SURVIVAL OF PERSONS STARTING HAART IN HIV/ AIDS CARE FACILITY IN NAIROBI, KENYA

BY

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DECLARATION

I declare that this dissertation is my original work and has not been submitted anywhere else for examination, award of a degree or publication. Where other people's work or my own work has been used, this has properly been acknowledged and referenced in accordance with the requirements of the University of Nairobi.

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…………………………………	……………….……………
Signature	**Date**

DEDICATION

*I dedicate this project work to my parents **Mr and Mrs Kiptallam**, colleagues and friends for their unreserved support in my two years of studies at the University of Nairobi (UoN).*

*I also dedicate this work to my daughter **Vivien** for her unwavering support to me where and whenever necessary to accomplish this research write up.*

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ACRONYMS

AHR	Adjusted Hazard Rate
AIDS	Acquired immune deficiency syndrome
ART	Antiretroviral Therapy
CI	Confidence Interval
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
LTFU	Lost to Follow – up
OIs	Opportunistic infections
UNITID	University of Nairobi Institute of Tropical and Infectious Diseases

DEFINITION OF TERMS

Survival probability	The chance of survival of study participants.
Hazard rate	The probability of dying after surviving for specified time
Cohort	Participants enrolled at the same time to the study.
Demographic data	Information describing study participant
Clinical data	Measurements collected from study participants.
Kaplan Meier model	The Kaplan-Meier procedure is a method of estimating time-to-event models in the presence of censored cases.
Cox Regression Model	The model produces a survival function that predicts the probability that the event of interest has occurred at a given time t for given values of the predictor variables

Contents

List of Tables

List of figures

ABSTRACT

Background: Variations in survival rates between males and females initiated on HAART have been reported in many HIV intervention programs showing increased mortality in males. It is desirable to have estimates of expected survival rates of persons living with HIV. Such variables that influence survival are important for; projecting future numbers of AIDS cases, understanding of the pathology of the disease, clinical decision making and planning health service interventions. In addition results are useful for; monitoring the progress of the HIV/AIDS epidemic, changes of treatments, enabling mathematical modeling and health care professionals to estimate future needs.

This study presents survival comparisons between males and females enrolled at the same time and observed until the end of the study. These will contribute to improve health outcomes in different population settings. In addition this study identified some of the factors influencing survival by gender of persons in HAART presents the determined survival rates of HIV-infected patients treated with HAART in comprehensive care facility, in Nairobi Kenya.

Objectives: Assess the survival of persons starting highly active antiretroviral therapy in a comprehensive care facility in Nairobi, Kenya with aim of determining demographic gender characteristics and survival probabilities.

Design This was a cross-sectional retrospective study of those HIV/ADS persons on management at a HIV/AIDS health care delivery facility in Nairobi.

Main study Variables: The main study variables are demographic and clinical data. The demographic data are age, gender, marital status, occupation, level of formal education, region the person is coming from (place of residence) and monthly income. Clinical data are; whether the patient is on ART, calendar year of ART initiation, first date of clinic visit, last date of clinic visit, and mortality date.

Study population: Persons on follow up and starting HAART in a HIV/ AIDS care facility in Nairobi, Kenya.

Results: The study was conducted from 2006 to 2011 and enrolled 2453 participants; 62% female and 38% males. Mean, median and standard deviation of their ages were 33.17, 33.00 and 10.144 years respectively.

At the end of the five-year with 3-month interval visits within the study period, more men than women were more likely to be marked as lost to follow up (LTFU) with adjusted hazard ratio of 1.19 at 95% Confidence interval (1.15–1.26).

After adjusting for covariates at mean levels, survival and hazard functions curves showed higher survival probabilities for females compared to males and higher hazard probabilities for males compared to females. The factors that contributed significantly to the differences in mortality are levels of education, occupation and marital status of persons under study. Despite the fact that most of the data elements had no responses from the study participants, mean covariates had within - significance to the survival rates.

Conclusion: HIV-infected males have higher mortality on ART than females in this program. The variations can be attributed to differences in response to treatment. Future studies should be undertaken to determine whether the gender difference in survival rates are wholly or partly to this factor and/or Lost to follow up of target study participants.

CHAPTER ONE INTRODUCTION

Survival rates of AIDS patients and variables that influence them are important for not only projecting future numbers of AIDS cases but also increasing understanding of the patho-physiology of the disease, management decision making and planning health service care provision interventions [1 - 3]. In addition for monitoring the progress of the HIV/AIDS epidemic as new treatments, there are studies showing that survival studies provide information on the response and enable mathematical modeling and health care professionals to estimate future needs [1, 4, 5].

As at the end of the year 2014 approximately 37 million people were infected with HIV virus that causes AIDS and also there is a notable increase in the uptake of ARVs as compared to the first, second and early part of the 3rd decade of the HIV/AIDS epidemic [6, 7]. The HIV treatment brought about by combining antiretroviral therapy (HAART) in 1996 has changed the course of the disease among those living with HIV in high-income countries but had only reached a fraction of people in low income countries [8, 9]. Observably the ARV experienced persons live longer and healthier lives unlike those not on treatment. However, persons living with HIV in resource-poor countries like Kenya have higher mortality rates, particularly the first months after initiating ART. *"In Ethiopia the adult prevalence of HIV was estimated to be 1.5% in 2011"* [10 - 12]. The antiretroviral therapy has led to reduction in hazard probabilities and enhanced quality of life for persons infected with the HIV virus.

Currently there is increased number of persons starting HAART after diagnosis of the disease. However gender differences in number and survival rates for persons initiating HAART is evidently increasing [13, 14]. Mortality rates among males are higher than for females especially in 3rd world economies. This is presumably as a result of several factors including environmental and circumstantial factors. It is also documented that the advancement of the disease after ART initiation among males is faster than for females [15]. The result of this is a high rate of mortality among men compared to females [1 - 3]. Studies mainly from India as well as other resource poor countries have also shown high early mortality among patients accessing ART care 2,11,14,15.

However other studies have documented no gender influence on survival [16 - 18]. A study revealed that after initiation of the treatment, HIV-positive people had estimated nearly 4 years median survival time. This same study documented among the variables included in the study namely; education level, marital status, study area and gender did not have significant impact on survival [19, 20].

Observably the ARV experienced persons live longer and healthier lives unlike those not on treatments [21 – 23]. Some of the factors to this improvement include support to the body immune system to fight opportunistic infections. The HIV virus destroys CD4 lymphocytes cells among other immune system cells thereby increasing infected persons vulnerability to opportunistic infections [24, 25].

In 2014, about 2 Million new HIV infections were reported and documented and reported around the world and about the same number (2 Million) died as a result of AIDS related illnesses [6].

The AIDS scourge reported in most countries around the world in the nineties had statistics of life span of the infected persons averaging 9-10 years. "*Early in the AIDS epidemic, most HIV-infected people died within 10 years of becoming infected*" [7, 26]

The HIV epidemic continues to be a serious health and socioeconomic concern particularly in limited resource countries in Africa and some parts of Asia. With the development of antiretroviral therapy in the late nineties, severity of the epidemic began to ease off. This however presented a new challenge on the socioeconomic welfare and capacity of the infected persons. Most infected persons in this limited resource settings could not afford the cost of antiretroviral drugs and management of the disease through good eating habits [27, 28]. "In 2003, this situation was declared a global emergency, and governments and international agencies began to implement plans to increase ART coverage in resource-limited countries" [7, 29]. The declaration of the AIDS epidemic as a global emergency led to the initiation and implementation of programs that enhance management of HIV virus through constant and consistent supply of antiretroviral medicines to all categories of resource settings worldwide. Through grants and agreements between governments and agencies, there was increase in supply of ART in communities. This resulted in increased number of persons starting HAART after diagnosis of the disease. The number of programs handling ART has increased exponentially since 2010 [30 – 33].

