SURVIVAL OF PERSONS ON HAART IN COPTIC HOSPITAL, 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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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** who was always to support 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
LB	Lower Bound
LTFU	Lost to Follow – up
OIs	Opportunistic infections
UB	Upper Bound
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 High antiretroviral therapy (HAART) have been reported in many HIV intervention programs and studies that show evidence of increasing mortality in males compared to females. It is desirable and of greater interest to have estimates of expected survival rates of both males and females living with HIV/AIDS. The indicators of variation that yield the difference in survival are considered important in: future disease estimates in numbers and projections; generate interest in further study on the science of HIV/AIDS; review of curative and treatment mechanisms; modelling of the disease and other infections; progressive monitoring of the epidemic and making informed decisions on health, healthcare workers and interventions at all levels of healthcare delivery.

This study presents survival comparisons between males and females enrolled at the same time and observed until the end of the study. It also identifies some of the factors influencing survival of persons in HAART by gender and presents the determined survival rates of HIV-infected patients treated with HAART. It is expected that this contribute to improve health outcomes in different population settings.

Objective: To assess the survival of persons starting HAART with the aim of determining demographic gender characteristics and survival probabilities.

Design A longitudinal study of HIV/AIDS persons on HAART.

Main study Variables: The main study variables are both demographic and clinical. The demographic data variables 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, it was observed that more men than women (adjusted hazard ratio, 1.19, 95%; CI 1.14 – 1.27)on HAART were identified to be missing appointments and thereby needing follow ups.

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: Variation in mortality rates of males and females on HAART 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

The rates of survival of HIV/AIDS persons and indicators determining its outcome are significant when ascertaining future numbers and proportions of cases related to HIV/AIDS; greater understanding of the HIV disease; progressive monitoring of the epidemic and making informed decisions on health and related mediations [1 - 3].

As at the end of the year 2016, nearly 37 million persons contracted the HIV virus causing AIDS. Intuitively, this certainly led to the 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]. In the care and treatment of HIV persons, uptake of a combination of more than one ART resulted in transformation of the disease particularly in the high per capita income countries in comparison with low per capita income countries [8, 9]. By observation, the ARV experienced persons' live longer and healthier lives unlike those not on treatment. However, HIV/AIDS persons in low income countries including Kenya record relatively higher death rates in the early months of start of HAART. *"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. 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, socioeconomic and circumstantial factors. It is also documented that the advancement of the disease after ART initiation among males is faster than for females [15] resulting in high rates of mortality among men compared to females [1 - 3]. Several studies majorly from the South Asian region and low income countries evidenced the high rates of death in persons under antiretroviral therapy (2, 11, 14, and 15). However other studies have documented no gender influence on survival [16 - 18]. Upon start on treatment, a study on persons infected with HIV revealed the following: The survival time of these persons was about 4-median years with variables including gender, status of marriage, level of education and area of study having no major effect 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. Increase in predisposition of HIV persons to opportunistic infections is as a result of CD4 lymphocytes cells that make up the immune system getting destroyed by the virus [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 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].

Despite the fact that no conclusive assessment on the explanations advanced on variance in mortality rates by gender, likely interpretations have nevertheless been recommended for further interrogation. Vital and most fundamental features on mortality and rates point to the fact that progression of HIV disease among persons on ART is greater in males than in females. The likelihood of a case of missed clinical appointments resulting to recurrent cases of lost-to-follow-up (LTFU) being a male is higher than it being a female. This is a commonality in many research and HIV care and treatment settings. 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].

In view of the aforementioned therefore, it is considered critical to seek understanding on these variances with the main aim of developing mechanisms and strategies towards enhanced health outcomes in dissimilar population locations.

1.2. STUDY OBJECTIVES

1.2.1 Broad objective

To determine survival of persons on HAART

1.2.2 Specific Objectives

The specific objectives of this study are

1. To define male and female demographic characteristics in the study.
2. To determine the difference and assess survival probabilities of study participants.
3. To identify the determinants of survival by 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. Are survival probabilities between males and females different?
3. 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 increasing evidence from many HIV studies, of significant decrease in admission and mortality rates of HIV infected persons as an outcome of use of HAART that enhance the ability of the immune system to fight HIV. The use of highly active antiretroviral therapy (HAART) has had value addition on the lives of HIV infected persons [1].

