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EVALUATING SURVIVAL OF HIV/AIDS AND TB CO-INFECTION USING ACCELERATED FAILURE TIME MODEL

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ABSTRACT: *Background: The relationship between Human Immunodeficiency Virus (HIV) and Tuberculosis (TB) is complex, resulting in the synergistic increases in their morbidity and mortality. The occurrence of both infections worldwide is a great public health problem. There is a looming threat of a pandemic emerging in Ghana as it has been in other African countries. The advent of the potent combination of antiretroviral therapy (ARV) in 1996 has been of immense effect in extending the life span of infected patients by slowing the wasting period, and boosting the CD4 cell count of an infected patient. This study aimed to evaluate the survival rate of HIV/AIDS and HIV/TB co-infection patients and to examine the influence of prognostic factors on the survival of patients and then fit Accelerated Failure time model for monitoring the performance of patients on HIV/AIDS and co-infection chemotherapy. Methods: The study considered a real-life data set obtained from St. Mathias Hospital, a referral center for health centers in the Pru District of the Brong Ahafo Region of Ghana. The hospital has a unit for both anti-retroviral therapy (ART) and tuberculosis (TB). The study considered patients above five years of age on treatment regimen between 2008 to 2013.The patients were followed retrospectively until the outcomes of either the event (treatment failure) or being censored. Accelerated Failure time model was used to explore the survival rate and prognostic factors of HIV/AIDS and HIV/TB co-infected patients. Results: Within the follow-up period 2008 to 2013, out of the 295 HIV/AIDS patients followed, 58 (19.7%) died and 25 (32.9%) died from the 76 HIV/TB co-infected. The survival estimates at the end of 70th month for HIV/AIDS and the co-infection were respectively 0.4110 and 0.1892. This suggests that the patients with co-infection experienced a worse survival rate compared to the HIV/AIDS patients. The best fitted model for survival analysis in HIV/AIDS and TB co-infection is the Gamma model. Among the several prognostic factors evaluated by the Gamma model, gender, weight, CD4 cell count, and WHO Clinical Stages I and III were identified as significant prognostic factors at 5% significance level for the HIV/AIDS patients. In the HIV/TB co-infection, however, only weight and CD4 cell count of the patients are significant at 5%. The significant prognostic factors indicated that a unit increase in these prognostic factors would significantly improve the survival time of the patients at different rates. Holding all covariates constant, the survival time is 6.44 and 1.084 times longer for a unit increase in the weights of a HIV/AIDS and HIV/TB co-infected patients respectively. Conclusion: More sexually active people contract the HIV and the TB co-morbidity of HIV/AIDS develops more in the older patients but may occur at any stage in the course of the immunodeficiency. From both the survivorship time table method and the best fitted AFT model, the Gamma model, HIV/TB co-infected patients experienced the worse survival rate. In both disease situations, weight and CD4 cell count*

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prognostic factors could be used to effectively and efficiently monitor the survival rate of patients on ART chemotherapy by implementing Gamma AFT modelling.

KEYWORDS: Accelerated failure time model, Cox-Snell residual, HIV/TB co-infection, prognostic factors, CD4 cell count.

INTRODUCTION

Background

The complex relationship between Human Immunodeficiency Virus (HIV) and Tuberculosis (TB) results in synergistic increases in their morbidity, and mortality. The occurrence of both infections worldwide is a significant public health problem. The situation in Africa is no different. There is a looming threat of the pandemic emerging in Ghana as well as in other African countries [1].

HIV is a virus that attacks and destroys the infection-fighting CD4 cells of the body's immune system. It is noteworthy that the loss of CD4 cells makes it very difficult for the immune system to fight infections. When the immune system is progressively damaged by HIV, the infected person becomes immunosuppressed and is, therefore, vulnerable to other opportunistic infections, especially tuberculosis. The advanced and symptomatic form of HIV is called Acquired Immunodeficiency Syndrome (AIDS). The HIV epidemic is one of the most destructive health crises of modern times, destroying families and communities around the world, causing huge socio-economic burdens. HIV is transmitted through body fluids such as blood, semen, genital fluids, or breast milk of an infected person. Among the modes of transmission, unprotected sex or sharing drug injection equipment with an infected person are the most common ways that HIV is spread [2]. Despite tremendous researches being conducted in the field of HIV/AIDS, there is currently remains no cure for the infection. There are, however, steps that can be taken to delay the onset of full blown AIDS and to reduce its progression. The most promising advance has been the advent of potent combination of therapy, the Antiretroviral therapy (ARV) in 1996. The ARV can prolong the life of the infected patient by slowing down the wasting period as it boosts the CD4 count in the immune system [3].

The main opportunistic infection, Tuberculosis is caused by the tubercle bacillus *Mycobacterium tuberculosis*, and is spread through air [4]. Tuberculosis attacks the lungs, but also sometimes affects other parts of the respiratory system. TB that affects the lungs is called the pulmonary TB; otherwise it is called extra-pulmonary TB. There are two forms of TB; latent and active TB. Latent TB infection is the inactive form; the TB germs in the body are dormant and do not make a person sick. Some people have a strong immune system that can quickly destroy the bacteria once they enter the body. A person with latent TB cannot spread it to unaffected persons. Without treatment, however, the latent TB infection can advance to active TB disease [5].

