Post renal transplant patients' and allograft survival at Kenyatta National Hospital Renal Unit: A four Year Retrospective Cohort Study

By

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DECLARATION

I, Mwangi Elijah Githinji, hereby declare that this is my original work except where otherwise acknowledged and has not been submitted either to this or any other university for the award of any degree or for any award.

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DEDICATION

This study is dedicated to my family: my mother Rebecca Wanjiru for always believing in me and encouraging me throughout my study. It is also dedicated to my wife Edith N. Githinji and our wonderful children Judebec, Margaret and Mary, for their understanding and sacrifice in the course of preparation of this work.

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ACRONYMS

DWGF - Death with Graft Function

ESRD - End Stage Renal Disease

HLA - Human leukocyte antigen

KNH - Kenyatta National Hospital

SLE - Systemic Lupus Erythematosus

USA - United States of America

USRDS - US Renal Data System

WHO - World Health Organization

DEFINITION OF TERMS

Age: the number of years the patient lived from birth to date of transplantation

Date of entry: the date when the transplant was done

Diabetes mellitus: Defined as a patient who has been diagnosed by a medical specialist to have diabetes mellitus

Event: The event is the response variable i.e. patients death or kidney allograft failure

Gender: This is a qualitative measure of whether the patient is male of female

Graft survival: Time from transplant to graft failure (the time a kidney graft remains patent), censoring for death with a functioning graft and grafts still functioning at time of analysis

Hypertension: Defined as the patient having a blood pressure of above 140/90 mmHg during the period after transplantation of the allograft

Patient survival: Time from transplant to the time the patient experiences event of interest (death)

Rejection: Allograft rejection will be considered to have taken place if the patient went back to hemodialysis or undergoes another transplant

Smoking status: This is a qualitative measure of whether the patient has been smoking or not during the period of the study

Time to event: The variable measures the duration to the event defined by the status variable;

a) The time taken until there is rejection of the kidney

b) The time taken by the patient from time of transplant to experiencing the event death

The time of enrollment: This will be the month of transplant. Time will be measured in months.

ABSTRACT

Renal transplantation has become the treatment of choice for most patients with end stage renal disease (ESRD). Marked improvements in early graft survival and long-term graft function have made kidney transplantation a more cost-effective alternative to dialysis.

This study was aimed at determining the patient and renal allograft survivals and identifying the factors impacting on survival following kidney transplantation at Kenyatta National Hospital.

94 kidney transplant recipients who underwent renal transplant at Kenyatta National Hospital from January 2010 to February 2014 were considered for the study. Survival analysis was used in the analysis to assess the role of explanatory factors in time to death of a patient and time to rejection of a kidney allograft. Outcome measures studied were patient and graft survival. Graft loss was defined by the need for permanent renal dialysis, repeat transplantation or death with a functioning graft. Kaplan-Meier method was be used to determine patient and graft survivals. Cox proportional hazard model was used to determine the factors affecting survival. The patients' survival for the first year was 88.7%, second year 88.7%, third year 88.7% and 82.6% for the fourth year. The trend showed that the survival was the same for the first three years then a drop on the fourth year. For the patients who survived the operation, their survival was 92.7% for the first, second and third year post transplant. The fouth year survival was 85.7%. The renal allograft survival was 92.01% for the first and the second year, and 83.01% for the third and fourth year. The graft survival for those who survived the transplant was 97.36 for the first and the second year and 88.02% for the third and fourth year.

The factors that significantly influenced survival of renal transplanted patients were presence of diabetes mellitus (p-value- 0.032) and the level of antigens of the human leukocyte antigen (HLA) mismatch (p-value<0.0001). Factors that significantly influenced allograft survival were

presence of Systemic lupus erythematosus (SLE) (p- value =0.025) and employment (p-value =<0.0001). The results of the study concurred with other studies done elsewhere. In conclusion, the study established that the survival rates in Kenyatta national hospital were good.

CHAPTER ONE: INTRODUCTION

1.1 Background

The function of healthy kidneys in the body is to remove excess fluid, minerals, and wastes from the blood and regulate blood pressure. If the kidneys are damaged, they don't work properly. Harmful wastes build up in the body and blood pressure may rise. The body may retain excess fluid and not make enough red blood cells. This defines kidney failure. If the kidneys fail, treatment is needed to replace the work normally done by the kidneys. Treatment options available are dialysis or kidney transplant. Each treatment option has its benefits and drawbacks. Some changes in lifestyle need to be made after choosing any of the treatment options, including eating and planning daily activities. But with the help of healthcare providers, family, and friends, most people with kidney failure can lead full productive and active lives.

