Original Research Article

An application of the Growth Model to HIV/AIDS Patients on Antiretroviral Therapy with Coinfections in a District Hospital in Ghana

Abstract

Lethargic opportunistic diseases like Tuberculosis andHepatitis C are deeply ingrained complications for patients diagnosed with human immunodeficiency virus (HIV). The effect of Highly Active Antiretroviral Therapy(HAART) on Hepatitis C and Tuberculosis in HIV patients in Ghana continues to be unpredictable, especially in younger patients. This study aimed to describe the patient survival time distribution on antiretroviral treatment using Statistical Growth model.A retrospective cohort of 634 patients were selected from the District Health Information Management System 2 (DHIMS 2), a secondary source, using a random sampling approach. These patients were diagnosed with HIV and put on antiretroviral therapy between 2000 and 2019 at St. Martins Catholic Hospital in Amansie South District of the Ashanti Region. The probability of survival for almost all of the risk factors decreases gradually at different clinical states, i.e., from state 1 through to state 4. Hepatitis C or Tuberculosis can also be diagnosed chronically in approximately one in ten patients. Age, sex and the CD4 cell count of patients substantially (p- value less than 20 percent in log-rank tests) contributed to the prevalence of human immunodeficiency virus.Survival of children, aged <1year, after treatment was of negative effect.The statistical growth analytical approach offers a good estimate of survival rate ($R^2 = 79.82\%$) among major risk factors for children, aged <1yearon ART with proportion of survival growth of 0.95, hence the survival time of children, aged <1yearon HAART is negatively affected irrespective of the treatment initiation period.

Keywords: Statistical growth model, antiretroviral, transition, treatment, survival

1.0 Introduction

In 2016, one million deaths out of approximately 36.7 million HIV-infected people were reported (UNAIDS, 2020). Sub-Saharan Africa, recorded very high figure of the HIV-infected patients (WHO, 2015). HIV/AIDS is known as a pandemic because its infection spreads over a large geographical area. During the early period of 2014, 39 million deaths were recorded due to this disease (Kallings, 2008; Center for Disease Control and Prevention, 2005). Awareness of trends in HIV/AIDS epidemics is critical in tracking and monitoring progress in preventing and managing actions in countries (Pandey et al., 2019).

However, Highly Active Antiretroviral Therapy (HAART) fights the disease progression by improving the principal immune system of the body or decreasing the concentration of RNA blood content. Although we may conclude that HAART enhances the immune system, there are some questions regarding numerical progression that can be asked. After patients have initiated HAART, the state of the immune system, determined by the CD4+ cells count changes and this varies depending on the gender, age, educational status, and other functional status of the patient.

In Ghana and other sub-Saharan African countries, the government's assessment of HIV prevalence is based primarily on HIV sentinel surveillance (HSS), which focuses on reviewing pregnant women visiting prenatal clinics. Between September and December 2014, the latest sentinel surveillance was conducted at the Noguchi Memorial Institute for Medical Research (NMIMR), integrating the External Quality Assurance Test (EQA) for the HIV component into the Ghana Demographic and Health Survey (GSS, 2015).

The Statistical Growth model is used to fit the progression rate of CD4 count among HIV/AIDS infected people. The CD4 count is an important immunological marker for patients with HIV and the rate of decline in the CD4 count is often much faster at the onset of clinical stage IV. Survival analysis, also referred to as "duration analysis," evaluates the time to failure, where failure indicates a single discrete event analysis (Basavarajaiah, 2020).

Opportunistic infections (OIs) are ailments that affect HIV patients more often and with serious complications. This is directly attributable to the compromised immune systems (Sterling, 2020). Tuberculosis has been proven to be one of such opportunistic diseases when paired with HIV/AIDS (Ngwerume, 2008).

Several scientific researches on HIV/AIDS epidemiology and geographic co-morbidities have resorted to different descriptive and empirical statistical methods. Relative risks (RRs) and Odds ratios (ORs) are widely adjusted to identify and assess the relationship between risk factors and health outcomes (Basavarajaiah, 2020). On the other hand, proportional hazard models (PHM) are used to define and clarify the association among survival time and risk

factors in particular: HIV status, opportunistic disease status, WHO HIV/AIDS levels, CD4 count, age, sex and alcohol use (Zachariah R., Fitzgerald, M., Massaquoi, M et al., 2006).

