Survival Analysis of HIV/AIDs Patients under Antiretroviral Treatment at Central Hospital, Agbor, Delta State, Nigeria

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Abstract- This study is designed to relate the Cox Proportional Hazard model to evaluate the determinant factors of survival time, predict the clinical progression of HIV/AIDs ailment by means of secondary data obtained from the Antiretroviral Rehabilitation Unit of Central Hospital, Agbor, Delta State, Nigeria. The statistics were extracted from Regular Patient Medical Registration. A study was undertaken on a sample of 1000 HIV/AIDs patients who were followed for a minimum predetermined period of 11 years and 3 months. From the sample, 64.2 per cent were female and 35.8 per cent were male, 8.6 per cent of the patients were report dead; while 91.4 per cent patients were censored. The Cox regression result indicated that the survival time of the HIV/AIDs patient is significantly related to gender, on ART, enrolment date, and current age.

Index Terms- Survival analysis, Antiretroviral, Hazard rate, Proportional model

I. INTRODUCTION

Survival analysis is a collection of statistical procedures for data analysis for which the outcome variable of interest is time until an event occur Liu (2102). By time, we mean years, months, weeks, or days from the beginning of follow-up of an individual until an event occurs; on the other hand, time can refer to the age of an individual when an event occurs. By event, we mean death, disease incidence, relapse from remission, recovery (return to work) or any designated experience of interest that may happen to an individual Klembaum (1996). Survival analysis is a statistical method for data analysis where the product variable of concern is the time to the incidence of an event. Klembaum (1996). Survival modeling or methods of analysis are generally used in experimental, biostatistics and epidemiology research to model time until event data. According to Nakhaee & Law (2011), Survival analysis can also be described as a statistical procedures premeditated to take into account the quantity of time an investigational unit contributes to a study period, that is, the time between entry into study and occurrence of event of interest Survival analysis deal with methods that measure the risk of death or progression of a disease and provide predictions that can help clinicians to estimate trends in the patient outcomes. Monitoring the duration of survival after diagnosis is therefore, an important component of the surveillance of HIV/AIDs as it provides the basis for evaluating individual prognostic factors as described in Assefa and Wencheko, (2012). As noted in Nakhaee & Law (2011), these techniques also allow health planners to predict the Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDs) burden on the health system and to allocate health services resources appropriately. Health care planning relies on a good understanding of disease incidence which requires an precise information of survival patterns Heller et.al., (1998). The survival of HIV/AIDs patients depends on a variety of factors including but not limited to the individual patient's demographic factors, serological baseline factors and presence of co-morbidities. The most widely used survival modelling techniques include the Cox's proportional hazards models and the accelerated failure time (AFT) models. In the last two to three decades, quantile regression (QR) models as introduced by Koenker & Bassett Jr, (1978) have become an alternative technique to describe and contextualize the distribution of a response variable given a set of explanatory variables. Quantile regression models are very flexible in assessing covariate effects on event times, thereby attracting huge interest in their application to survival modelling. Survival data is frequently skewed and the marginal distribution of response variable is characterized by marked skewness. Quantile regression methods are robust in characterizing and exploring the distribution of skewed data (for example duration or survival data) hence, emerging as popular techniques in survival modelling. According to Fitzenberger and Wilke (2005). Whilst the Cox's proportional hazards models estimators show that the survival times or failure times recognize the presence of some risk factors quantile regression analysis adds a new dimension to the literature Jonas et.al., (2000). It was further suggested by Hosmer et.et., (2008) that the influence of the risk factor on the survival times varies across the survival time distribution and for patients with higher duration (survival) times, the survival function will barely recognize some risk factors whilst for patients with the lowest survival times; their survivor function is particularly sensitive to the presence of some risk factors. Thus, quintiles regression techniques can help us get a more complete picture of the underlying connection connecting risk factors and the survival time. In Hogan et.all.,(2004) noted that; Censored quantile regression (CQR) like proportional hazards models

tackled the issue of right censoring of the response variable, which is frequent in survival study by modeling. the distribution of the survival time in a flexible semi-parametric way Ider and Kasl (1991) quantile regression does not entail modelling suppositions that may not be pragmatically valid like in the case of the proportional hazards postulation for the Cox's proportional hazards regression models. Censored quantile regression models are flexible than the AFT models or the Cox's proportional hazard model because they do not restrict the variation of estimated coefficients over the quantiles (Fitzenberger& Wilke, 2005).

