SURVIVAL OF UGANDA'S HIV POSITIVE SERVICE MEN ON TB TREATMENT

By

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DECLARATION

I, Acleo Ndyabambireki kale declare that this dissertation is my original work and that it has never been submitted for any academic award in this or any other higher institution of learning

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DEDICATION

To the people who have helped and motivated me in various ways to pursue my education and mostly this level. May the good Lord reward you abundantly?

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LIST OF ABBREVIATIONS AND ACRONYMS

AHR	Adjusted Hazard Ratio
AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretrouiral Therapy
BFM	Body Fat Mass
BIA	Bioelectrical Impedance Analysis
BMI	Body Mass Index
CPT	Co-trimoxazole Prophylactic Therapy
EPTB	Extra Pulmonary Tuberculosis
FFM	Fat Free Mass
GMH	General Military Hospital
HIV	Human Immunodeficiency Virus
KARNOFSKY	Patients status
MOH	Ministry of Health
NACP	National AIDS Control programme
P-Pos	Pulmonary Positive
SERVICE MEN	UPDF combats
TASO	The AIDS Support Organization
TB	Tuberculosis
UNAIDS	Joint United National Programme on HIV/AIDS
WHO	World Health Organization

ABSTRACT

This study aimed at investigating factors associated with the survival of Uganda's HIV/TB positive service men on TB treatment in the General Military Hospital (GMH), Bombo army barracks. The source of data was from the clinical and laboratory case reports in the files of patients at GMH between January 2009 to December 2011 sample size of 143 patients. The analysis was made using a time-to-event analysis based on the Kaplan-Meier estimate, the Log-rank Chi-square test and Cox-Proportional Hazard Model.

The results showed that the survival of the HIV/TB patients on treatment was overall low (most survived up to 20^{th} weeks of the initiation of ART treatment). By area of residence, most of the servicemen treated at the GMH came from barracks found in rural areas (37.8%) followed by those in urban barracks (32.8%) while the least were those from the Peri urban barracks (29.4%). Majority of the patients on treatment in GMH were bed ridden.

The survival of the HIV patients in stage 1 and stage 2 was different from those at stage 3 and stage 4 who were at high risk of death compared to those in stages 1 and 2. The survival of the patients with low CD4 of $\leq$ 200 cell/m^3 was different from that of patients with high CD4 of 500cell/mm^3, and those were at high risk of death compared to those with high CD4 of 200cell/mm^3 $\leq$ 500cell/mm^3. Patients who were bed ridden had lower chances of survival compared to those at working stage of Karnofsky. Furthermore, HIV infected TB patients who were drinking alcohol and were on ART and TB treatment had lower chances of survival compared to those who were not drinking alcohol.

Old age is associated with poor survival, whereas being male is associated with better survival. Patients who develop TB prior to start ART their mortality was high with increasing risk of death (52.5%) compared to those who develop TB while on ART (47.5%).

It is recommended that reduction of deaths among HIV/TB patients requires early screening, diagnosis, and faster treatment within 3 months to 8 months for TB infection especially for patients on antiretroviral therapy.

CHAPTER ONE

INTRODUCTION

1.1 Background to the study

This study is about the survival among Human Immune Deficiency Virus (HIV)-positive TB patients among Uganda's service men in General Military Referral Hospital (GMH). The GMH is the only referral hospital in Luwero district and it is mainly used by Uganda's service men. The study is based on the socio- demographic characteristics, disease related factors, wasting and treatment related factors affecting survival among HIV-infected TB patients on treatment.

On a global basis, nine million cases of tuberculosis are registered annually and two million deaths among HIV-TB patients (World Health Organization, 2010). Similarly, the HIV pandemic has been responsible for the increment of deaths and TB incidence since HIV leads to increased risk of developing TB related disease and complicates its diagnosis and treatment (Varma et al., 2009).

The global TB Report 2012 shows that 46% of TB patients were also HIV positive and this increases their mortality rate (TASO, 2013). Nsubuga (2012) argues that TB is the leading cause of death globally among HIV- positive clients and accounts for forty percent (40%) of deaths in sub Saharan Africa.

In Sub-Saharan Africa, Tuberculosis is considered as the leading cause of death among HIV positive people in several countries (Balewgiziesileshi, 2013). HIV therefore has brought several challenges in the control and treatment of tuberculosis at different levels. TB is considered to be a catalyst of mortality and HIV is a leading cause of TB among HIV positive clients living in the Sub Saharan. Franke et al. (2011) argue that HIV infection among people has worsened the global tuberculosis epidemic and in Sub-Saharan Africa, some countries have seventy percent

(70%) of people with TB also being HIV positive and the management of these clients is therefore a public health issue that must be addressed.

In East Africa, HIV/TB infection is still a challenge. For instance in Kenya, 50-60% of the people who are HIV positive were estimated to be co-infected with TB (Ministry of Health Kenya 2006). Tanzania had prevalence of HIV/TB patients of (8.5%) (Ngowi et al. 2008). Similarly Niyongabo et al.(1999) found out that 76.9% of HIV patients were co-infected patients with TB and in Rwanda it was indicated that the rate of TB was at 37% among HIV co- infected patients and TB was ranked as the leading cause of death among Rwandans (Ministry of Health, 2005).

TB and HIV remain leading public health problems in Uganda. Uganda ranks 16 out of the 22 high burden TB countries in the world. In regard to TB, the world Health Organization estimates that 80,000 people develop TB each year in Uganda (209/100,000 population). However, only 50% of these cases are detected currently. On the other hand, the adult HIV prevalence has risen from 6.4% in 2005 to 7.3% in 2011. Nearly half (50%) of the TB cases notified in the country are co-infected with HIV. The dual TB and HIV epidemics increase the burden of one another. On the one hand, HIV is the number one risk factor for one to develop TB disease. On the other hand, TB is the most common cause of death among people living with HIV accounting for 30% of the deaths among this population.

In Uganda the existence of TB and HIV among people is still high and a burden as HIV is still an active developer of TB among infected clients. At present fifty percent (50%) of the TB patients are also infected with HIV MOH-NTLP (2011) and TB is still a leading cause of death among Ugandans with HIV with thirty percent (30%) of all death occurring due to Tuberculosis thus making the survival of these clients low (MOH-NACP, 2012). The causes of the rise in TB cases

in Uganda are mainly due to the deadly association between TB and HIV. The HIV/AIDS pandemic is driving a resurgence of a silent new TB epidemic in the country owing to an increasing association between HIV and TB. TB is now the leading cause of death of people living with HIV in Uganda.

Adatu (2010) argued that tuberculosis is the major health problem in Uganda. About 60% of TB patients in the country are also infected with HIV, which increases their chances of dying if the two diseases are not handled properly. Some people in Uganda describe TB as a disease for the poor and of people with high prevalence of HIV/AIDS. It has been found to mostly affect young adults living in congested areas (Adatu, 2010).

The president of the Republic of Uganda has made a numerous efforts to sensitize the Uganda's service men about HIV/AIDS and TB disease through Ministry of Health and her Partners like National Tuberculosis, WHO, National Reference Laboratory and others. With the objective of ongoing counseling, caring of the Ugandan's services men living healthier and longer hence reducing mortality due to HIV/AIDS and Tuberculosis.

With the information above, there is need to carry out this study to determine the survival of the Uganda's HIV positive service men with TB on treatment in GMH by focusing on the socio-demographic characteristics, disease, wasting and treatment related factors that affect survival among HIV- infected TB patients on TB treatment in GMH.

1.2 Statement of the problem

The government of Uganda has made numerous efforts to sensitize people about HIV/AIDS and Tuberculosis diseases through Ministry of Health and her partners like National Tuberculosis and Leprosy program, World Health Organization, National TB Reference Laboratory, Stop TB and AIDS Control program. In here, clients are given services of counseling, treatment and care with

ongoing counseling, with an objectives of clients living healthier and longer hence reducing mortality rate caused by HIV/AIDS and Tuberculosis.

The factors associated with survival of these clients are still unclear. If factors that facilitate the survival of HIV/TB clients of Uganda's service men continue to be unclear, then survival of HIV/TB clients will remain low. Therefore this study will seek to determine those factors that are associated with the survival of the Uganda's HIV positive service men on TB treatment in GMH will guide policy makers in building the capacity of heather workers to manage patients with TB and HIV / AIDS thus reducing the mortality rate in Uganda's positive service men on TB treatment.

1.3 Objectives of the study

The overall objective of this study was to determine factors influencing the survival of Uganda's HIV infected service men on TB treatment.

Specific objectives

The following were the specific objectives of the study:

1) Determine the influence of socio-demographic factors that affect survival of Uganda's HIV positive service men on TB treatment.
2) Examine the disease related factors associated with survival among HIV positive Uganda's service men on TB treatment.
3) Examine the treatment related factors that affect survival among HIV positive Uganda's service men on TB treatment.
4) Describe the survival outcomes of HIV-infected Uganda's service men on TB treatment.
5) Assess the effects of wasting on survival of HIV-positive Uganda's service men on TB treatment.

1.4 Research Hypotheses

The following were tested hypotheses:

1. Age of the patient has no effect on survival of Uganda's HIV positive service men on TB treatment.
2. Nature of TB disease has no effect on survival of HIV positive service men on TB treatment.
3. Timing of ART has no effect on survival of Uganda's HIV positive service men on TB treatment.
4. Smoking has no effect on survival of Uganda's HIV positive service men on TB treatment.
5. Weight of the patient has no effect on survival of Uganda's HIV positive service men on TB treatment.
6. Stage of HIV of the patient has no effect on survival of Uganda's HIV positive service men on TB treatment.

1.5 Significance of the study

Survival of HIV-infected patients on TB treatment has remained poor in Uganda. Most of the studies conducted have not been focusing on other disease like HIV/AIDS and TB independently and this has been attributed to the existing policy and knowledge gaps that exist.

The few studies conducted on survival of HIV-infected TB patients on TB treatment have been conducted in urban centers or the National Referral Hospital Mulago that are relatively well facilitated compared to Military Referral Hospitals. Therefore, it is vital to carry out this study in GMH and compare the results with those studies carried out in the urban centers like Mulago

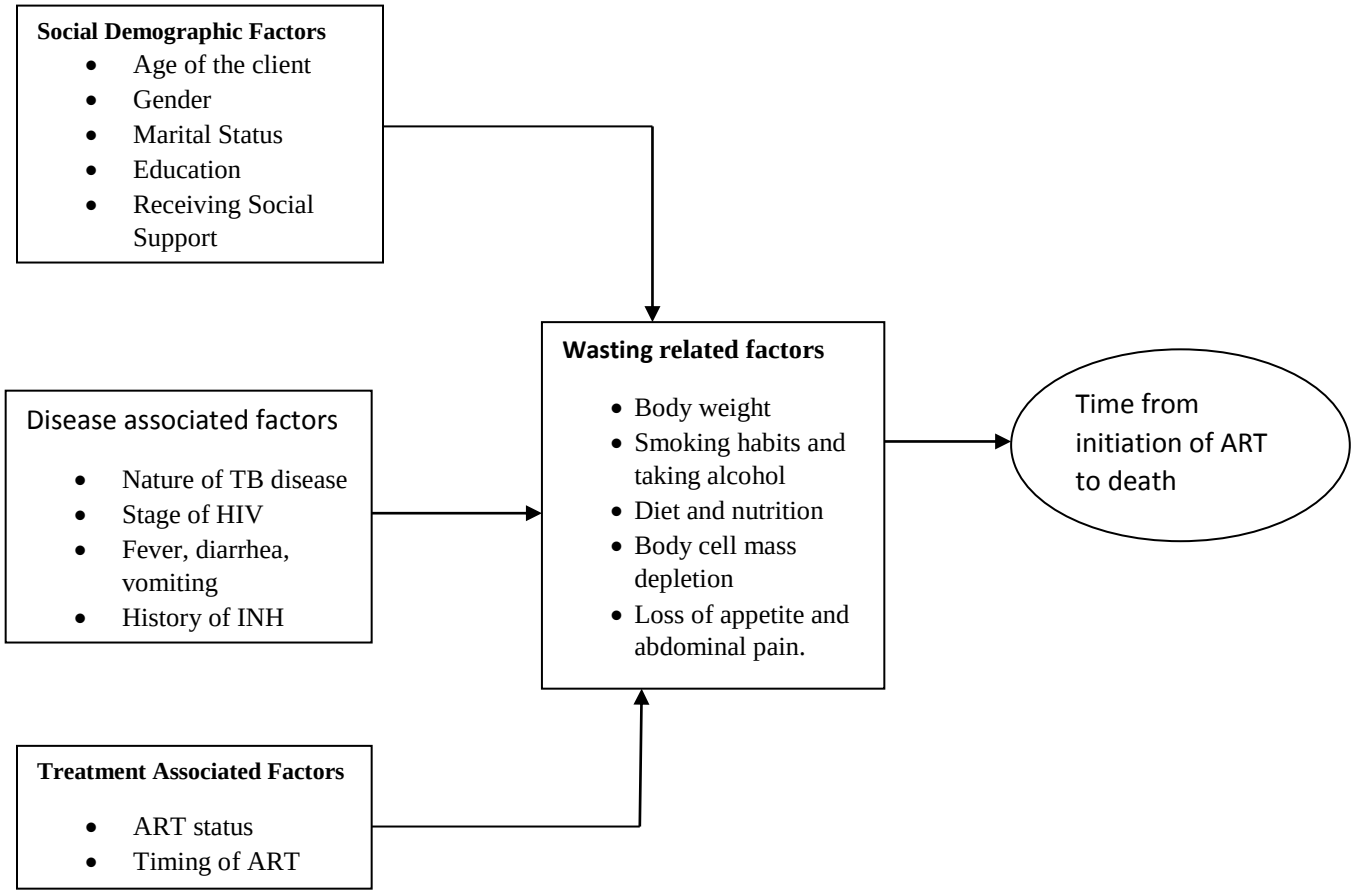
National Referral Hospital in order to develop effective care and support services for HIV-infected TB clients to have improved treatment outcomes and survival.

This study therefore will determine the survival of HIV positive service men infected with TB on treatment in GMH Referral Hospital by looking at socio-demographic, disease, wasting and treatment related factors associated with survival of HIV TB infected patients as to provide evidence to guide care and treatment policies of HIV-infected TB patients within Uganda's service men in General Military Referral Hospital. To the researchers and academia the results of this prove insights regarding factors associated with survival among HIV/TB patient focusing on those who were seeking for care and treatment from General Military Referral Hospital.

1.6 The conceptual Frame Work

The figure on next page presents factors for survival as independent variables, survival of the HIV-infected TB patients as the dependent variables. The independent variables are categorized under several factors for example, socio-demographic factors (age of the client, gender, marital status, occupation and education) treatment associated factors (ART status, Timing of ART, Duration of ART and History of INH) wasting associated factors (age, sex, HIV-status, weight loss, Extent on chest x-ray, smoker, taking alcohol) and Disease associated factors(Nature of TB disease, stage of HIV, CD4 at TB treatment initiation and Karnofsky score) and economic factors (levels of income, area of residents, access to hospital). There is an interaction among these factors as they affect the dependent variable and this determines the survival of HIV-TB patient of Uganda's service men in Bombo General Military Referral Hospital. The outcomes is survival time from initiation of ART to death

Figure1.1: Conceptual Framework



Conceptual framework of survival of Ugandan's HIV- positive service men on TB treatment

1.7 Structure of the Dissertation

The dissertation has been organized into five chapters. Chapter one constitutes the background to the study in relation to general information about TB and HIV, problem statements, study objectives, hypotheses, significance of the study and conceptual framework for Time from initiation of ART to death and patient's characteristics. Chapter two is about the literature that was reviewed. This includes; literature on TB, TB diagnosis, TB and HIV co-infection in relation to time from initiation of ART. Chapter three covers the sources of data that were used in the study, data selection, study variables, statistical data analysis, ethical clearance and study limitations. Chapter four presents the findings and discussions of the study. Chapter five states

the summary, conclusions and recommendations of the study. This dissertation also includes references of the materials consulted during the study and forms that were used in the collection of information and data that was used in the study.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

The chapter presents the literature and studies conducted by different authors about the study objectives presented in sections and subsections.