Generally, a relatively small proportion of people infected with *Mycobacterium tuberculosis* will develop active TB disease. Those with HIV have a much higher chance of developing the active disease. Tuberculosis cases are more prevalent among men than women, and TB mainly affects adults in their productive years. The burden of TB continues to increase due to poverty, population growth, and HIV/AIDS [6]. TB is the most common opportunistic infection

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complicating HIV infection, especially in developing countries, and may occur at any stage in the course of immunodeficiency [7].

Tarekegn (2011) conducted a retrospective study in which a total of 632 patients(316 in ART and pre-ART cohort) were followed for a median of 32.9 months in pre-HAART and 35.4 months in HAART. The study aimed to identify factors that increase the risk of TB in People Living with HIV/AIDS (PLWHA). The result from Cox Proportional hazard (Cox PH) model indicated that WHO stage III or IV patients who were bedridden and had hemoglobin levels less than 10mg/dl had an increased risk of TB in PLWHA. [8].

Shaweno and Worku (2012) also employed a retrospective cohort study to compare the survival rate between 370 HIV positive and 370 HIV negative TB patients, during an eight month DOTS period. They considered TB patients' HIV status and follow-up time until death, was taken as an outcome. Cox PH regression model was used to determine the hazard ratio of death for each predictor. Their study revealed that co-infected patients were less likely to survive [9].

Musenge *et al*., (2013) modeled the contribution of spatial analysis to understanding HIV/TB mortality in children using the structural equation modeling approach. They used multiple logit regression model with and without spatial household random effects. Structural equation models were also used in modeling the complex relationships between multiple exposures and the outcome of HIV/TB child mortality. A protective effect was found in households with better socio-economic status and older children. Spatial models disclosed that the areas which experienced the greatest child HIV/TB mortality were those without any health facility [10].

Nawumbeni *et al.*, (2014) compares the performance of Cox PH model and the Accelerated Failure Time (AFT) model using HIV/TB Co-infection Survival data. This study revealed that the AFT model has the best predictive power compared to the Cox PH model, based on the Akaike Information Criterion (AIC) and Bayesian Information Criterion BIC values [11].

This research is aimed to:

- Evaluate the mortality rate of HIV/AIDS, and co-infected patients;
- Examine the influence of prognostic factors on the survival of patients;
- Fit an appropriate Accelerated Failure time model.

MATERIALS AND METHODS

Ethical consideration

Ethical approval was obtained from the Research Department of the District Health Directorate of Ghana Health Service, Yeji before the commencement of the study. An informed written consent was also sought from the management of the hospital and no consent sought from patients since the research involves secondary data and does not include any direct contact with human subjects. The data collection procedures and the purpose of the study were free of any identification. The extracted data from the patients' folders and the analysis were stripped off any identifiable information to ensure confidentiality and anonymity.

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Study area

The study population is Pru District, one of the 27 districts in the Brong-Ahafo Region of Ghana with Yeji as its administrative capital. It was originally created from the Atebubu-Amantin District in 2004 by an Act of Parliament through a Legislative Instrument. Pru District is bordered to the north by East Gonja District in the Northern Region and to the south by Atebubu-Amantin and Nkoranza Districts. To the east, it shares boundaries with the Sene District and to the west with Kintampo South and Kintampo North Districts (12).

Data used and data collection procedure

The study considers a real-life data set obtained from St. Mathias Hospital in the Pru District of the Brong Ahafo Region of Ghana. This hospital serves as a referral center for health centers in the District. The hospital has a unit for both HIV/AIDS and tuberculosis (TB) patients on treatment. The hospital started giving free anti-retroviral therapy (ART) services in 2008. The study considered patients above five years of age. The study period was from 2008 to 2013 and the patients were followed retrospectively until the outcomes of either the event (treatment failure) or censored (in this case not treatment failure).

The prognostic factors were also extracted from the patients' folders but without any personal identifier.

Estimation of the survivorship function

We used the Life table method to estimate the survivorship function. The Gehan's method (1969) was employed where the midpoint of the interval was used to estimate the hazard and the density functions and the upper limit used to estimate the survival function [13].

Log rank test**:**

This was used to compare the death rate between two distinct groups, conditional on the number at risk in the groups. The log rank test hypothesis that;

H_0 : All survival curves are the same

H_1 : Not all survival curves are the same.

Log rank test approximates a chi-square test which compares the observed number of failures to the expected number of failures under the hypothesis.

$$\chi^2 = \sum_{f=1}^{k} \frac{(O_f - E_f)^2}{E_f} \qquad (1)$$

where, $k-1$ is the degrees of freedom. A large chi-squared value implies a rejection of the null hypothesis for the alternative hypothesis.