1.1 Acronyms and Abbreviations

AIDs	Acquired Immunodeficiency Syndrome
HIV	Human Immunodeficiency Virus
CQR	Censored Quantile Regression
PHM	Proportional Hazards Model
LTFU	Loss to Follow-Up
MIS	Management Information Systems
UNAIDS	United Nations Programme on HIV/AIDS
AFT	Accelerated Failure Time models
ART	Anti-Retroviral Therapy
ARD	Antiretroviral drugs
WHO	World Health Organization
OR	Odds Ratio
RR	Relative Risk
HR	Hazard Ratio
ANC	Anti-Natal Care clinics
OLS	Ordinary Least Squares
IQR	Interquartile Range
CD4	Cluster of Differentiation 4
CI	Confidence Interval
(OIs)	Opportunistic infections

II. LITERATURE REVIEW

Antiretroviral medications are designed to prevent the replica of HIV in the human. The main effect of antiretroviral treatment is to restrain viral reproduction, allowing the individual's immune system to recuperate and protect a patient from increasing AIDs. The clinical benefit of ART for AIDs patients, in terms of mortality reduction and improved quality of life, is well established but shows regional differences, with higher case fatality rates in poor countries Braitstein *et al.*, (2006).With the dawn of antiretroviral therapy (ART), the morbidity and mortality of HIV disease are decreasing considerably in Europe and the USA Crimmins *et al*., (1996). 10 Million People living with HIV and who are eligible for treatment under the new WHO guidelines are still in need (UNAIDS, 2010). The examination of the survival likelihood of AIDs patients using socio-demographic factors and the idea that all demographic, socioeconomic, health and risky behavioral factors may perhaps have momentous relationship through survival of patients is supported by many researchers such as; Marie *et al*., 2001; Monica 2006; Holmes *et al*., 2003; Monica *et al*., 2006; and Cawley 2006.

According to the report of Sieleunou *et al*. (2009) age, is the significant predicator of survival of HIV/AIDs patients. According to Sandra *et al*., (2009) showed that, HIV sero-prevalence (regulating for such factors as age and gender) was 2.7 times higher among married than single patient, 5.5 times higher among the divorced and separated, and 7.9 times higher among the widowed. Antiretroviral therapy (ART) has reduced the incidence of opportunistic infections for certain patients with access to care. However, opportunistic infections may continue to cause substantial morbidity and mortality in patients with HIV infection (Holmes et al., 2003). In a related study in Kisesa, Tanzania, four rounds of village-based HIV testing and twenty rounds of household-based demographic examination on three hundred and sixty-nine HIV patients were conducted between 1994 and 2006. The dates of infection were roughly ascertain for individual sero-converters by allocation of a date between the last negative and first positive test, (Gregson *et al*., 2001). Person-years lived post-infections were computed, allowing for left truncation and right censoring, and Kaplan-Meier survival functions were constructed, truncating the analysis at the start of 2005 when ART first became available in the community Weibull models were fitted to estimate median survival time and parametric regression methods were used to investigate the control of sex and age at infection. The Kaplan-Meier function showed 67% surviving 9 years' post-infection, and the overall predicted median survival was 11.5 years. Survival was strongly related to age at infection (hazard ratio 1.06 for each additional year of age, and weakly to sex. A strong effect of age was evident even after allowing for mortality from non-HIV-related causes using cause deletion methods to estimate net mortality. The researchers are therefore of the view that, the survival of HIV-infected individuals was comparable to that reported in developed country studies before the beginning of HAART and that Survival patterns in Kisesa are marginally more favorable than those reported in cohort studies in Uganda with tha application of Kaplan-Meier survival estimate showed that patients with weight loss <10% of usual body weight survived 12 months, that is 2.5 times longer than patients with >20% weight loss (Chaisson et al. 1995). In Cawless (1998) The Cox proportional hazards model was use to study factors linked with evolution of AIDs and death and the result showed that lower CD4 cell count and adult age were associated with an bigger risk of death but there was no association between disease succession and sex Maria (2001) assessed AIDs patients' survival on 12 years' study of 486 adult patients using Kaplan-Meier survival analysis models to examine the impact of variables on patient survival, the log rank test to evaluate possible statistical differences between sub-groups and multivariate analysis using Cox proportional hazards model for assessing the performance of prognostic factors. The result demonstrated that there was no statistically significant difference between mean survival of male and female patients, among different age groups but CD4 count and antiretroviral drugs had a significant impact on increased survival of AIDs patients. Horsburgh (1991) also illustrated that age was not a significant predictor of survival in HIV infection. According to Endale et al. (2006), the identification prognostic markers where time to death is the main outcome variable, the Kaplan-Meier and Cox regression survival analysis is better for application as this was carried out in Ethiopia using data from 162 patients treated with HAART and the result confirm the highest death rate occurred in the first month of the treatment.

