

Survival Experience and its Predictors among TB/HIV Co-infected Patients in Southwest Ethiopia

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Abstract

Background: HIV-TB co-infection is “bidirectional and synergistic”. HIV promotes the progression of latent tuberculosis infection to disease and tuberculosis accelerates the progression of HIV disease to its advanced stage. To date, there have been limited clinical data regarding survival rates among TB/HIV co-infected patients and the impact of antiretroviral therapy on clinical outcomes in developing countries. Therefore, this study assessed the predictors of TB/HIV associated mortality in a cohort of HIV infected patients treated with antiretroviral therapy in Jimma University Teaching Hospital.

Methods: Retrospective study was conducted in Jimma University Teaching Hospital from September 01, 2010 to August 31, 2012. All records of adult TB-HIV co-infected patients who follow TB-HIV care in Jimma University Teaching Hospital between 01 September of 2010 and 31 August of 2012 were retrieved. Data were entered by Epi-data and was exported to SPSS version 19. Data were analyzed using proportional hazards cox model with stepwise variable selection to identify independent predictors. P value below 0.05 was considered statistically significant in the final model.

Results: Fifty five (20.2%) Tb HIV co-infected patients were died in the year September 2010 to August 2012, and 272 study subjects contributed 3, 082.7 person month observations. Age between 35-44 years (AHR=2.9; 95%CI: 1.08-7.6), being commercial sex worker (AHR=9.1; 95%CI: 2.7-30.7), bed ridden functional status (AHR=3.2; 95%CI: 1.2-8.7), and WHO stages 2 (AHR=0.2; 95%CI: 0.06-0.5), 3(AHR=0.3; 95%CI: 0.1-0.8) and 4(AHR=0.2; 95%CI: 0.04-0.55) were the independent factors affecting mortality of TB-HIV co-infected patients.

Conclusions: More than 1 in 5 TB-HIV co-infected individuals died. The independent predictors were age between 35-44 years, being student and commercial sex worker, bed ridden functional status, and WHO stages 2, 3, and 4. Therefore, attention should be given to reduce the considerable amount of death, and specific intervention should be designed focusing on the independent predictors.

Keywords: TB-HIV; Survival; Retrospective cohort; Ethiopia

Introduction

TB/HIV co-infection is “bidirectional and synergistic in which HIV promotes the progression of latent tuberculosis infection to disease, and tuberculosis accelerates the progression of HIV disease to its advanced stage [1]. HIV is the main reason for failure to meet Tuberculosis (TB) control targets in high HIV settings; as well TB is a major cause of death among people living with HIV [2]. According to 2010 WHO report on TB profiles of different countries, Ethiopia is classified as high burden TB, High burden HIV and high burden MDR-TB [2]. The prevalence rate was estimated to be 394 (173-623) per 100000 populations including those co-infected with HIV, and there were 152,030 new cases of which 3,190 are below 15 years of age [2].

Globally, TB remains among the leading causes of death from an infectious agent. In 2008, of the estimated 9.4 million incident cases of TB, 1.4 million were in people living with HIV and TB accounted for 23% of AIDS-related deaths [3-5]. Different studies stated that, TB is often the first manifestation of HIV infection, and it is the leading cause of death among HIV-infected patients in Africa [6,7]. It is estimated that almost 33% of all people living with HIV-1 are co-infected with TB. In parts of sub-Saharan Africa up to 70% of Tb patients are co-infected with HIV [8]. In Ethiopia, a cross-sectional study revealed that the rate of HIV infection in TB patients was 18% ranging from 8.3% (in Silte zone) to 35.3% (in South Omo zone) [9].

There are different factors affecting the survival of Tb/HIV co-infection. Age, gender, marital status, level of education, religion, occupation, residence, weight, AIDS staging, TB clinical presentation and calendar year were predictors [10,11]. To date, there have been limited clinical data regarding survival rates among HIV/TB co-infected patients and the impact of antiretroviral therapy (ART) on

clinical outcomes in developing countries like Ethiopia. Besides, few studies have analyzed factors associated with survival in HIV-infected TB patients taking into account drug susceptibility patterns of *Mycobacterium tuberculosis*. We, therefore, conducted this study to look at the survival rate of TB/HIV co-infected patients and to gain better insight on associated factors.