Accelerated Failure Time Models (AFTM)

AFT models follow a known distribution. The models include the: Exponential model, Weibull, Lognormal, Log-logistics and Gamma models. The underlying assumption for this model is

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that the effect of the covariate is multiplicative with respect to the survival time. The model regresses the natural logarithm of the survival time (*log t*) over the covariates. It is expressed as a linear function of the covariates.

$$\log t = X_j \beta + z_j \qquad (2)$$

Where X_j is the vector of covariate, β is the vector of regression coefficient, z_j is the error term.

In diagnosing the model, the Cox-Snell residual plot was fitted to determine whether the AFT model is adequate for prediction.

RESULTS AND DISCUSSIONS

There were 295 HIV/AIDS patients, 58 (19.7%) died; and 76 were HIV/TB co-infected, 25 (32.9%) died during the study period of 2008 to 2013. Table 1 presents the descriptive statistics for continuous covariates of the patients involved in this study. The maximum, median and mean ages of the HIV/AIDS patients were 75, 34 and 35 years respectively while that of TB co-infected patients were respectively maximum age was 70, 35.5 and 37 years but same minimum age of 6 years in both patients. The median and mean ages revealed that youths are the most infected with HIV leading to the TB co-infection. This could be justified that the youthful stage is the sexually active stage with high possibility of unprotected sex or sharing drug injection equipment which are the most common modes of HIV transmission [2]. Comparison of the two groups from their ranges (maximum-minimum) and the mean also indicated that as younger people contract the HIV, the co-morbidity of HIV/AIDS which is the TB co-infection develops in the older patients because TB mainly affects adults in their productive years [6]. It also seemed that being the commonest opportunistic infection, TB may occur at any stage in the course of the immunodeficiency [7] as depicted in the same minimum age. The minimum and maximum weights were 8 and 90 kg respectively for the HIV/AIDS patients but respectively slightly higher in the HIV/TB co-infected patients (minimum of 9 kg and maximum 93kg). It was generally revealed, however, from the comparison of the median (50 kg for HIV/AIDS and 43 kg for TB co-infection) and the mean (50.98 and 42.96 kg for HIV/AIDS and the TB co-infection respectively) that the co-infected patients were losing more weights than their HIV/AIDS counterparts. This was clear because the co-infected patients were actually been confronted with double tragedy.

Even-though the patients were put on ARV chemotherapy to prolong their lifespan by slowing down the wasting period through boosting the CD4 count in the immune system [3], there is a vast difference in the survival rate of HIV/AIDS and TB co-infected patients. Thus the more deteriorating nature in co-infected patients was further shown in comparatively lower immunity level of the co-infected patients as measured by the CD4 counts. The HIV/AIDS patients recorded a minimum CD4 count of 5 (which was 1 for TB co-infected patients) and a maximum CD4 count of 1907 as against 1011 for TB co-infection. The mean CD4 cell count for the co-infected patients was 327 which were below the mean CD4 cell count (368.96) of the HIV/AIDS patients. With regard to survival time, both categories of patients again had the same minimum survival time of 1 month but different median, mean and maximum survival times whereby co-infected patients had shorter survival period in all cases as shown in table 1. That is to say that as stated earlier and in other findings, co-infected patients experienced faster rate of deterioration and hence has shorter lifespan [9].

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The survival rates of the HIV/AIDS and TB co-infected patients were then estimated using the Life table method proposed by Gehan's (1969) and the results given in Tables 2 and 3 respectively. The survival estimates at the end of the 70th month for HIV/AIDS and the co-infection were respectively 0.4110 and 0.1892.This further suggests that the co-infected patients experienced a worse survival rate compared to the HIV/AIDS patients. The result agrees with the finding by Interagency Coalition on AIDS and Development (2010), stating that up to 33% of all AIDS deaths worldwide can be attributed to TB. This could also be a result of the difficulty in diagnosing HIV patients who are also infected with TB, since HIV patients are more susceptible to contracting TB outside the lungs [7].

The hazard plot in Figure 1 for HIV/AIDS showed the 59th month of treatment as the most risky month while the 63rd month of HIV/TB co-infection was the riskiest month. The sharp rise and then fall in the hazard in both patients may be due to non-adherence to treatment protocol, side-effects or other biological and therapeutic factors that need to be researched. Additionally, in the case of the co-infected patients, it could imply that HIV/AIDS patients were not diagnosed early as being positive for TB in order to receive the required additional chemotherapy, resulting in the greater deterioration in the health of these patients in the later stages of treatment of HIV/AIDS. From the test of equality using the log rank test (Table 4), only WHO Clinical Stage is statistically significant in the HIV/AIDS patients but rather religious affiliation in HIV/TB co-infected patients. However, covariates including gender, marital status, disclosure to sexual partner, and drug regimen were statistically insignificant in determining the survival rates of patients between the two groups.

In modeling the survivorship of patients, the study revealed that among the AFT models, Gamma model best fit the data since it has the least AIC and BIC values (Table 5).