Weight loss is also shown to have connection with increased death among the 259 HIV/AIDs patients because as noted in Nuredin (2007) who carried out a retrospective study in Adama Hospital ART clinic with 259 HIV/AIDs patients.

In the literature as discussed, sharp out the use of survival analysis in the studies of time-to-event data such as; patients living with HIV/AIDs disease, in particular the use of Kaplan-Meier analysis and proportional hazards models for the detection of clinical and socio demographic variables with the assumption that the variables influences the survival of AIDs patients.

III. METHODLOGY

3.1. Method of Data Collection

A secondary data collection method was employed to extract a sample of 1000 out of the total registered 2000 HIV/AIDs cases that have been followed up for 12 years (January 2006 to December 2018) at Central hospital, Agbor, Delta State, Nigeria.

3.2 Proportional Hazards Modelling (PHM)

Cox's Proportional Hazards Modelling (PHM) is a partial likelihood perspective in which the baseline hazard rate is an unspecified nuisance function Liu (2102). it can also be described as the basic modeling or technique used in exploring the relationship between the survival experiments and potential risk factors in survival data analysis. This model was proposed by Cox in the year 1972; (Cox and Oakes, 1984) and it has come to be identified as the Cox Proportional Hazards Regression Models (CPHRM). Although, the model is based on the theory of hazards proportionality as such, no particular form of likelihood distribution is assumed for the survival times. The model is thus semi-parametric in nature and very flexible.

3.3 Model Specification for the PHM

Examining the bond between survival time and illustrative variables (risk factors) entails the condition of a linear-model for the log-hazard. For instance, each surveillance under examination is presume to be subject to an instantaneous hazard rate $h(t)$ of experiencing a unique invent. Where$1 \leq t \leq \infty$. Analogous to the parametric proportional hazard model, the effect of covariate in the Cox model is specified by a multiplicative effect term $exp(x'\beta)$, given the nonnegative of the Hazard function. The basic equation for the Cox model is given by

$$h(t/x) = h_0(\mathrm{t})\exp(x'\beta) \quad (3.1)$$

Given the hazard function, the survival probability is

$$S(t;x) = [S_0(t)]^{\exp(x'\beta)} \quad (3.2)$$

Where,

$$S_0(t) = \exp[-H_0(t)] \quad (3.3)$$

From equation (2.1) and (2.2) above, the density function is

$$f(t;x) = h_0(\mathrm{t})\exp(x'\beta)exp\left[-\exp(x'\beta)\int_{\mathrm{o}}^{\mathrm{t}} \mathrm{h}_0\,(\mathrm{u})\mathrm{du}\right]$$

3.3 Fitting the Proportional Hazards Model

To fit a proportional hazards model given in equation 3.5 to an observed set of survival data, requires estimating the unknown coefficients of the illustrative variables $(X_i,)$ in the linear component of the model β_i and the baseline hazard $h_0(t)$, may also need to be estimated. The estimation of this parameters can be done independently. After estimating the β_i , the result we then be used to construct the baseline hazard function. This aspect is important of paramount to make inferences about the effects of p-explanatory variable $(X_i,)$ on the relative hazard, $\frac{h_1(t)}{h_0\,(t)}$, as noted in collett, (2015) and Allison, (2010) we do not need an estimate of $h_0(t)$.