2.2 HIV TB Prevalence in Uganda

According to WHO (2011) 8.7 million people developed TB worldwide in (2011)13% of people with TB were living with HIV, the interaction of TB and HIV is increasing the burden of both diseases. .It is also widely acknowledged that HIV presents a massive challenge to the control of TB, while TB is one of the common causes of morbidity and the leading cause of mortality in PLHIV (MoH, 2006). An estimated 30% of all deaths among PLHIV are attributed to TB (MoH, 2006). It is therefore, a big challenge especially in the medical circles where efforts have been devised to deal with HIV among TB patients.

2.3 Survival Outcomes among HIV Infected TB Patients

Harries (2007) found out that in sub-Saharan Africa TB diagnosis death among the participants in their study was high in the first two months of TB treatment. This was attributed to several factors that were associated with treatment, disease that affected patient's level of adherence to treatment.

Furthermore, in a retrospective study carried out by Alenmayehu and Debebe (2012) in southern Ethiopia, it was found that all HIV/TB patients on TB treatment were more likely to die at the time of DOTS and this risk was higher in patients at the continuation phase which led to a shorter survival among patients and therefore, the survival probability was lower in HIV positive TB patients (Alemayehu and Debebe,.2012).

Zhang et al. (2012) revealed that despite the fact that China has the most burden of HIV/TB in the whole world there was a problem of limited study on the epidemiology. In the study they carried out to ascertain survival among HIV/TB co-infected patients from four clinics in Guangxi from the month of August 2006 to December 2008,it was found that among the201 HIV/TB co-infected patients included in the study, 47(23.0%) died within 12 months and thus, survival among the participants was rated high (Zhang et al,.2012).

It was further found out by Curran et al.(2012) that the rate of death among HIV/TB co-infected patients was significantly lower among those who started ART treatment earlier compared to those who started the treatment later (Curran et al, 2012). Thus in this study, the survival outcome among patients was linked to timing of ART initiation among patients.

In a study by Mashimbye (2009) carried out in south Africa, the survival outcome among HIV/TB infected patients on ARV rollout between November,2005 and March 2008 was 7.5%percent and at treatment completion, results indicated that mortality was 8.44%. This was because of alcohol consumption, age and marital status that were found statistically significant.

Lastly, Beth et al. (2011) found that 27.5% of the patients died before starting TB treatment and for the patients who survived, 13.6% percent died before completing TB treatment and 42.7% of the patients died during the median days of follow up. This survival outcome was partly associated to limited low utilization of HIV/TB health care points.

2.4 Socio-Demographic Factors and Survival among HIV infected TB Clients

It has been aurged that socio-demographic characteristics of HIV- infected TB patients have a critical bearing on their survival. Manosuthi et al. (2012) found out that clinical characteristics and treatment outcomes among patients with tuberculosis after one year of treatment, 52% were

cured or completed treatment, 19% transferred out, 12% defaulted and 9% were still no-going TB treatment.

In a prospective cohort study by Getahum (2010) risk factors for death and treatment relapse were associated with being female, age ≥ 30 years. This is perhaps so because HIV is most prevalent among females in this age group. Although this is the case, chart reviews in most TB clinics in Uganda reveal that death occurs mostly among males in the same age group.

Bulgiba et al. (2013) found that ethnicity was the only social risk factor among HIV-infected TB patients in Malaysia, patients with ethnicity were 5 times on higher risk of death as compared to the patients without the ethnicity group as other (HR 4.48,95% CI 1.73-11.64)

Mahletsemu et al. (2013) in Addis Abada, Ethiopia, results indicated that employment status, place of residence and gender were some of the significant factors associated with HIV and TB among HIV/TB co-infected persons (Mahlet et al, 2013).

In relation to social support Jaworsky et al. (2011) in their study found that HIV/TB patients who had partners reported receiving support and this increased their chances of survival. Support from partners was in form of ongoing counseling, reminders to take drugs and visiting the health facility as well as providing transport during the days of visitation respondents and identified two main sources of support. HCPs and family and/ or friends HIV/TB co-infected patients also mentioned the possibility of acting as support for other couples in similar situations (Tecimer et al, 2011).

2.5 Disease Related Factors Associated with Survival among HIV infected on TB treatment

Timothy et al. (2010) argued that the primary risk factor for TB recurrence among HIV-infected patients with TB appears to be low CD4Tlymphocyte count, with the risk highest among persons

with a CD4 Tymphocyte count ≤100 cells/mm. In a study conducted by Manosuthi (2009) one hundred forty-two(142) patients randomized into 2 groups equally had a mean body weight of 53kg and it was found that low body weight is an important predictive factor for treatment failure.

Additionally a study conducted in Southern India by Kumar et al. (2011) found that a CD4 count among HIV/TB clients below 200/mm was not statistically associated with a higher mortality rate.

Uria et al. (2012) in a study conducted in India found that two thirds of HIV/TB CO-infected patients were presented with extra pulmonary tuberculosis. The most common form of extra pulmonary tuberculosis was tuberculosis meningitis followed by pleuritis, abdominal tuberculosis, and lymphadenitis cumulative incidence of mortality was 16%, 26% ,39% and 46% at 1, 3, 12 and 24 months respectively.

Zakumumpa (2011) argued that in Uganda the existence of TB among people is associated with HIV and this has claimed many lives of the HIV positive patients even worldwide. In Uganda about 60% percent of HIV positive clients are also co-infected with TB and the case of those who die is high (Zakumumpa, 2011).

Hyun et al. (2010) in their study carried out in Uganda, found that 99% of the participants were having a good Karnofsky score performance (≥80) and they were mildly ill during the recruitment process. He concluded that the number of symptoms among the HIV/TB co-infected clients as well as the energetic status was responsible for the increased morbidity and mortality despite TB preventive therapies.

According to Peus et al. (2013) Karnofsky score refers to a test performed to measure and make a comparison between the function status of a person/patient. This tool is widely used and it described the patients' status basing on the 11 point (Scalepeus et al., 2013).

Lastly in the study conducted by Mahlet et al. (2013) it was found that among the factors that were statistically significant to survival of HIV/TB co-infected clients were WHO stage of HIV (3&4).

2.6 Wasting related Factors Associated With Survival among HIV-infected patients on TB treatment

The high risk of TB in AIDS patients extends to those infected by HIV who have not yet developed clinical signs of AIDS. Alcoholics and intravenous drug abusers are also at increased risk of contracting tuberculosis. Until the economic and social factors that influence the spread of tubercular infection are remedied, there is no real possibility of completely eliminating the disease.

An evaluation of controlled chemotherapy study conducted among the in home and sanatorium patients in south India shows that diet plays a role in treatment of pulmonary tuberculosis. Although the Incidence of wasting has declined since the advent of HAART, weight loss and malnutrition continue to be significant problems in HIV clinical care. Significant and progressive HIV-related weight loss is related to diminished functional capacity, increased risk for secondary infection, hospitalization and by itself can be an independent cause of death. Those with body cell mass depletion were not as healthy as those without body cell mass depletion in terms of immune status as indicated by lower CD4 counts (Vanltallie et al, 1990).

The WHO uses BMI to grade nutritional status (wasting) of adults in the following manner: mild malnutrition (17.00<BMI <18.49), moderate malnutrition (16.00 <BMI <16.99), and severe malnutrition (BMI < 16.00). Several studies have been conducted on wasting in pulmonary TB in relation to TB-HIV co infection. However, there are limitations and differences in the findings due to cofounders such as alcohol intake, smoking, prior nutrition counseling of the subjects, dietary practices to mention but a few. In one short term clinical trial, nutrition counseling with or without oral supplementation achieved a substantial increase in energy intake in about 50% of malnourished HIV-infected patients. However further studies were needed to evaluate long-term effects, these findings suggest that nutrition counseling has an important role in the management of malnourished HIV-infected patients but research to support such findings is minimal as evidence based nutrition interventions are lacking. In China, a study of more than 42,000 elderly persons found that TB incidence was significantly lower in overweight persons than in normal-weight controls. This can otherwise suggest an increase in TB in the wasted subjects or the otherwise normal weight subject therefore, not only does TB cause wasting but wasting can also be a precursor of TB ending in a vicious cycle of under nutrition and TB infection (Mupere et al, 2012).

Nutritional changes during and after tuberculosis treatment has not been well described. We therefore determined the effect of wasting on rate of mean change in lean tissue and fat mass as measured by bioelectrical impedance analysis, and mean change in body mass index during and after tuberculosis treatment. In a prospective cohort study of 717 adult patients, BMI and height-normalized indices of lean tissue and fat mass as measured by BIA were assessed at baseline, 3, 12, and 24 months (Zalwango et al, 2012).

Mupere et al (2014) found out that wasted tuberculosis patients regain weight with treatment but the type of gain differs by gender and patients may remain underweight after the initial phase of treatment.

In South Africa researchers came to a conclusion that primary healthcare clinic attendees need evidence-based information on the detrimental effects of alcohol consumption on HIV infection one of which detrimental effect might be wasting in TB HIV co-infection which questions this study serves to answer.

Weight loss among those with TB can be caused by several factors, including reduced food intake due to loss of appetite nausea and abdominal pain; nutrient losses from vomiting and diarrhea metabolic alterations caused by the disease. Although malnutrition is associated with tuberculosis, there have been few studies addressing nutritional status in HIV-infected adults with tuberculosis. These studies have been limited to assessment of body weight and serum albumin concentrations. A recent study from Burundi among adults with tuberculosis, including pulmonary, extra-pulmonary and disseminated infection, suggests that those infected with HIV have significantly lower weight, BMI and fat-free mass compared with individuals without concurrent HIV infection (Glenn et al, 2010).

As measured by bioelectric impedance analysis, 58 (31%) of 187 enrolled HIV+ men had significant body cell mass depletion at some point during the study, of who 23 subsequently lost at least an additional 5% of body cell mass in the 6 months between any two consecutive study visits. This additional body cell mass depletion was associated with significant increase in fatigue, global distress depressive Symptomatology, and reduced life satisfactory.

Expressing fat-free mass and body fat mass as percentages of body weight or by weight is un-satisfactory. Tall patients with protein energy malnutrition can exhibit value for FFM and BFM similar to those of shorter well-nourished individuals (Vanltallie, 1990).

Wasted tuberculosis patients regain weight with treatment, having appetite, stop smoking and taking alcohol this reduce the mortality rate of patients and this is in line with the literature study by (Muperel et al , 2012).

2.7 Treatment Related Factors Associated With Survival among HIV-infected on TB treatment

In a study comparing earlier versus later start of ART in HIV infected adults with tuberculosis, it was confirmed that initiating ART two weeks after the start of tuberculosis treatment significantly improved survival among HIV infected adults with CD4 +T cell counts of 200 per cubic millimeter or lower (Blanc et al., 2011).

Furthermore it was been confirmed that ART(Antiretroviral Therapy) reduced mortality among individuals with low CD4 counts and improved retention in care, regardless of CD4 count (Mugabo et al ,2011).

Similarly according to the study carried out by Varma et al. (2009) in Thailand, it was found that one of the factors associated with survival for HIV/TB patients was use of ART as the treatment. However, he added that research has to be done to confirm that early start of ART among HIV-TB patients increases chances of survival.

In addition, Harries et al. (2009) in their study carried out in Sub-Saharan Africa, argued that ART treatment needs to be started by the HIV/TB client immediately after TB diagnosis and this as a result of discovering that death among the participants in their study was high in the first two months of TB treatment.

Furthermore, it was revealed by TB- TASO (2013) that early initiation and diagnosis of HIV/TB clients on ART facilitates survival and this can be done through the creation of linkage

facilitations at the health center to oversee the life state of the clients in order to ensure that there is adherence to treatment which saves the HIV/TB client (TB -TASO, 2013).

Wehbe et al. (2013) argued that the duration of ART is key in determining survival among HIV-TB Co-infected patients since it reduces mortality. In their study Cortes et al. (2013) found that 68% of HIV/TB co-infected patients received ≥180 days of the ART therapy, and there was a decreased risk of death among participants but this was due to other factor like timing of ART among patients, level of CD4 Count among others. They concluded however, that the effect of duration of ART treatment in relation to ART imitation on mortality needs to be studied.

According to Granich et al. (2010) INH Prophylaxis acts as preventive method of spreading TB and reduces the risk of active TB, the incidence, prevalence and transmission among members in the community. In a study carried out by Heather et al. (2007) to investigate the impact of isoniazid prophylaxis on mortality as well as incidences of TB among children living with HIV, it was found that mortality was low among participants under isoniazid prophylaxis and the results further confirmed a low TB incidence among isoniazid group. This led to a conclusion that survival benefit was associated with early prophylaxis with isoniazid among children co-infected with TB

Padmapriyadarsin et al. (2011) argued that INH prophylaxis if taken daily for 6 months, reduces the incidence of TB by about two thirds among HIV-TB patients and the most widely recommended regimen for TB prevention treatment is isoniazid 300 mg taken on a daily for 6months. However according to the WHO guidelines (2010) the use of 6H regimen is recommended and with 36H that is 3 years of isoniazid but this entirely depends on the available local need as well as resources.

According to Swaminathan et al. (2000) early screening as well as treatment of TB among HIV/TB clients was mentioned as one of the factors that can increase survival among HIV/TB patients. They added that early treatment of active TB makes the patient able to survive and reduces chances of spreading the rate of death among other clients. It was further emphasized that there is need to develop a comprehensive TB screening program at hospital and health centers within the country to effect screening and early treatment (Swaminathan et al., 2000)

Lastly, community sensitization about TB and HIV/AIDS need to be carried out for especially the co-infected patients, this has to be accompanied by TB prevention care and support services done at the health facility during the clinic days or at the community drug distribution points.

The above information is about the literature that was reviewed. This includes; literature on TB and HIV/AIDS, HIV/TB diagnosis, conclusions and recommendations on TB/HIV co-infection patients in relation to time from initiation of ART.

CHAPTER THREE

METHODOLOGY

3.1 Introduction

This Chapter presents the methodology that was adopted in the study based on the objectives. It discusses the source of data, variable description and their measurements, data analysis, regression diagnostics, ethical considerations as well as the study limitations.

3.2 Sources of Data

Data from clinical and laboratory case reports in the files of patients in GMH has been used in this study. Most of the data had already been captured in electronic form. This study selected out only data of servicemen at GMH who were HIV positive on TB treatment between January 2009 and December 2011.

3.3 Variables and their Measurements

The following were the Variables and their Measurements that have been included in the study.