The Gamma model for HIV/AIDS and HIV/TB co-infected patients and the time ratios for significant covariates are presented in tables 6, 7 and 8 respectively. The Gamma model for HIV/AIDS patients (Table 6) revealed that female, weight, CD4 cell count, and WHO clinical stages I and III are significant at 5% significance level but only weight and CD4 cell count are significant at 5% significance level for HIV/TB co-infection (Table 7). In both disease conditions, age, religion, marital status, regimen, disclosure of status to partner and WHO clinical stages II and IV are insignificant. The estimated survival time of the significant factors shows increase in survivorship since the time ratios are greater than one (Table 8). This implies that a unit increase in these prognostic factors would improve the estimated survival time of the patients but at different rates. Holding all factors constant, the survival time is 6.44 and 1.084 times longer for a unit increase in the weights of HIV/AIDS and HIV/TB co-infected patients respectively. This finding was revealed in other studies [14,15] affirming that the mortality rate among patients with higher CD4 count and weight is proportionally lower compared to patients with lower CD4 count and weight. In a similar way, HIV/AIDS (but not so for the HIV/TB co-infected) patients who are at WHO Clinical Stages I and III experienced an improved survival time. This could be as a result of the opportunistic infections at stage IV. The HIV/AIDS patient at WHO Clinical Stages I and III would have their predicted survival time accelerated by 3.72 and 3.71 respectively (Table 8). The model also deduced that the HIV/AIDS female patients had a better and longer predicted survival time (Table 6 and 8). This is consistent with Owiti, (2013) proposition that men naturally seek healthcare later and find it difficult to visit the hospital regularly, resulting in a higher mortality rate.

Although not statistically significant, the non-significant factors may also correspond to increase in survivorship to some extent. It was noticed that patients on a combined drug

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regimen (AZT/3TC/EFV) had lower predicted survival time (Table 6) and patients who practice Christianity and Islam have better survival rates ($TR = e^{0.0217}$=1.022) and ($TR = e^{0.0103}$=1.010) respectively (Table 7).

The diagnostic evaluation of the Gamma model using the Cox-Snell residual plot revealed that the graph is closer to the bisector than the rest of the models. As a result, the gamma model best fits the HIV/AIDS and HIV/TB co-infection data in the study as shown in Figure 3 and Figure 4, respectively.

CONCLUSION

The study followed two hundred and ninety-five (295) patients who were diagnosed of HIV/AIDS and seventy-six (76) HIV/TB co-infected patients on treatment within the periods 2008 to 2013. The AFT modelling of the survival rates of patients from the prognostic factors selected Gamma as the best fitted model based on AIC and BIC. The Cox-Snell residual plot further confirmed the Gamma model as well fitted for evaluating the survival of HIV/AIDS and HIV/TB co-infection. It was disclosed that the HIV/TB co-infected patients experienced the worse survival rate. The prognostic factors such as weight, CD4 count, gender (female), and WHO clinical stages I and III significantly determine the survival of the HIV/AIDS patients. However, only weight and CD4 count significantly determine the survival of the co-infected patients. Hence, irrespective of the disease condition (HIV/AIDS or HIV/TB co-infection), weight and CD4 cell count will significantly determine the patient's survival rate.

We, therefore, recommend that governments and stakeholders should support healthcare providers to initiate routine testing for opportunistic infections in HIV/AIDS patients to reduce deterioration in the health of the patients due to comorbidities. In addition, health authorities should be very cautious and devote extra attention to patients who have lower weights and CD4 cell counts because it is observed that these factors significantly affect the survival of the patients while closely monitoring the WHO clinical stages and the gender as well. Gamma model will be of great help to evaluate the performance of chemotherapeutic treatment of the patients.

Abbreviations

3TC	Lamivudine
AFTM	Accelerated Failure Time Model
AIC	Akaike Information Criterion
AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral therapy
ARV	Antiretroviral
AZT	Zidovudine
BIC	Bayesian Information Criterion
CD4	Cluster of Differentiation Four
DOTS	Directly Observed Treatment Short-Course
EFV	Efavirenz
GHS	Ghana Health Service
HIV	Human Immunodeficiency Virus
HR	Hazard Ratio
KM	Kaplan-Meier Estimator
LR	Likelihood Ratio

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NVP Nevirapine
PH Proportional Hazard
PLWHA People Living with HIV/AID
TB Tuberculosis
TR Time Ratio
WHO World Health Organization

Competing interest

The authors have no competing interest to declare.