According to Naicker (2009), several studies have demonstrated a high incidence of chronic kidney disease among black Americans. Unfortunately, lack of functioning registries in most of Sub-Saharan Africa has resulted in a lack of reliable statistics. There is a general impression that it is at least three to four times more frequent than in more developed countries; uremia accounted for 1.0% - 1.5% of total annual deaths among Egyptians, both in the pre-dialysis era and for two decades after (Naicker, 2009). The figures are comparable with those of other countries of similar social economical standards.

Chronic kidney disease affects mainly young adults aged 20–50 years in sub-Saharan Africa and is primarily due to hypertension and glomerular diseases. In the developed countries chronic kidney disease presents in middle-aged and elderly patients and is predominantly due to diabetes mellitus and hypertension (Arogundade & Barsoum 2008).

The availability of renal replacement therapy in much of the Sub-Saharan Africa is limited because of their high costs. Lack of available therapy is responsible for high rate of morbidity and mortality. In 2004, renal replacement therapy was accessed by approximately 1.8 million people worldwide. Five percent of the dialysis population was from Sub-Saharan Africa (Grassman, Gioberge, Moeller, & Brown 2005).

There are more than one million Kenyans who suffer from kidney disease. There are less than 100 working dialysis machines in the country (Singh 2012). Most of the patients in Kenya with end-stage kidney failure either do not have access to a dialysis clinic or they cannot afford to go to the very few available dialysis clinics (which are less than 10) since they are very expensive (Singh 2012). The main causes of kidney disease in Kenya are mainly hypertension and diabetes. Kenya also suffers from acute shortage of kidney specialists with one nephrologists catering for a 100,000 people (Singh 2012). There is urgent need to train more kidney specialists and renal nurses to cater for the increasing number of patients in the country.

According to the latest WHO data published in April 2011, Kidney Disease Deaths in Kenya reached 2,912 or 0.92% of total deaths. The age adjusted Death Rate is 19.59 per 100,000 of population ranks Kenya at position seventy seven (77) in the world.

Transplantation is limited by cost, donor shortages, and lack of a brain-death law in most of sub-Saharan Africa (Naicker, 2009). Renal transplantation has become the treatment of choice for most patients with end stage renal disease (ESRD). Marked improvements in early graft survival and long-term graft function have made kidney transplantation a more cost-effective alternative to dialysis (Collins & Kulkarni 2013). According to Collins & Kulkarni (2013), studies show that renal transplantation prolongs patient lifespan when compared with dialysis. Increasingly, patients on dialysis are being referred for transplant evaluation, which has resulted

in burgeoning waitlists and increased waiting times for patients in need of kidney transplants. As at 2013, more than 82,000 patients are waiting for kidney transplants in the United States.

1.2 Problem Statement

There is an increase in the number of patients suffering from chronic kidney failure in Kenya. More than one million Kenyans suffer from kidney disease. Most of the patients in Kenya with end-stage kidney failure either do not have access to a dialysis clinic or they cannot afford to go to the very few available dialysis clinics (which are less than 10) since they are very expensive (Singh 2012). The world health organization (WHO) (2011) reports the age adjusted Death Rate in Kenya for kidney disease as 19.59 per 100,000 of population. The availability of renal replacement therapy in much of the Sub-Saharan Africa is limited because of their high costs. Lack of available therapy is responsible for high rate of morbidity and mortality (Grassman et. al. 2005).

Renal transplantation has become the treatment of choice for most patients with end stage renal disease (ESRD). KNH performs approximately four renal transplants per month. Transplantation is limited by cost, donor shortages, and lack of a brain-death law in most of sub-Saharan Africa (Naicker, 2009). Most patients in Kenya prefer hemodialysis because it is economical in short term. Patients undergoing hemodialysis at KNH are dialyzed once a week due to the patient machine ratio. Studies show that in the long term renal transplant is cheaper and convenient compared to hemodialysis. Although long term survival following renal transplantation remains below that of general population, it is much superior to that experienced by patients undergoing dialysis. Lack of understanding of factors that influence the survival of the kidney graft and transplant patients may lead a high rejection and death rate.

1.3 Study Justification

The number of patients undergoing hemodialysis can be reduced if the uptake for renal transplant is improved. This can also reduce the patient machine ratio and will lead to better survival of the patients. KNH is the only public hospital offering renal transplant services in Kenya and there is no research done on patient and kidney allograft survival at the Renal Unit. The results will also provide information to success of renal transplant and the factors that affect renal survival. If the results show a high survival rate, the study will be used to improve the uptake of renal transplantation in Kenya. If the results of the study show low survival rate, it will be used to formulate policies to improve the service and survival.