As the virus infects the body, the CD4 + T cells which are immune cells start to deplete as the HIV infect the body. For HIV-infected individuals, these cells are regarded as essential progression biomarkers (UNAIDS, 2020). CD4 + T cells are the prime determinant of prognostic information and an antiretroviral therapy guide for HIV-positive individuals, considering the disease's close connection to the immune system. Mostly, for a group of patients, we would like to know the number of CD4 + T cells to learn more about the progression of the disease on their first visit to the medical centre.However, since it is not very instructive to comment about the disease status of the number of CD4 + T cells in one state, change in the number of cells over time is a reasonable predictor of disease status. Many papers on HIV biomarkers using various regression methods have been published (Culshaw, 2006), (Kuller, L. H., Tracy, R., Belloso, W., 2008), (Duprez, D. A., Neuhaus, J., Kuller, L., 2012). Under HIV/AIDS progression modeling, Markov models are reasonably straightforward to evaluate both CD4 step or death or failure in a single model as opposed to survival models. The Markov models can handle censored data, risks (censorship), multiple outcomes, repeated outcomes, unpredictability and survival probability inconsistency. (Abassi et al., 2017).

A 7-state Markov model recently published by Shoko and others to determine the progression of HIV/AIDS patients on ART at a Bela clinic in 2018 in South Africa showed that patients spent less time in good states than in bad states when treatment is effective. They concluded that there should be more frequent monitoring of deleterious drug reactions, checking patients with HIV/AIDS for any symptoms and signs of TB, and monitoring for variables that may affect gender differences. (Shoko et al., 2018,). Another study using joint modelling to estimate risks associated with different variables and covariates with a mixed longitudinal impact sub-model for CD4 counting and a Cox relative risk survival sub-model with time-dependent covariates by Deo and colleagues concluded that quality adjusted lifetime years were estimated for each person for their lifetime horizon (Deo et al., 2019).

However, none of these studies considered the inclusion of survival rate with survival growth proportion, formation of CD4+T cells after patients start HAART with or without covariate (Hep C or TB), which shows how the disease progresses while ART is initiated.

2.0 Objectives

This study seeks to provide an alternative way of understanding treatment survival while on HAAT among HIV patients, estimate survival rate with proportion of survival growth and compare the effect patterns of different covariates using the Statistical Growth model.

3.0 Methods

3.1 Study population and setting

Amansie South District Assembly is one of the thirty District in Ashanti Region. The district was established in 1988 as part of Ghana's Decentralization Strategy by Legislative Instrument (L. I.) 1403 to introduce administration to the citizenry at the local level and to foster development. This led to Manso Nkwanta becoming its District capital. The total land area is 1230sq.km, which is about 5% of Ashanti Region's total land area. The 2010 Population and Housing Census puts the District's population at 134,331, representing 2.8% of Ashanti Region's population (GSS, 2014).

3.2 Study design

A Retrospective cohort of 634 patients were selected from the District Health Information Management System 2 (DHIMS 2), a secondary data, using the simple random sampling technique. Individuals that comprise the subset of the larger group are randomly selected as identified in DHIMS 2. In most cases, everyone in the large population set has the same likelihood of being chosen. This results in a balanced subset with the best chance of accurately representing the larger group as a whole. Simple random sampling technique is free of bias. These patients were diagnosed with HIV and put on antiretroviral therapy between 2000 and 2019 at St. Martins Catholic Hospital in Amansie South District of the Ashanti Region.The time to death was the outcome variable in this analysis. For patients who died before December 31, 2019, the time to death was calculated from the date of initiation to the date of death (the end of the study period). Those who did not witness the event of interest before the end of the report, as well as those who were lost to follow-up, were considered censored. The Kaplan-Meier test was used to predict survival after the start of ART, and log-rank tests were used to compare various groups' survival prospects. The variables with p- value less than 20 percent in log-rank tests were selected as potential risk factors. The collected data was cleaned, coded and then analysed using **R** (**version** "**4.0**")

3.3 Covariate description

For the purposes of this study and also due to the limitations associated with secondary data collected from the District Health Information Management System 2 (DHIMS 2) database, the study covariates were limited to the patient's gender, World Health Organisations (WHO) clinical stages of HIV, age category and CD4 count.

We fit the model to the data from time to event. The period is the outcome variable of interest, typically called period of loss, or time of survival or lifetime. For instance:

(a) Duration from treatment commencement to failure

(b) Birth-to-death duration (lifespan)

(c) Time spent on AIDS infection

(d) Duration from birth to onset of a disease (starting age)

3.4 Model Description

Some notable terms are used in the survival model or "time" to assess events, concentrating on measuring the time leading to an incident. In this study, the incident is defined as *death, lost to follow-up and delayed care*. There are two basic data components of survival analysis. These are non-normality and censorship.