According to Cox 1972, the conditional probability that an individual experience a particular event at time t_i given that he or she is among the k individual at risk $R(t_i)$ of experiencing the event. This conditioner probability can be transform to a continuous hazard function as

$$\frac{harzad\ at\ t_i\ for\ individual\ i\ with\ covariate\ x_i}{\sum_{l\epsilon R(t_i)} hazard\ rate\ at\ t_i\ for\ individual\ l}$$

This equation can be represented as

$$\frac{h(t_i;x_i)}{\sum_{l\epsilon R(t_i)} h(t_i;x_i)} = \frac{h_0(t_i)\exp(x'\beta)}{\sum_{l\epsilon R(t_i)} h_0(t_i)\exp(x'\beta)} \quad (3.6)$$

Eliminating the common term, it provided an incomplete hazard function without specifying the distribution of the baseline h_0. Hence, the only parameter to be estimated in the Cox model is simply specified as the log of the likelihood of equation…

$$logL_p(\beta) = \sum_{i=1}^{d}\left\{x_i'\beta - \sum_{i-1}^{d}\log\left[\sum_{l\epsilon R(t_i)}\exp\,(x_i'\beta)\right]\right\} \quad (3.7)$$

IV. ANALYSIS OF RESULT

In this section, we consider the descriptive analysis of the data and concluded the section with the survival analysis. Basically, we first examine the bio-data of HIV/AIDs patients and we consider the stay time of the patient on treatment and cross tab with the final status of the patient whether dead (status =0), active (status =1), LFTU (status =2) or Transferred out (status =3)

4.1.Exploratory Data Analysis (EDA) on Gender, Current Age, ART and Enrolment date

Table 4.11; Distribution of Cases by Gender

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	358	35.8	35.8	35.8
	Female	642	64.2	64.2	100.0
	Total	**1000**	**100.0**	**100.0**	

Table 4.13; Gender Outcome Cross Tabulation

		OUTCOME		Total
		DEAD	ACTIVE, LTFU, TRANSFERRED OUT	
GENDER	Male	38	320	**358**
	Female	48	594	**642**
Total		**86**	**914**	**1000**

Table 4.13; Categorical Variable Codings[a,c]

		Frequency	(1)
GENDER[b]	0=Male	358	1
	1=Female	642	0
CRNT_STA[b]	0=NOT ON ART	628	1
	1=ON ART	372	0

(a) Category variable: GENDER (GENDER)
(b) Indicator Parameter Coding
(c) Category variable: CRNT_STA (CRNT ART STATE)

Table 4.14; Current Age Outcome Cross Tabulation count

		OUTCOME		Total
		DEAD	ACTIVE, LTFU, TRANSFERRED OUT	
CURRENT AGE	11-20yrs	4	40	**44**
	21-30yrs	6	57	**63**
	31-40yrs	34	271	**305**
	41-50yrs	28	319	**347**
	51-60yrs	9	138	**147**
	60yrs above	5	89	**94**
Total		**86**	**914**	**1000**

Table 4.15; Case Processing Summary

		N	Percent
Cases available in analysis	Event[a]	86	8.6%
	Censored	895	89.5%
	Total	981	98.1%
Cases dropped	Cases with missing values	0	0.0%
	Cases with negative time	0	0.0%
	Censored cases before the earliest event in a stratum	19	1.9%
	Total	19	1.9%
Total		**1000**	**100.0%**

Block 0: Beginning Block

Omnibus Tests of Model Coefficients

-2Log Likelihood
1042.208

Table 4.16; Omnibus Tests of Model Coefficients[a]

-2 Log Likelihood	Overall (score)			Change From preceding Step			Change From preceding Block		
	Chi-square	df	Sig.	Chi-square	df	Sig.	Chi-square	df	Sig.
730.811	287.554	4	.000	311.397	4	.000	311.397	4	.000

