



SURVIVAL ANALYSIS OF LONG-TERM SURVIVORSHIP OF HIV PATIENTS UNDER ANTIRETROVIRAL THERAPY AT GENERAL HOSPITAL, UGBA, BENUE STATE, NIGERIA

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ABSTRACT

Survival model plays a vital role in the understanding of prognosis and hence management of diseases. In this study, the long-term survival of HIV/AIDS patients under antiretroviral therapy (ART) is evaluated using Survival models. In particular, the Kaplan-Meier Estimator was used to estimate the Long-term survival of HIV/AIDS patients under ART. A retrospective data was obtained on HIV/AIDS patients who enrolled on ART at General Hospital, Ugba Logo Local Government Area, Benue state, Nigeria from year 2018 to 2022 for the study. Results revealed that 96% of HIV/AIDS patients under antiretroviral therapy had suppressed viral load for at least 8.8 years. Further test on the equality of survival distributions of female and male gender based on the Log-Rank, Breslow (generalized Wilcoxon) and Tarone-Ware statistic revealed that the survival distributions of the female and male patients are similar at 0.05 level of significance. It is recommended that people living with HIV/AIDS should accept antiretroviral therapy so that they could live healthy lives.

Keywords: Survival Analysis, Kaplan-Meier Estimator, HIV/AIDS, Antiretroviral Therapy

INTRODUCTION

Human immunodeficiency virus (HIV) attacks and destroys CD4 cells, a type of immune cell. This damage to the immune system makes the body vulnerable to infections and certain diseases. To date, there is no vaccine that can permanently cure HIV. Therefore, people who contract HIV require lifelong medical treatment. Without treatment, HIV can severely damage the immune system, leading to acquired immunodeficiency syndrome (AIDS) (Khaled, 2019). Although there is no cure for HIV/AIDS, proper care for those already infected remain a viable approach to addressing the public health concerns. Antiretroviral therapy plays a vital role in improving the lives of people with HIV in this regard. The widespread use of antiretroviral therapy has led to better prognoses and fewer AIDS-related deaths (Williams et al., 2011).

Despite advances in scientific understanding and public health campaigns targeted at combating the menace of HIV/AIDS the disease remains a major public health concern with more people becoming infected of the virus daily (Sanni et al., 2018). In 2014, the Joint United Nations Program on HIV/AIDS (UNAIDS) established the 90-90-90 global target to control the HIV epidemic. This target envisioned that by 2020, 90% of people living with HIV would have known their status, 90% of those diagnosed would have received antiretroviral therapy, and 90% of those on treatment would have achieved viral load suppression. However, as of 2018, Nigeria fell short of the 90-90-90 goal, with only 67% diagnosed, 53% on treatment, and 42% virally suppressed. The North-Central region of Nigeria showed worse results, with just 9% of those on antiretroviral therapy achieving viral suppression (NACA, 2020). In 2020, UNAIDS set a more ambitious 95-95-95 target with the third 95 implying a 95% viral load suppression of HIV patients who are on ART (NACA, 2020).

Since Nigeria's introduction of free antiretroviral therapy in 2002, AIDS incidence has drastically declined over the past decades (NACA, 2022). Antiretroviral therapy (ART) helps in stabilizing the deteriorating immune system by reducing the viral load in the blood. The decision to initiate ART is generally based on two clinical measurements: CD4 count and viral load, which quantifies HIV levels in the blood. The

purpose of ART is to suppress viral load to undetectable levels in the body. If successful, ART enables the infected person to live a healthier, longer life without transmitting the virus (Gurprit et al., 2020). Hence, an HIV patient who achieves an undetectable viral load could be considered functionally cured. Since suppressed viral load is associated with increase in survival rate and low transmission, it becomes imperative to periodically assess the effectiveness of ART programs on HIV/AIDS patients. Such assessment would help in monitoring progress on UNAIDS target of 95-95-95 by 2025. The aim of this paper is to evaluate long-term survivorship of HIV/AIDS patients under Antiretroviral therapy (ART) using survival analysis model. It is believed that findings of this paper will provide information for the appraisal of ART intervention in the study area and also enlighten HIV/AIDS patients on the benefits of ART.