Gender differences in survival rates for persons initiating HAART is evidently increasing. Mortality rates among males are higher than for females especially in 3rd economies. This is presumably as a result of poor adherences to drug schedules, individual behaviors, late start of ART when the disease has advanced and the ever common factor of lost to follow up. Compounded by environmental and circumstantial factors, the advancement of the disease after ART initiation among males is faster than for females. The result of this is a high rate of mortality among men compared to females [13, 14].

1.1 STATEMENT OF THE PROBLEM

Persons starting HAART have low Cluster of differentiation 4 (CD4) cell counts. Antiretroviral therapy (ART) is used to support and improve their immune systems. Uptake of ART is important to the survival of these person(s). Although there has been growing interest among scientists to determine the factors that influence survival of persons in HAART, little is however known about the male-female differences. Specifically, information on the disparities in survival probabilities of persons in ART by gender remains scanty [1, 31].

A range of possible explanations for gender differences in mortality on ART have been suggested but there has been no comprehensive evaluation of the reasons put forward. Baseline characteristics strongly predict mortality on ART, and men initiating ART have more advanced HIV disease than females. In addition, loss to follow-up (LTF) is associated with mortality, and men are more likely to become LTF than females in many settings. Evidence regarding gender differences in immunologic and virologic responses is mixed. This study therefore sets to identify some of these factors and make inferences on the survival of persons in ART. Survival comparisons are made in males and females enrolled at the same time and observed until the end of the study [34].

It is important to understand such differentials in order to improve health outcomes in different population settings.

1.2. STUDY OBJECTIVES

1.2.1 Broad objective

To assess the survival of persons starting highly active antiretroviral therapy in a comprehensive care facility in Nairobi, Kenya

1.2.2 Specific Objectives

The specific objectives of this study are

1. To define demographic characteristics of males and females in the study.
2. To determine survival probabilities of study participants.
3. To assess the difference in survival probabilities of the two categories of study participants.
4. To identify the determinants of survival of each gender.

1.2.3 Study questions

The following are the study questions intended to achieve the overall objective

1. What are the demographic characteristics of study participants?
2. What are the gender specific survival probabilities?
3. Are survival probabilities between males and females different?
4. What are the factors that influence survival of gender specific group of persons starting HAART?

CHAPTER TWO JUSTIFICATION

Dissimilarities in survival of study population of males and females receiving antiretroviral treatment have been the subject of deliberations by many study groups in health institutions. This is because statistics on records of mortalities of persons on ART show that the number of males is higher than that of females. In any study setting in developed and developing countries, male mortality is higher than mortality in females [35, 36].

Many reasons have been advanced to justify this trend of high mortality in male population starting ART compared to females. In the developing nations and Africa in particular, males starting HAART deliberately or due to stigma stay away from clinic facility offering care and treatment services for HIV persons while females seek early medical attention and therefore are able to be helped early enough to contain the severity of the disease. In this case, males become lost to follow up and more at risk of experiencing mortality earlier than females [37].

Males and females may also have different immune response to HIV treatment. Under the same line of regimen, persons starting HAART may experience differing failure rates or better still no failure rates resulting from use of the specified regimen [38, 39]. The covariates are not limited to the two aforementioned but also marital status, occupation, levels of income and education would be attributable to the dissimilarities in gender survival and hazard probabilities among persons starting HAART.

This study therefore examines dissimilarities in gender survival and hazard probabilities among persons starting HAART with a focus on marital status, occupation, levels of income and education [40]. Variables such as CD4 count and lost to follow up cases were not included in the overall model because of insufficient data on the two and thus excluded from the final survival model. The study will help in furthering understanding of the differences in survival probabilities of male and female populations [41].

CHAPTER THREE LITERATURE REVIEW

There is a growing and general manifest in many HIV studies that HAART has provided dramatic reductions in hospitalization and mortality rates. It has also increased the quality of life for many individuals living with HIV [1]. Mortality rate increases among male population compared to female population is documented by many investigators. In a study conducted in ART centre at Banaras Hindu University (BHU), Varanasi, Uttar Pradesh, India, a large ART centre catering to approximately 16,000 patients with a drainage area covering eastern part of Uttar Pradesh, Bihar and Jharkhand established increased male mortality [18]. The objective of that observational study was to assess the factors determining survival of patients on ART under routine programme conditions five years after its inception. The hazard of death was 2.01 (CI: 1.49-2.72) times higher in males than females, 1.33 (CI: 0.98-1.81) and 1.48 (CI: 0.91-2.41) times higher in patients of age 30-50 yr and >50 yr, respectively as compared to patients of age < 30 yr [16, 17, 18].

Many researches have attributed Males starting HAART to late reporting of disease progress and thus becomes difficult to handle in males, frequent lost to follow ups by male population and difference in responses to treatment [8, 41].

"…Since the advent of ART, mortality rates for people living with HIV/AIDS have decreased substantially both in resource rich and resource-limited settings with conflicting reports about gender-related differences in mortality. Where differences have been reported, little is known about the reasons. Identifying whether men and females benefit equally from ART and ascertaining the reasons underlying any difference could inform strategies designed to address these differences and optimize ART delivery" [42]. This is especially important in resource limited settings (where ART scale-up is a major focus), and particularly among specific occupational sub-groups of the population who contribute significantly to the socio-economic development in a society and whose skill-base continues to be depleted by HIV/AIDS [41, 43].

A study carried out in a population of persons not in HAART showed that the life expectancy was 18.3 years less for men compared to 11.4 years less for females. The female cohort had greater life expectancy compared to the male cohort. Though differences for the two cohorts remain unclear due to disparities in socioeconomic settings it is believed that for HAART persons, the difference could be over 10 years [44].

The pattern of mortality observed in our cohort is consistent with findings from other resource-poor settings. In Arba Minch Hospital patients, mortality in the first year of follow-up was 15.4/100 person-years and most of deaths occurred within first three months [8, 11].

The incidence mortality rate of 3.8/100 person-years in our cohort is comparable to Arbaminch Hospital cohort in the first year. In Tanzania, a regular decline in mortality from 35.7 during pretreatment follow-up to 17.5 per 100 person-years during the first month of treatment is reported [9]. Another similar study conducted by Johannessen et al. estimated mortality was 19.2, 24.5, and 29.0% with respect to at 3, 6, and 12 months, respectively, with the majority of deaths occurring within three months of starting ART. These findings are similar to what has been reported elsewhere [45, 46].

CHAPTER FOUR STUDY METHODS

This chapter presents the methods used to study selected persons, the design and the eligibility criteria. It also presents the scope and limitations of the study.

4.1 Study Design, Population, and Eligibility Criteria

This is a cross-sectional study on the survival of persons starting ART in the period (2006 – 2011). A total of two thousand four hundred and fifty three (2453) study participants enrolled into the program and starting HAART In the five years were assessed.

Participants were selected from a total of three thousand three hundred and ninety seven (3397) enrolments at the facility. The selection was based on the following criteria.