In this study, we employed the survival function of time (Chen, 2013; Rodríguez & Lin, 2013) where survival analysis is used to follow subjects over a period of 9 years.

Typically, three functions describe or characterize the distribution of survival times:

3.5 Concept of the Model

The survival time distribution is typically represented or defined by three functions.

i. Survival Function

$s(t)=P(\text{an individual survivor longer than } t)$

$=P(T> t)$ (1)

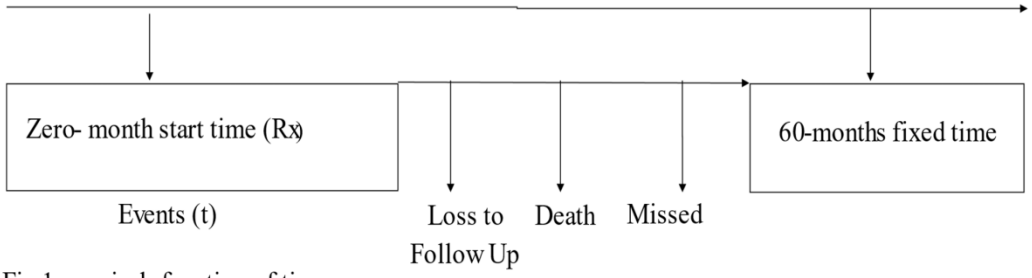

Fig 1: survival function of time

$S(t)=1-P(\text{an individual die before fixed time}).$

$S(t)=1-F(t)$ (2)

$S(60)=P(\text{ an HIV-infected patient's survival longer than 60 months})$

$=P(T>60 \text{ months})$ (3)

$P(t=60 \text{ months}).$

$S(60)=1-P(\text{ an HIV-infected patient dies before 60 months})$

$=1-F(60 \text{ months})$(4)

Estimation of S(t):

$\hat{s}(t)=\frac{\text{No. of patients who survive longer than "t"}}{\text{Total no. of patients in cohort}}$ (if the observations are not censored)

ii. Probability Density Function

$f(t)=\lim_{\Delta t\to 0}\frac{P(\text{an individual dying in the interval } t, t+\Delta t)}{\Delta t}$

$f(t)=-\frac{ds(t)}{dt}=$(The slope of the survival function)

$$\hat{f}(t)= \frac{\text{No of patients dying in the interval beginning at "t"}}{\text{Total no. of patients} \times \text{internal width}} \quad (5)$$

iii. Hazard Function (Hz)

$$h(t)= \lim_{\Delta t \to 0} \frac{1}{\Delta t} P(\text{an individual dies in the time interval } (t, t+\Delta t))$$

$$h(t)= \lim_{\Delta t \to 0} \frac{1}{\Delta t} P(t<T<t+\Delta t)/T>t)$$

$$= f(t)/1- f(t) = f(t)/S(t) \quad (6)$$

Estimation of h(t) :

$$\hat{h}(t)= \frac{\text{No of deaths in } (t, \Delta t)}{\text{No of alive patients at } t \times \Delta t}$$

$$= \frac{\text{No of deaths in } (t, \Delta t)/\text{Total pts}}{\Delta t \times (\text{No of patients at } t)/\text{Total pts}} \quad (7)$$

3.6 WHO Clinical States/Levels

The WHO system assigns patients to one of four systematic clinical state, varying from state 1 (asymptomatic) to state 4 (AIDS). Patients are allocated to a specific state when they show at least one health disorder under the parameters of that state. Patients assume a progressive state after rehabilitation from the health condition that positioned them at that state. The following states have been indicated by the WHO with complaints received from patients living with HIV (PLHIV):

Clinical state I: A favourable treatment state with Cd4 cell count above $750/mm^3$. Complaints received at this state include Acute Retroviral Primary and Asymptomatic Syndrome.

Clinical state II: A mild favourable treatment state with Cd4 cell count between $500/mm^3$ and $\leq 750/mm^3$. Complaints received include: mild unexplained weight loss, recurrent infections of the respiratory tract, herpes zoster, angular cheilitis, persistent oral ulceration, common pruritus, seborrheic dermatitis, infections of the fungal nail infection etc.

Clinical state III: This is a treatment state of a patient with Cd4 cell count between $300/mm^3$ and $\leq 500/mm^3$. Complaints received include: Extreme weight loss (> 10% body assumed or measured weight), unexplained recurrent diarrhoea over 1-month, unexplained persistent

fever, oral candidiasis, oral hairy leucoplakia, suspected pulmonary tuberculosis, documented extreme bacterial infections, and acute ulcerative necrotizing stomatitis.