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APPENDIX

FIGURES

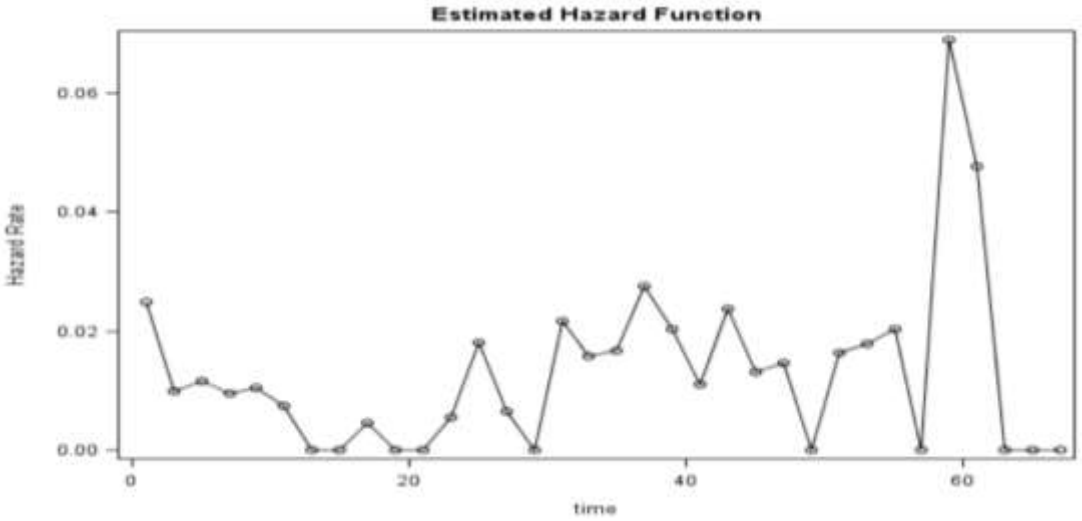

Figure 1: Hazard curve for HIV/AIDS

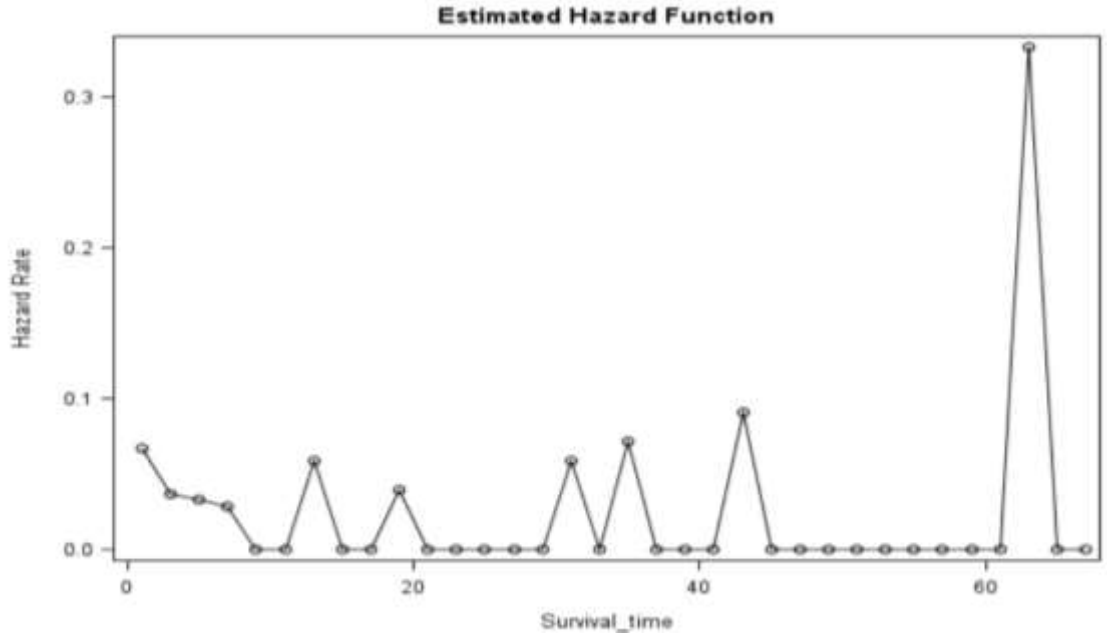

Figure 2: Hazard Curve for Co-infection

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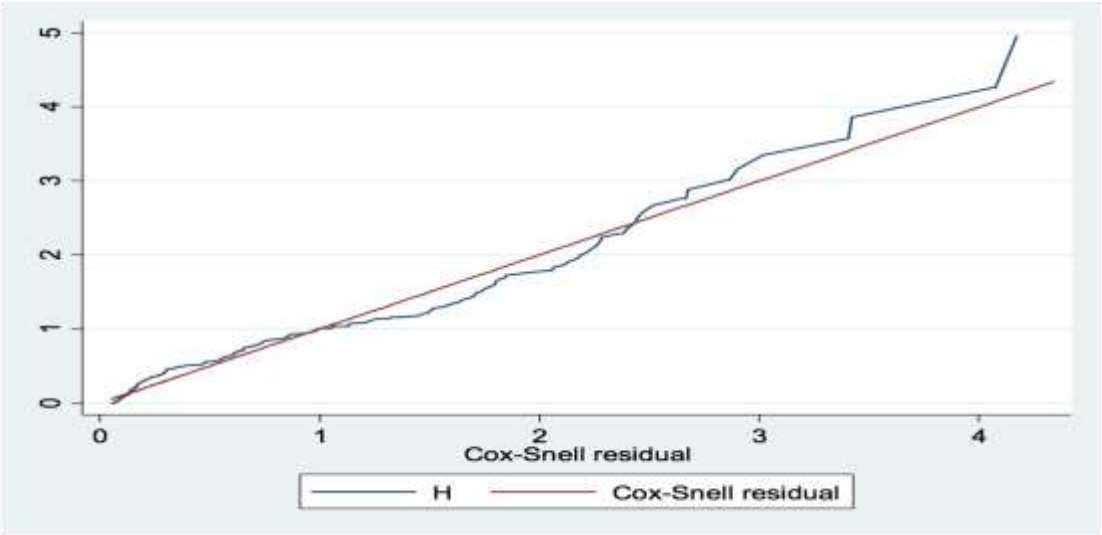