Table 3.1: Independent variables

Variable	Definition	Measurement	Type
Age	The age of patients who are HIV/ TB positive on TB treatment in GMH	Years	Continuous
Gender	Refers to a female or a male HIV/TB patient on treatment	Male or Female	Categorical
Diagnostic category	Diagnostic result of the TB	Pulmonary TB Extra-pulmonary TB	Categorical

Table 3.1: cont'd

Education level	Informal Formal	levels	Binary
Social support	Receiving support	Yes No	Binary
Marital status	Type of union	Married ,single, separated, widow , cohabiting	Categorical
Occupation	Deployment status	Inactive force In reserve force	Binary
Duration on Anti retroviral therapy	Time patient has been on Anti retroviral therapy(ART)	Numerical	count
History of INH	History status for INH	Ever had INH prophylaxis Never had INH prophylaxis	Binary
Nature of TB disease	Type of TB	Pulmonary TB or Extra Pulmonary TB	Binary
Stages of HIV at initiation of ART	WHO HIV Stages, stage 1,stage2,stage3 and stage4	Stages from stage one to stage four of HIV	Ordinal
CD4 at Tb treatment initiation	Most current CD4 count	Numerical	Count
Weight of the patient	Under weight Normal weight	Nominal	Nominal
Smoker habit of the patient	Patients smoking characters	Smokers Non-smokers	Binary
Drinking alcohol	Alcohol behavior	Drinks Not-drinking	Binary
Over sweating due to TB	Sweating at night because of the disease Not sweating at night because of the disease	Over sweat at night Not sweating at night	Binary
Extent on chest X-ray	Current X-ray use service	Uses X-rays Non users	Binary
Karnofsky score	Patients characters	Working, Ambulatory, Bed-ridden	Nominal

3.4 Dependent variable

The dependent variable was the time from initiation of ART to death.

3.5 Data Analysis

A survival data analysis approach was adopted in the investigation using Stata 12. Prior to the analysis, a failure and time variable were generated. The failure variable represents the status of survival for all patients and it was denoted by 1, patients who had died where coded by zero 0.The analysis was carried out at three levels namely univariate, bivariate and multivariate analysis. At the univariate analysis patient's characteristics were summarized using frequency distribution tables.

At bivariate analysis, log-rank test was used to compare overall mortality rate between the two groups the log-rank test takes the form

$$\chi^2 = \frac{(O_1+E_1)^2+}{E_1}\frac{(O_2+E_2)^2}{E_2} \text{---------- (3.1)}$$

where

n_{1t} were at risk of death at time t in group 1

n_{2t} were at risk of death at time t in group 2

d_t time to death

O_1 were total death in 1

O_2 were total death in 2

$$e_{1t} = \left[\frac{n_{1t}}{(n_{1t}+n_{2t})}\right] * d_t$$

$$E_1 = \sum e_{1t}$$

$$E_2 = O_1 + O_2 - E_1$$

The probability of Patient survival was summarized using the Kaplan-Meier estimate

$$St_{(j)} = d_{j=1}^{i-1}(1- d_j/r_j) \text{---------- (3.2)}$$

Where

r_i= were the patient at risk of death at i^{th} time.

d_i= were the number of patient die at $t_{(i)}$

The Cox-proportional hazard model was used in determining the relationship between the time from the initiation of the treatment to censored that is death, or competition of treatment. The Cox-proportional hazard model was the most suitable general regression model because it was not based on any assumptions concerning the nature or shape of the underlying survival distribution. The model assumes that the underlying hazard rate is a function of the hazard function.

The hazard function model takes the form

$$h\left(\frac{t}{x}\right) = h_o(t)\exp(b_1x_1 + b_2x_2 + \cdots + b_kx_k) \quad \text{.....(3.3)}$$

Where X_1 ... X_k are a collection of predictor variables and h_o(t) was the baseline hazard at time t, representing the hazard for a person with the value 0 for all the predictor variables.

h(t) was the hazard function at time t

$h_{o(t)}$ was the baseline hazard for individual when the value of all the independent variables.

χ_i were the independent variables

b_i were the coefficients

3.6 Regression Diagnostics

Three diagnostic tests were performed on the fitted Cox-PH model. Firstly, the assumption of constant proportional hazard time was estimated based on the diagnostic test and assumption to test for the proportionality of the model as a whole (Grambsch & Therneau, 1994). If the tests in the table are not significant at 5% level, then proportionality cannot be rejected and hence there was no violation of the constant proportional assumption.

Secondly, the link test was used to test the appropriateness of using the Cox PH regression model (Mackinnon, 1992). The link test investigated whether the Cox PH regression model was the correct specification for the outcome variable and whether the Cox PH regression was explained by the linear combination of the predictors. For this to hold, the result for the Hat-statistic was supposed to be significant ($p < 0.05$) if the Cox PH regression model was appropriate and at the same time, the result for Hat- squared statistic would not be significant to verify that no additional variables were significant ($p > 0.05$), unless by chance (Rogers, 1994).

3.7 Limitations of the study

Data was got from clinical and laboratory case reports in the files of patients which patients I never got a chance to observe and interact with, this limited the research to only the available information hence affecting the scope of the study.

Data was availed from the electronic data base and this data was collected and stored for other purposes other than this research. Hence, key information that would be resourceful to this research could have been missed which may have led to some errors in the study.

Data was obtained from all the HIV/TB co-infected patients who were receiving HIV comprehensive care from GMH. Hence, data concerning those HIV/TB Patients not on treatment and those on partial treatment was not captured. This may have caused bias in results as well as errors in the study.

This information was obtained from the old files of patients some of which had missing information. This may have contributed to inaccuracies in the study.

This being the first study conducted about the subject in GMH, there was limited access to vital information, research materials, statistics and this prolonged the research period the planned time in a bid to acquire this new information.

3.8 Ethical Issues

Because the data used was secondary, the researcher sought for a letter of introduction from the school of statistics and planning in order to obtain the data from GHM the official producers of the data. Confidentiality of the information pertaining to the dataset was ensured in the study that GHM provided filtered dataset without identifiers.

CHAPTER FOUR

SURVIVAL OF HIV/TB POSITIVE PATIENTS ON TB TREATMENT

4.1 Introduction

This chapter presents the findings based on the objectives and it focuses on the survival outcome, socio-demographic related factors, disease related factors, wasting related factors and the treatment related factors that affect survival among HIV infected TB patients on TB treatment in GMH.

4.2 Background characteristics for the Respondents

Table 4.1 indicates the respondents characteristics of the study.

Table 4.1: Distribution of patients by Social-demographic, Disease, Wasting, Treatment related factors

Variables	Category	Sample size (n=143)	Percentage (%)
Area of Residence	Rural	54	37.8
	Urban	47	32.8
	Peri-Urban	42	29.4
Receiving social support	Yes	70	49.0
	No	73	51.0
Gender	Male	83	58.0
	Female	60	42.0
Marital status	Married	69	48.3
	Single	26	18.2
	Separated/divorced	17	11.8
	Widow	20	14.0
	Cohabiting	11	7.7
Deployment and location	In actives service	118	82.5
	Reserve force	25	17.5
Stage of HIV at initiation of treatment	Stage 1	3	2.1
	Stage 2	19	13.3
	Stage 3	90	62.9
	Stage 4	31	21.7

Table 4.1 cont'd

CD4 count on treatment	$\leq 200\ cells/mm^3$	89	62.2
	$200 \leq 500 cells/mm^3$	32	22.4
	$\geq 500 cells/mm^3$	22	15.4
Karnofsky	Working	40	28.0
	Ambulatory	18	12.6
	Bed ridden	85	59.4
Taking alcohol	Yes	81	56.6
	No	62	43.4
Weight	Under weight	85	59.4
	Normal weight	58	40.6
Smoker	Yes	75	52.5
	No	68	47.5

Table 4. 2: Age of the patients

Age	**n**	**Median**	**Std-dev**	**Min**	**Max**
	143	38.13	14.68	18	85

The distribution of TB patients by selected background characteristics is displayed in Table 4.1. By area of residence the results shows that most of the servicemen treated at the GMH came from barracks found in rural areas (37.8%) followed by those in urban barracks (32.8%) while the least were those from the peri urban barracks (29.4%).

The distribution shows that most servicemen treated at GMH were in active service (82.5%). In regard to marital status almost half (48.3%) of servicemen were married followed by the single servicemen (18.2%) and lastly those cohabiting (7.7%).

In addition the distribution shows that there were more male servicemen treated at GMH (58%) compared to female service men (42%). Patients on the TB treatment at GMH in stage3 ($\geq$ 200 cells/mm^3) of HIV had the highest percentage of 62.9% followed by those in Stage 2(200$\leq$500cell/mm^3) with 22.4%.

The distribution also indicates that patients on treatment in GMH at bed ridden stage of karnofsky were the majority with 59.4% followed by those at working stage with 28%. The distribution shows that most of the servicemen treated at the GMH were smokers with 52.5%.

4.3 Survival outcomes of HIV infection TB patients

An analysis was carried out between the selected background characteristics and dependent variable (Area of residence, Gender, Education level, Religion, Marital status, Receiving support and Deployment). The results are displayed in Table 4.2.

Results were obtained basing on the detailed of socio-Demographic factors (area of residence, gender, education level, religion, marital status, receiving support and occupation or deployment location), treatment (ART status, starting ART, History INH), Disease related factors (nature of TB, pulmonary, stages of HIV, CD4 treatments, karnofsky, fever, diarrhea, vomiting, cough, over sweating at night) and Wasting related factors(wasting, sex, weight, X-rays status, smoker, taking alcohol, Appetite status) that affect the survival of HIV patients on TB treatment.

Among the socio-Demographic related factors, the receiving of social support, area of residence and the occupation or deployment of the service men, had an effect on the survival of the Uganda's service men and the rest were not. And those include gender, marital status, education level and age. Table 4.3: presents the results.

Table 4. 3: The relationship between Social-demographic related factors and time from initiation of ART to death.

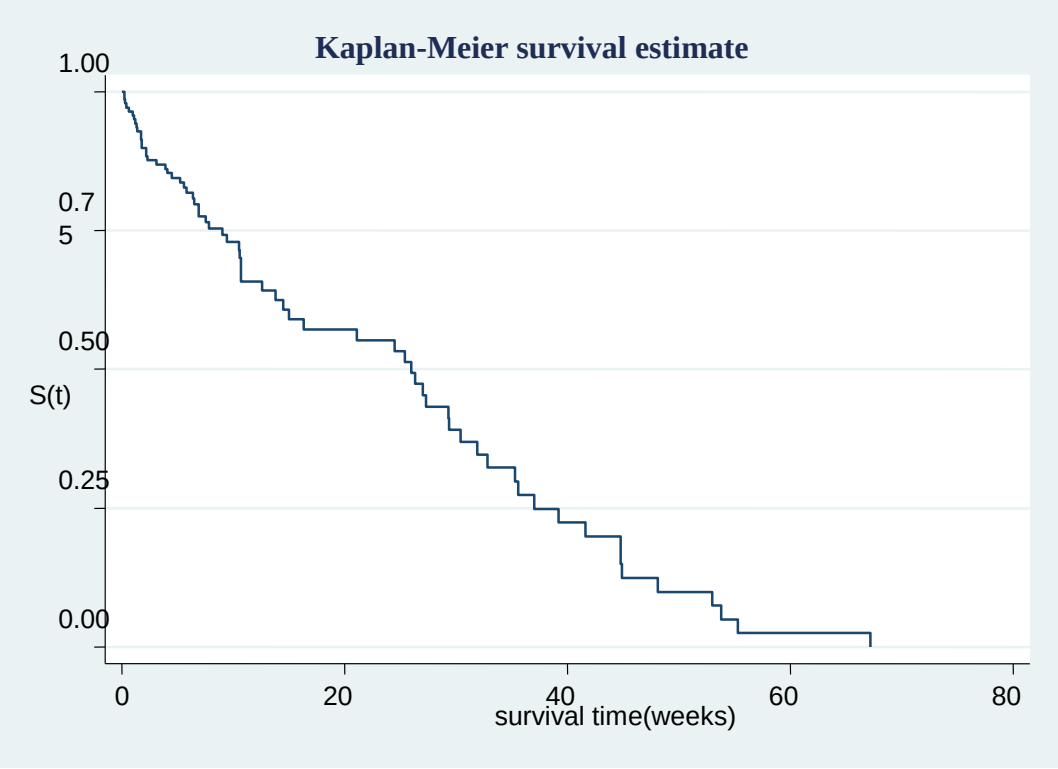
Variables	Category	Sample size	Number of patient who die	Expected death	χ^2	P-value
Area of Residence	Rural	54	26	14.6		
	Urban	47	17	21.7		
	Peri-Urban	42	24	30.7		
					12.5	0.00
Gender	Male	83	42	45.1		
	Female	60	25	22.0		
					0.7	0.41
Education level	Informal	64	31	28.6		
	Formal	79	36	38.4		
					0.4	0.54
Religion	Catholic	47	22	20.7		
	Protestant	29	15	9.2		
	Sevens day	18	11	12.5		
	Muslim	26	14	18.0		
	Other specify	23	5	6.6		
					5.5	0.24
Marital status	Married	69	34	41.8		
	Single	26	14	7.7		
	Separated	17	6	4.4		
	Widower	20	9	8.5		
	Cohabiting	11	4	4.6		
					8.5	0.09
Receiving support	Yes	70	30	26.2		
	No	73	37	40.8		
					10	0.32
Deployment	In service force	118	49	40.6		
	In reserve force	25	18	26.4		
					6.0	0.01

The survival function for patients living in the rural, urban and Peri-urban area was the same. The married, single, separated and those who were in relationship had a different survival function and those who were married had a higher risk of death compared to those in other marital status. The survival function for patients who were in active services was the same with servicemen in reserve force service with those in active services being at higher risk of death compared to those in reserve force service.

4.4 The overall survival of HIV/TB positive

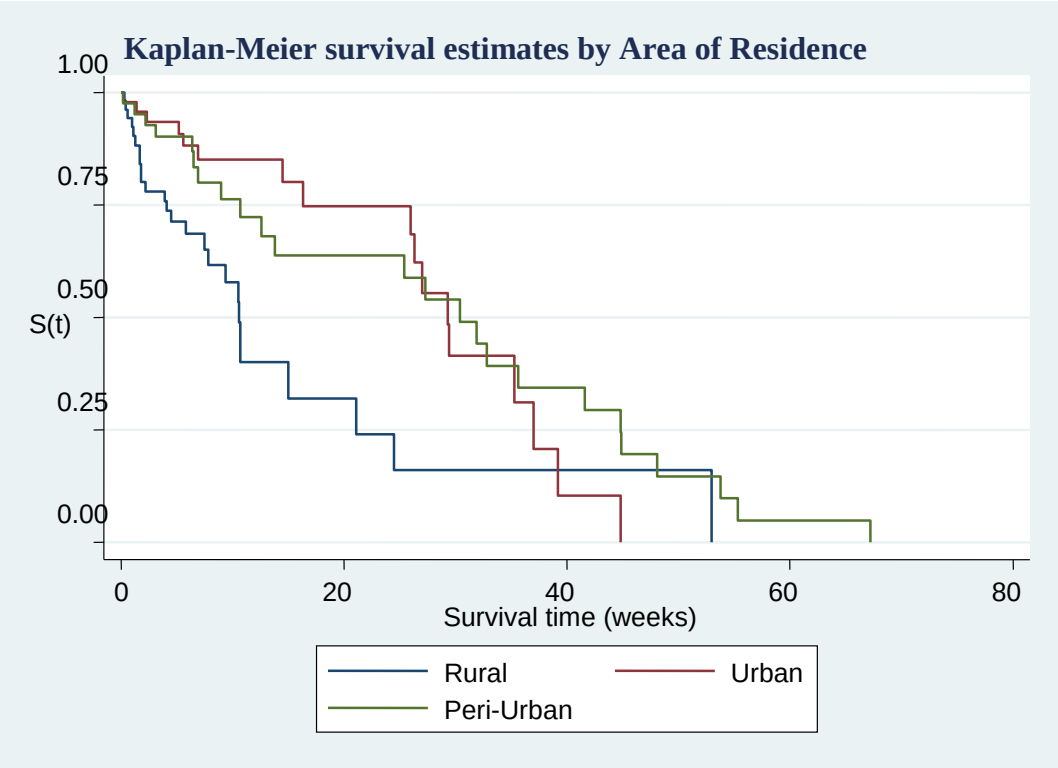
Figure 4.1 shows the overall survival of HIV/TB positive patients on TB treatment from time of ART initiation to death.