Clinical state IV: This is a worse treatment state with Cd4 cell count below $300/mm^3$. Complaints received include: Persistent severe or, chronic herpes simplex infection, radiological bacterial pneumonia, oesophageal candidiasis, extrapulmonary tuberculosis, HIV encephalopathy, Kaposi sarcoma and toxoplasmosis (WHO, 2014).

4.0 Results

Table 1: Descriptive analysis of CD4 count.

Variable	Patients mean ± SD	P-value
Age (year)	24.31 ± 7.20 (203–41.21%)	0.028
Baseline CD4	115.39 ± 57.12(203)	0.489
CD4 before 6 months end	301.65 ± 161.31(198)	0.037
CD4 before 1-year cohort end	369.97 ± 95.97(194)	0.005
CD4 before2-year cohort end	378.98 ± 64.98(192)	0.020
CD4 before3-year cohort end	409.97 ± 50.12(190)	0.084
CD4 before4-year cohort end	444.00 ± 40.97(186)	0.010
CD4 before5-year cohort end	449.97 ± 35.88(184)	0.002
WHO clinical state	Nil	
State II	9(1.90%)	0. 529
State III	84 (16.21%)	0.431
State IV	108 (22.01%)	0.477
Occupation assessment up to 5years	149(30.17%)	0.068
Death	65(12.04%)	0.031
HIV/TB co-infection		
Yes	19(7.01%)	0.202
No	183(36.98%)	0.887
HIV-HEP C co-infection		
Yes	14(6.34%)	0.201
No	201(39.79%)	0.89
Mean period of Rx from beginning to completion of fifth cohort		

Mean days	1741 ± 49.01(187)	0.002

P-value < 0.05

From Table 1, the average patient age is 24.31 ± 7.20/mm^3, the mean baseline CD4 count before the start of Highly Active Antiretroviral Therapy is below the CD4 count baseline of 115.39 ± 57.12/mm^3. After subsequent periods of HAART completion, the average CD4 count is increased to (301.65 ± 161.31/mm^3) for the first 6 month, the average CD4 count is increased to (369.97 ± 95.97/mm^3) at 1 year, the average CD4 count is increased to (378.98 ± 64.98/mm^3) at 2 years, the average CD4 count is increased to (409.97 ± 50.12/mm^3) at 3 years, the average CD4 count is increased to (444.00 ± 40.97/mm^3) at 4 years and the average CD4 count is increased to (449.97 ± 35.88/mm^3) at 5 years. WHO clinical states are assessed on the basis of CD4 count baseline. From Table 5, WHO clinical state II is 9(1.90%), state III is 84(16.21%), state IV is 108 (22.01%) .and are all considered to be statistically insignificant. The physical and clinical assessment on the Cronbach scale of the occupational PLHIV is 149(30.17%, p-value<0.05), mortality 65(12.04%, p-value <0.05), Hep C (6.34%) and HIV-TB co-infection 7.01%.

From the results, the average period of initiation at HAART at p-value= 0.002 is 1741 ± 49.0 days (Table 1). This means that the paradoxical clinical deterioration after HAART start which is the Immune Reconstitution Inflammatory Syndrome (IRIS) is improved.

Table 2: Survivability of a particular CD4 class with HAART interval

Survival Time (weeks)	Survival Proportion	Standard Error	Survival Proportion	Standard Error
9	–	–	0.950	0.0517
12	0.992	0.0134	0.900	0.0709
13	0.980	0.0180	–	–
14	0.967	0.0221	–	–
18	–	–	–	–
19	0.949	0.0250	–	–
20	0.919	0.0289	–	–
22	0.916	0.0319	–	–
23	0.869	0.0379	0.839	0.0841
24	0.821	0.0451	0.741	0.121
25	0.797	0.0470	–	–
26	0.749	0.049	–	–
30	0.741	0.0509	–	–
34	0.709	0.0519	0.620	0.120
35	0.698	0.0531	–	–
36	0.600	0.0571	0.561	0.121
38	–	–	–	–
40	–	–	–	–
44	0.539	0.0590	–	–
45	0.349	0.0571	0.479	0.119
46	0.310	0.0549	–	–
47	0.289	0.0551	–	–
48	–	–	–	–
52	0.281	0.0541	–	–
53	0.261	0.0531	–	–
54	0.200	0.0491	0.391	0.140
55	0.191	0.0480	0.260	0.140
56	0.0920	0.0360	0.135	0.120
58	0.0741	0.0331	–	–
60	0.0489	0.0300	–	–
63	0.0	0.0	–	–