Survival analysis is the branch of statistics that study data that normally associate with the duration of time until the occurrence of an event of interest. What makes the survival analysis a particular area of interest in event history analysis is the specific characteristic to take into account incomplete observations, or also called, censored information. With the presence of censoring, it may be impracticable to apply some standard statistical method for analyzing such data (Liberato, 2017). Survival models have found applications in several HIV/AIDS studies. The empirical review of some of the studies are outlined below.

Okoro (2024) assessed gender differences in response to antiretroviral therapy among people living with HIV/AIDS at Federal Medical Center (FMC), Abuja using retrospective cross-sectional study among 595 HIV adult patients who enrolled between January 2021 and December 2022. The study found that 96% of the total study participants had viral load suppression and female gender were equally virally suppressed as the males. A retrospective cohort study of the survival of HIV/AIDS patients under ART at the University Hospital, Northwest Ethiopia was undertaken by Teka, et al. (2021). The Kaplan-Meier and Cox proportional hazard models were adopted to study the survival and also identify factors influencing HIV/AIDS patient survival rates. The study reported Educational status, Age, alcohol consumption, family size, baseline and current weight, tobacco and chat

usage, baseline hemoglobin, and tuberculosis (TB) diseases as significant predictors of HIV/AIDS patients' survival. Elsewhere, Cescon, et al. (2013) in a cohort study examined differences by gender in clinical responses to antiretroviral therapy (ART). It investigated gender differences by injection drug use (IDU) history in virologic responses to ART and mortality using data from the Canadian Observational Cohort (CANOC) collaboration. Results revealed that HIV-positive women in CANOC are at heightened risk for poor clinical outcomes.

Genzeb et al. (2021) conducted a study on the survival of people living with HIV after initiation of HAART. The study looked at survival time and associated factors among adults with HIV in south Gondar, Northwest Ethiopia. A 5-year retrospective cohort study design was conducted by the researcher using patient records among 746 adults living with HIV/AIDS. The study employed systematic random sampling technique to select respondents after proportional allocation was made for all health facilities included in the study. Result showed that mortality rate was highly observed in the early phase of antiretroviral treatment. Age of respondents >43 years, past TB treatment, baseline WHO stage IV, pneumonia after HAART, INH prophylaxis, and disclosure status were independent predictors of mortality. Melaku (2018) conducted a study to investigate major risk factors, which contributed to shortened survival time and death of HIV patients on antiretroviral therapy. Using Six-hundred HIV patients from two different hospitals and six health centers recorded from January 2003 to December 2017, the Kaplan–Meier and Cox proportional hazard model were employed in the study. Results indicated that tuberculosis comorbidity was a significant risk factor to the survival of patients at 5 % level significance. From the Cox regression result, the risk of death for patients who lived with tuberculosis was about 2.872-fold times higher than those patients who were negative. Maskew et al. (2013) investigated the gender differences in treatment response among HIV positive patients virally suppressed within six months of treatment initiation. They found that male patients had a 20 % greater risk of death at both 24 months and 36 months of follow-up compared to females. Older patients and those with a low hemoglobin level or low body mass index (BMI) were at increased risk of mortality throughout follow-up and men gained fewer CD4 cells after treatment initiation than did women.

Birhanu et al. (2021) conducted a study to assess unsuppressed viral load (>1,000 copies/mL) and associated factors among HIV patients taking first-line antiretroviral treatment at public health facilities in Jimma, Ethiopia with 669 patients where 258 (38.6%) were aged 25–34 years. Median age was 35 years. Multivariate logistic regression analysis was performed to identify factors independently associated with viral no suppression, considering a 95% confidence interval. Results revealed that, among the participants, prevalence of unsuppressed viral load was 20.3%. Risk of unsuppressed viral loads was 91% lower among ART patients who had been taking ART. Ghobadi et al. (2023) used mixture cure models to estimate factors affecting short- and long-term survival of HIV patients. Findings of the study revealed that antiretroviral therapy, tuberculosis infection, history of imprisonment, and mode of HIV transmission were the factors that influenced short-term survival time (p -value < 0.05). Results also showed that, prison history, antiretroviral therapy, mode of HIV transmission, age, marital status, gender, and education were significantly associated with long-term survival (p -value < 0.05). The people with prison history, who received ART treatment, and contracted HIV through injection drug users

survive longer. Health professionals should pay more attention to these findings in HIV prevention and treatment. Other studies on HIV/AIDS patients survival and associated risk factors could be found in Ketema and Eshetu (2012); Gurprit et al. (2013); Million, (2018); Lodwick et al. (2010) and Titou et al. (2022).