Figure 4.1: Overall survival of HIV positive TB patients



From the Figure 4.1 it can be observed that the survival of HIV/TB patients on treatment was overall low. For example most survived up to 20th weeks.

Figure 4.2: Kaplan-Meier survival estimates by Area of Residence



The results from Figure 4.2 show that service men in urban areas of residence were more likely to survive than those in rural and peri-urban areas. This may be because of distances, poor health service, care and treatment, for patients in rural and peri urban areas compared to their counterparts in urban areas. Patients from different areas of residence had a different survival function. With those from rural area (37.8%) being at high risk of death followed by those in urban areas (32.8%). It was also noted that the hazard ration for patients in rural areas was also high (1.000) to that in other areas of residence with urban (0.399) and peri-urban (0.431).

Figure 4.3: Kaplan –Meier survival estimates by Martial status

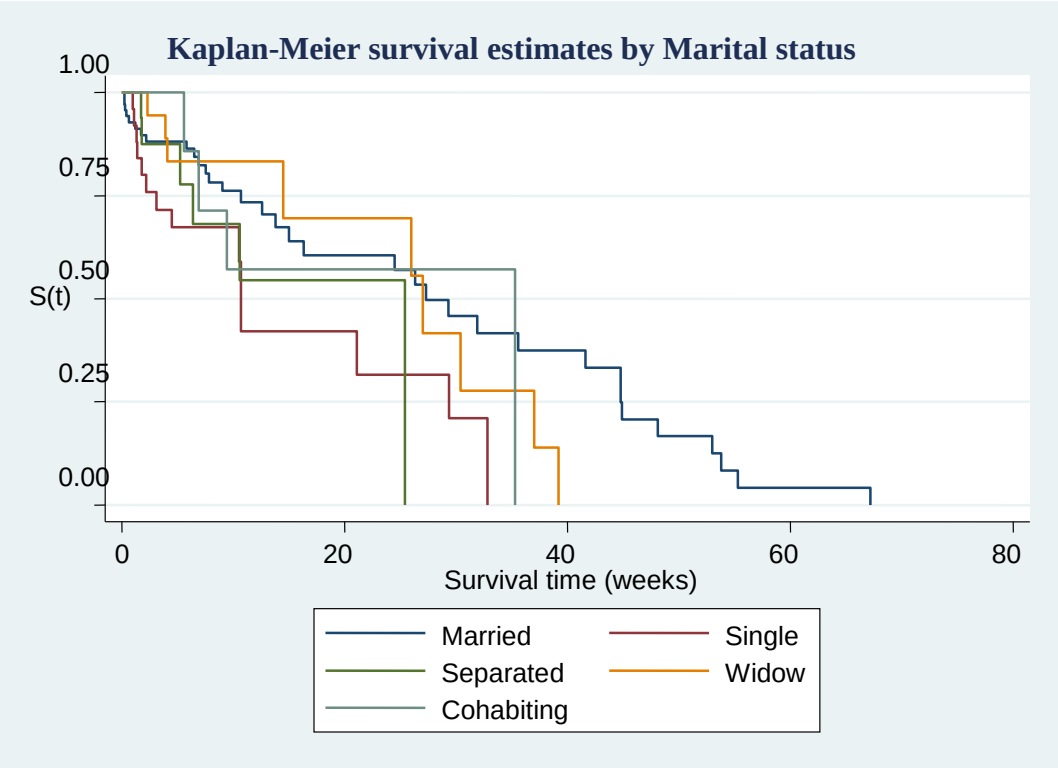


Figure 4.3 shows that co-infected patients on ART and TB treatment that were married were more likely to die of HIV/TB disease compared to those in other categories. The married, single, separated and those who were cohabiting had different survival function from each other, with the married having the highest risk of death (48.3%) followed by the single (18.2%) and lastly those in a relationship (7.7%). Also it was noted that single patients on TB treatment had a high increasing hazard of 2.439 which was associated with poor survival.

Figure 4.4: Kaplan –Meier survival estimates by Education level

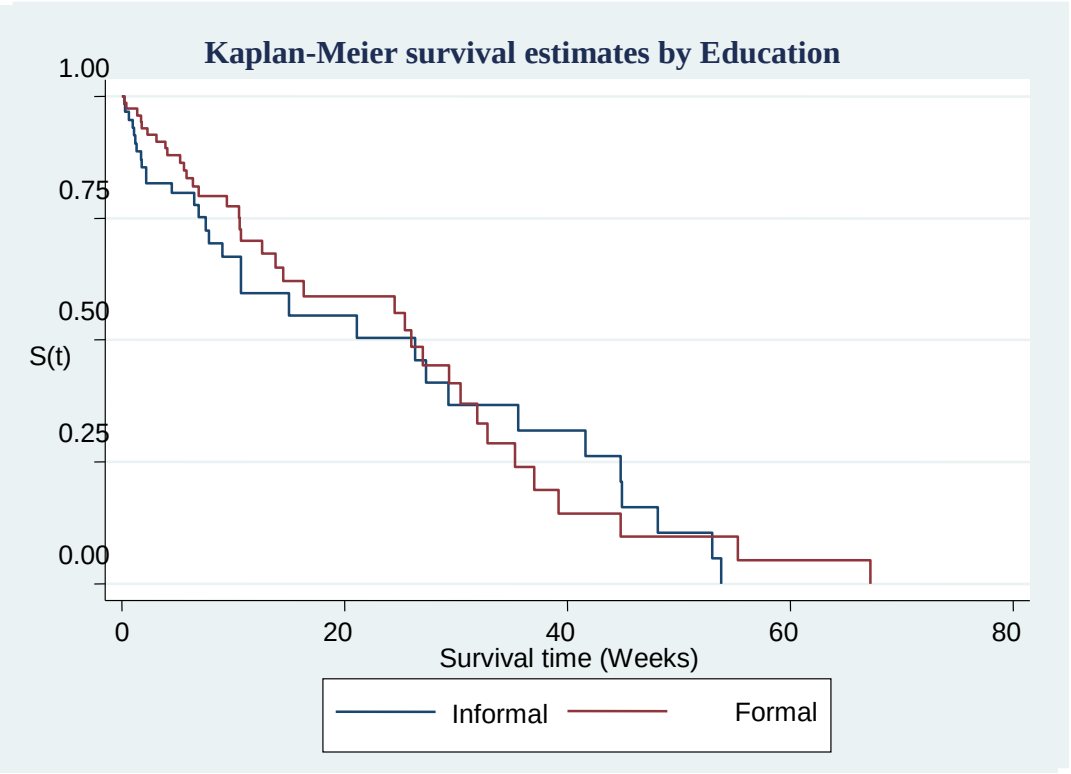
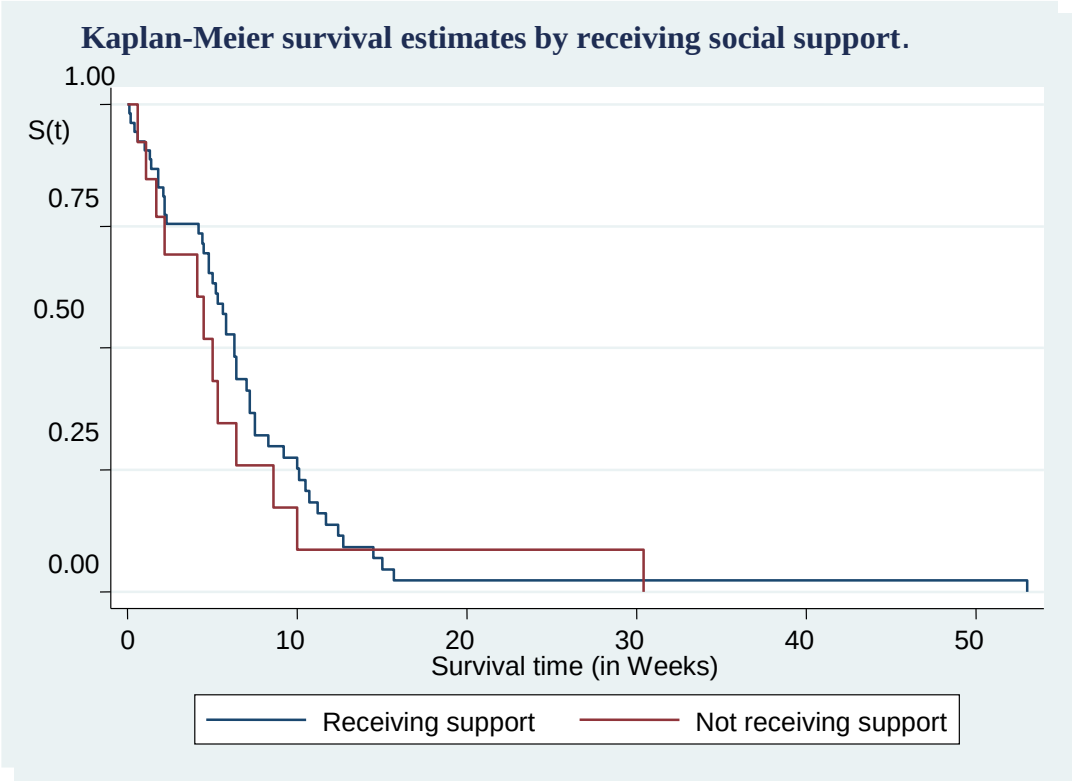


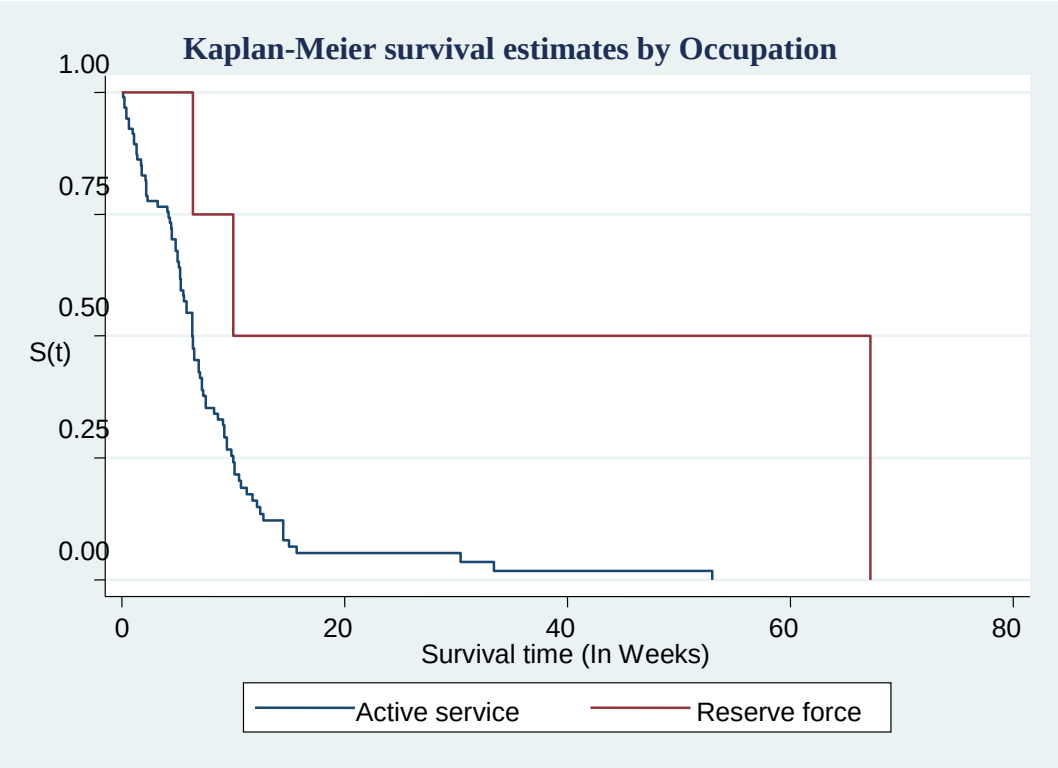
Figure 4.4 Shows that Uganda's service men who had formal education had higher chances of survival compared to those with Informal education. It was also noted that patients with informal and formal education had different survival function with informal education patients having high risk of death (55.2%).

Figure 4.5: Kaplan –Meier survival estimates by receiving social support



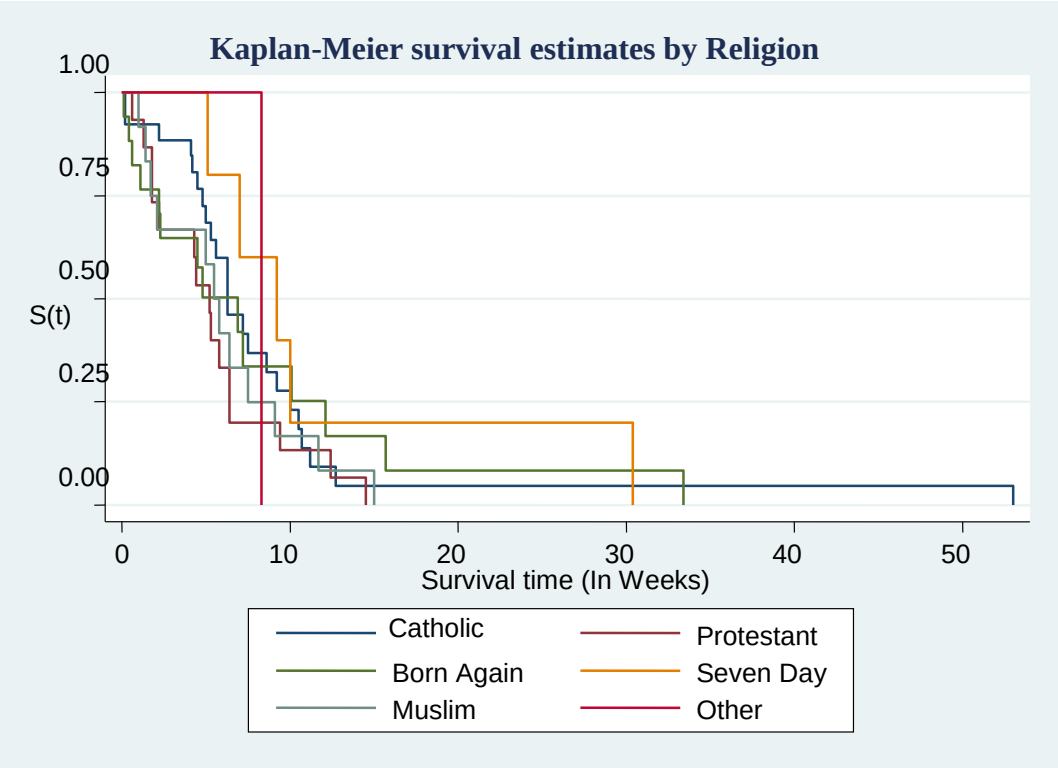
The results in Figure 4.5 shows that patient who were receiving social support on ART and TB treatment were more likely to survive compared to those who were not receiving social support on ART and TB treatment. The survival function of patients receiving support and the patients that were not receiving support were different. Patients who were not receiving support were at higher risk of death (51%) compared to their counterparts who were receiving support (49%).