Table 4.16; Variables in the Equation

	Parameter estimate	Standard error	Wald	df	Mean	Sig.	Hazard ratio	95.0% CI	
								Lower	Upper
GENDER	.347	.225	2.390	1	.357	.122	1.415	.911	2.197
AGE	-.233	.094	6.194	1	3.779	.013	.792	.659	.952
CRNT_STA	-.799	.227	12.420	1	.635	.000	.450	.289	.702
ENROL_DAT	.000	.000	77.552	1	13392364447.706	.000	1.000	1.000	1.000

V. DISSCUSION OF FINDINGS

From table 4.14 above, the minimum age recorded is eleven (11) years and the maximum age is eighty-nine (89) years also, age groups between 31 and 50 years has the higher numbers of the HIV infection for both sexes at Central hospital, Agbor. In the programme outcome of the information, the dependent variable, the censoring status variable and censoring values is reported first. Given a long period of observation (12 years) 86 out of 1000 individuals are deceased (actual event) and the remaining 914 HIV/AIDs patients are right censored the Model Fit Statistics (MFS) Section display three indicators of model fitness, with their values being very close and obviously generating the same conclusion about model fitting. All three test in the "Testing Global Null Hypothesis Beta = 0" section demonstrate that the null hypothesis $\hat{\beta} = 0$ should be rejected. For example the chi-square of likelihood ratio test is 287.554 with 4 degree of freedom which is very strongly significant ($P < 0.0001$).

In the table of "Analysis of Maximum likelihood Estimate" the regression coefficient of gender is 0.347 (standard error =0.225) statistically significant at 0.05 ($x^2 = 2.390$; $P < 0.0001$). (It should be noted however, that the Wald statistical test is use to test the maximum likelihood estimate of the parameters of interest is compared with the proposed value with

the assumption that the difference between distributed, hypothetically the significance of the difference is compared to chi-square distribution as such, it is also known as the Wald chi-square test) by exponentiation, the regression coefficient generates the hazard ratio between the males and the females HIV/AIDs infected persons taking antiretroviral drugs at Central Hospital, Agbor, Delta State. As presented in the seventh table in conclusion, the estimate of this hazard ratio is 1.415 suggesting that the mortality of female is 42% higher than the males of other covariates being equal. The regression coefficients of the three control variables are statistically significant. Age is negatively associated with the hazard rate of 0.792 ($\hat{\beta}_2 = -0.233, x^2 = 6.194; P < 0.0139$) as expected likewise, CRNT ART state the patient on Anti-Retroviral Therapy is having 45% hazard rate which is less than those that are not on art with hazard rate of about 65% so, mortality is higher among those who are not on ART. ($\hat{\beta}_3 = -0.799, x^2 = 12.420; P < 0.001$) in other words additional increase in the Anti-Retroviral Therapy would however the mortality rate of HIV/AIDs patients. Also, the enrolment date, is also very significant with hazard rate of 1.000. The primary goal of ART is to improve health, prolong the life of the HIV-infected persons and reduction in HIV-related mortality, Delta State Government should make improvement towards the provision of safe, effective, equitable and sustainable ART services to those infected by HIV/AIDs.

REFERENCES

[1] Achalu, I. E. (2008). Aids and other sexually transmitted diseases: what everyone should know (3rd Ed). Nigeria, Simarch Ltd.

[2] Assefa, T., and Wencheko, E. (2012). Survival analysis of patients under chronic HIV care and antiretroviral treatment: specialized hospital, Addis Ababa, Ethiopia Ethiopian Journal of Health Development, 26 (1), 22-29.

[3] Braitstein, P., Brinkhof, M.W., Dabis, F., Schechter, M., Boulle, A., (2006) Mortality of HIV-1-infected patients in the first year of antiretroviral therapy: comparison between low-income and high-income countries. Lancet 367: 817–824

[4] Cawley, J. F. (1988). Social and legal issues for people with HIV. UK, Nam publication.

[5] Chaisson, R.E., Keruly, J.C., Moore, R.D. (1995). Race, Sex, Drug Use, and Progression of the Human Immunodeficiency Virus Disease. N Engl J Med, 333(42): 751-756.