1. The person is starting HAART at the time the study begins.

2. Participants should have been enrolled into the program and on Highly Active antiretroviral Therapy (HAART).

4.2 Variables of the study

The response variable in this research that was the "survival time" was defined as the number of months from the month of enrollment of a patient in the HIV-care till one of the events "death", "lost to follow up", "dropped out", "stopped", "transferred out to other health centers or hospitals" occurred. This meant that the survival data studied here were "right-censored".

The predictor variables relate to the social, demographic, medical and clinical background of the patients having these respective classifications; gender (male, female), area of residence, age at the start of ART (in full year), marital status at the start of treatment (single, separated, divorced, widowed), level of education at the start of treatment (no education, primary, secondary and above; and employment status at the start ART (unemployed, not working due to illness, on the job).

Specifically, main study variables were demographic and clinical data. Age, gender, marital status, occupation, Levels of formal education, region the person is coming from (place of residence) and monthly income were classified as demographic data. Clinical data were; whether the patient is on ART, calendar year of ART initiation, first date of clinic visit, last date of clinic visit and mortality date.

Baseline characteristics measured when patients report and enrolled at the facility were demographic data on age, gender, marital status, occupation, sources of income, place of residence and cell phone contacts; and calendar year of ART initiation.

The primary endpoint was mortality. Mortality cases were reported either through phone calls by social workers, follow up on patient or admissions at the facility. Transfers were recorded by programs and observation time was right-censored at the date of transfer. Patients were defined as Lost to Follow-up if there was no patient contact between the patient and the facility for a period of one year.

4.3 Data analysis

The statistical analytic method used in this study is known as Survival Data Analysis. Survival data analysis involves the modeling and analyses of data that have a principal end point the time until an event occurs (time-to-event data). Survival Analysis considers conditional information on the remaining time of a subject's survival given current survival time. Survival data were censored in the sense that they did not provide complete information since, for a variety of reasons, subjects of the study may not have experienced the event of interest.

Descriptive analysis of survival data utilizes non-parametric methods to compare the survival functions of two or more groups. The Kaplan-Meier estimator (product-limit-estimator) of the survival function [10] was employed for this purpose. The log-rank test was utilized to test whether observed differences in survival experience between/among the groups was significant or not.

Data was analyzed using SPSS v20.0. Baseline characteristics were described with summary statistics by gender. Differences between proportions and medians were tested with Pearson's chisquared test for proportions and the log rank-sum test. Two-sided statistical tests were used at alpha = 0.05. Time to death was analyzed from date of ART initiation using Kaplan-Meier curves.

Cox's proportional hazards regression models were used to assess crude and adjusted associations between patient characteristics and outcomes. All available plausible demographic and clinical variables were considered potential confounders and were included in multivariable models if they altered the association between gender and mortality or were significantly associated with the outcome under study. Results are presented as hazard ratios (HRs) with a 95% CI by duration on ART. The proportional hazards assumption was confirmed by testing gender/time and gender/log time interaction terms. The gender mortality ratio was defined as the male divided by the female mortality rate.

4.4 Survival data analysis and functions

Survival data analysis is the determination of survival times and probabilities from data with time as a measure of an event of interest. The event may be death or recovery of study participant (s) or the working rate of device(s) in a manufacturing or processing industries and companies.

Definition of variables for survival analysis

Let *n* be the number of study elements and are at risk of experiencing event of interest.

Let *T* be a continuous variable that represents the future life time of any of the study elements. Then the probability distribution of *T* is described by probability density function *f(t).*

The survival and hazard functions (S(t) and H(t) respectively) that describe the pattern of the random variable *T* are given by

$S(t) = P(T>=t)$.

But $S(t) = P(T>=t) = 1 – F(t)$ where

F(t) is the cumulative distribution function of *T*.

The hazard function H(t) specifies the instantaneous rate of failure at *T-t* represented by ∂. This is a conditional case on survival to time *t.*

S(t) is given by $\sum\pi[1-(d_j/ r_j)]$

Censoring

Censoring of study elements occurs when the study element becomes a lost to follow up (LTFU) and experiences event directly or indirectly and for which the time is not known, experiences the event before the study begins or does not experience after the study is complete.

4.6 Kaplan Meier survival models

The Kaplan-Meier model is based on estimating conditional probabilities at each time point when an event occurs and taking the product limit of those probabilities to estimate the survival rate at each point in time.

4.7 Cox Regression models

The shape of the survival function and the regression coefficients for the predictors are estimated from observed subjects; the model can then be applied to new cases that have measurements for the predictor variables.

The model takes into consideration information from censored participants, (those persons who do not experience the event of interest during the time of observation), because they contribute usefully to the estimation of the model.

CHAPTER FIVE RESULTS

This chapter presents results from the analysis of data collected from 2453 persons starting HAART in a Healthcare facility in Nairobi, Kenya. The results and comments are presented as follows.

5.1. Demographic characteristics of study participants

The purpose of the demographic analysis is to provide characteristics of the persons in the study in terms of gender, age group, place of residence, marital status, occupation, monthly earnings (income).

The tables below show the distribution of persons in terms of number of gender, age group, place of residence, marital status, occupation and monthly earnings.

Table 1 Gender of Study Participants

Gender of study participants		
Gender	Number of Persons	Percentage (%)
Male	931	38.0
Female	1522	62.0
Total	2453	100.0

Comment

The 2453 persons evaluated show dominance of female as M:F is 0.61:1. This is approximately the Kenya National gender proportions.

5.1. Mean, standard deviation and Percentiles of age of Study Participants

Table 1.1 Mean, standard deviation and Percentiles

Persons in the study		2453
Mean Age		33.17
Median Age		33.00
Mode		34
Std. Deviation for Age		10.144
Percentiles	25%	28.00
	50%	33.00
	75%	39.00

Mean age of participants was 33.17 years and deviation from the central mean is 10.144. This means that majority of persons in the study are aged 33.17years or within approximately 10 years above or below 33 years. Again this is reflecting the overall national levels.

Table 2 Education level and Sex of the participants.

Formal Education	Gender		Total	Percentage (%)
	Male	Female		
No Education	16	32	48	2
Lower primary education (less than 5 years education)	29	51	80	3
Five to eight years of primary education	121	247	368	15
Beyond primary education	241	282	523	21
Level not shown	524	910	1434	59
Total	931	1522	2453	100

Comment

Notable is 59% who had not indicated the level of formal education and there were more females than males.

Table 3 Marital status of Study Participants

Marital Status	Gender		Total	Percentage (%)
	Male	Female		
Married (monogamous)	284	222	506	20.6
Married (Polygamous)	18	26	44	1.8
Cohabiting	5	10	15	0.6
Divorced	1	4	5	0.2
Widowed	34	95	129	5.3
Single	33	152	185	7.5
Child	28	23	51	2.1
Separated	27	106	133	5.4
No response on Marital Status	501	884	1385	56.5
Total	931	1522	2453	100

Comment

A similar trend as for income is observed on marital status. The more than half persons who did not respond on their status of marriage and majority being females can be attributed to the sensitive nature of the question on marriage. Most people prefer not giving response to it. The high number of persons in marriage setup compared to 'single' status informs of the degree of prevalence of the AIDS epidemic among marriage partners compared to single persons.