Figure 4.6: Kaplan –Meier survival estimates by occupation



From Figure 4.6 it shows that co-infected patients on ART and TB treatment in reserve force had higher chances to survive compared to those in actives force. It was also noted that the survival function of patients in actives service force and reserve force was different.

Figure 4.7: Kaplan –Meier survival estimates by Religion



The Figure 4.7 shows that Catholics were more likely to die of HIV/TB disease compared to those in other categories.

This study also found out that survival among HIV/TB co infected patients depend on social support. This finding is centrally to the literature and findings by Newmeyer et al. (2011) where HIV/TB co infected patients who reported receiving support and this increased their chances of survival, therefore despite the existence of social support, death among HIV/TB co infected clients occurs.

4.5 Disease related factors

Among the disease related factors as per the study it was found out that karnofsky score (Bed-ridden), having Fever, Nature of TB, pulmonary TB, stages of HIV (WHO, HIV stage) the CD4 count at treatment initiation, over sweating at night and constant Cough of more than two weeks

had significance effects on the survival of HIV positive service men on TB treatment. Table 4.4 presents results:

Table 4. 4: The relationship between Diseases related factors and Time from initiation of ART to death.

Variable	Category	Sample size n=(143)	Number of patient who die	Expected death	χ^2	P-value
Type of TB	Pulmonary TB	100	43	36.2		
	Extra-Pulmonary TB	43	24	30.8		
					3.1	0.08
Stages of HIV at treatment	Stage 1	3	3	5		
	Stage 2	19	16	14.6		
	Stage 3	90	34	35.6		
	Stage 4	31	14	11.7		
					1.8	0.62
CD4 count at treatments	≥ 200 cell/mm^3	89	32	35.1		
	≤ 200 cells/mm^3	32	21	17		
	≥ 500 cell/mm^3	22	14	15		
					1.36	0.51
Karnofsky	Working	40	29	29.6		
	Ambulatory	18	10	9		
	Bed ridden	85	28	28.4		
					0.13	0.94
Fever	Yes	118	47	41.3		
	No	25	20	25.7		
					2.6	0.11
Diarrhea	Yes	78	26	23.5		
	No	65	41	43.5		
					0.47	0.49
Vomiting	Yes	78	27	23.6		
	No	65	40	43.4		
					0.85	0.36
Constant Cough of more than two weeks	Yes	116	49	43.6		
	No	27	18	23.4		
					2.3	0.13
Over Sweating at night	Yes	114	53	57.5		
	No	29	14	9.6		
					2.5	0.11

The survival function of the patients in stage1 and stage 4 was different, and patients at stage 3 and stage 4 were at high risk of death to those in stages 1 and 2. The survival function of the patients with low CD4 of ≥ 200 cell/mm^3 were different from those patients with high CD4 of 500cell/mm^3, many of patients with ≥200cell/mm^3 were at high risk of death compared to those with high CD4 of 200≤ 500cell/mm^3. Patients who were Bed ridden had lower chances of survival compared to those at working stage of Karnofsky. The patients who had constant fever were at higher risk of death compared to those with no fever and their survival function was different.

Figure 4.8: Kaplan –Meier survival estimates by Nature of TB

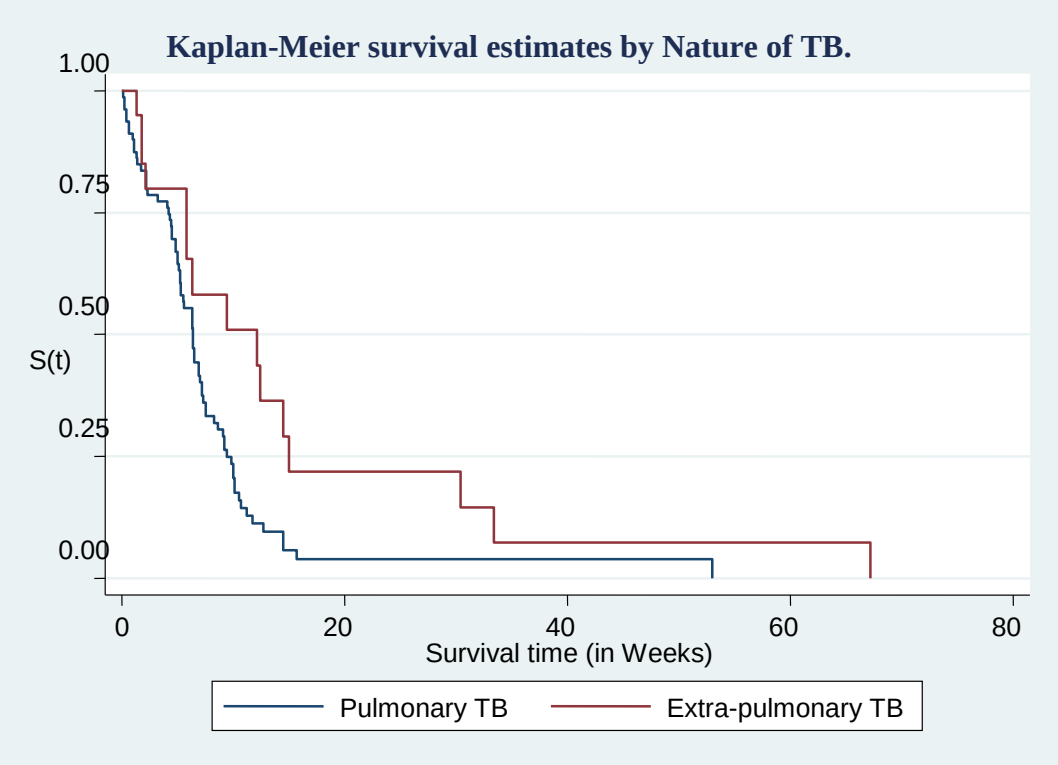
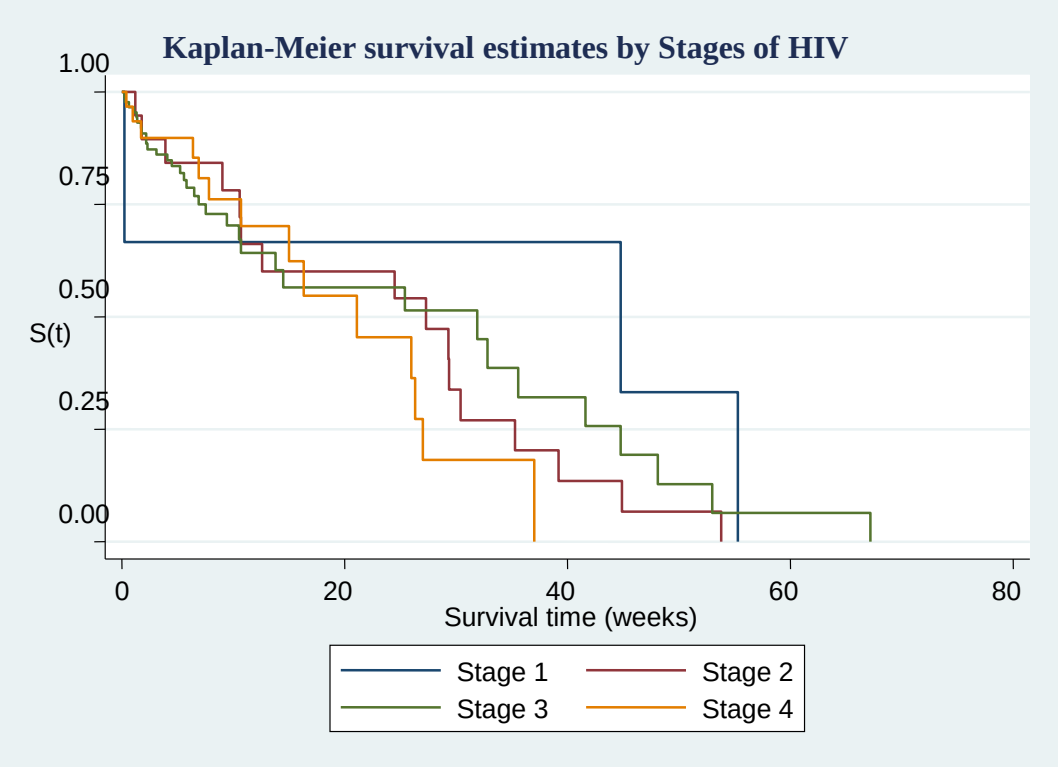


Figure 4.8 shows that HIV/TB co-infected patients on ART and TB treatment with pulmonary TB had lower chances of survival compared to those with Extra-pulmonary TB. Also the survival function of patients with pulmonary TB were different from that of patients with extra-

pulmonary TB and patients with pulmonary TB were at higher risk of death compared to those with extra-pulmonary TB.

Figure 4. 9: Kaplan –Meier survival estimates by Stage of HIV



The Figure 4.9 Shows that patients at stage 1 and stage 2 of HIV on ART and on TB treatment were more likely to survive compared to those in stage 3 and stage 4 of HIV. The survival function of the patients in stage1 and stage 4 was different, and patients at stage 3 and stage 4 were at high risk of death compared to their counterparts in Stage 1 and 2.

Figure 4. 10: Kaplan –Meier survival estimates by CD4 treatments

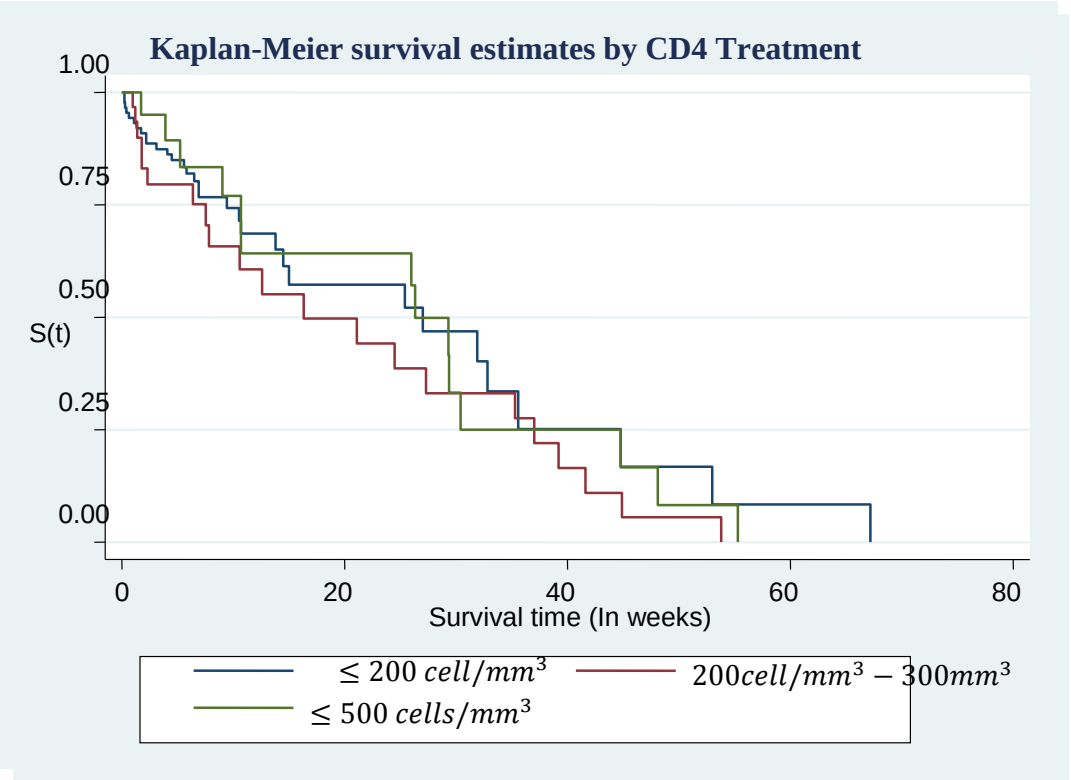


Figure 4.10 indicates that patients with a CD4 count less than 200 cells/mm^{3}had lower chances of survival compared to those patients with CD4 count $300 cells/mm^3 \leq 500 cells/mm^3$. The survival function of the patients with low CD4 of less than 200 cells/mm^3 was different from those patients with high CD4 of 500cell/mm^3. Patients with low CD4 count of less than 200cell/mm^3 were at higher risk of death compared to those with high CD4 of 500cells/mm^3.

Figure 4. 11: Kaplan –Meier survival estimates by Karnofsky

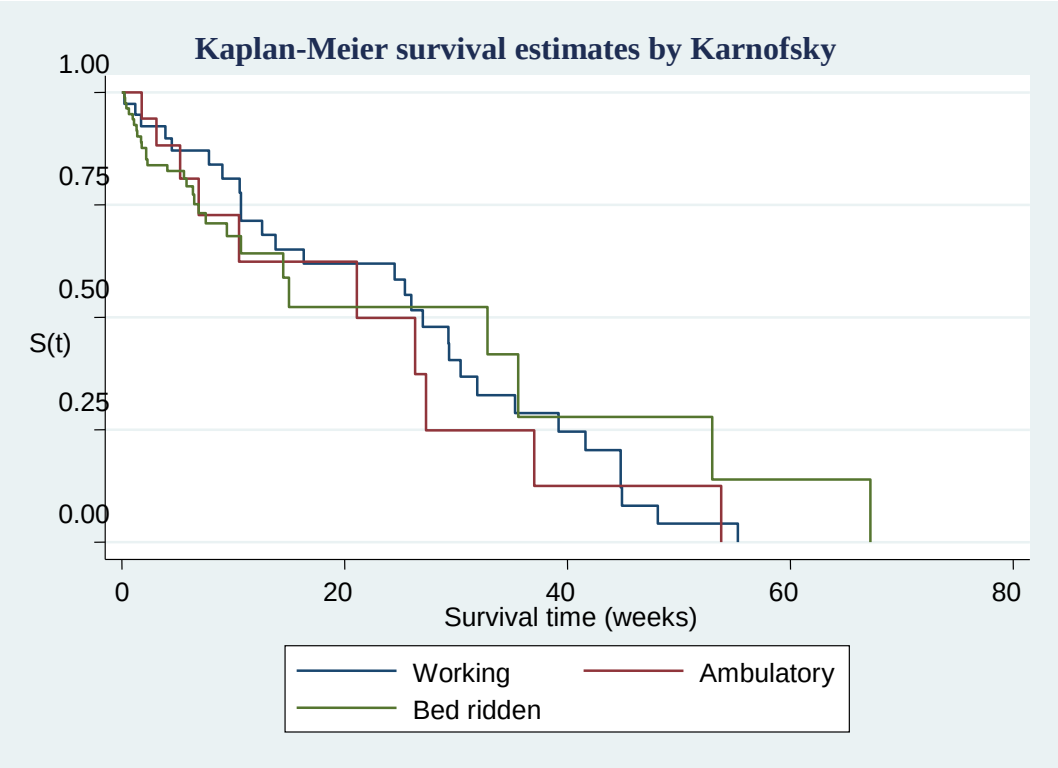
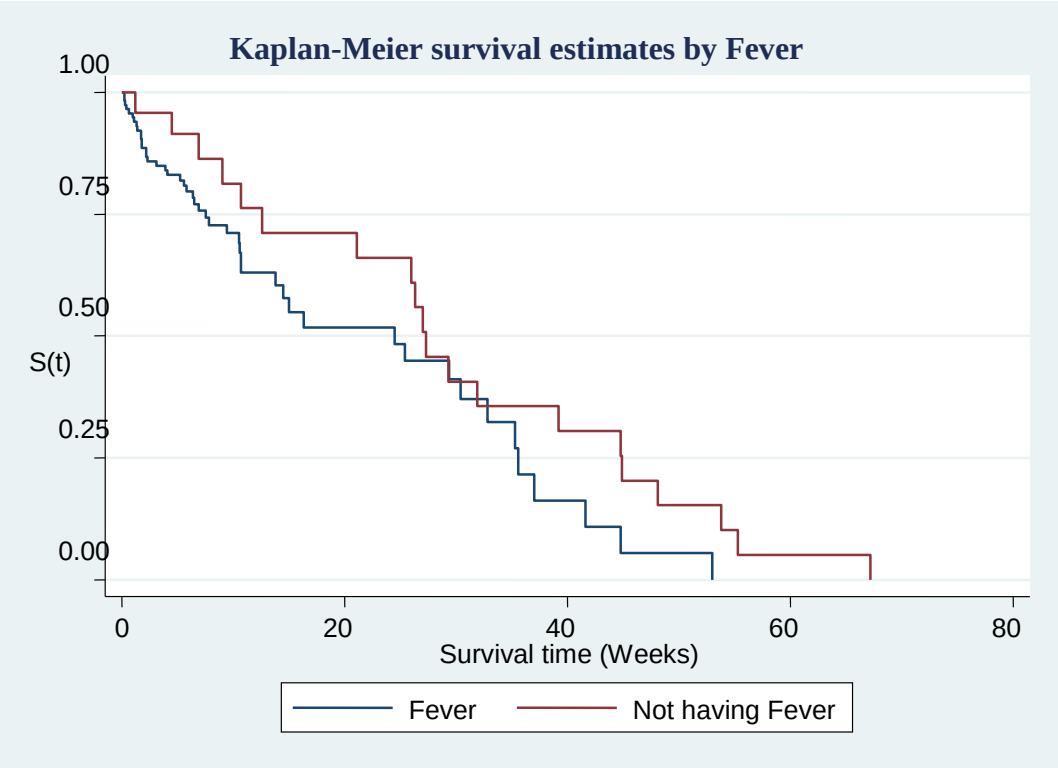