[6] Fitzenberger, B. and Wilke, R. A. (2005). Using Quantile Regression for duration Analysis. Springer, 2 (3), 103-118.

[7] Holmes CB., Losina E., Walensky RP., Yazdanpanah Y., Freedberg KA. (2003). Review of Human Immunodeficiency Virus: type 1-related Opportunistic Infections in Sub-Saharan Africa. Clin Infect Dis; 36:652-62.

[8] Klembaum, D. G.(1996) Survival Analysis: A Self learning text. Springer, New York,.

[9] Koenker, R. and Bassett Jr, G. (1978). Regression Quantiles. Econometrical, 46, 33-50.

[10] Xia Liu (2102). Models and Applications, First Ed. A john Wiley & Sons, Ltd., Publication.

[11] Maria, F.G., Ligia, R.S., Kerr-Pontes, Rosa, S.M., Marcondes, C.F., Fábio F. and Iusta C. (2001). Survival of Adult AIDS Patients in a Reference Referral Hospital of a Metropolitan Area in Brazil. Rev Saude Publica, 36(3): 278-84.

[12] Monica, M. and Patrizio P. (2006). Comparing costs and effectiveness of different starting points for highly active antiretroviral therapy in HIV positive patients. Acquired Immune Deficiency Syndrome, 11: 197-202.

[13] Nakhaee, F. and Law, M. (2011). Parametric modeling of survival following HIV and AIDs in the era of Highly Active Antiretroviral Therapy: Data from Australia. Eastern Mediterranean Health Journal, 7: 232-233.

[14] Nuredin, I. (2007). Education of factor affecting the chance of survival/death status among hiv positive people under the antiretroviral treatment program: The Case of Adama Referral Hospital, M.Sc. Thesis, Addis Ababa University, Ethiopia.

[15] Patrick, I. O. (2007). Adolescent sexual and Reproductive Health in the Niger Delta Region of Nigeria – Issues and challenges. African Journal of Reproductive Health, 11(10): 113-124.

[16] Sandra, E., Min, Y., and Juan, M. (2009): Multilevel survival analysis of health inequalities in life expectancy. International Journal for Equity in Health 8:31

[17] Sieleunou, I., Mohamadou S., Anne-Marie, S., Joris M. and Marleen, B. (2009) Determinants of survival in AIDs patients on antiretroviral therapy in a rural centre in the Far-North Province, Cameroon. Tropical Medicine and International Health. Jan; 14(1): 36-43

[18] Stringer J.S., Zulu I., Levy J., Stringer EM., Mwango A., Chi BH., Mtonga V., Reid S., Cantrell RA., Bulterys M., Saag MS., Marlink RG., Mwinga A., Ellerbrock TV., & Sinkala M..(2006). Rapid Scale-up of ART at Primary Care Sites in Zambia: Feasibility and Early Outcomes. JAMA, 296:782-793.

[19] UNAIDS (2010). UNAID report on the Global AIDs Epidemic. Geneva, UNAIDS

[20] Wesley, T, (2008). AIDs Day, keynote speaker. Davidson University, Davidson, New City

[21] Andersen,P.K.,Bentzon,M.W., and Klein,J.P.(1996). Estimating the survival functions in the proportional Harzard Regression Model: a study of small sample size propertie. Scandinavian Jouenal of Statistics, 23, 1-12

[22] Hogan, J.W., Roll, J., and WKorkontzelou, C.(2004) tutorial in biostatistics: handling drop-out in longitudinal studies. Statistics in Medicine, 23 17-30

[23] Ilder, E.L. and Kasl. S. (1991) Health Perception and Survival: do global evaluation of health status really predict mortality? Journal of Gerontology: Social Science, 46, S55-S65

[24] Jonas, B.S. and Mussolino M.E.(2000) symptoms o depression as a perceptive risk factor for stroke, Psychosomatic Medicine. 62, 463-471

[25] Crimmine, E.M., Hayward, M.D. and Saito, Y. (1996) Differentials in active life expectancy in the older population of the United States. Journal of Gerontology: Social Science, 51B, S111-S120

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