Increase in mortality rate in male population compared to female population is documented by many investigators around the world. In a study conducted on about 17,000 HIV / AIDS patients in Uttar Pradesh ART center, India to evaluate the elements that determine survival of HIV persons on HAART for a period of 5 years, established increased male mortality [18] with 2.01 (with confidence interval of between 1.48 and 2.73) hazard rate difference in multiples in male persons than in females. For study elements of ages between 30 years to 50 years and higher, the hazard rate was 1.48 (with confidence interval of between 0.92 and 2.40) times in comparison with elements under 30 years of age [16, 17, 18] and thus becomes difficult to handle leading to recurrent lost-to-follow-ups 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 finding is of significance particularly in little resource settings inhabited by a hardworking and active population with necessary and required skills to drive forward the economy, depended upon for socio economic growth and development but with notable negative effects of HIV/AIDS infection and in which scale up of ART is urgently needed [41, 43].

A similar 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 aforementioned studies exhibit a form of mortality among HIV infected persons which resonates with outcomes from other low income and resource settings. With Arba Minch Hospital patients, mortality was recorded at 15.4/100 person-years in the first study year and most of deaths occurred within first three months [8, 11].

The incidence mortality rate of 3.8/100 person-years in the study group can be likened to the characteristics and mortality pattern of Arbaminch Hospital group investigated in year 1 of study. In Tanzania, a notable and steady reduction in incidences of mortality (35.7 before start of HAART to 17.5 /100 person years) during the first month of treatment is reported [9]. Another similar study conducted by Johannessen et al. estimated mortality at 19.2%, 24.5%, and 29.0% at 3, 6, and 12 months, respectively, many of the deaths recorded in the first 3 months of ART. Concurrence of these study results with others from elsewhere is noted [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 longitudinal study on the survival of persons starting ART between the years 2006 and 2011. 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.

A total of two thousand four hundred and fifty three (2453, 72% of 3397) study participants enrolled into the program and starting HAART in the five year period that the study was undertaken.

4.2 Eligibility

1. Participants are 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 Definition of Indicators (variables) used in this study

In this study, survival time is defined as the number of times (in years) enrolled participant is actively on ART and is followed until event of interest – death occurs. In the course of following, the study participant may drop out of care, become lost-to-follow-up or transfer out of current healthcare facility to other health centers or hospitals. Any of the events occurring in course of study on a participant leads to having the participant rightly censored.

Independent variables in the survival model are described as the determiners of the effect on the overall survival of participants of specific cohort. These variables include: the social and demographic descriptions of study participants (age, gender, marital status, employment and education level).

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. Transfer of patients to other health facilities was recorded by program teams. Upon transfer of a participant, the participant or cohort of participants transferred are censored.

A study participant is regarded as Lost to Follow-up if there was no contact with the facility for a period of one year.

4.3 Data analysis and methods

This study involved observing elements over a period of 5 years and determining if they experienced event of interest. The time-to-event data collected have ‘time’ and ‘event’. This is survival data and the modelling and analysis takes into consideration the probability of study cohorts and different times of the study before experiencing the event. Censored elements are either lost to follow up, dropped from the study or transferred to other healthcare centers. These elements are excluded from the final data used to draw comparative information on survival of persons under HAART.

This analysis of survival data utilizes a number of popular statistical techniques including the Kaplan-Meier estimator of determining survival model of study elements. To test the significance of observed variations in survival with respect to gender, the log – rank test technique was used.

Statistical Package for Social Science (SPSS) v20.0 was used to analyze the data from the study.

Vital characteristics including gender distribution, level of education, spread in income, marital status and occupation were considered fundamental description of the study participants. Statistical tests at α=0.05 informed the difference in rates and measures of central tendency and the survival of persons initiating HAART.