Figure 4.11 it was indicated that HIV/TB co-infected patients on TB treatment at karnofsky= working were more likely to survive compared to those who were at karnofsky =Bed ridden and karnofsky =Ambulatory stage. Patients who were Bed ridden had lower chances of survival to those at working stage of Karnofsky and also their survival function was different.

Figure 4.12: Kaplan –Meier survival estimates by Fever



This Figure 4.12 Shows that HIV/TB co-infected patients on ART and TB treatment with fever had lower chances of survival compared to those who had no fever. The survival function of the patients with fever and those with no fever was different.

The findings above are consistent with the literature by Uria et al. (2012) in the study conducted in India where the cumulative incidence of mortality was high among the HIV/TB co infected patients with TB. This is probably because patients who are PTB smear positive were highly immune compromised.

Survival of HIV/TB patients significantly depended on the CD4 count of the patients in this study. Patients with low CD4 count had a great risk of dying than those with high CD4 counts. The reason is that the higher the CD4 the greater the body immune system and low CD4 count

weakens the body immune system so death can easily occur since the body cells cannot fight opportunistic infections brought by both diseases.

Also it was found out that survival of HIV infected TB patients does depend on the nature, type of TB which are in line with the findings by Balewgizie et al. (2013).

It has also been noted that positive HIV and TB patients with high CD4 count at TB treatment initiation of $\leq$ 500 cells/mm^3had a lower mortality rate compared to those whose TB treatment initiation are at $\leq$ 200 cells/mm^3. This is because of a good immune system the body keeps TB infection quiet and sleeping ('latent TB').

The findings are in line with the literature by Zakumumpa (2011) who argued that in Uganda the existence of TB among people is associated to HIV and this has claimed many lives of the Ugandan's who are HIV and TB positive that affect the body immune system as well as the nature of treatment at time.

Also it was noted that WHO stage was associated with survival among HIV infected TB patient and results showed that HIV positive TB patients in stage 3 were more likely to die compared to those in stage 1 and stage2 and this finding is in line with results of (Mahlet et al. ,2013).

Contrary to the findings conducted by Vijay et al. (2011) in Southern India who found that a CD4 count among HIV/TB patients that are below 200cells/mm^3 was not statistically associated with a higher mortality rate. However this deference between the results of this study and that of Vijay et al. (2011) can be attributed several factors including difference in the levels of CD4 counts among participants of this study and that of Vijay et al.(2011).

The findings are in line with the literature by Stering et al.(2010) were he found that the primary risk factors for TB recurrence among HIV infected patients with TB appears to be low CD4+ T

lymphocyte count, with the risk highest among persons with a CD4+ T lymphocyte count<100 cells/mm^3. Similarly a study by Mahlet et al. (2013) patients who had a low CD4 count< 200 were more likely to die as compared to their counterparts who had more CD4 count.

Also the study shows that the survival was high among those patient who were at walking stage than bedridden, not having constant diarrhea, not vomiting, no constant cough of 2 weeks or more, no fever of 2 weeks or more and ambulatory patients. The findings are in line with literature by Lim et al. (2010) where he said that HIV/TB infected patients are more likely to survive if they are at walking stage unlike any other stage.

Similarly study found out that 99% of the participants were having a good Karnofsky score performance and they were mildly ill. We expect the patient to fairly respond to treatment and thus chances of survival are high as compared to other levels. This implies that if a patient performs fairly as far as Karnofsky score is concerned the higher are the chances of survival.

4.6 The treatment associated factors

Table 4.5: presents the treatment characteristics associated with the survival of the positive Uganda's service men on the TB treatment.

Table 4. 5: The relationship between treatment related factor and time from initiation of ART to death.

Variable	Category	Sample size n=(143)	Number of patients who die	Expected death	χ^2	P-value
ART status	Develops TB while on ART	68	40	38		
	Develops TB prior to start ART	75	27	29	0.26	0.61
Starting ART	Early ART initiation (within two weeks)	69	44	47.7		
	Delayed ART initiation (latter three weeks)	74	23	19.3	1.20	0.27
History INH	Yes	59	35	41		
	No	84	32	26	2.6	0.11

The survival function of patients who develops TB while on ART and those develop TB prior to start ART on TB treatment who are HIV/TB positives they were not the same and this was indicated with patients develop TB prior to start ART having high risk of death to those who develops TB while on ART. The survival function of patients who delay ART initiation with that of patients who initiate in time is not the same. Also patients who delay to initiate were at high risk of death to those that initiate in time.

Figure 4. 13: Kaplan –Meier survival estimates by ART status

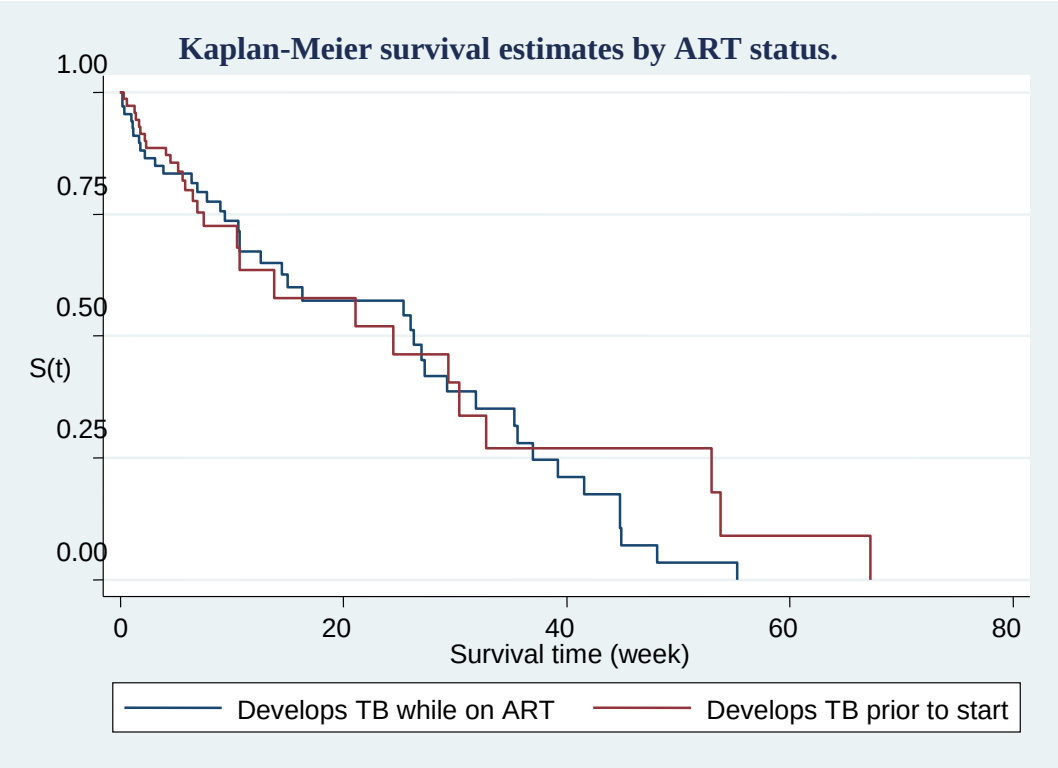


Figure 4.13 Shows that HIV /TB co-infected patients on ART and TB treatment that developed TB prior to starting ART were associated with poor survival compared to those on ART. The survival function of the patients who develops TB while on ART and patients who develops TB Prior to start treatment was different.

Figure 4.14: Kaplan –Meier survival estimates by timing of ART

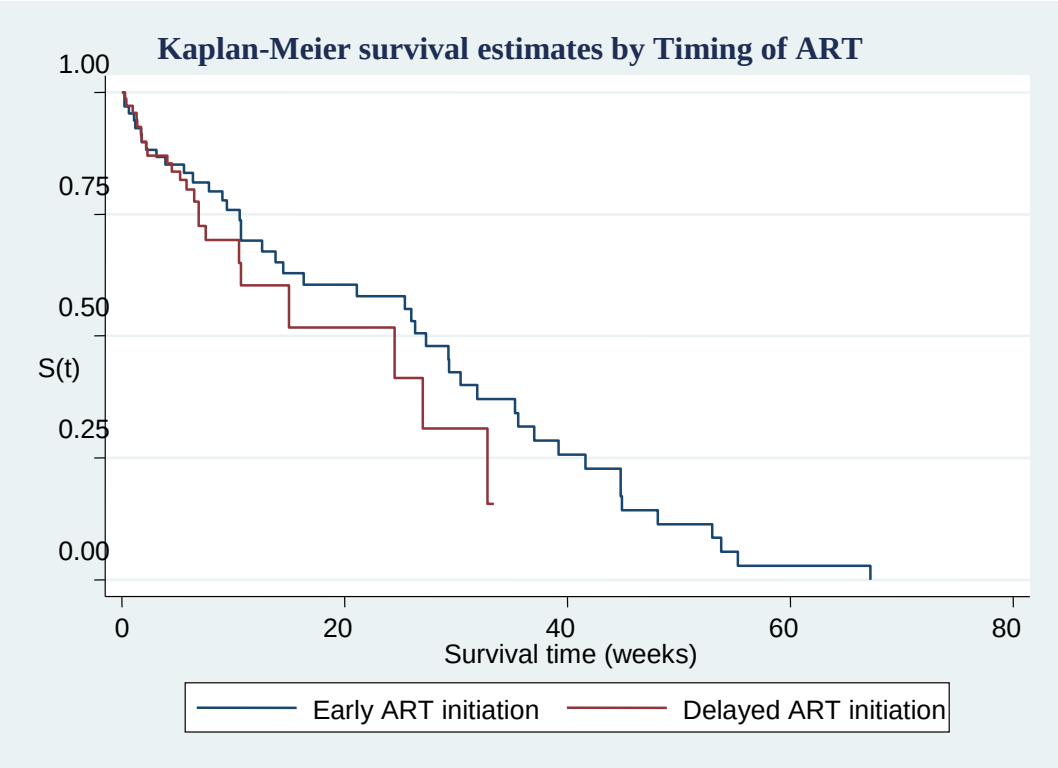


Figure 4.14 Shows that HIV /TB co-infected patients on ART and TB treatment at Early ART initiation (within two weeks) were more likely to survive compared to those who delayed ART initiation (after three weeks). The survival function of patients who were initiated on ART early were different from those who delayed ART initiation.

Figure 4.15: Kaplan –Meier survival estimates by INH prophylaxis

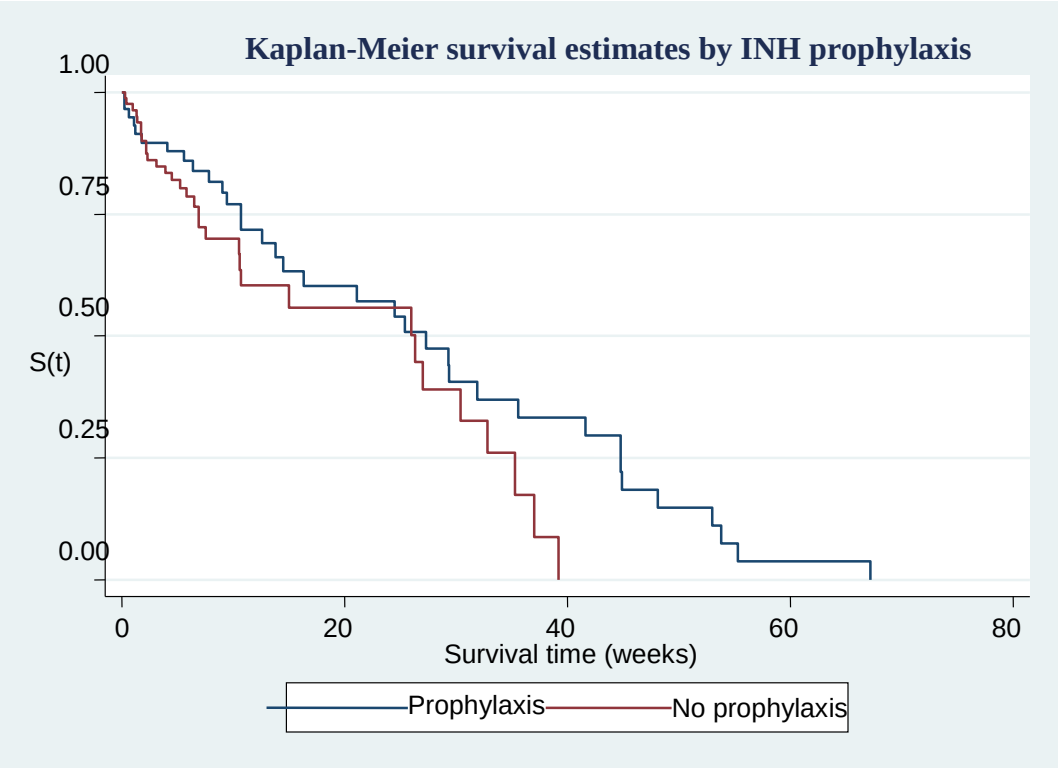


Figure 4.15 Shows that co-infected patients on ART and TB treatment with no history of INH were more likely to survive compared to those who had history of INH.