Methods and Participants

Study design

A retrospective cohort study using ART records from September 01, 2010 to August 31, 2012 was conducted in Jimma University Teaching Hospital (JUTH). The hospital is located in 355 km towards southwest of Ethiopia.

Population

All adults aged 15 years and above who follow TB-HIV care in JUTH were the population. Incomplete records were excluded from analysis.

Variables

Death due to TB/HIV co-infection was the event. Age, religion, educational level, ethnicity, marital status, employment status, residence, number of rooms past opportunistic infection, TB incidence, functional status, baseline CD4 cells count, baseline weight, drug regimen, WHO clinical stage, risk behavior and substance use were an independent variables.

Statistical analysis

Data extraction checklist was used to extract information from the patient cards, registration and log books. Data were entered by Epi-data and was exported to SPSS version 19.0 for windows for analysis. The data were cleaned and edited before analysis. Data exploration was undertaken to see if there are odd codes or items that were not logical and then subsequent editing was made. The main end point in

this study was death from TB/HIV co-infection. Individuals defaulted, lost to follow up, transfer out and survivors at the end of the study period were considered as censored. Finally, the out-come of each subject was dichotomized in to censored or recovered. The patient cohort characteristics was described in terms of mean, median, standard deviations, and range values for continuous data; percentage, frequency tables and charts/graphs for categorical data. For the comparison of time to recovery among the different groups of patients, Kaplan Meir curve was used. The proportional hazards cox model with stepwise variable selection procedural was used to identify independent predictors of survival. The assumption for proportional hazard was assessed graphically by log minus log survival curve. P-value less than or equal to 5% was considered significant.

Ethical consideration

Ethical clearance was obtained from the Office of Institutional Review Board of college of Public Health and Medical sciences, Jimma University. Consent was obtained from Jimma University Teaching Hospital.

Results

Baseline socio-demographic and economic characteristics of the study subjects

A total of 272 TB-HIV co-infected patients were followed for a mean of 340 days. In this study, the mean age of the study subjects were 32(+8.53) years with a majority of them lying between 25-34 years age. Females (58.1%), daily labourers (31.6%), formally educated (51.5%), Muslim (49.3%), married (60.7%) and urban dwellers (69.5%) were the dominant study participants. Almost three fourth of them live with less than 5 people and do have water and electricity. A considerable amount (44.5%) of study participants has 1 living room (Table 1).

Socio-demographic variable		n=272	Percentage
Age (in years)	15-24	38	14.0
	25-34	140	51.5
	35-44	69	25.4
	>=45	25	9.2
Sex	Male	114	41.9
	Female	158	58.1
Occupation	Government employed	48	17.6
	NGO	46	16.9
	Farmer	80	29.4
	Daily labor	86	31.6
	Commercial sex worker	12	4.4
Educational status	Illiterate	81	29.8
	Read and write	51	18.8

	Formal education	140	51.5
Religion	Orthodox	76	27.9
	Muslim	134	49.3
	Protestant	50	18.4
	Catholic	12	4.4
Marital status	Married	165	60.7
	Single	58	21.3
	Divorced	36	13.2
	Widowed	13	4.8
Residence	Urban	189	69.5
	Rural	83	30.5
Number of people living with	<5 people	210	77.2
	>=5 people	62	22.8
Water	Yes	207	76.1
	No	65	23.9
Electricity	Yes	207	76.1
	No	65	23.9
Room	1	121	44.5
	2	110	40.5
	3	31	11.4
	4	10	3.7

Table 1: Baseline socio-demographic characteristics of 272 adult TB-HIV Co-infected patients enrolled to HIV at Jimma University Teaching Hospital, South West Ethiopia, 2013.