Figure 3: Gamma Cox-Snell residual for HIV/AIDS

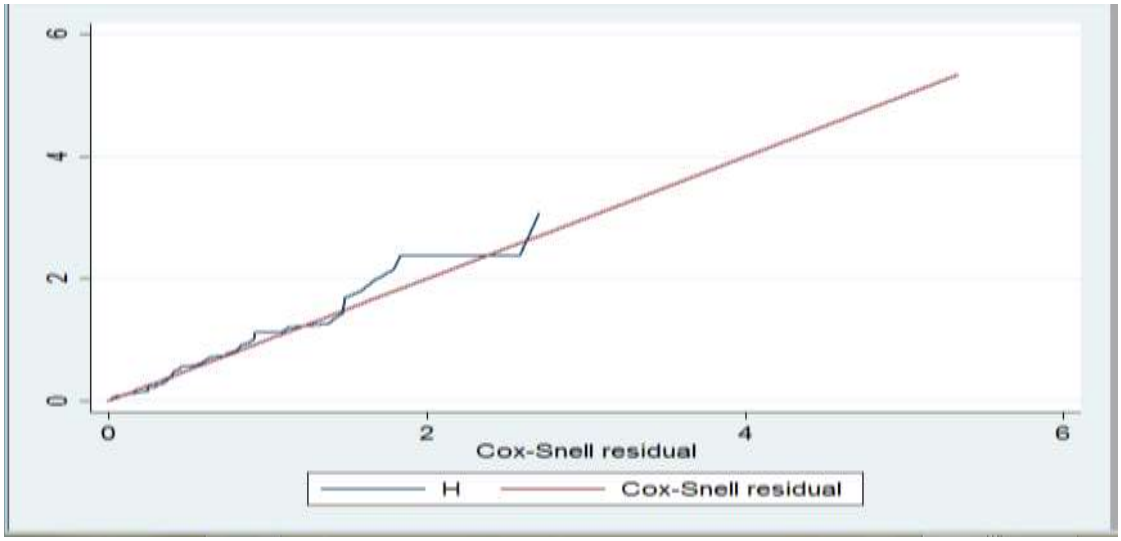

Figure 4: Cox-Snell residual plot for HIV/TB co-infection

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TABLES

Table 1: Descriptive statistics for continuous covariates for the patients

Variables	Mean	Median	Std. Dev.	Min.	Max.
HIV/AIDS					
AGE	35.47	34.00	11.51	6.00	75.00
WEIGHT	50.98	50.00	11.22	8.00	90.00
CD4	368.96	322.00	301.52	5.00	1907.00
TIME	17.07	8.00	19.30	1.00	69.00
CO-INFECTION					
AGE	37.09	35.500	14.96	6.00	70. 00
WEIGHT	42.96	43.00	13.77	9.00	93.00
CD4	327.00	219.50	307.27	1.00	1011.00
TIME	11.24	6.00	15.50	1.00	68.00

Table 2: Hazard, density and survival estimates of HIV/AIDS patients

Mid-point	Hazard	SE	Density	SE	Upper limit	Survival	SE
1	0.0249	0.0069	0.0243	0.0066	2	1.0000	0.0000
3	0.0098	0.0049	0.0092	0.0046	4	0.9514	0.0131
5	0.0117	0.0058	0.0107	0.0053	6	0.9329	0.0158
7	0.0096	0.0055	0.0086	0.0049	8	0.9114	0.0187
9	0.0104	0.0060	0.0092	0.0053	10	0.8942	0.0209
11	0.0074	0.0052	0.0064	0.0045	12	0.8757	0.0230
13	0.0000	0.0000	0.0000	0.0000	14	0.8629	0.0244
15	0.0000	00000	0.0000	0.0000	16	0.8629	0.0244
17	0.0046	0.0046	0.0039	0.0039	18	0.8629	0.0244
19	0.0000	0.0000	0.0000	0.0000	20	0.8550	0.0254
21	0.0000	0.0000	0.0000	0.0000	22	0.8550	0.0254
23	0.0055	0.0055	0.0047	0.0047	24	0.8550	0.0254
25	0.0181	0.0104	0.0150	0.0085	26	0.8456	0.0268
27	0.0065	0.0065	0.0053	0.0052	28	0.8156	0.0310
29	0.0000	0.0000	0.0000	0.0000	30	0.8051	0.0323
31	0.0216	0.0125	0.0170	0.0096	32	0.8051	0.0323
33	0.0157	0.0111	0.0120	0.0083	34	0.7710	0.0364
35	0.0168	0.0118	0.0123	0.0086	36	0.7471	0.0390
37	0.0275	0.0159	0.0194	0.0109	38	0.7224	0.0415
39	0.0204	0.0144	0.0137	0.0095	40	0.6837	0.0448
41	0.0110	0.0110	0.0071	0.0070	42	0.6564	0.0470
43	0.0240	0.0168	0.0149	0.0104	44	0.6421	0.0481
45	0.0132	0.0132	0.0080	0.0079	46	0.6122	0.0503
47	0.0147	0.0147	0.0086	0.0086	48	0.5963	0.0515
49	0.0000	0.0000	0.0000	0.0000	50	0.5791	0.0528
51	0.0164	0.0164	0.0093	0.0092	52	0.5791	0.0528
53	0.0179	0.0179	0.0098	0.0097	54	0.5604	0.0543
55	0.0204	0.0204	0.0108	0.0107	56	0.5407	0.0558
57	0.0000	0.0000	0.0000	0.0000	58	0.5191	0.0576
59	0.0690	0.049	0.0335	0.0224	60	0.5191	0.0576
61	0.0476	0.0476	0.0206	0.0198	62	0.4521	0.0669
63	0.0000	0.0000	0.0000	0.0000	64	0.4110	0.0723
65	0.0000	0.0000	0.0000	0.0000	66	0.4110	0.0723
67	0.0000	0.0000	0.0000	0.0000	68	0.4110	0.0723
69	0.0000	0.0000	0.0000	0.0000	70	0.4110	0.0723