Survival Curve Comparison (log-rank test)

Table 3: Survival rate for patients with HAART - Statistical Growth model

Variable	Co-efficient	Standard	R^2 (%)	Survival	P-value(rate)

		error		Growth	
Intercept (year)	4.221	0.0814	46.01%	0.649	p-value ≥ 0.05
Beginning HAART below 350/mm^3 CD4 cell count.	0.071	0.006			
Intercept (year)	9.391	0.0669	79.82%	0.990	p-value ≤0.05
Beginning HAART above 350/mm^3 CD4 cell count.	0.076	0.003			

P-value < 0.05

Tables 2 and 3 indicate that there is an average input age of 23 years (time 0:2000), an average output age of 30 years and 488 total failures in the survival analysis model.

Patients with chronic problems between 53 and 104 weeks (1–2 years) are 64% more likely to die than those with any persistent signs of infirmities between 0 and 26 weeks (6 months). Patient reporting between 157 and 209 weeks of illness (3-4 years) have a 94% higher mortality risk than the baseline population, showing a weak statistical significance and impact on an estimated survival rate relative to those reporting chronic disease. Age was not statistically significant among individuals starting HAART above 350 CD4/mm^3. Patients between 21-26 years had a lower risk rate and a more survival rate. Individuals between 26 and 35 years have a 61% higher chance progressing to death than those in the median age category starting Highly Active Antiretroviral Therapy below 350 CD4/mm^3. There is a high risk of progression to death among patients between 18-25 years (65%) and those between 26-34 years (87%).

The CD4 count is tested for chronic symptoms, with statistically significant chronic weight loss (p-value <0.05) being the best indicator of risk of death (WHO, 2010). Over 95 percent of patients respond to treatment. The cumulative survival growth or rate after commencing Highly Active Antiretroviral Therapy is 0.990 (p-value < 0.05, $R^2 = 79.82$ %). Starting HAART with a count of CD4 above 350/mm^3 is probably more effective. In addition, the

CD4 count is a significant predictor for patients with HIV infections; the rate of the decrease in CD4 count is always much faster if the initiation of HAART is applied to subjects with CD4 below 350/mm^3 and in clinical state IV.

The likelihood of dying increases with the person's reduced CD4 count at enrolment. This is confirmed by the results of (Agan et al., 2012). Therefore, both CD4 cell count and viral load need to be used to monitor treatment efficacy. Younger patient below 40 years have a higher chance of immune restoration than the aged.