Table 4 Income of Study Participants

Income of Study Participants	**Gender**		**Total**	**Percentage (%)**
	Male	Female		
2,001 – 5000	64	76	140	5.7
5,001 - 10,000	78	73	151	6.2
10,001 - 20,000	67	47	114	4.6
20,001 - 30,000	30	7	37	1.5
30,001 - 50,000	16	10	26	1.1
> 50,001	12	5	17	0.7
< 2,000	140	397	537	21.9
No source of Income	524	907	1431	58.3
Total	931	1522	2453	100.0

Comment

More than half of study participants did not have any known source of income and majority being females. Major income categories are dominated by males. This corresponds with the national income earnings and self-employment rating by gender.

Table 5 Occupation of Study Participants

Occupation of Study Participants	**Gender**		**Total**	**Percentage (%)**
	Male	Female		
Unemployed	62	169	231	9
Employed	180	123	303	12
Self-employed	89	162	251	10
Farmer	1	29	30	1
Housewife	17	86	103	4
Casual labourer	54	46	100	4
NA (Child)	27	23	50	2
Did not respond	501	884	1385	57
Total	931	1522	2453	100

Comment

The high number of males with formal employment as compared to the females in informal employment point to the already evident disparities in employment in Kenya at all levels by gender.

Table 6 Age Groups of Study Participants

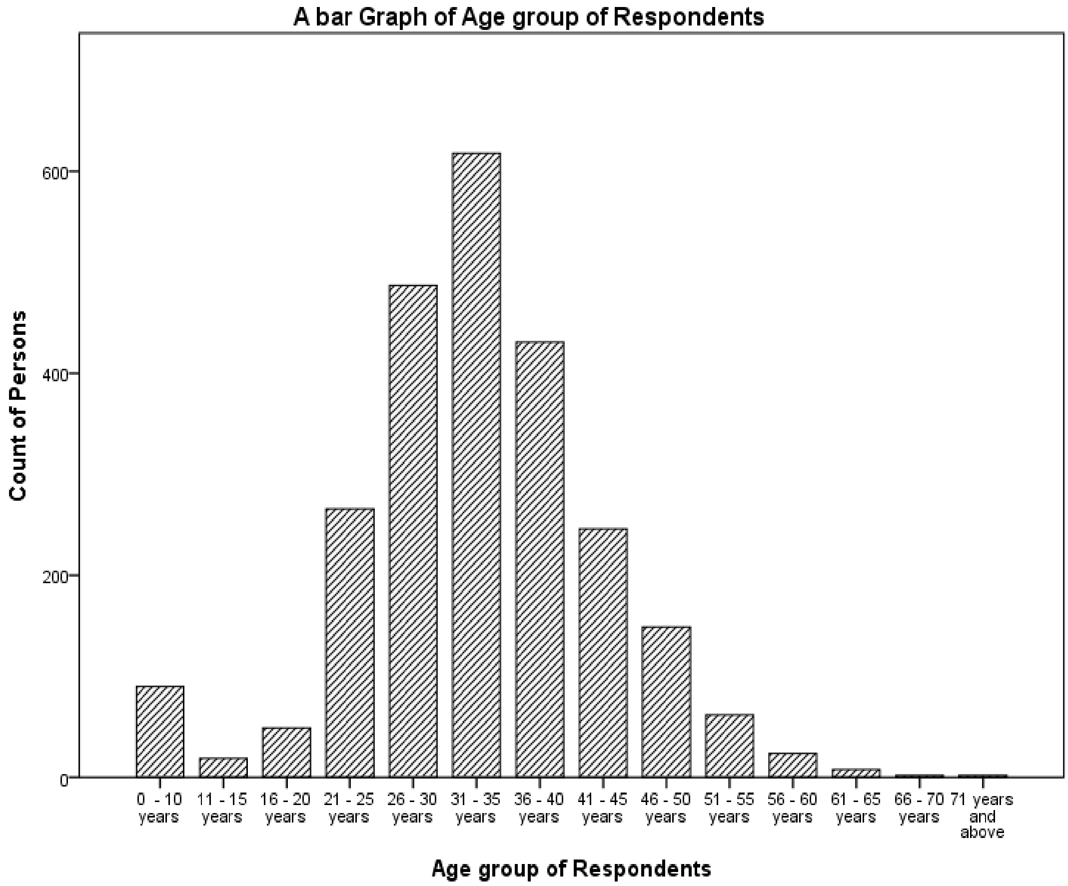
Age groups of Study Participants	Gender		Total	Percentage (%)
	Male	Female		
0 - 10 Years	49	41	90	3.7
11 - 15 Years	11	8	19	0.8
16 - 20 Years	7	42	49	2
21 - 25 Years	34	232	266	10.8
26 - 30 Years	122	365	487	19.9
31 - 35 Years	232	386	618	25.2
36 - 40 Years	199	232	431	17.6
41 - 45 Years	136	110	246	10
46 - 50 Years	85	64	149	6.1
51 - 55 Years	37	25	62	2.5
56 - 60 Years	14	10	24	1
61 - 65 Years	4	4	8	0.3
66 - 70 Years	1	1	2	0.1
71 Years and above	0	2	2	0.1
Total	931	1522	2453	100

Comment

Most persons are aged between 26 years to 40 years. The age bracket is most productive and sexually active men and females.

The figure below illustrates in detail the distribution of Study Participants in the 14 age groups.

Figure 1 Illustration of Age groups of participants



Distribution of study persons by age group simulates a normal curve with mean age group of 31-35 years.

5.2. Survival of persons in HAART

The survival rates (probabilities) of persons in the study were analyzed using statistical package for social sciences (SPSS). The variables were time (t_j) in years the event of interest (death), the number of persons (r_j) at the start of the study - number of persons at risk number of persons who experienced the event (d_j) and the number of persons censored (c_j).

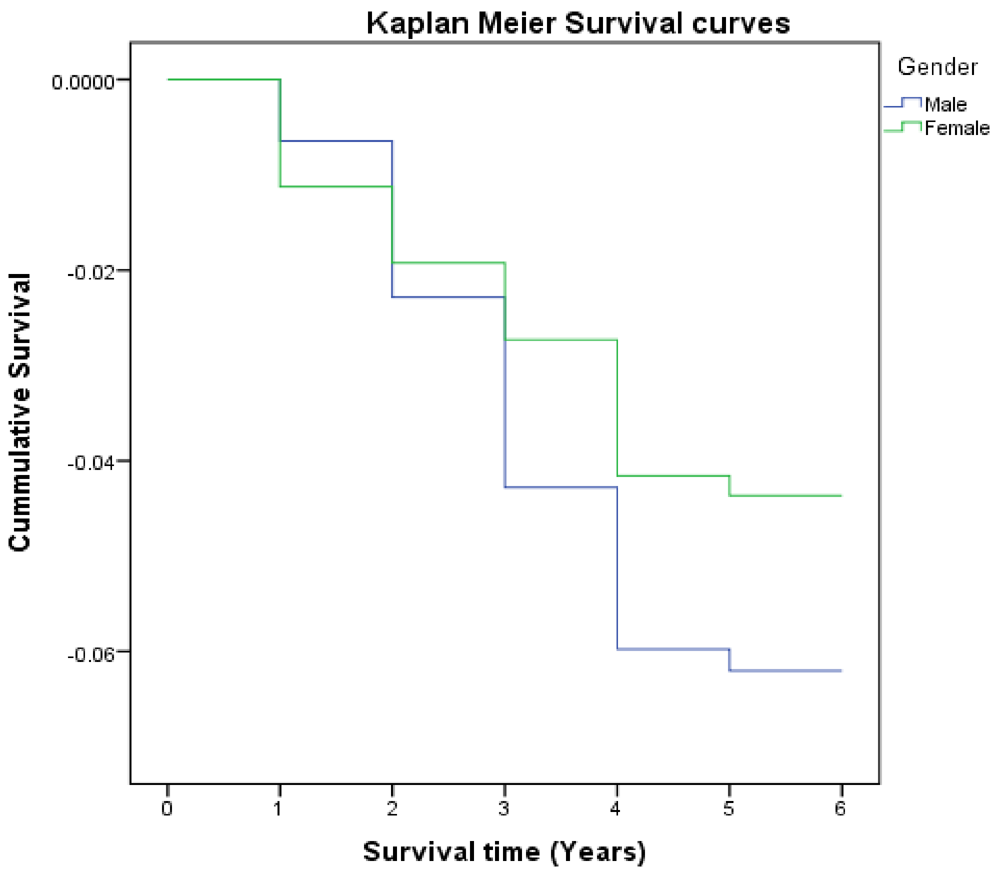
The table below is a survival table by gender of 1453 persons assessed. It gives the survival probabilities $\{1-(d_j/r_j)\}$ of males and females at different years of the study.