To find out on the relationship between participant descriptions and survival, the Cox's regression proportional hazard model was utilized in this analysis. The descriptions, both demographic and clinical are considered significant and strongly associated with the outcome of survival of persons on ART.

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 predisposed to the outcome event.

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 *f(t).*

The pattern of the random variable *T* and are described by survival and hazard functions as follows.

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

But S(t) = P(T>=t) = 1 – F(t) in which,

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.

4.5 Kaplan Meier survival models

The Kaplan-Meier function of analyzing time-to-event data uses conditional odds at each point of occurrence of the event and obtains product multiple of the odds when estimating time specific interval survival rates.

4.6 Cox Regression models

Survival functions take standard shapes and with estimated regression coefficients from the observed study elements. The model so obtained can be used to predict survival of new cases.

The model takes into consideration information from censored participants since determine the final 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 socio-demographic features of study participants is to provide general information with respect to their gender marital status and occupation of participants with monthly income earnings as shown in the tables below.

Table 1: 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. Measures of central tendency of study Participants

Table 1.1 Measures of central tendency

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 with a 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 (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

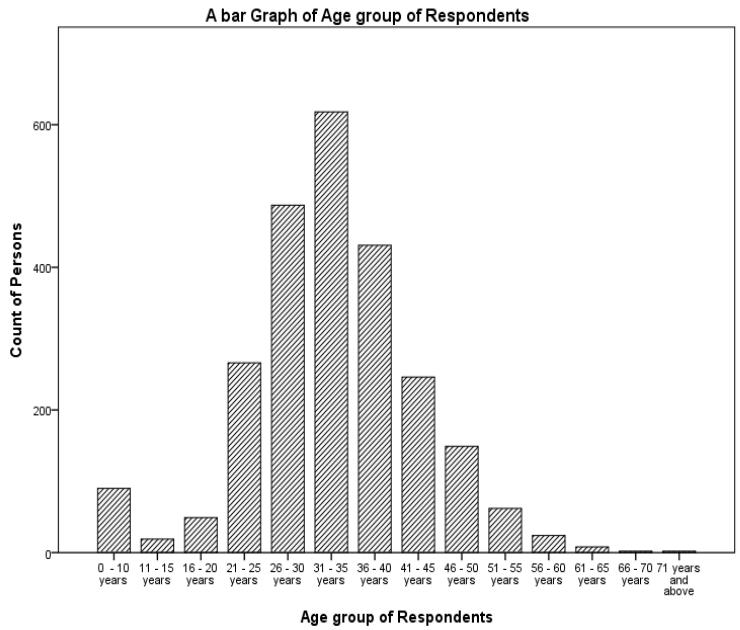
Age groups of Study Participants	Gender		Total	Percentage (%)
	Male	Female		
0 - 10 Years	49	41	90	3.7
11 - 15 Years	11	8	19	0.8
16 - 20 Years	7	42	49	2
21 - 25 Years	34	232	266	10.8
26 - 30 Years	122	365	487	19.9
31 - 35 Years	232	386	618	25.2
36 - 40 Years	199	232	431	17.6
41 - 45 Years	136	110	246	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

In the analysis of data to determine survival rates (probabilities) of persons in the study, the indicators used include time (t_j) (in years) to 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).