From the foregoing, the study of HIV/AIDS patients survival and associated risk factors using survival models is a common theme in epidemiology literature. However, findings on gender differences on HIV/AIDS patients' response to ART treatments and recovery are divergent hence there is still need for further empirical investigations.

MATERIALS AND METHODS

This section presents methods used at the stage of design of the survey, collection of data, analysis and interpretation of the result on the estimation of long-term survival of HIV/AIDS patients under antiretroviral therapy.

The Data

A retrospective cohort study was conducted on HIV patients who were enrolled on ART at General Hospital Ugba, Logo Local Government area, Benue State, Nigeria up to December, 2022 irrespective ART start date. Health records of HIV patients who were enrolled on ART were reviewed and relevant information such as ART start date, current viral load, date of current viral load, gender and treatment status were obtained. A total of 2360 HIV patients were enrolled on ART at the hospital. However, the study did not consider all the enrollees. Their inclusion/exclusion was based on the following criteria:

Inclusion

- i. HIV patients who were on ART up to 2022.

Exclusion

- i. All cases with incomplete data.
- ii. HIV patients with no follow up information.
- iii. HIV patients who were transfer out.
- iv. Patients who died prior to the commencement of the study.

Consequently, the remaining sample for the study was 2288 cases.

Viral load suppression or otherwise has a direct link to HIV/AIDS patients survival. Under normal circumstances, suppressed viral load would lead to longevity while unsuppressed viral load decreases life span and even dead. Here interest is on the event where an HIV/AIDS patient on ART experience unsuppressed viral load. The probability that an HIV/AIDS patient does not have unsuppressed viral load beyond time t defines the survival function, $S(t)$.

Statistical Models

This section presents the survival models which were applied in the study due to Kleinbaum and Klein (2012).

Survival Model Specification: Survival and Hazard Function

Let T represents the survival time of HIV/AIDS patients under ART with a probability density function $f(t)$, then the cumulative distribution function (CDF) would be presented as in Equation (1).

$$F(t) = \Pr\{T \leq t\} = \int_0^t f(t)dt \quad (1)$$

which gives the probability that the event has duration less than or equal to t .

The survival function $S(t)$ is defined as the complement of CDF of T , that is,

$$S(t) = \Pr\{T > t\} = 1 - F(t) = \int_t^{\infty} f(t) dt \quad (2)$$

where T is a non – negative random variable representing the time to event of interest.

Survival function, $S(t)$ represents the probability that an HIV/AIDS patient under ART will survive at least up till to time t . Given that an individual has survived up to the beginning of the interval t , the probability that an event of interest will occur within a specified interval of time

It can be expressed as:

$$h(t) = \frac{-d[S(t)]/dt}{S(t)} \quad (3)$$

such that the cumulative hazard is given by Equation (4).

$$\int_0^t h(t)dt \quad (4)$$

Kaplan-Meier Estimator

The Kaplan-Meier Estimator, also known as product limit estimator is a non-parametric method used to estimate the survival function from life data. The Kaplan-Meier estimator is defined as follows:

$$\hat{S}(t) = \prod_{t_i < t} \frac{n_i - d_i}{n_i} \quad (5)$$

where d_i are number of death event at time t

n is the number of subject at risk of the death to the time

Log Rank Test

The Log Rank statistics is a large sample Chi square test that is used to test the equality of survival distributions. Akin to the Chi square test, it uses the observed against the expected cell counts over categories of outcomes defined by ordered failure times (Kleinbaum and Klein 2012). The test statistic is defined as:

$$\text{Log – Rank Statistic} = \frac{\sum (O_i - E_i)^2}{\text{Var}(O_i - E_i)} \sim \chi^2 \quad (6)$$

where O_i and E_i are the observed and expected cell counts for the i^{th} group respectively.

Tarone-Ware tests

The Tarone-Ware test is a variant of the Log Rank test but with the assumptions that the two populations to be compared are identically distributed, equal variances with temporal stability. However, time points are weighted by the square root of the number of cases ($\sqrt{n_i}$) at risk at each time.

Breslow (Generalized Wilcoxon) Test

The Breslow (Generalized Wilcoxon) Test is equally a variant of the Log Rank test that is used to compare the equality of survival distributions. In contrast to the Log Rank test, the time points are weighted by the number of cases (n_i) at risk at each time.