So the results of the study and the literature given agree that HIV & TB infected patients can survive while on ART, but this calls for early initiation to ART for an HIV/ AIDS for client, availability of ART drugs at the health centers and early screening against TB infection. HIV/TB clients who were not on ART had their risk of death increased especially at first months, so treating TB with ART would translate into saving lives of HIV/TB clients especially during the first month at TB treatment. Patients who Delayed ART initiation latter than two months were at high risk of dying (38.19/70) compared to those of Early ART initiation (63.81/32). Similarly, Varma et al. (2009) in this study found out that the risk of death increased as longer as ART was delayed among the study participants.

The study found that timing of ART was associated with survival among HIV/TB co-infected patients. This is in line with the literature by Zachariah et al. (2009) who argued that ART treatment needs to be started by the HIV/TB patients immediately after TB diagnosis. But in relation to this study, it can be argued that many HIV/ TB infected patients who did not get started on ART and developed TB were likely to be ill and therefore unable to benefit from ART treatment. The finding of this study also indicates that duration on ART is associated with survival among HIV/TB infected patients. This finding is in line with literature by Cortes et al. (2013) who argued that the duration of ART is vital in determining survival among HIV/TB infected patients, since it reduces mortality.

INH prophylaxis was not associated with survival among HIV/TB infected patient. This finding are related to the literature by Granich et al. (2010) who noted that INH prophylaxis acts as a preventive method of spreading TB reduces the risk of actives TB, the incidence, prevalence and transmission among members in the community. Also the findings are related to the results by Heather et al. (2007) who investigated the impact of isoniazid prophylaxis on mortality as well as incidence of the TB among children living with HIV and found low mortality among participants under isoniazid prophylaxis. This is probably because INH prophylaxis reduces the incidence and rate of infection among HIV/TB infected patients and increases the rate of survival.

Beth et al. (2011) found that 27.5% of the patients died before starting TB treatment and for the patients who survived, 13.6% percent died before completing TB treatment and 42.7% of the patients died during the median days of follow up. This survival outcome was partly associated to limited low utilization of HIV/TB health care points.

The findings in this study were in line with Varma et al. (2009) who found out from the study participant in Thailand that survival for HIV/TB patients was associated with ART treatment. In

line with the findings of this study, an HIV/TB infected patient who develops TB while on ART has a higher chance of survival because ART treatment strengthens the body immune system and he or she will be in position to positively respond to treatment unlike in the situation where TB develops before ART treatment.

HIV/TB co-infected patients in this study who developed TB while on ART treatment had a lower risk of death. This finding is consistent with studies carried out by Balewgizie et al. (2013), Cain et al. (2009) and Manosuthi et al. (2006) among others where appositive effect of ART on the survival outcome for HIV/TB co-infected clients, involving a successful immune restoration and reduce morbidity and mortality were obtained.

The patients who were not on ART treatment were at a higher risk of death, and this can be attributed to the factors like delayed presentation of the patients leading to advance HIV/AIDS. According to study by Moolphate et al. (2011) the first month of the TB treatment had the highest number of death among HIV/TB co-infected clients. Therefore this brings emphasis that ART needs to be started as soon as TB diagnosis has been carried out.

4.7 The wasting associated factors

Among the wasting related factors as per the study it was found out that gender, weight, X-rays status, smoking, taking alcohol and apatite status that were statistically significance on the survival of the Uganda's service men on TB treatment and it is shown in Table 4.6:

Table 4. 6: The relationship between Wasting related factors and Time from initiation of ART to death.

Variable	Category	Sample size n=(143)	Number of patient who die	Expected death	χ^2	P-value
Gender	Male	81	44	45.6		
	Female	62	23	21.5		
					0.19	0.67
Body cell mass depletion	Positive	102	25	39.9		
	Negative	41	22	27.1		
					1.7	0.19
Body Weight	Under weight	85	28	22.8		
	Normal weight	58	39	44.2		
					2.14	0.14
Diet and nutrition	On diet	126	56	51.2		
	On poor diet	17	11	15.6		
					2.01	0.16
Smoker	Yes	75	24	24.2		
	No	68	43	42.8		
					0.00	0.96
Drinking alcohol	Yes	81	26	25.2		
	No	62	41	41.9		
					0.05	0.82
Eating habits	Yes	56	40	38		
	No	87	27	29		
					0.29	0.59

The survival function of male and female patients on TB treatment who are HIV/TB positives they were not the same and this was indicated with male having high risk of death to that of female. It was also indicated that smokers on ART and TB treatment were at a higher risk of death smoke attributed to reduced body immune system. Patients who were drinking alcohol and were on ART treatment had higher risk of death compared to those who were not drinking alcohol, and their survival function of patients drinking alcohol with those not drinking alcohol were not the same as in table 4.6.

Figure 4. 16: Kaplan –Meier survival estimates by eating habits and abdominal pain

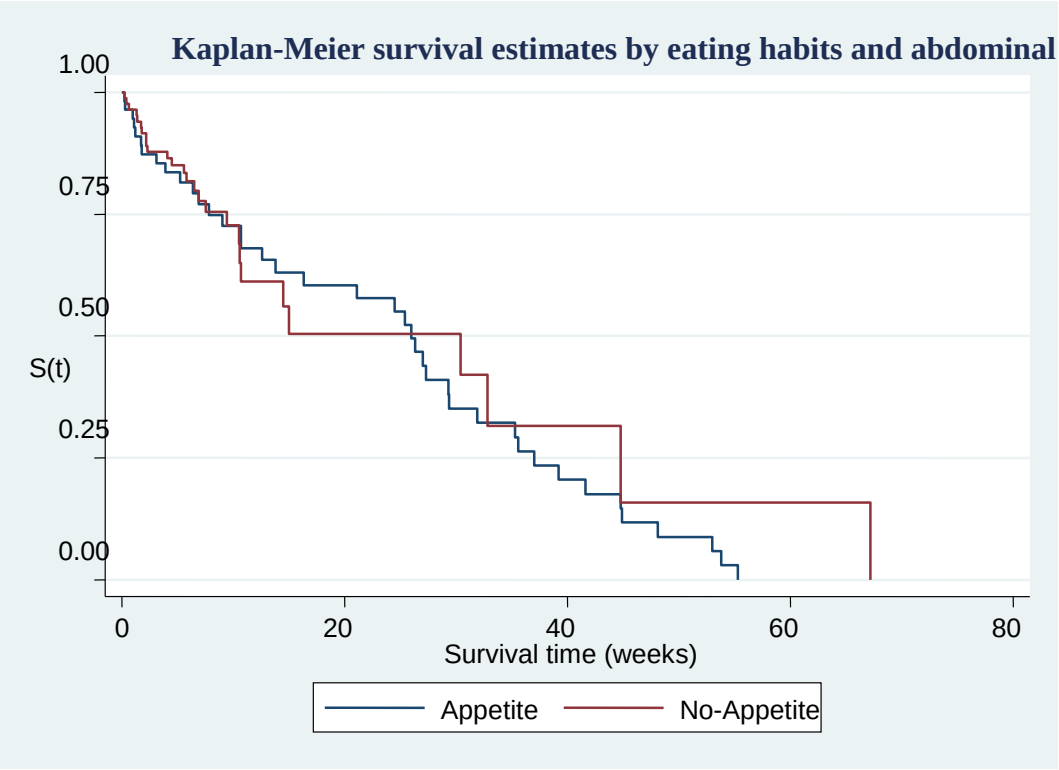


Figure 4.16 Shows that the co-infected patients on ART and TB treatment with appetite were more likely to survive compared to those who had lower appetite and had abdominal pain. The survival function of the patients with appetite and patients with no appetite was different.

Figure 4. 17: Kaplan –Meier survival estimates by body weight

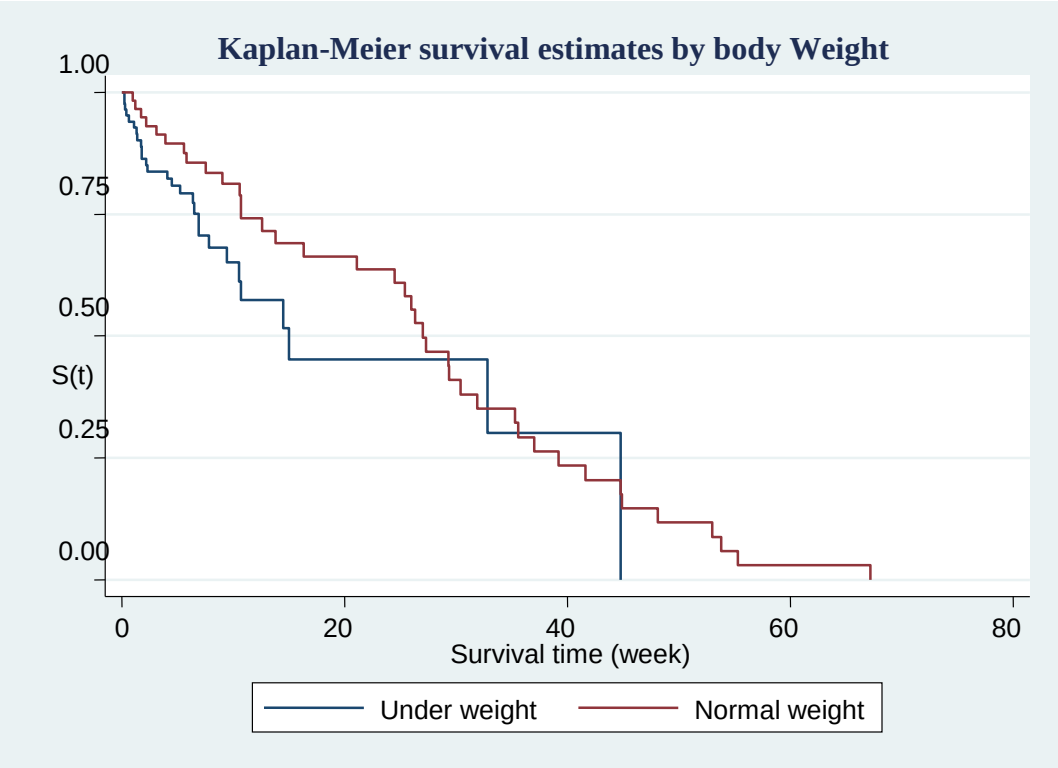
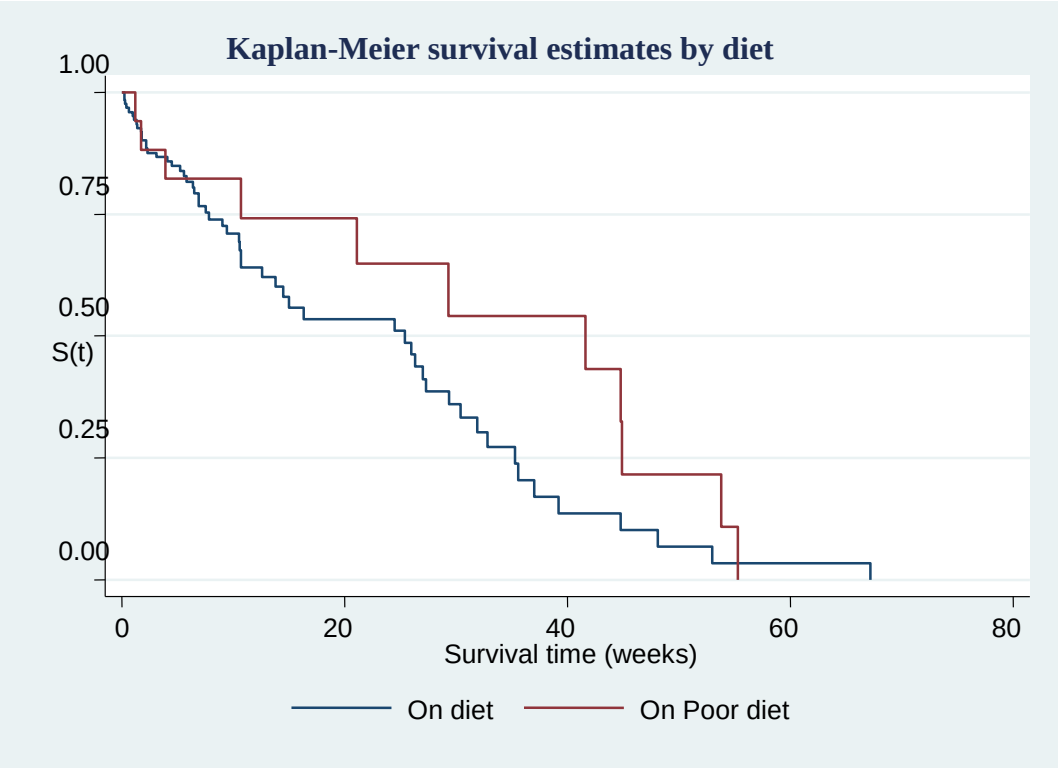


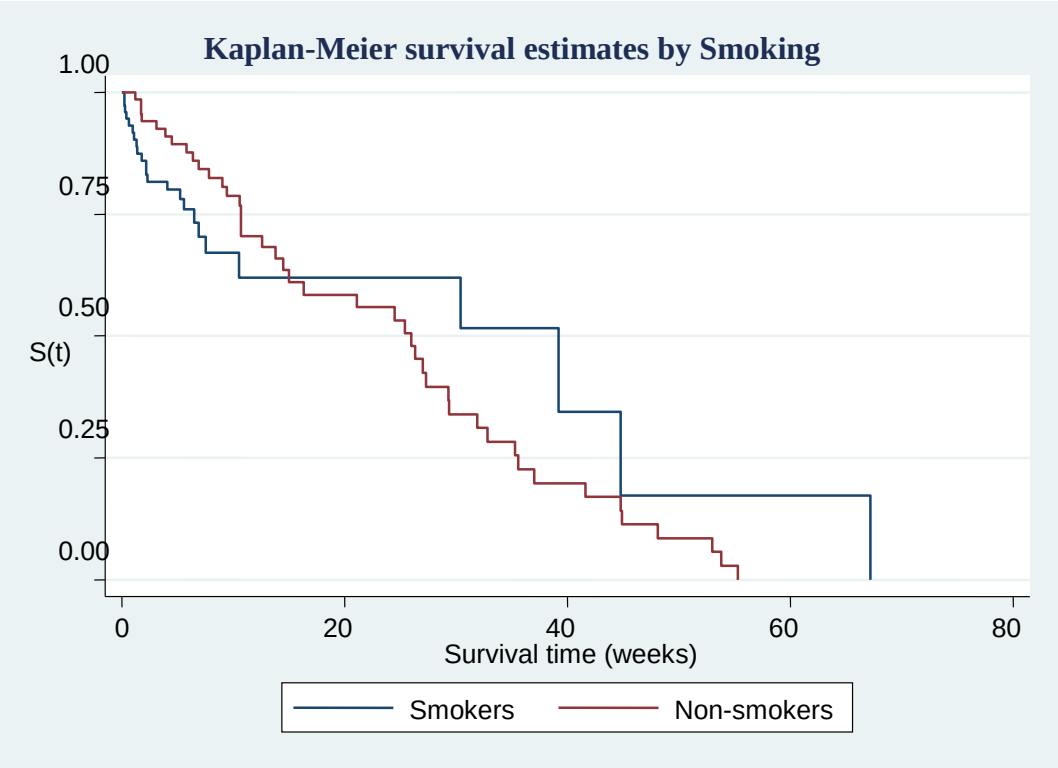
Figure 4.17 Shows that HIV/TB co-infected patients on ART and TB treatment with normal weight were more likely to survive compared to those who were under weight.