Clinical and behavioral characteristics of the study subjects

In the cohort, 176 (64.7%) study subjects had disclosed about their status to the nearest person. Majority of the patients were on first line regimen, working functional status and WHO stage-III. Pulmonary TB accounted more than extra pulmonary or mixed TB type and the

mode of entry was relapse in above 85% of the participants. Nearly 70% of their partners were positive and above 70% of study participants had risky behaviour. Surprisingly, 83% of them didn't use condom (Table 2).

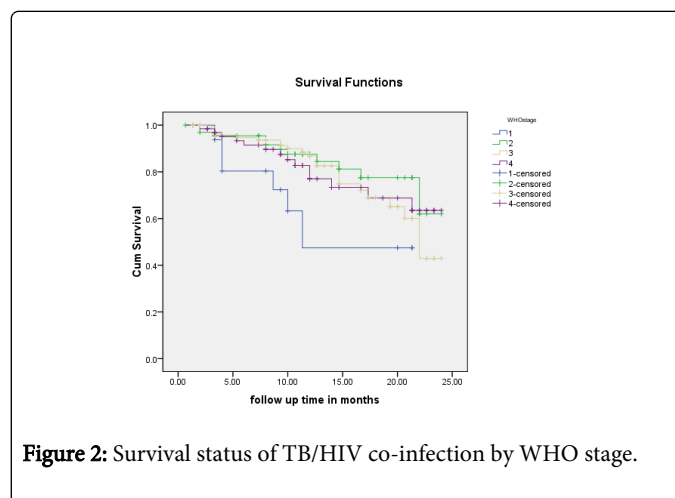
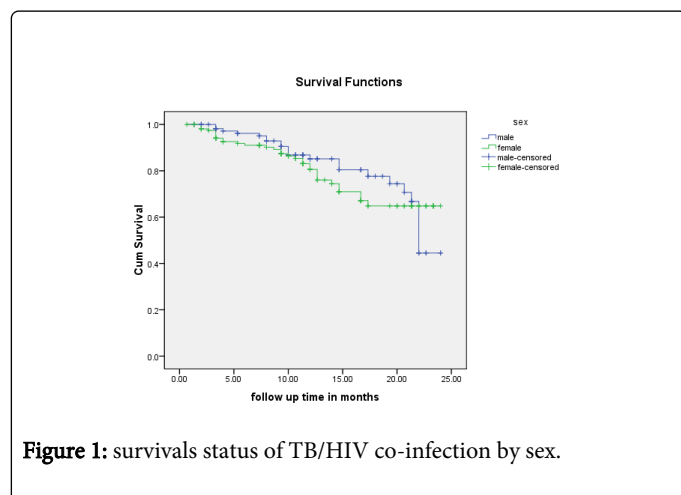
Variable	Value/level	n=272	Percentage
Disclosure	Yes	176	64.7
	No	96	35.3
Function	Work	138	50.7
	Ambulatory	95	34.9
	Bed ridden	39	14.3
WHO stage	1	17	6.2
	2	67	24.6
	3	124	45.6

	4	64	23.5
Regimen	First line	229	84.2
	Second line	43	15.8
CD4	<200 cells/copies	163	59.9
	>=200 cells/copies	109	40.1
TB type	Pulmonary	213	78.3
	Extra pulmonary	14	5.1
	Mixed	45	16.5
Mode of TB entry	New	232	85.3
	Relapse	27	9.9
	Dropout	13	4.8
Partner HIV status	Positive	189	69.8
	Negative	1	0.4
	Unknown	82	30.1
Risky behaviour	Yes	191	70.2
	No	81	29.8
Condom use	Yes	47	17.3
	No	225	82.7
Tobacco smoking	Yes	126	46.3
	No	146	53.7
Alcohol drinking	Yes	76	27.9
	No	196	72.1

Table 2: Clinical and behavioural characteristics adult TB-HIV Co-infected patients enrolled to HIV at JUTH, South West Ethiopia, 2013.

Survival status of study participants

A total of 55 (20.2%) Tb HIV co-infected patients were died in the year September 2010 to August 2012.