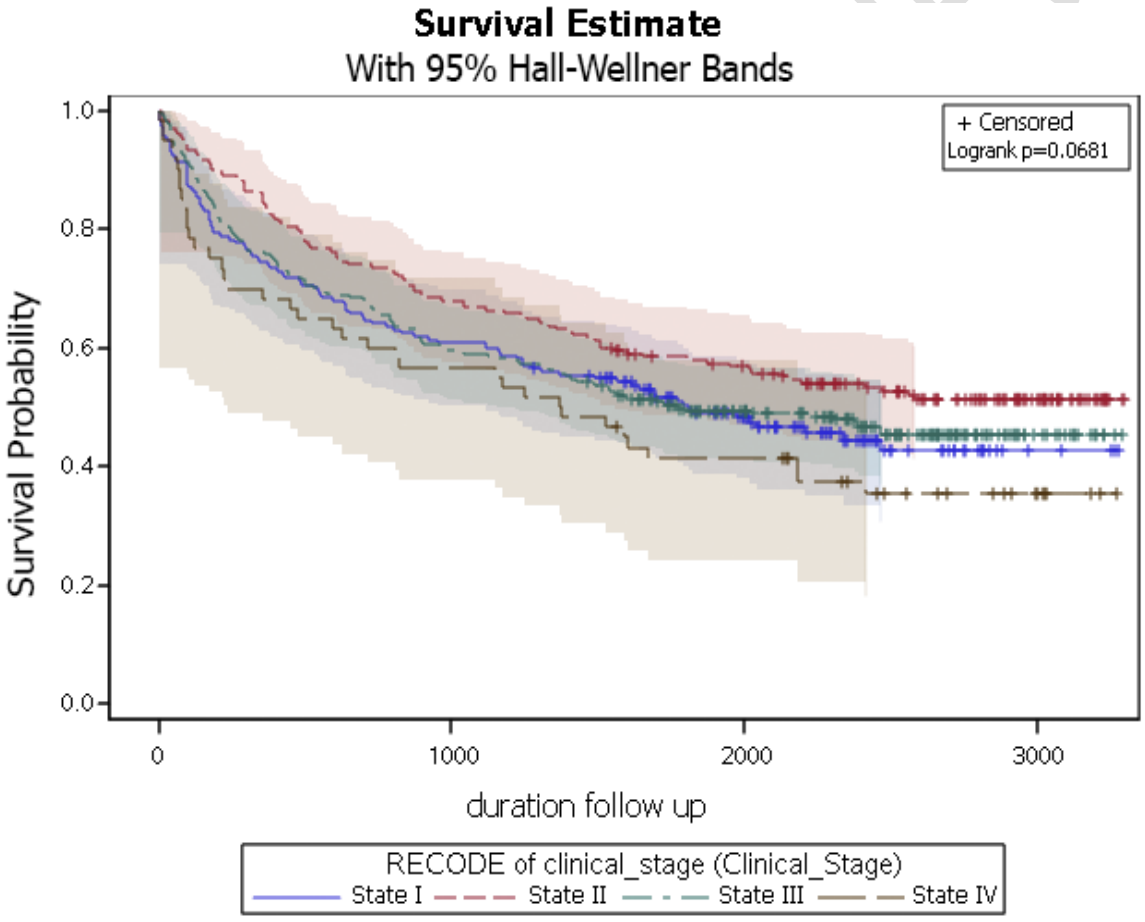

Figure 1: Survival estimates among children on ART.

The likelihood of survival of children was determined based on the state levels. From Figure 1, younger patients less than 15 years who start ART in state 4 have the least probability curve over the entire review era. This means that younger patients who start ART at the late

detection state of the virus infection have least or no chances of survival. Hence children who are put early on ART are more likely to survive in clinical states of the disease.

A log-rank statistic of 7.1120 and a P-value of 0.0681 show that the odds of survivors do not vary statistically for the various states. Nonetheless, a low p-value less than or equivalent to 0.05 may suggest a potential variation in children's survival expectations starting at various states. This suggests that starting Highly Active Antiretroviral Therapy (HAART) with higher CD4