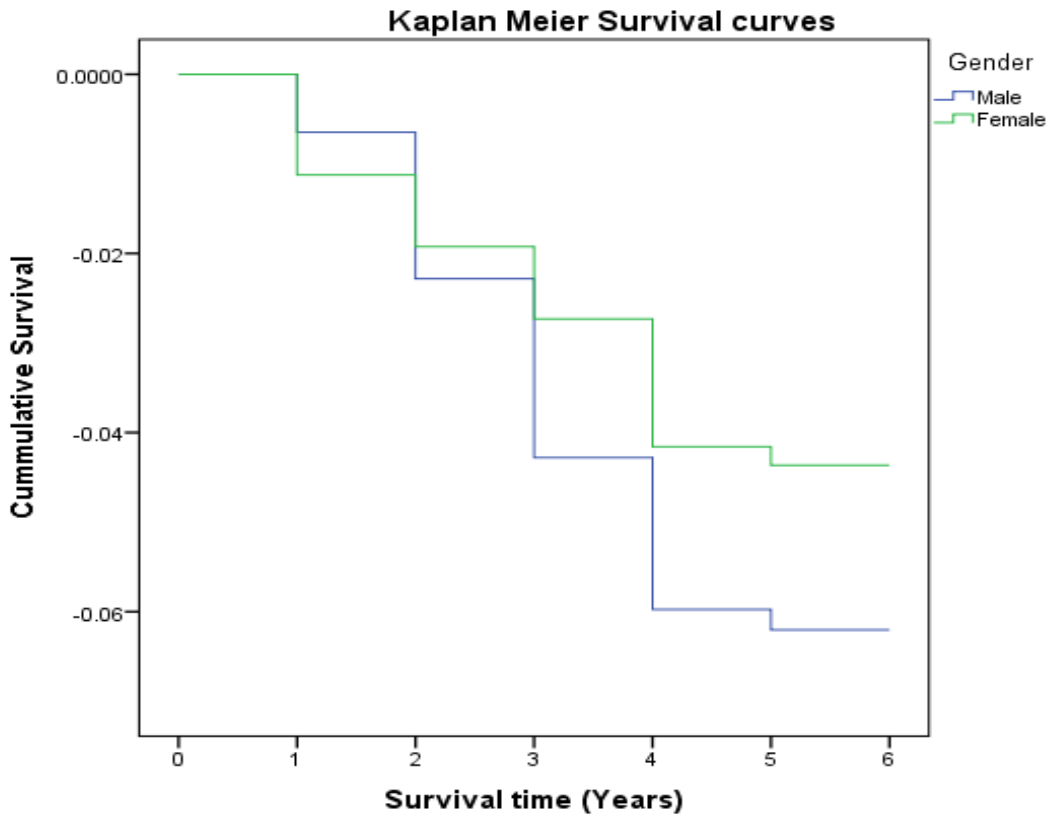
The table below is a survival table by gender of 1453 persons assessed. It gives the survival probabilities $\{1-(d_j/r_j)\}$ of males and females at different years of the study.

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 (cj)	Number Exposed to Risk (rj)	Number of Terminal Events (dj)	Proportion Terminating (dj/ rj)	Proportion Surviving 1-(dj/ rj)	Cumulative Proportion Surviving at End of Interval S(tj)	Hazard Rate F(tj)	Std. Error of Hazard Rate
Male	0	0	931.000	6	.01	0.99	.99	.01	.00
	1	0	925.000	15	.02	0.98	.98	.02	.00
	2	0	910.000	18	.02	0.98	.96	.02	.00
	3	0	892.000	15	.02	0.98	.94	.02	.00
	4	0	877.000	2	.00	1.00	.94	.00	.00
	5	875	437.500	0	.00	1.00	.94	.00	.00
Female	0	0	1522.000	17	.01	0.99	.99	.01	.00
	1	0	1505.000	12	.01	0.99	.98	.01	.00
	2	0	1493.000	12	.01	0.99	.97	.01	.00
	3	0	1481.000	21	.01	0.99	.96	.01	.00
	4	0	1460.000	3	.00	1.00	.96	.00	.00
	5	1457	728.500	0	.00	1.00	.96	.00	.00