RESULTS AND DISCUSSION

Descriptive Analysis of Data

This section begins with a descriptive analysis of the variables used in the study. These variables are: recovery status, age group, and gender of HIV/AIDS patients. Table 1 shows that out of a total number of 2288 HIV/AIDS patients considered in the study, 1670 (73%) were females and 618 (23%) males. This gender distribution is in support of previous findings which revealed that HIV is more prevalent among females than males (Girum, et al., 2018; Lawal, et al., 2024). Out of 2288 samples, 2193 cases achieved viral load suppression with only 95 cases of unsuppressed viral load which translate to 95.9% and 4.2% respectively. This implies that the UNAIDS target of 95% viral load suppression (< 1000 copies/ml) for HIV/AIDS patients on ART by 2025 is already achieved at the treatment centre.

Table 1: Descriptive Analysis of HIV Infected Cases (n=2288)

Variables	Total N (%)	Patients Status	
		Suppressed N (%)	Unsuppressed N (%)
Gender			
Male	618 (27.0)	590 (26.9)	28 (29.5)
Female	1670 (73)	1603 (73.1)	67 (70.5)
Total	2288	2193 (95.8)	95 (4.2)

Kaplan-Meier Estimate

The Kaplan-Meier (K-M) survival plots for the whole data and that of the female/male gender are presented in Figures 1 and 2 respectively. It is observed that in Figure 1, the survival graph has a downward slope which indicates that the proportion of patients who did not experience suppressed viral load decreased with time. The survival plot reaches a plateau at almost 0.0 cumulative survival rate and in about 3200 days. This implies that there is barely 0.04 probability that an HIV/AIDS patient under ART would not achieve viral load suppression by 3200 days (approximately 8.8 years). In other words, the point up until the point of plateau should consist of subjects with suppressed viral load. Based on the K-M model,

Table 2 presents estimated mean time to achieving suppressed viral load for the whole dataset as 2084 days (approximately 5.7 years) with standard error of 14.21. To assessed the impact of gender on the survival rate of HIV/AIDS patients under ART, a Kaplan-Meier plots for female and male gender is presented in Figure 2 with no visible difference in the plots when compared with that of the whole data in Figure 1. However, the estimated mean time to suppression as presented in Table 2 shows a slight difference between the female and male gender with values 2092 (approximately 5.7 years) and 2062 days (approximately 5.6 years) with standard deviations 16.797 and 26.204 respectively.