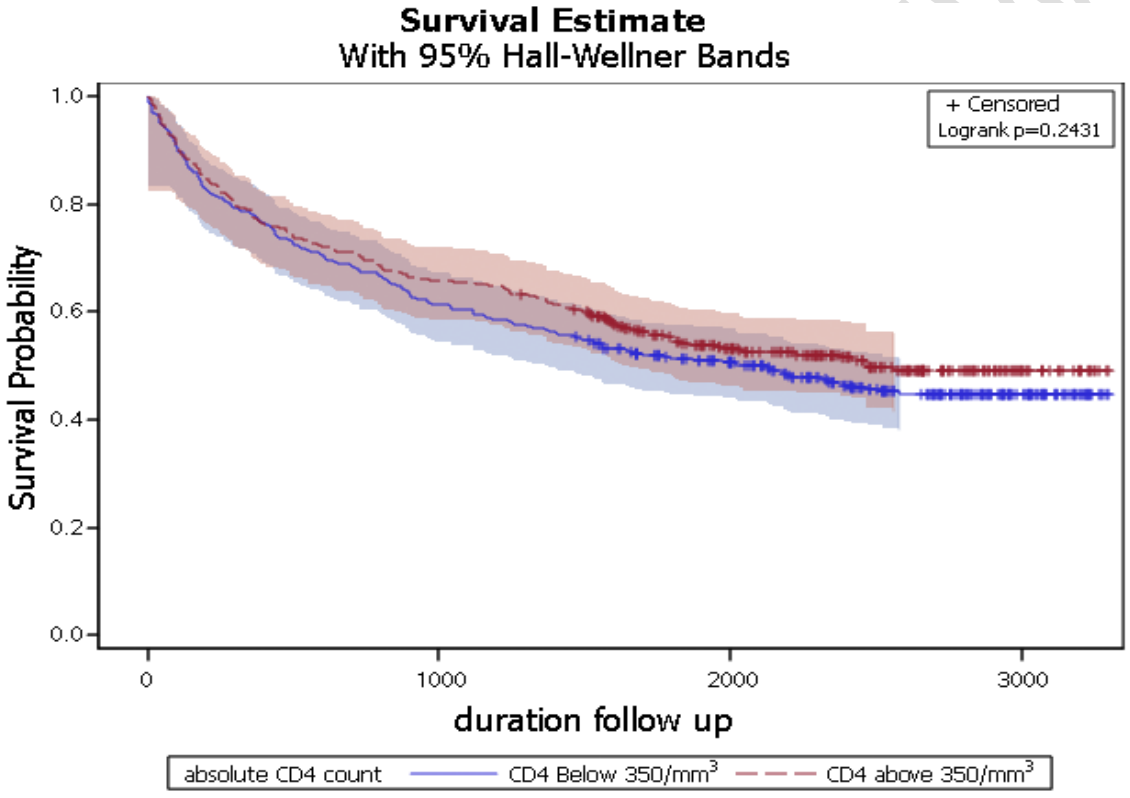

Figure 2: Kaplan-Meier survival curve by state level.

count can lower TB/Hep C incidence in children. A CD4 count less than 350/mm^3 appears to have an estimates of lower survival probability in relation to patients of equal age who start an antiretroviral therapy above 350 /mm^3 CD4 count level as shown in Figure 2. A log rank of 1.2991 and the corresponding p-values of 0.2431 show no significant difference in the prognosis for survival of children beginning with their CD4 counts below 350 /mm^3 and those beginning with a CD4 above 350/mm^3. Figure 3 shows an overlapping and therefore 95%

Hall-Wellner Bands indicating no significant difference in care opportunities for male or female babies. Therefore, starting HAART with CD4 count above 350/mm^3 is probably more effective and the likelihood of dying increases with the patients' reduced CD4 count at enrolment.

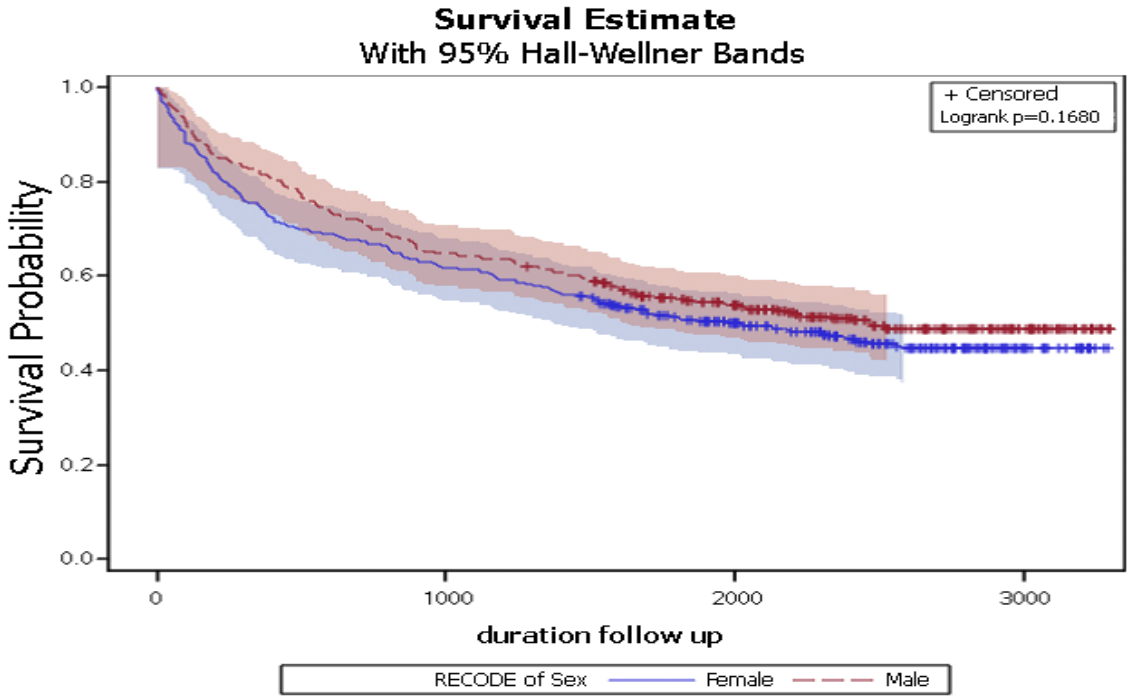

Figure 3: Kaplan-Meier survival curve based on sex

The log rank figure of 1.6990 and an equivalent p -value of 0.1680 shows that sex has no major consequences on children's survival on hospital care.

From Figure SM1, children less than 15 years of age have significantly lower survival prognosis. A log rank value of 32.011 and an equivalent p-value less than 0.0001 is a characteristic of a significant difference in the impact of the age category on the chances of survival of the child.