Figure 2 Illustration of Kaplan Meier Survival curves

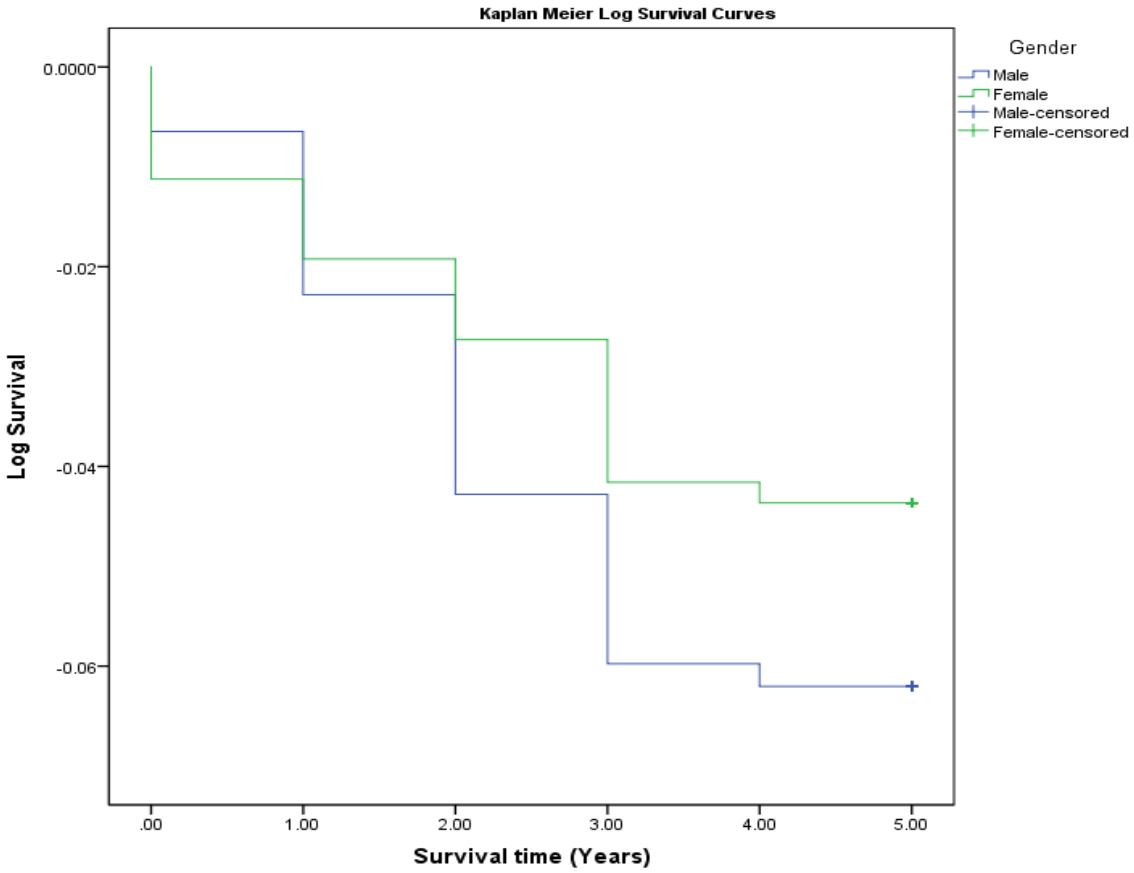


Comment

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

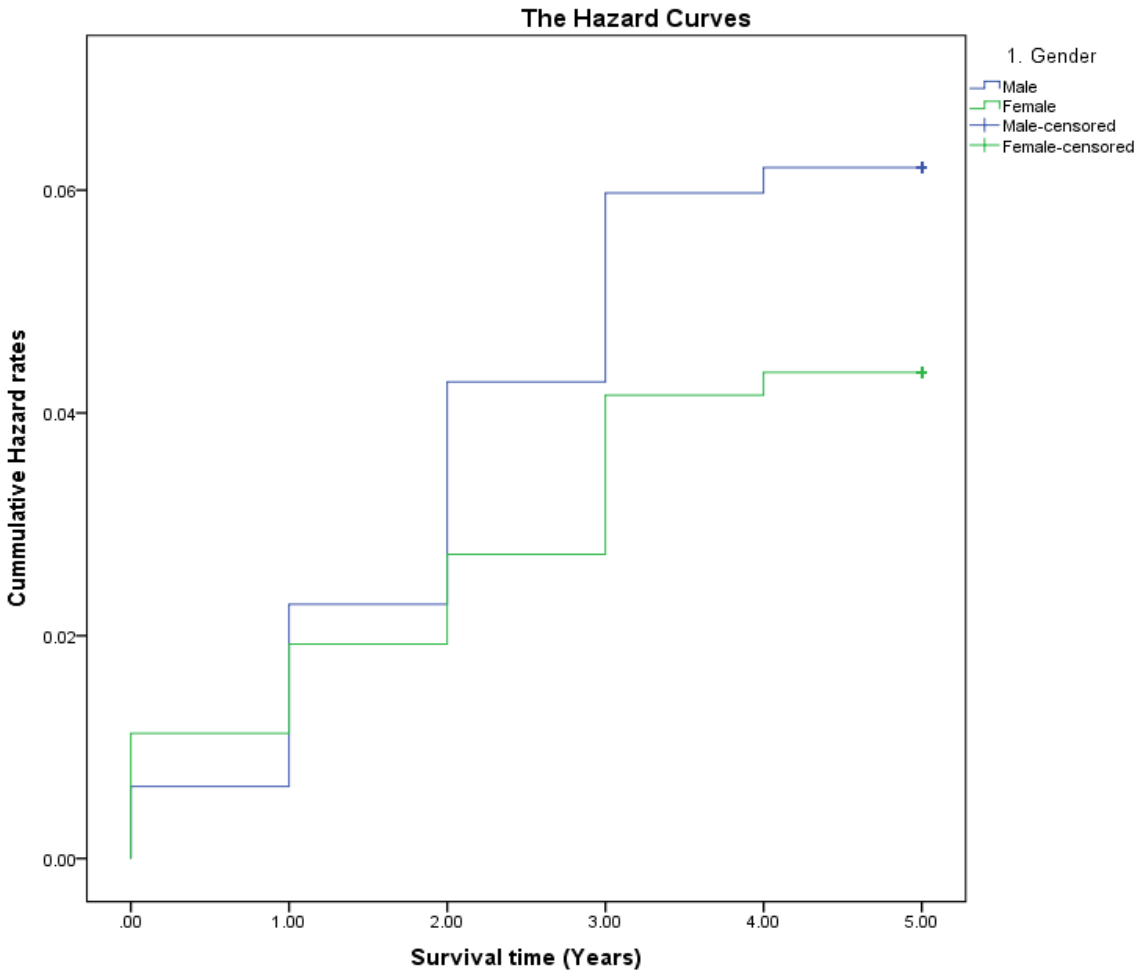


Comment

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 variance in observed and expected values.

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

Where

U_L - result observed mortality cases

d_j - observed mortality cases

d_{1j} - Expected mortality cases

Table 8: The mean and median survival time of study participants

Gender	Mean[a]				Median			
	Estimate of β	Std. Error	95% CI		Estimate	Std. Error	95% CI	
			LB	UB			LB	UB
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. This indicates survival time estimated on cases with limited times of survival								

Comment

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

Table 9: Log Rank estimates

	χ-Square	Degrees of freedom (df)	Level of significance
Log Rank (Mantel-Cox)	3.716	1	.054

Comment

Overall comparisons provide test result in spread of survival times of males and females in the study. With a chi – square of 3.716 at 0.05 level of significance the calculated value of 0.054 the cognitive hypothesis that the different levels of gender are the same is rejected 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

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			

Comment: The cases available in the event were 4.9% while the censored cases were 95.1%

Table 11: Gender Stratum Status

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				

Comment: Total participants who experienced event of interest was 121 (56 Males and 65 Females).

The large number of females is attributed to the disproportionate ratio of M: F (0.61:1).

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									
Survival Time[a]	Parameter	B	Std. Error	Wald	df	Sig.	Exp(B)	95% CI for Exp(B)	
								LB	UB
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 curve at mean of independent variables**