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Table 3: Hazard, density and survival estimates for co-infected patients

Mid-point	Hazard	SE	Density	SE	Upper-limit	Survival	SE
1	0.0667	0.0222	0.0625	0.0195	2	1.0000	0.0000
3	0.0367	0.0183	0.0310	0.0150	4	0.8750	0.0390
5	0.0333	0.0192	0.0262	0.0147	6	0.8131	0.0469
7	0.0286	0.0201	0.0211	0.0146	8	0.7606	0.0528
9	0.0000	0.0000	0.0000	0.0000	10	0.7183	0.0577
11	0.0000	0.0000	0.0000	0.0000	12	0.7183	0.0577
13	0.0588	0.0415	0.0399	0.0268	14	0.7183	0.0577
15	0.0000	0.0000	0.0000	0.0000	16	0.6385	0.0739
17	0.0000	0.0000	0.0000	0.0000	18	0.6385	0.0739
19	0.0400	0.0399	0.0246	0.0238	20	0.6385	0.0739
21	0.0000	0.0000	0.0000	0.0000	22	0.5894	0.0829
23	0.0000	0.0000	0.0000	0.0000	24	0.5894	0.0829
25	0.0000	0.0000	0.0000	0.0000	26	0.5894	0.0829
27	0.0000	0.0000	0.0000	0.0000	28	0.5894	0.0829
29	0.0000	0.0000	0.0000	0.0000	30	0.5894	0.0829
31	0.0588	0.0587	0.0327	0.0312	32	0.5894	0.0829
33	0.0000	0.0000	0.0000	0.0000	34	0.5239	0.0962
35	0.0714	0.0712	0.0349	0.0331	36	0.5239	0.0962
37	0.0000	0.0000	0.0000	0.0000	38	0.4541	0.1057
39	0.0000	0.0000	0.0000	0.0000	40	0.4541	0.1057
41	0.0000	0.0000	0.0000	0.0000	42	0.4541	0.1057
43	0.0909	0.0905	0.0378	0.0356	44	0.4541	0.1057
45	0.0000	0.0000	0.0000	0.0000	46	0.3784	0.1120
47	0.0000	0.0000	0.0000	0.0000	48	0.3784	0.1120
49	0.0000	0.0000	0.0000	0.0000	50	0.3784	0.1120
51	0.0000	0.0000	0.0000	0.0000	52	0.3784	0.1120
53	0.0000	0.0000	0.0000	0.0000	54	0.3784	0.1120
55	0.0000	0.0000	0.0000	0.0000	56	0.3784	0.1120
57	0.0000	0.0000	0.0000	0.0000	58	0.3784	0.1120
59	0.0000	0.0000	0.0000	0.0000	60	0.3784	0.1120
61	0.0000	0.0000	0.0000	0.0000	62	0.3784	0.1120
63	0.3333	0.3143	0.0946	0.0725	64	0.3784	0.1120
65	0.0000	0.0000	0.0000	0.0000	66	0.1892	0.1450
67	0.0000	0.0000	0.0000	0.0000	68	0.1892	0.1450
69	0.0000	0.0000	0.0000	0.0000	70	0.1892	0.1450

Table 4: Test of equality using the log rank

Variable	df	χ^2		*p-value*	
		HIV	Co-infected	HIV	Co-infected
Gender	1	0.50	0.71	0.4811	0.3991
Mstatus	3	1.92	4.36	0.5890	0.2254
Religion	2	2.09	6.37	0.3520	**0.0414**
WHO	3	39.17	1.62	**0.0000**	0.6555
Disclosure	1	0.66	0.39	0.8819	0.5313
Regimen	2	7.43	0.31	0.1901	0.8559