Hazard rates for both males and females are also provided.

Table 7: Survival Life Table

Life Table									
	Time in years (t_j)	Number Withdrawing during Interval (c_j)	Number Exposed to Risk (r_j)	Number of Terminal Events (d_j)	Proportion Terminating (d_j/r_j)	Proportion Surviving $1-(d_j/r_j)$	Cumulative Proportion Surviving at End of Interval $S(t_j)$	Hazard Rate $f(t_j)$	Std. Error of Hazard Rate
Male	0	0	931.000	6	.01	.99	.99	.01	.00
	1	0	925.000	15	.02	.98	.98	.02	.00
	2	0	910.000	18	.02	.98	.96	.02	.00
	3	0	892.000	15	.02	.98	.94	.02	.00
	4	0	877.000	2	.00	1.00	.94	.00	.00
	5	875	437.500	0	0.00	1.00	.94	0.00	0.00
Female	0	0	1522.000	17	.01	.99	.99	.01	.00
	1	0	1505.000	12	.01	.99	.98	.01	.00
	2	0	1493.000	12	.01	.99	.97	.01	.00
	3	0	1481.000	21	.01	.99	.96	.01	.00
	4	0	1460.000	3	.00	1.00	.96	.00	.00
	5	1457	728.500	0	0.00	1.00	.96	0.00	0.00

Figure 2 Illustration of Kaplan Meier Survival curves

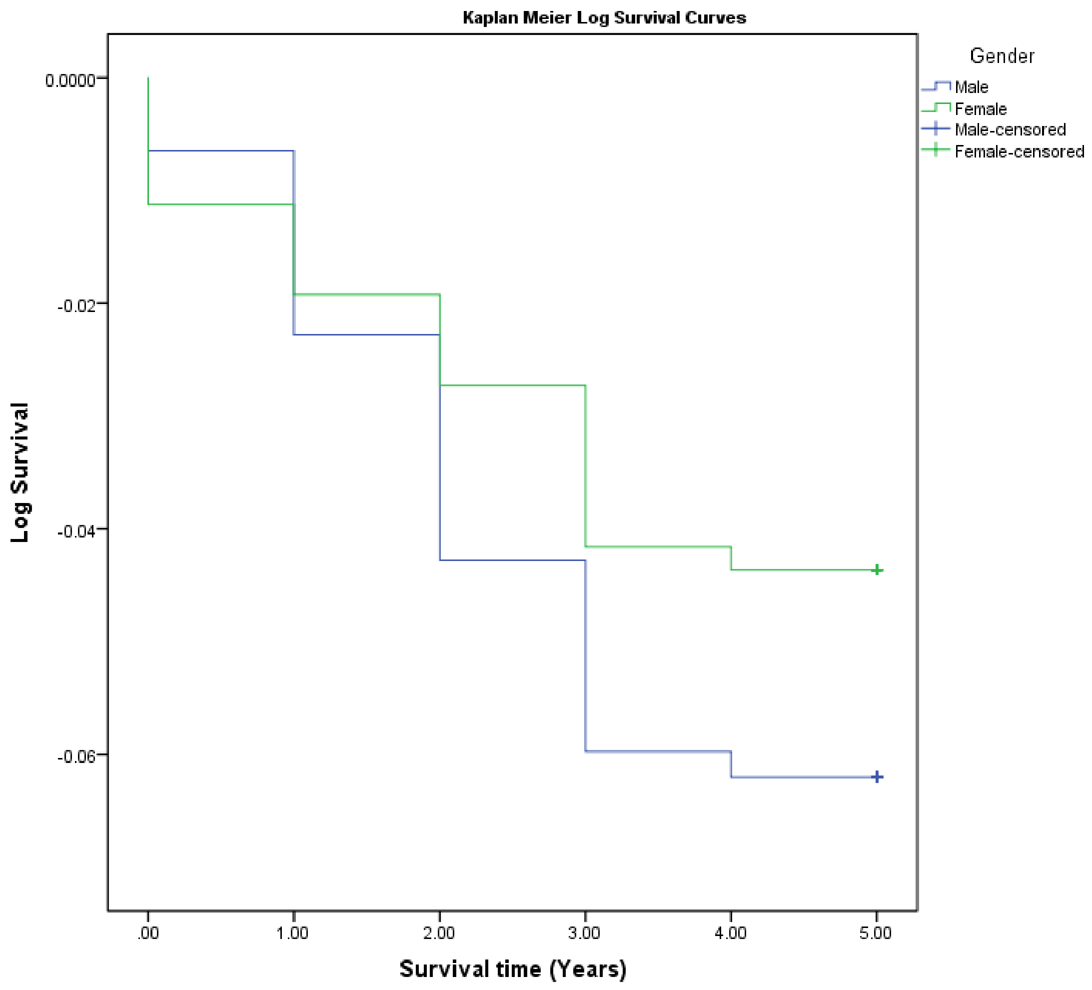


Comment

The Kaplan Meier graph is a plot of the cumulative survival probabilities $S(t_j)$ against survival time (t_j).

The graph shows survival curves for both male and female. From the graph, females have a higher survival rates than males.