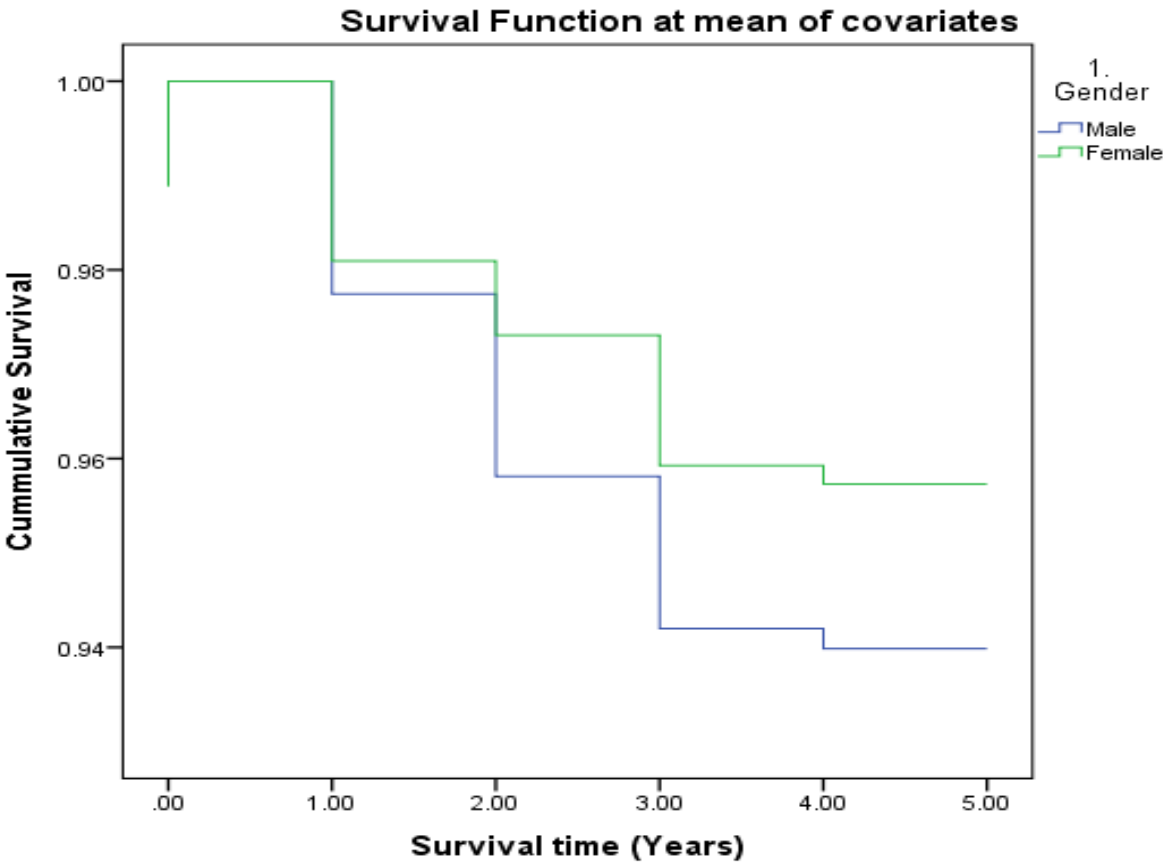
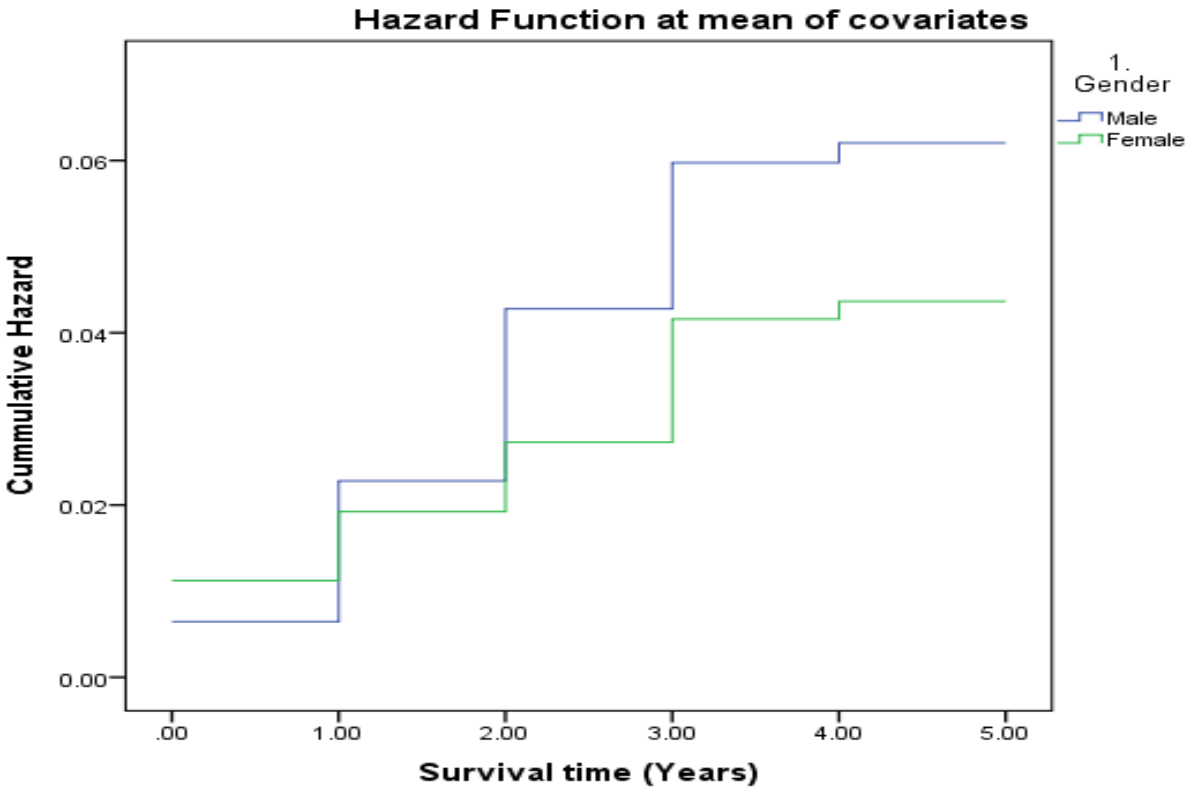