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Table 5: Model comparison

Criterion	Weibull	Exponential	Gamma	Llogistic	Lnormal
HIV/AIDS					
AIC	246.224	246.955	215.699	253.342	260.326
BIC	304.818	302.103	277.740	311.937	318.921
Co-infection					
AIC	137.066	136.345	128.962	137.406	138.410
BIC	176.688	173.637	170.916	177.028	178.032

Table 6: Gamma model for HIV/AIDS patients

Parameter	Level	df	β	SE	95% C.I			*p*-value
Intercept		1	-1.1675	1.8767	-4.8457	2.5107	0.39	0.5339
Gender	Female	1	0.7085	0.3555	0.0117	1.4054	3.97	0.0463
Age		1	0.0076	0.0126	-0.0170	0.0322	0.37	0.5439
		Religion compared with Traditionalist						
Religion	Christian	1	1.3727	1.1854	-0.9508	3.6961	1.34	0.2469
	Islam	1	1.0280	1.2654	-1.4522	3.5081	0.66	0.4166
		Marital status compared with Widowed						
Mstatus	Divorced	1	0.8257	0.9309	-0.9989	2.6503	0.79	0.3751
	Married	1	0.9068	0.8200	-0.7003	2.5139	1.22	0.2688
	Single	1	-0.0603	0.7974	-1.6231	1.5026	0.01	0.9398
Weight		1	1.8633	0.7646	0.3648	3.3619	5.94	0.0148
CD4		1	0.0065	0.0018	0.0031	0.0100	13.81	0.0002
		Regimen compared with (CBV/NVP)						
Regimen	AZT/3TC/EFV	1	-0.3505	0.2096	-0.7613	0.0604	2.80	0.0946
	AZT/3TC/NVP	1	-0.6714	0.5652	-1.7793	0.4364	1.41	0.2349
		WHO Clinical Stage compared with IV						
WHO	I	1	1.3132	0.5721	0.1920	2.4344	5.27	0.0217
	II	1	0.7970	1.0384	-1.2383	2.8322	0.59	0.4428
	III	1	1.3118	0.5113	0.3096	2.3140	6.58	0.0103
Disclosure	No	1	0.3566	0.7495	-1.1125	1.8256	0.23	0.6342
Scale		1	0.1897	0.0560	0.1064	0.3383		
Shape		1	8.5412	2.4599	3.7199	13.3625		

Table 7: Gamma model for Co-infection patients

Parameter	Level	df	β	SE	95% C.I			*p*-value
Intercept		1	-1.5663	1.3328	-4.1785	1.0459	1.38	0.2399
Gender	Female	1	0.1896	0.4136	-0.6209	1.0002	0.21	0.6465
Age		1	-0.023	0.0166	-0.0563	0.0088	2.05	0.1522
		Religion compared with Traditionalist						
Religion	Christian	1	0.0345	0.4395	-0.8269	0.8959	0.01	0.9374
	Islam	1	0.0727	0.5178	-0.9422	1.0877	0.02	0.8883
		Marital status compared with Widowed						
Mstatus	Divorced	1	0.3388	0.4999	-0.6409	1.3185	0.46	0.4979
	Married	1	-0.3664	0.4826	-1.3123	0.5795	0.58	0.4477

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	Single	1	1.1728	0.8236	-0.4415	2.7871	2.03	0.1545
Weight		1	0.0809	0.0217	0.0383	0.1235	13.85	0.0002
CD4		1	0.0043	0.0007	0.0029	0.0056	36.12	0.0001
		Regimen compared with (CBV/NVP)						
Regimen	AZT/3TC/EFV	1	-0.1321	0.5415	-1.1934	0.9292	0.06	0.8073
	AZT/3TC/NVP	1	0.0747	0.3916	-0.6929	0.8422	0.04	0.8487
		WHO Clinical Stage compared with IV						
WHO	I	1	-0.6574	0.4447	-1.5290	0.2142	2.19	0.1393
	II	1	-0.3376	0.4639	-1.2469	0.5718	0.53	0.4669
	III	1	-0.5659	0.5295	-1.6037	0.4719	1.14	0.2852
Disclosure	No	1	-0.0312	0.5751	-1.1583	1.0959	0.00	0.9568
Scale		1	0.6596	0.2525	0.3114	1.3969		
Shape			-2.1927	1.0823	-4.3139	-0.0715		

Table 8: Time Ratio (TR) for significant Covariates for HIV/AIDS and HIV/TB Co-infection

HIV/AIDS			**HIV/TB Co-infection**	
Covariate		TR=e^{β}	Covariate	TR=e^{β}
Gender	Female	$e^{0.7085} = 2.03$		
Weight		$e^{1.8633} = 6.44$	Weight	$e^{0.0809}$ =1.084
CD4		$e^{0.0018} = 1.00$	CD4	$e^{0.0043}$ =1.004
WHO clinical stage	I	$e^{1.3132} = 3.72$		
	III	$e^{1.3118} = 3.71$		

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