Figure 3 Illustration of Log survival curves

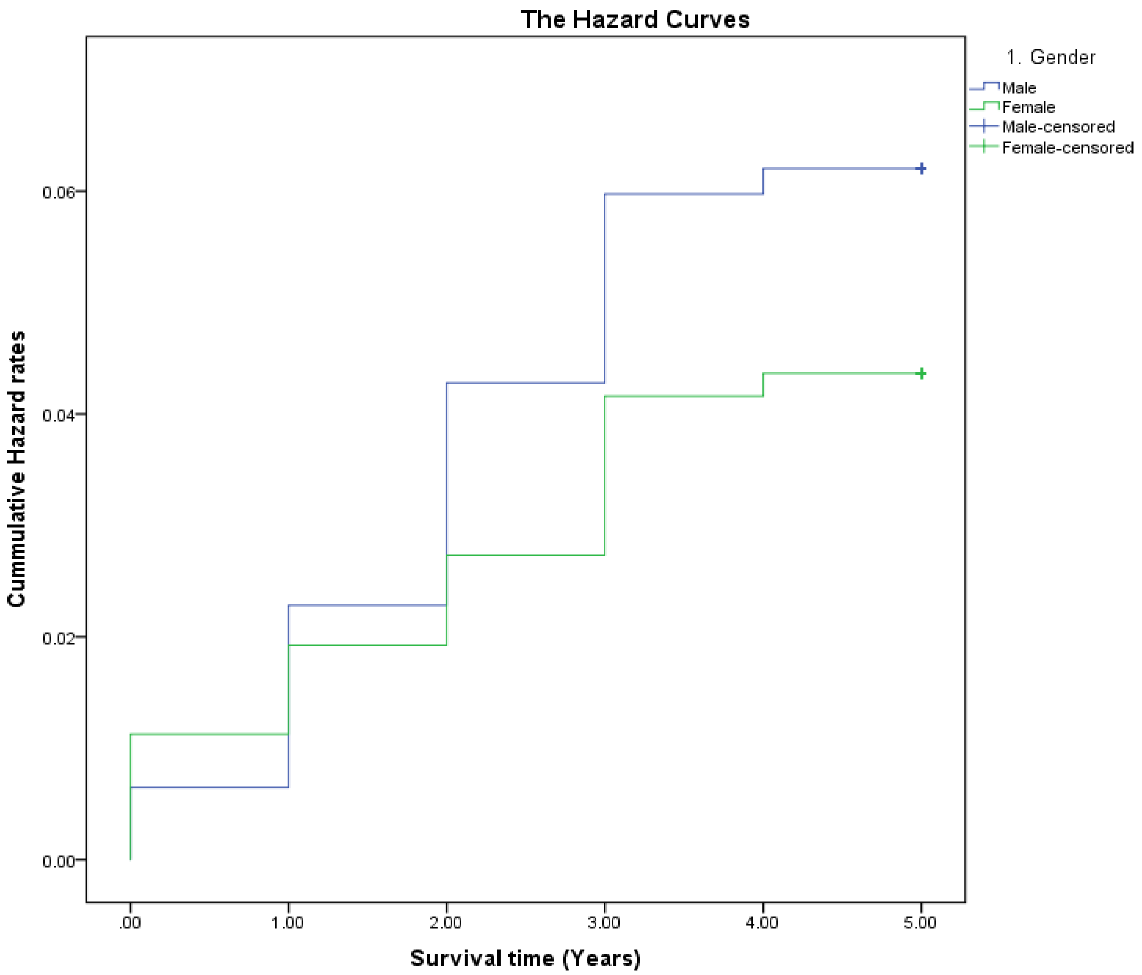


Comment

Logarithms were calculated on the survival data to adjust for variations (deviations) and effects of confounding. The curve was then plotted against survival time in years as shown above.

The findings from above Kaplan Meier illustrations show that the female cohort compared to the male cohort infected with the disease at the same time tends to live longer before experiencing event of interest - death.

Figure 4 Illustration of Hazard curves



Comment

Censored persons were excluded from calculation of hazard rates. The cumulated hazard rates (probabilities) for male and female were then plotted in a hazard graph against survival time in years.

From the graph, the male population has a higher hazard rate than female population.

Mean and median survival times of persons starting HAART

Mean and median survival times are the average periods of the study time participants lived.

The Log rank test derives the difference between the observed values and expected values.

$$U_L = \sum[dj - E(d_{1j})]$$

Where

U_L - result observed mortality cases

d_j - observed mortality cases

d_{1j} - Expected mortality cases

Table 8: Means and Medians for Survival Time

	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
Gender	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
Male	4.811	.026	4.760	4.862	0.000	0.000		
Female	4.859	.018	4.823	4.895	0.000	0.000		
Overall	4.841	.015	4.812	4.871	0.000	0.000		
a. Estimation is limited to the largest survival time if it is censored.								

The estimated mean survival times by gender, of persons starting HAART is lower for males (4.811 years) compared to females (4.859).

Table 9: Over all Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	3.716	1	.054

Comment

Overall comparisons provide test result of survival distributions for the different levels of gender. With a chi – square of 3.716 at 0.05 level of significance the calculated value of 0.054 then we reject the null hypothesis that the different levels of gender are the same and conclude that the different levels of gender are not the same.

5.3. Cox Regression Models

Table 10: Summary of Event and Censored cases

		N	Percent
Cases available in analysis	Event[a]	121	4.9%
	Censored	2332	95.1%
Total		2453	100.0%
a. Dependent Variable: Survival time in Years			

Table 11: Gender Stratum Status

Stratum Status[a]				
Stratum	Strata label	Event	Censored	Censored Percent
1	Male	56	875	94.0%
2	Female	65	1457	95.7%
Total		121	2332	95.1%
a. The strata variable is : Gender				

Table 12: Variable categories and their levels of significance

Variable Category	Score	d.f	Level of Significance.
Education level	2.293	4	.682
Education - No Education	.797	1	.372
Education - Lower primary education	.353	1	.552
Education - Five to eight years of primary education	.200	1	.655
Education - Beyond primary education	1.124	1	.289
Marital Status	5.653	8	.686
Marital status - Married (monogamous)	.289	1	.591
Marital Status - Married (Polygamous)	.316	1	.574
Marital Status - Cohabiting	.746	1	.388
Marital Status - Divorced	.236	1	.627
Marital Status - Widowed	2.936	1	.087
Marital Status – Single	.786	1	.375
Marital Status – Child	.661	1	.416
Marital Status - Separated	.001	1	.979
Occupation	9.804	7	.200
Occupation - Unemployed	3.088	1	.079
Occupation - Employed	2.798	1	.094
Occupation - Self-employed	.147	1	.701
Occupation – Farmer	.069	1	.793
Occupation - HouseWife	2.652	1	.103
Occupation - Casual Labourer	.968	1	.325
Occupation - Did not Respond	.740	1	.390
Earnings	4.669	7	.700
Earnings - 2,001 - 5000	.572	1	.449
Earnings - 5,001 - 10,000	2.034	1	.154
Earnings - 10,001 - 20,000	.186	1	.666
Earnings - 20,001 - 30,000	.442	1	.506
Earnings - 30,001 - 50,000	1.439	1	.230
Earnings - > 50,001	.005	1	.943
Earnings - < 2,000	.209	1	.647
a. Residual Chi Square = 25.303 with 25 df Sig. = .445			