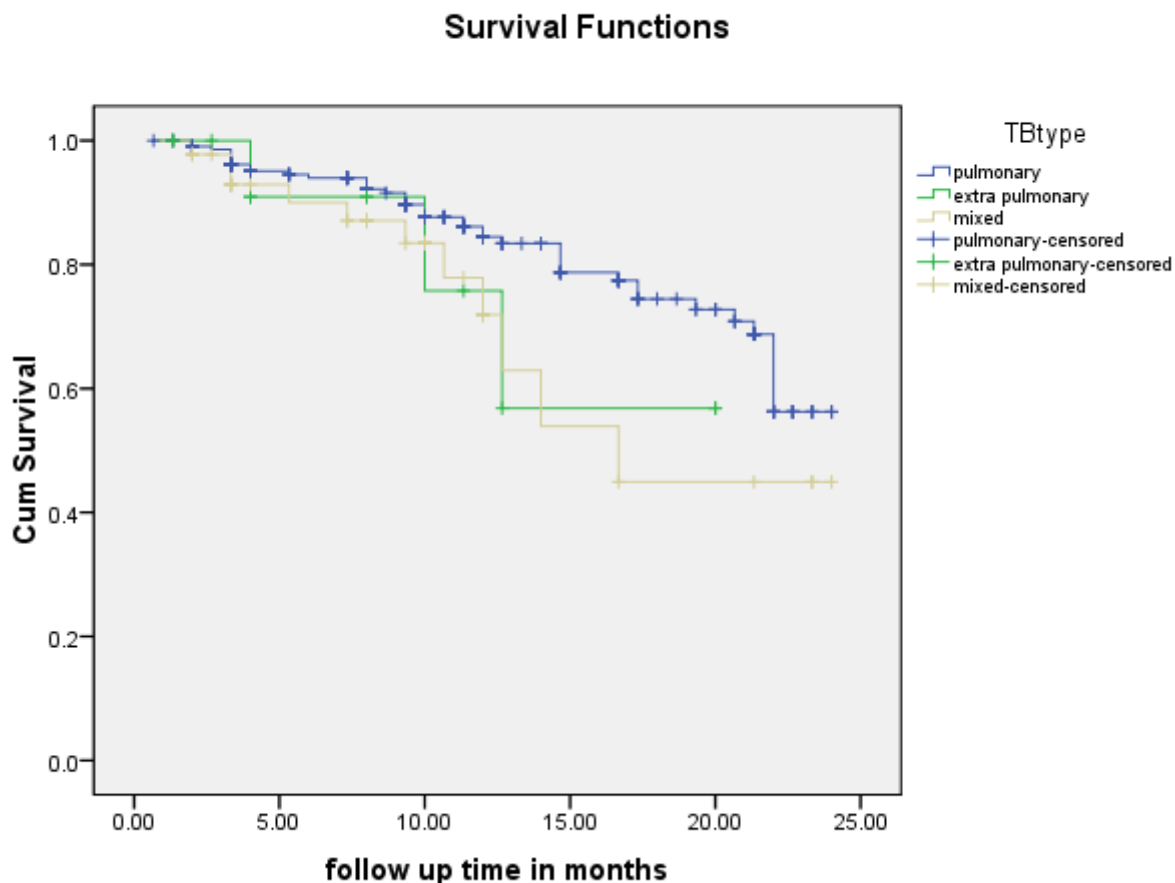


Figure 3: Survival status of TB/HIV co-infection by tuberculosis type.

The 272 study subjects contributed 3, 082.7 person month observations (PMO) to this study.

The survival status by sex, functional status, WHO stage and CD4 category is described by the Kaplan-Meier figures (Figures 1-3).

Predictors of mortality in TB-HIV co-infected patients during TB treatment

Bivariate cox regression analysis showed that the risk of death was statistically different by age, educational status, occupation and WHO stage.

After adjustment, checking for interaction and fitness of the model, age between 35-44 years, being student and commercial sex worker, bed ridden functional status, and WHO stages 2, 3, and 4 were independent predictors in the multiple Cox regression analysis (Table 3).