Figure 6 **Illustration of Hazard curve at mean of independent variables**



Comment

Covariates (variables that describe social demographics of the respondent) factored in the regression hazard model to assess relationships between characteristics and survival of study participants included marital status, occupation, education levels and monthly earning.

The covariates; Education (Beyond primary education, Education - No Education); Marital Status (Cohabiting, Marital Status – Widowed); Occupation (Employed & Unemployed); and Occupation (Employed, Housewife, and Casual Laborer) were found to be significant in the survival of persons starting HAART (P-values less than computed chi – square level of significance (0.445).

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 HIV/AIDs care and treatment facilities dedicated for HIV/AIDS persons, serving a diverse population in high HIV-burden settings. In Kenya, the high mortality of HIV persons on ART comparing with 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. 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 evidently high deaths among male persons in ART with advanced stage of HIV disease means that the cohort requires early diagnosis with enhanced counselling, testing and start of HAART.

In Arba Minch Hospital patients, mortality was recorded at 15.4/100 person-years in the first study year [50 – 53]. In Tanzania, a notable and steady reduction in incidences of mortality (35.7 before start of HAART to 17.5 /100 person years) in 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.

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.

The efficacy of ART in reducing cases related to mortality among HIV persons varies across countries mainly as a result of levels of income, adherence to treatment, the quality of HIV care and descriptions of patients on ART [4, 24]. Aspects including HIV staging and start of ART factored in survival model of males and females showed male patients at 31% great risk of dying as compared to females. The great risk of males is attributed to gender descriptions that endear them to become lost-to-follow-up although females who missed clinical appointments and eventually become lost-to-follow-up are similarly likely to die. Female patients however were identified to have enhanced 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 $\chi 2$ value of 3.716 at 0.05 level of significance, the different in probabilities 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]".

The study in Nepal was explicit in giving findings of male HIV persons being at greater risk of dying compared to female HIV persons.

This study similarly showed a 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].

6.1 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. These persons were excluded from the final survival analysis IFF there were no reports of having experienced the event of interest.

Censoring was applied on persons who did not experience event of interest within the time of this study.

6.2 Strengths and Limitations

Strength: 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.

Limitations: 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 the 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.

A study on the reasons for high number of lost to follow ups among males on HAART is critical in addressing factors that exacerbate high mortalities.

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