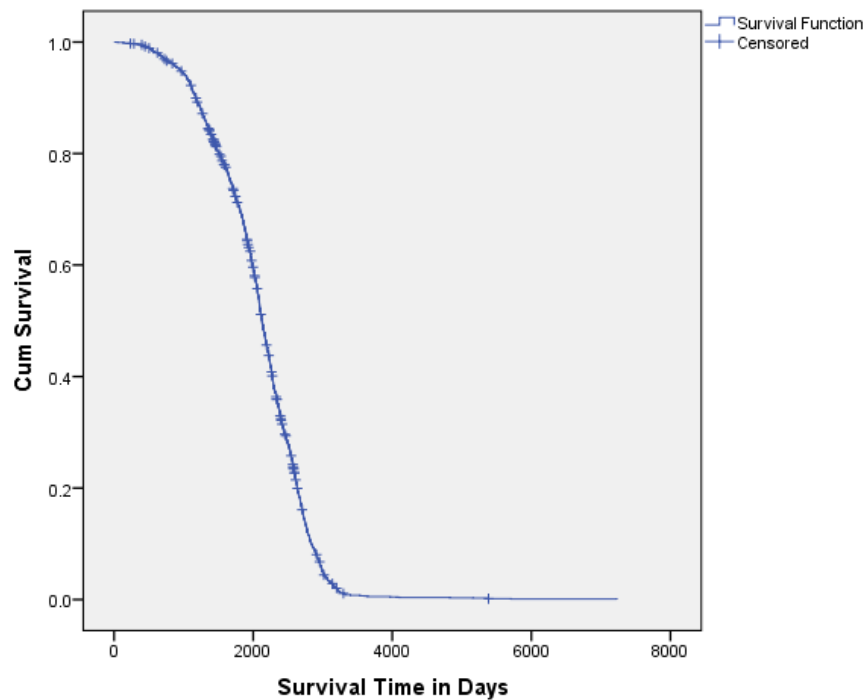


Figure 1: Kaplan-Meier Survival Plot for Whole Data Set

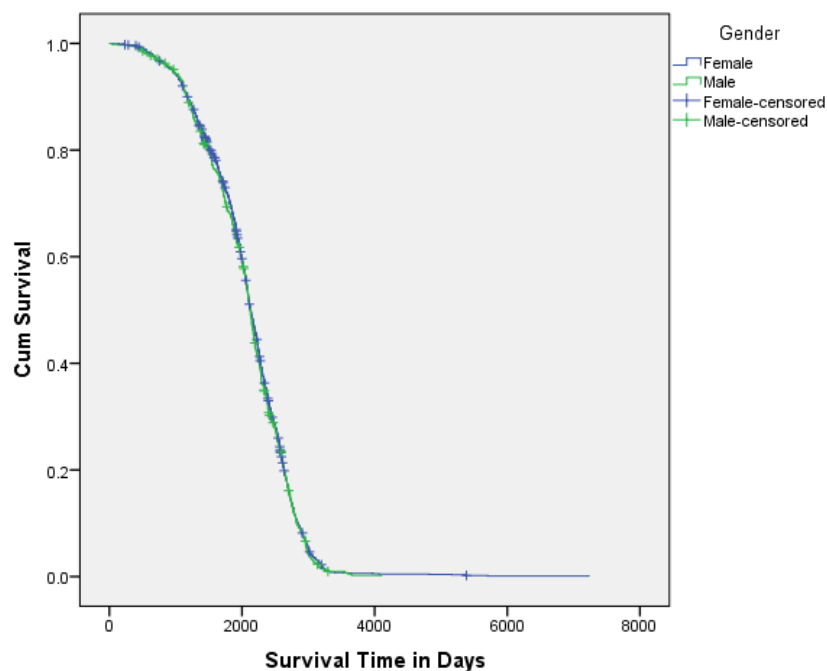


Figure 2: Kaplan-Meier Survival Plot for Females and Male

Table 2: Mean Survival Time from K-M Model: Female, Male and Entire Subject

Gender	Estimate	Std. Error	Mean ^a	
			95% Confidence Interval	
			Lower Bound	Upper Bound
Female	2092	16.797	2059	2125
Male	2062	26.204	2011	2114
Entire Subject	2082	14.214	2056	2112

Test for Equality of Survival Distributions

A test for equality of the survival distributions for the female and male gender was carried out using the Log-Rank, Breslow (Generalized Wilcoxon) and Tarone-Ware tests with the results presented in Table 3. Results in Table 3 shows that

there is no significance difference between the survival distribution of female and male HIV patients under ART since the significant values for the Log-Rank, Breslow (Generalized Wilcoxon) and Tarone-Ware tests; namely 0.507, 0.539, and 0.552 are all greater than 0.10. In other words, the slight

difference in the female and male survival times that was observed in Table 2 is due to chance. Hence, the survival distributions of female and male HIV/AIDS patient under

ART are the same. This result is in line with previous findings in Okoro (2024).

Table 3: Test of Equality of Survival Distributions for Female and Male Gender

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	0.440	1	0.507
Breslow (Generalized Wilcoxon)	0.378	1	0.539
Tarone-Ware	0.354	1	0.552

CONCLUSION

The focus of this study was to evaluate long-term survivorship of HIV/AIDS patients under Antiretroviral therapy (ART) using a retrospective information from a health facility in Ugba, Benue State, Nigeria. Survival plots from K-M model revealed a downward slope which indicates that the proportion of patients who did not experience suppressed viral load decreased with time.

It was obtained that 95.9% of HIV/AIDS patients under antiretroviral therapy survived for at least 8.8 years after the commencement of therapy. This implies that the UNAIDS target of 95% viral load suppression (< 1000 copies/ml) for HIV/AIDS patients on ART by 2025 is already achieved at the treatment centre. Some tests on the equality of survival distributions of the female and male gender based on the Log-Rank, Breslow (Generalized Wilcoxon) and Tarone-Ware statistics revealed that the survival distribution of female and male patients are similar at 0.05 level of significance. It is recommended that the results obtained from this study be used to educate people living with HIV/AIDS accept antiretroviral therapy so that they can live healthy and long lives. More research should be conducted to isolate the risk factors associated with long term survival of HIV/AIDS patients in the study area. It is recommended that people living with HIV/AIDS be educated to accept antiretroviral therapy so that they may live healthy lives.

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