5.0 Discussion

The study reveals that, HIV patients with chronic problems between 53 and 104 weeks (1–2 years) are 64% more likely to die than those with any persistent symptoms between 0 and 26

weeks (6 months). Women reporting between 157 and 209 weeks of illness (3-4 years) have a 94% higher mortality risk than the baseline population, showing little statistical significance and impact on a computed survival rate relative to those reporting chronic disease. This corroborates the findings by (Samb et al., 2007). The diagnosis of a doctor for a chronic disease has little impact on the estimated death risk. Age is statistically of a limited significance for a category of individuals starting HAART above $350/\boldsymbol{mm^3}$ CD4 count. Individuals between 21-26 years have a lower risk rate and a higher survival rate. Individuals between 26 and 35 years have a 61% higher chance progressing to death than those in the median age category starting Highly Active Antiretroviral Therapy below $350/\boldsymbol{mm^3}$ CD4 count. There is a high risk of progression to death among patients between 18-25 years (65%) and those between 26-34 years (87%).

Computed hazard ratios are not statistically significant for other age groups and are therefore not presented in the table. Although the use of demographic and biological data for survival analysis is made, survival models have multiple constraints. First, there are very few variables used to diagnose chronic health symptoms. No physical test or in-depth examination of each symptom is required as supported by (Tuboi et al., 2007). However, the emerged results depend heavily on the willingness of the patient to regularly report chronic and opportunistic infections symptoms, and for how long they have been. Unless the data are stated inconsistently, the findings of the study would only be incomplete. Second, the CD4 count is tested for chronic symptoms, with statistically significant chronic weight loss alone (p-value=0.05) being the best indicator of risk of death as supported by (WHO, 2010). Most patients adhered very well to treatment (> 95%). After beginning HAART, the cumulative survival rate is 0.98 (p-value= 0.05, $R^2 = 79.82\%$). HAART with a count of CD4 above $350/mm^3$ is probably more effective. This corroborates the findings by (Weidle et al., 2006). In addition, the CD4 count is a significant predictor for patients with HIV infections; the rate of decrease in CD4 count is always much faster if the initiation of HAART is CD4 < $350/mm^3$ in clinical state IV. This also corroborates the work by (Wools-kaloustain et al., 2006).

The likelihood of dying increases with the person's reduced CD4 count at enrolment. This is confirmed by the results of (Agan et al., 2012), who have concluded that being at the critical state of AIDS leads to a greatest likelihood of dying. Research has also shown that despite inhibited viral load particularly in older patients, CD4 cell count rises gradually.Therefore, both CD4 cell count and viral load need to be used to monitor treatment efficacy. The study

shows that younger people under 40 have a higher chance of immune restoration than the aged. The CD4 mean count in older patients is lower than in younger ones. This corroborates the findings by (Alinaghi et al., 2014).

The results of this study show that patients usually begin ART in an advanced HIV/AIDS state IV. Close monitoring on children on ART therapy and other measures should be introduced to minimize deaths in the children population. Considerable amount of work should also be done to determine how infant survival times are adversely influenced by start of ART while the therapy is expected to have beneficial implications.

The contributions of this study include a clear illustration of the merits of using the statistical growth model in survival analysis and modelling when identifying risk factors for patient survival on treatment. Using this method enables an exploration of the dynamics of risk factors throughout the survival time distribution. The other significant contribution is that the statistical growth model's approach can be implemented to augment the proportional hazards model in a very effective and insightful way.

6.0 Conclusion

The growth analytical approach offers a better estimate of the survival rate ($R^2 = 79.82\%$) with the proportion of survival growth at 0.95 when changing the survival and development model. This implies that our model provides a better estimate of the survival rate with a major risk factor for infants on ART. Getting a baby may have significant negative implications on the survival time. Diagnosis by a doctor for a chronic disease have little impact on the estimated death risk. Age is statistically not significant for a group of individuals starting Highly Active Antiretroviral Therapy (HAART) above $350/mm^3$cd4 count. HAART with CD4 count above $350/mm^3$is probably more effective. The CD4 count is a significant predictor for patients with HIV infections; the rate of the decrease in CD4 count is always much faster if the initiation of HAART is below $350/mm^3$in clinical state IV. Despite inhibited viral load particularly in older patients, CD4 cell count improves gradually. Therefore, both CD4 cell count and viral load need to be used to monitor treatment efficacy. Younger people under 40 years receiving ART have a higher chance of immune restoration than the aged.

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