Variable	Crude hazard ratio (95%CI)	Adjusted hazard ratio (95% CI)
Age in years		
15-24	1	1
25-34	1.1(0.5-2.8)	1.4(0.6-3.8)

35-44	2.2(0.9-5.4)**	2.9(1.08-7.6)**
>=45	0.6(0.1-2.7)	0.3(0.05-1.6)
Sex		
Male	1	1
Female	1.1(0.7-1.9)	1.7(0.8-3.5)
Educational status		
Illiterate	1	1
Read and write	0.7(0.3-1.3)	0.9(0.3-2.4)
Formal education	0.4(0.2-0.7)**	0.6(0.2-1.8)
Occupation		
Gov't employed	1	1
NGO	1.1(0.4-2.9)	0.9(0.4-2.6)
Farmer	1.06(0.4-2.6)	0.7(0.3-1.9)
Daily labour	2.4(1.04-5.3)**	2.1(0.9-4.9)
Commercial sex worker	6.7(2.2-20.9)**	9.1(2.7-30.7)**
Disclosure		
Yes	1	1
No	0.7(0.4-1.1)	0.7(0.3-1.8)
Function		
Work	1	1
Ambulatory	0.6(0.3-1.09)	1.05(0.5-2.1)
Bed ridden	0.5(0.2-1.05)	3.2(1.2-8.7)**
WHO stage		
1	1	1
2	0.3(0.1-0.9)**	0.2(0.06-0.5)**
3	0.4 (0.2-1.02)	0.3(0.1-0.8)**
4	0.4(0.2-1.09)	0.2(0.04-0.5)**
TB type		
Pulmonary	1	1
Extra-pulmonary	0.6(0.3-1.07)	2.6(0.5-12.2)
Mixed	1(0.3-3.6)	0.9(0.3-2.7)
Risky behaviour		
Yes	1	1
No	0.9(0.5-1.6)	0.8(0.4-1.9)
Partner HIV status		
Positive	1	1

Negative	1.4(0.8-2.5)	0.5(0.2-1.5)
**Statistically significant at p<0.05		

Table 3: Cox regression analysis for predictors of mortality among TB-HIV coinfecting patients enrolled to HIV at Jimma University Teaching Hospital, South West Ethiopia, from 2010-2012.

Discussion

This study revealed the problem of high mortality of TB-HIV co-infected patients. More than 1 in 5 TB-HIV co-infected (20.2%) individuals died during TB treatment and this is consistent with the study conducted in Bahir Dar in 2012 [12].

Results from this study demonstrated that age between 35-44 years, being commercial sex worker, bed ridden functional status, and WHO stages 2, 3, and 4 were independent predictors affecting mortality of TB/HIV co-infected patients.

Study participants between 35-44 years old had nearly 3 times higher risk of (95% CI: 2.9, 1.08-7.6) death than those below 25 years old and this is similar with study done in Brazil [10] but different with the study done in Bahir Dar [12] stating that people aged 45 and above is more at risk of dying.

Regarding functional status, bedridden patients had three times (AHR=3.2, 95% CI: 1.2-8.7) an increased risk of mortality than in working status. This in agreement with the study conducted in Bahir Dar [12] stating that bedridden patients were nearly 4 times at risk of dying than in work functional status (AHR=3.88; 95%CI: 2.15-7.02).

Lastly, patients in WHO stages 2, 3 and 4 compared to stage 1 were found protective for mortality risk. The risk of death in patients diagnosed as WHO stage III was decreased by 70% (AHR=0.3; 95%CI: 0.1-0.8) compared to WHO stage I patients. The possible reason could be due to Immune reconstitution syndrome during their stage I, and their experience to develop self-care. The major limitation of this study is the small sample size on top of its being retrospective study.

In conclusion, more than 1 in 5 TB/HIV co-infected individuals died during TB treatment. Age between 35-44 years, being student and commercial sex worker, bed ridden functional status, and WHO stages 2, 3, and 4 were the independent predictors affecting mortality of TB-HIV co-infected patients. Therefore, since the death is a significant number, strategies to reduce this considerable amount including availability of ARVs should be applied to. A special attention should also be given for the independently associated factors. Researchers can

conduct using a primary study and/or large sample size to really deal out the predictors.

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