Table 13: Parameter estimates and levels of significance

`Parameter Estimates									
								95% Confidence Interval for Exp(B)	
Survival Time[a]	Parameter	B	Std. Error	Wald	df	Sig.	Exp(B)	Lower Bound	Upper Bound
0	Intercept	-2.708	.889	9.278	1	.002			
	Marital Status	.038	.084	.202	1	.653	1.038	.881	1.223
	Occupation	-.294	.106	7.678	1	.006	.746	.606	.918
	Income	.036	.101	.127	1	.722	1.037	.850	1.265
	Education	-.209	.235	.788	1	.375	.812	.512	1.287
	[gender=1]	-.441	.505	.762	1	.383	.643	.239	1.731
	[gender=2]	0[b]			0				
1	Intercept	-5.163	1.139	20.543	1	.000			
	Marital Status	-.149	.093	2.561	1	.110	.861	.717	1.034
	Occupation	-.055	.120	.212	1	.645	.946	.747	1.198
	Income	.070	.110	.407	1	.523	1.073	.864	1.332
	Education	.290	.307	.892	1	.345	1.336	.733	2.436
	[gender=1]	.585	.404	2.095	1	.148	1.796	.813	3.966
	[gender=2]	0[b]			0				
2	Intercept	-5.490	1.042	27.772	1	.000			
	Marital Status	-.020	.106	.035	1	.851	.980	.797	1.206
	Occupation	.088	.139	.401	1	.527	1.092	.831	1.435
	Income	.010	.132	.006	1	.939	1.010	.779	1.309
	Education	.051	.282	.033	1	.855	1.053	.606	1.828
	[gender=1]	.924	.381	5.868	1	.015	2.518	1.193	5.317
	[gender=2]	0[b]			0				
3	Intercept	-5.556	.959	33.552	1	.000			
	Marital Status	.080	.125	.407	1	.523	1.083	.848	1.384
	Occupation	.293	.173	2.858	1	.091	1.340	.954	1.883
	Income	-.115	.152	.568	1	.451	.892	.662	1.201
	Education	-.120	.262	.210	1	.647	.887	.531	1.482
	[gender=1]	.211	.344	.377	1	.539	1.235	.629	2.426
	[gender=2]	0[b]			0				
4	Intercept	-57.397	3873.391	.000	1	.988			
	Marital Status	1.591	340.479	.000	1	.996	4.907		
	Occupation	1.963	0.000		1		7.123	7.123	7.123
	Income	.472	417.764	.000	1	.999	1.603	0.000	.[c]
	Education	3.686	842.152	.000	1	.997	39.875	0.000	.[c]
	[gender=1]	.185	.915	.041	1	.840	1.203	.200	7.227
	[gender=2]	0[b]			0				

Figure 5 Illustration of survival function at mean of covariates

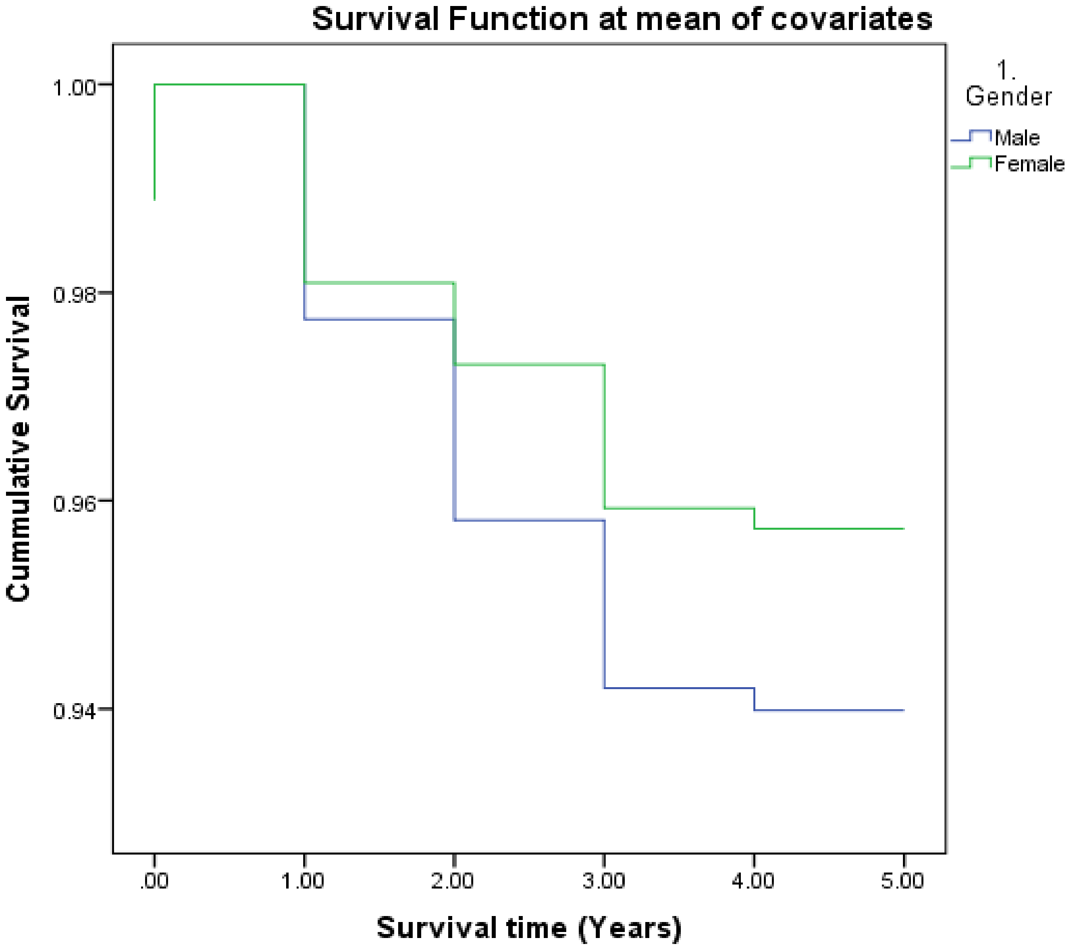
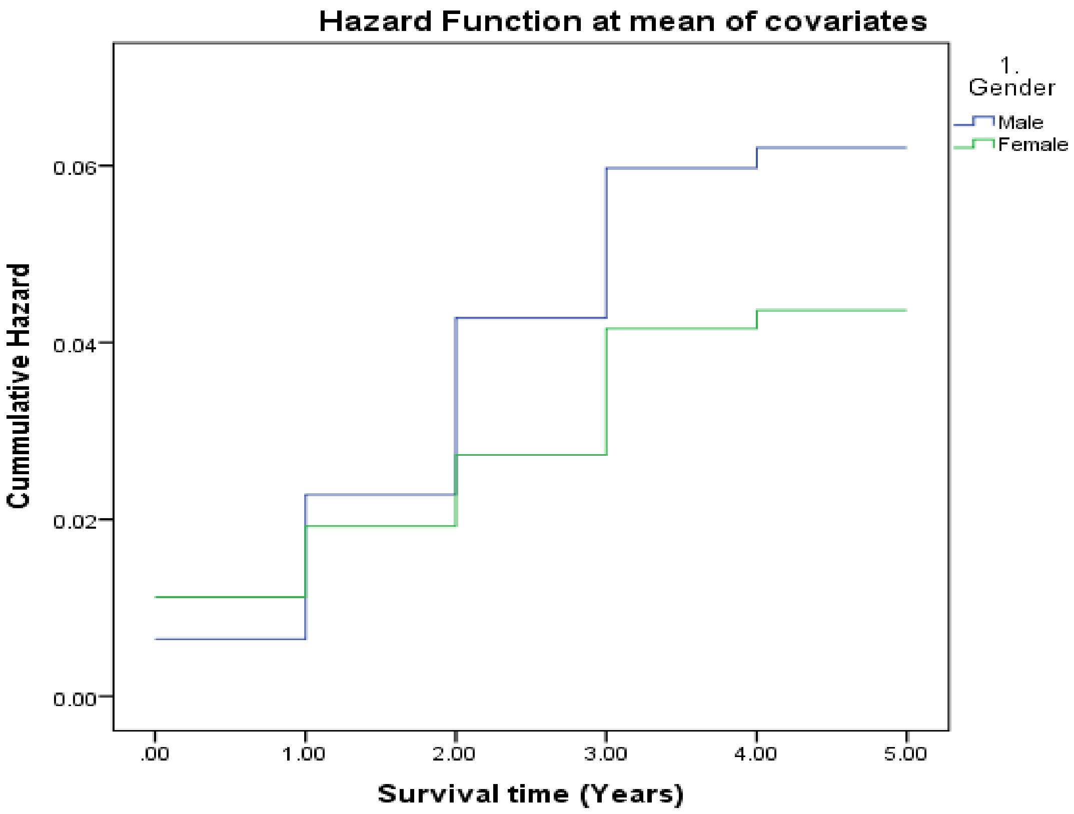


Figure 6 Illustration of Hazard function at mean of covariates



Comment

Cox's proportional hazards regression models assesses the crude and adjusted associations between patient characteristics and outcomes. The covariates (variables that describe social demographics of the respondent) factored in were marital status, occupation, education levels and monthly earning.