Figure 4. 18: Kaplan –Meier survival estimates by diet



The results from Figure 4.18 show that the HIV/TB co-infected patient on ART and TB treatment on diet were more likely to survive than those on poor diet.

Figure 4. 19: Kaplan –Meier survival estimates by Smoking



The Figure 4.19 Shows that HIV/TB co-infected patients on ART and TB treatment who were smokers had lower chance of survival compared to their counterparts who were non smokers. It was also noted that survival function of the patients who smoke and patients who are non smoker was different.

Figure 4. 20: Kaplan –Meier survival estimates by body cell mass depletion

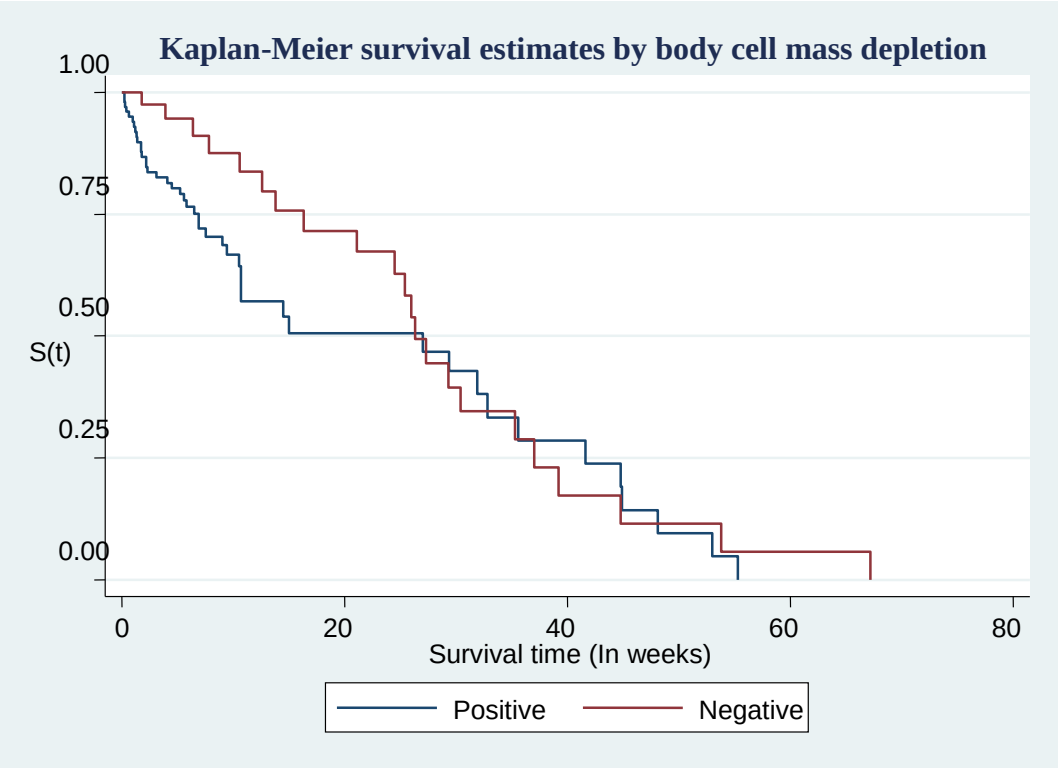
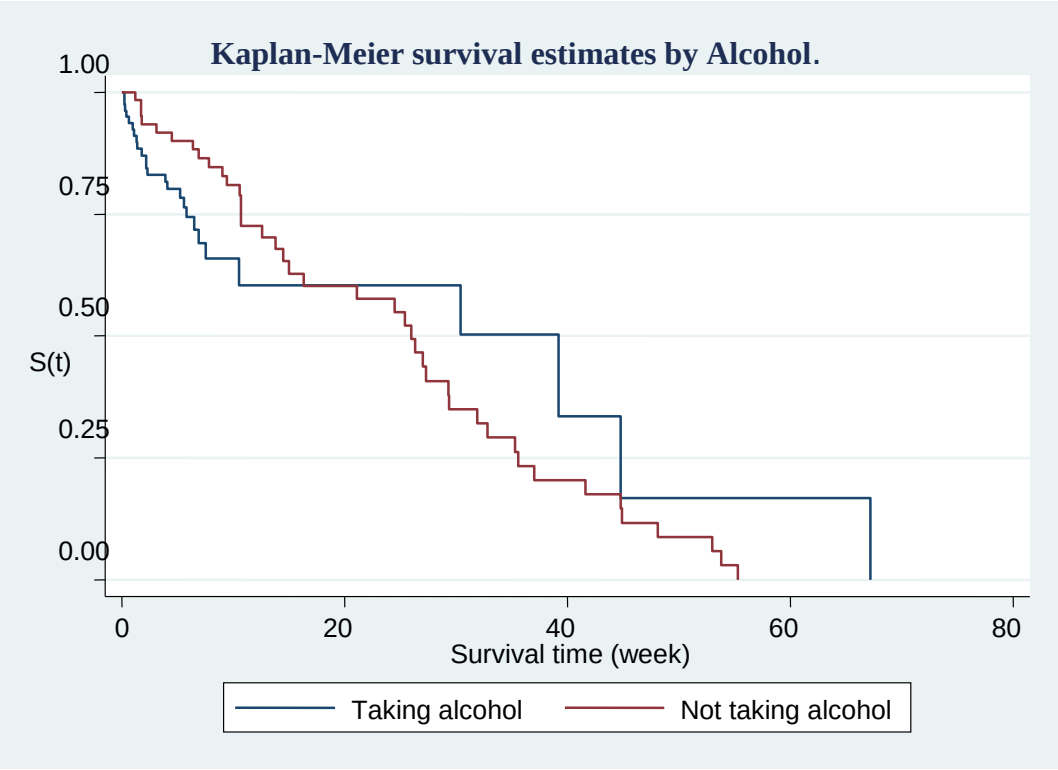


Figure 4.20 it was indicated that patients with body cell mass depletion were not as healthy as those without body cell mass depletion in terms of immune status as indicated by lower CD4 counts. Also the survival function of patients with body cell mass depletion was different from that of patients without body cell mass depletion, and patients with body cell mass depletion were at higher risk of death compared to those without body cell mass depletion.

Figure 4. 21: Kaplan –Meier survival estimates by Alcohol.



From the above Figure 4.21 it was indicated that the HIV/TB co-infected patients on ART and TB treatment who were not drinking alcohol were more likely to survive compared to those who were drinking alcohol.

The findings were in line with Vanltallie et al. (1990) who found out that, those with body cell mass depletion were not as healthy as those without body cell mass depletion in terms of immune status as indicated by lower CD4 counts.

This finding is centrally to the literature and finding by Glenn et al. (2010) a study from Burundi among adults with tuberculosis, including pulmonary, extra-pulmonary and disseminated infection, suggests that those infected with HIV have significantly lower weight, BMI and fat-free mass compared with individuals without concurrent HIV infection.

Wasted tuberculosis patients regain weight with treatment, having appetite, stop smoking and taking alcohol this reduce the mortality rate of patients and this is in line with the literature study by (Muperel et al , 2012).

4.8 Determinants of survival of HIV positive servicemen on TB treatment analysis (Cox proportional hazard model)

This model was aimed at examining the relationship between time from initiation of ART to death and independent variables in their different categories as presents in Table 4.7.

Table 4. 7: Cox regression model was used to analysis the relationship between the time from the initiation of treatment to completion or death.

variables	Category	Haz - Ratio	Std.err	p> | z |
Age	Age	0.965	0.013	0.010
Marital status	Married	1.000		
	Single	2.439	0.952	0.022
	Separated/divorced	1.674	1.846	0.308
	Widow	1.475	0.679	0.399
	In relationship	1.168	0.691	0.793
Nature of TB	Pulmonary TB	1.000		
	Extra-pulmonary TB	0.705	0.199	0.215
Area of residence	Rural	1.000		
	Urban	0.399	0.146	0.012
	Peri- urban	0.431	0.159	0.022
Karnofsky	Working	1.000		
	Ambulatory	1.034	0.564	0.951
	Bed ridden	0.568	0.331	0.332
ART status	Develops TB while on ART	1.000		
	Develops TB prior to start ART	0.486	0.449	0.016
Sweating	Sweating at night because of disease	1.000		
	Not sweating because of disease at night	1.703	0.559	0.105

From the table 4.7, old age is associated with poor survival, whereas being male is associated with better survival. The hazard of the patients with pulmonary TB was high and increased the risk of death by 71.3%.Karnofsky patients at bed ridden and ambulatory stage were associated with better survival with hazard increase of 0.568for bed ridden (p-value 0.332) and ambulatory hazard increase of 1.034 with p-value 0.951. Most of the patients treated at GMH from barracks in rural areas there hazard were high with increasing risk of (37.8%) followed by those from urban barracks (32.8%) hazard increase while the least were those from the peri-urban barracks with increasing hazard of (29.4%). Patients who develop TB prior to start ART there hazard were high with increasing risk of (52.5%) to those of who develop TB while on ART (47.6). Patients who were not sweating at night because of the disease there hazard were high to those that were Sweating at night.

The study also indicated that those with body cell mass depletion were not as healthy as those without body cell mass depletion in terms of immune status as indicated by lower CD4 counts and this is similar to a study carried out by (Ramakrishnan et al., 1961).

Weight loss and malnutrition continue to be significant problems in treatment of pulmonary tuberculosis in HIV clinical cases. Significant and progressive HIV-related weight loss is related to diminished functional capacity, increased risk for secondary infection and hospitalization and by itself can be an independent cause of death.

In this study it has been noted that on wasting in pulmonary TB in relation to TB-HIV co infection there are limitations and differences in the findings due to cofounders such as alcohol taking, smoking, prior nutrition counseling of the subjects and dietary practices. It was found out that patients who smoke and take alcohol had a high mortality rate and their treatment of

pulmonary TB was difficult compared to those that do not smoke, take alcohol and their treatment of Pulmonary TB was easy.

TB incidence was significantly lower in overweight persons than in normal-weight controls and patients with TB infection had symptoms and signs of TB such as cough, fever, weight lose compared to those who had no TB infection.

Wasted tuberculosis patients regain weight with treatment, having appetite , stop smoking and taking alcohol this reduce the mortality rate of patients and this is in line with the literature study by (Mupere1 et al. 2012). Tuberculosis Research Unit at Case Western Reserve University found out that wasted tuberculosis patients regain weight with treatment but the type of gain differs by gender and patients may remain underweight after the initial phase of treatment.

Similarly weight had significant effects that were associated with mortality of the Ugandan's service men who are HIV positive on TB treatment. It was also clear that patients who were underweight their mortality was high. This is in the relation with a study by Mashimbye (2009) who found out that influence survival among HIV/TB co-infected patients were gender ($p<0.001$) marital status ($p<0.03$), age ($p<.006$) body mass index ($p<0.001$) and alcohol consumption among the patients ($P<0.04$).

CHAPTER FIVE

SUMMARY OF FINDINGS, CONCLUSIONS AND RECOMMENDATIONS

5.1 Introduction

This chapter is about the summary of findings, conclusions and recommendations. It is based on the methodological process issues and the study objectives.

5.2 Summary of findings

This study revealed that the overall survival of HIV infected TB patients was low. However HIV/TB co-infected patients on ART and TB treatment were more likely to survive compared to those who were not on ART. The findings implied that HIV infected TB patients who had initiated ART treatment had more chances of survival compared to those who had HIV and TB but delayed to take on ART treatment. The existence of higher chances of survival among patients on ART in this study can be attributed to the increased immunity obtained from ART drugs; this makes the CD4 count to increase.

It was indicated that HIV/TB co-infected patients on TB treatment at karnofsky= working were more likely to survive compared to those who were at karnofsky =Ambulatory stage.

Old age is associated with poor survival.

The findings implied that HIV infected TB patients who were drinking alcohol and were on ART and TB treatment, had lower chances of survival compared to those who were not drinking alcohol.

The study shows that patients who were pulmonary TB and were on ART and TB treatment, had lower chances of survival than those who were Extra-pulmonary TB.

Most of the patients treated at GMH were from barracks in rural areas with increasing risk of (37.8%) followed by those from Peri-urban barracks with increasing hazard of 0.431 and P-value of 0.022 and lastly from urban barracks with hazard 0.399 and P-value of 0.012.

The overall survival of patients who were under weight because of HIV/TB diseases was lower compared to those patients with normal weight.

Patients on ART and TB treatment who had appetite were more likely to survive compared to those whose appetite was low.

Patients who develop TB while on ART had higher chances for survival compared to those who develop TB prior to ART (non-ART).

Patients who had constant cough for more than two weeks were more likely to die as compared to those with no constant cough of more than three weeks on ART and TB treatment.

Furthermore, it was noted that patients with high fever, vomiting, diarrhea, and karnofsky of bed ridden, on ART and TB treatment had lower chances of survival compared to their counter parts.

The co-infected TB patients with CD4 count $\leq$200 cells/mm^3 and 200 $\leq$500 cells/mm^3 on ART and TB treatment had lower chances of survival compared to those with CD4 of < 500 cells/mm^3.

The finding from the study show that patients on stage 1and stage 2 of HIV/AIDS treatment on ART and TB treatment were more likely to survive compared to those at stage 3and stage 4of HIV/AIDS treatment.

It was also noted in the study that death was high and common in patients with Pulmonary TB than those with Extra-pulmonary TB. Focusing on the distribution of HIV positive TB patients

according to time event (death), the results of this study revealed that 18% of HIV/TB Clients died and 82% censored. However, when you consider the time factor, there is a big difference in relation to when death occurred and the percentages.

5.3 Conclusions

Based on the study findings in chapter above, it can be decisively concluded that the overall survival of HIV co-infected TB patients was low and patients who were on ART treatment before developing TB were in better position than those patients who developed TB before starting ART treatment.

Among the socio-demographic related factors, patients who receive social support have higher chances of survival than those that did not receive social support.

Of the disease related factors patients with history of negative sputum smear WHO stage3, stage4, CD4 count $\leq$ 200 cell/mm^3 and patients who were ambulatory and bedridden at time of the initiation of treatment were at high risk and their mortality rate was higher compared to their counterparts.

Early ART initiation (within two weeks) increased the chances of survival of patients who are on TB treatment and patients who Delayed ART initiation treatment had low chances of survival.

Underweight patients had low chances of survival compared to those with normal weight.

Patients who were smokers and drinking alcohol on ART and TB treatment had lower chances of survival compared to their counterparts.

5.4 Recommendations

The regional referral hospitals and Health centers at all levels should make deliberate efforts to target and treat all HIV/TB co-infected patients with ART irrespective of the CD4 count levels as

one of the ways of improving their immunity for increased survival. This will reduce mortality among this category of patients.

It is recommended that reduction of deaths among HIV/TB patients requires early screening, diagnosis, and faster treatment within3 months to 8 months for TB infection especially for patients on antiretroviral therapy.

5.5 Areas for further research

Although the results of this study provide an explanation to factors associated with survival of HIV/TB positive service men on TB treatment, it is still debatable whether the findings will apply entirely too all positive service men. There is need to provide an exhaustive list of all the related factors associated with survival of positive service men on TB treatment. Further assessment is needed in the treatment of positive service men in fighting areas of operations.

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