Factors within covariates that were significant in survival of persons starting HAART were those with significant levels less than the computed chi-square significant level of 0.445. The factors were Education - Beyond primary education, Education - No Education

Marital Status – Cohabiting, Marital Status – Widowed, Occupation - Unemployed

Occupation – Employed, Occupation – Housewife, and Occupation - Casual Laborer.

On parameter significance, occupation is a highly significant factor in determination of survival probabilities by gender (P = 0.006) in the first year of survival.

CHAPTER SIX DISCUSSION

To my knowledge this is the first attempt at determining the survival rates of those living with HIV and start ART followed up for five years after starting ART in a HIV/AIDS health care facility in Nairobi, Kenya. This is particularly so for a Care Centre dedicated for HIV/AIDS persons, serving a diverse population in a high HIV-burden setting in Nairobi. The documented high early mortality in patients in Kenya starting ART, which was first reported in an earlier comparative analysis in some parts of Sub Saharan Africa was sufficiently compelling [39, 43]. Many studies had been done and hitherto documented varied survival rates but not in a Kenyan care providing facility at the start of ART [45, 47].

In this study ART-naïve adults were enrolled between June 2006 and December 2011. Participants were all living with HIV followed up until the initiation of HAART. This gives an insight into survival and its determinants in a hospital setting in Nairobi, Kenya [39, 45]. However specific interests were in the variations due to gender differences. The spectrum of persons enrolled, patterns of mortality and practical implications for managing HIV-infected persons was similar for many other start-up ART programs in Kenya and other resource-poor settings [46 - 48].

This study of gender variations in survival rates for initiating HAART is evident. Mortality rates among males are higher than for females especially in 3rd world economies. This is presumably as a result of poor adherences to drug schedules, individual behaviors, late start of ART when the disease has advanced and the ever common factor of lost to follow up. Compounded by environmental and circumstantial factors, the advancement of the disease after ART initiation among males is faster than for females. The result of this is a high rate of mortality among men compared to females.

The high early mortality in male patients with advanced disease implies the need for starting treatment earlier. This requires early diagnosis of HIV infection through improved counseling and testing practices.

In Arba Minch Hospital, mortality in the first year of follow-up was 15.4/100 person-years and most of deaths occurred within first three months [50-53]. In Tanzania, a regular decline in mortality from 35.7 during pretreatment follow-up to 17.5 per 100 person-years during the first month of treatment is reported [29, 45]. Although this statistic is not calculated in this study, the probabilities plotted against time showed that the number of mortalities recorded in the first year was more compared to the subsequent years of the study. This corresponds with the outcome of the studies stated above.

The overall mortality in this study is quite higher than in high-income countries but in line with low-income countries [6, 19 20].

This study considered income levels, education, occupation and marital status as major determinants of mortality or survival outcome. This however found out that occupation is a major and significant determinant of survival. More males than females have higher paying occupation. It is believed that other than unseen confounders, the busy schedules of this male cohort could have resulted in increased lost to follow up, poor adherence to drugs and poor clinic attendance resulting in missed appointments.

Variations in the mortality rates across different countries indicate that effectiveness of ART to reduce the mortality and increase the survival among HIV-infected patients could depend on the adherence, quality of service, and characteristics of persons on ART [4, 24].

After allowing for factors likely to affect mortality such as HIV disease stage at initiation, males on ART had a 31% higher risk of dying than females. Males were more likely to be lost to follow-up than females, but males and females who were lost to follow-up were equally likely to die. Females had a slightly better immunological response to HAART than men [27, 41].

The Kaplan Meier survival and hazard plots of cumulative probabilities against survival time show that females have higher survival probability than males. On the other hand, males have higher hazard (probability of dying) probabilities than females. This can be attributed to factors that influence survival of under study such as level of education, marital status, occupation and income earned.

In adjusting for variations (deviations) and effects of confounding from hypothetically identified covariates, and plotting survival and hazard curves for both male and female, output showed that females have higher survival rates than males. Overall comparisons provide test result of survival distributions for the different levels of gender. With a chi – square of 3.716 at 0.05 level of significance, the different in probabilities of by gender are significant. This means that the difference is not according to chance but due to some factors that directly and indirectly affect survival of each gender [60, 61].

The output of Cox's proportional hazards regression model showed how different levels of covariates influence survival probabilities of males and females. It can be deduced that levels of education, sources of income and marital status affect survival probabilities of both males and females.

In Nepal, male HIV-infected patients reported through HTC by July 2012 were double than female [25]. However, the proportion of male ART receivers was only 10% more than female in Nepal [26]. This indicates that female patients tend to enroll more frequently in ART service than men, and they would have early initiation of treatment due to the linkage between the community-based prevention of mother-to-child transmission (CB-PMTCT) and treatment and care program. Taking PMTCT service through community level had dramatically increased its utilization by pregnant mothers and it might have effectively encouraged females to get to know their HIV status and start early treatment through awareness and counseling services [27,28].

This study showed that male adult HIV-infected patients had higher risk of mortality. Our study recorded similar trend of high number of females enrolled and are starting HAART at earlier times than males [55 - 59]. This could also be attributed to the antenatal clinics that females in marriage settings attend. In these clinics females are taken through a provider-initiated testing and counseling. Thus females know their status earlier than males and subsequently get medical attention at early stages of the disease. Similarly the study could also be reporting late arrivals to medical facilities by males at late stages of the disease [65, 69].

Loss to Follow-up and Mortality Ascertainment

In this study persons who could not be traced for more than six months from the last clinic visit were considered to be lost to follow up. Lost to follow up persons were excluded from the final survival analysis IFF there were no reports of having experienced the event of interest. Persons with no outcome before analysis closure were censored at analysis closure.

Strengths and Limitations

Availability of data on factors that influence survival was a major strength of this study. The data enabled comparative analysis of the difference of survival by gender.

Missing data, incomplete documentation and loss to follow up cases were major limitations.

CONCLUSION AND RECOMMENDATIONS

This study had more females initiated into HAART than males. From other studies this is equally the trend. It can be concluded that factors that contribute to the difference in survival of HAART persons by gender are both direct and indirect. The factors included in the model to determine survival rates were considered direct. Occupation was identified as the most significant factor that determine survival differences in males and females. Marital status, level of formal education and levels of income also determine survival probabilities of males and females but at lesser significance compared to variable on occupation.

Recommendations

Regression model used to obtain parameter estimates need to be modified in future studies to include covariates that are likely to influence survival of study participants such as CD4 counts, WHO staging and lost to follow up. Their levels of significance on the response variable (time) would then be ascertained. This would bring out more clearly the degree of influence of covariates on survival differences of males and females.

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