1.4 Objectives of the Study

Aim of this study is to determine the patient and renal-allograft survival and to identify factors that may affect survival at Kenyatta National Hospital (KNH). The specific objectives are:

i. To determine renal transplant patient and renal allograft survival rates using survival analysis
ii. To identify risk factors that influence survival of renal kidney transplantees using Cox regression model
iii. To identify the risk factors the contribute to renal allograft survival using Cox regression model

1.5 Research Question

What were the post renal transplant patients' and allograft survival rates at Kenyatta National Hospital Renal Unit between the year starting January 2010 to February 2014?

CHAPTER TWO: LITERATURE REVIEW

2:1 Introduction

This chapter presents a review of available literature that is pertinent to the study. The review is divided into three main sections. The first section presents literature on renal transplant. The second section review literature and studies on survival of post renal transplant patients. The third section appraises studies on renal allograft survival**.**

2.2 Renal transplant

When a patient gets chronic kidney failure or end stage kidney disease, there are three treatment options available: hemodialysis, peritoneal dialysis and kidney transplant. Without long-term dialysis or a kidney transplant, the disease would prove to be fatal. A successful kidney transplant provides a better quality of life compared to the other options. It offers greater freedom and is often associated with increased energy levels and a less restricted diet. The source of transplantation kidney can be a living donor or a deceased (non-living/ cadaver) donor. The living donors can be related or unrelated to the patient. Cadaver organ comes from brain dead people who have willed their kidneys before their death. All donors are carefully screened and matched so that the recipient has maximum chances of a successful transplant.

The kidney transplant recipient is given immunosuppressant drugs to prevent the body's immune system from rejecting the new kidney. The transplanted kidney may function immediately or may take a few weeks to function normally. The recipient is more prone to infections due to the suppression of the body immunity. There is risk of rejection of the new kidney as the body considers it to be a foreign object. It may occur soon after transplantation, or several months or years after the procedure has taken place.

2.3 Survival of Renal Transplant Patients

In Europe the survival of patients who have undergone renal transplant has improved over the last three decades (Briggs 2001). Expected survival rates at one year are 95% and 90% at three to five (3-5) years. The risk of death has gone down over the years in all categories of patients. In mid 1970s, one year patient survival in those over 35 years of age was around 60 % while in the younger adults it was around 85 %. In the 1990s the difference narrowed to just over 5% with one year survival at or just below 90% for older patients and at just or below 95% for younger adults. Thus, renal transplantation offers a good prospect of survival for patients who are free of comorbid illness. Renal transplant survival is better for the young patients as compared to the older patients. This means that age is a factor that needs consideration.

Although long term survival following renal transplantation remains below that of general population, it is much superior to that experienced by patients undergoing dialysis. According to Briggs (2001), United States of America's long term mortality risk was 68% lower among those receiving transplants when compared with those remaining in the waiting list.

According to the scientific registry of transplant recipients (2013), the United States Kidney transplant life expectancy rates have continued to improve. The national deceased donor six-month kidney transplant survival rate was 94.4% in 2009. One year kidney transplant survival rate was 92% in 2008 while three year survival rate was 81.9% in 2009. The national living donor kidney transplant statistics shows a six month kidney transplant survival rate of 97.7% in 2009. The one year survival rate for the year 2008 was 96.5% while three year survival rate was 90.9 % in the year 2006. The statistics shows better survival for transplant from a living donor as compared to from a deceased donor.

Renal transplantation has been a treatment option for the treatment of end stage renal disease in Singapore since 1970 when the first cadaveric transplantation was performed. The first living kidney donor transplant was done in 1976. Marked improvement in post renal transplant patients' survival in Singapore has been noted more due to pharmacological and surgical advances but also more effective and stronger antiviral, antibacterial and antifungal agents. A ten (2000-2010) year patient survival rates in the transplant center was 83%. The advent of more portent immunosuppressant drugs, newer and better antibiotics and antifungals over the years, have all contributed to improved survival rates. The one, three, five and ten year survival rates were 96.7%, 94.8%, 91.5% and 82.7% respectively (Mok, Kee, & Goh 2012).

According to Foster et al (2002), the national shortage of suitable kidney donor organs has disproportional and adverse effects on African Americans due to the prevalence of type two diabetes mellitus and hypertension which are major etiologic factors for ESRD. The two conditions are more prevalent in African Americans than in the general population. The African Americans are more disadvantaged once kidney failure develops. This is because this patient cohort has longer median waiting times on the renal transplant list and they have higher rates of acute rejection.

As the immunosuppressive agents used to prevent acute rejection and the surgical techniques have improved, so have the graft and patient survival rates. Studies have shown improved life expectancy for patients who have undergone renal transplantation as opposed to patients who have remained on dialysis. After two years of functioning, a living donor renal transplant is less costly than maintaining the patient on hemodialysis. The quality of life of patients who have undergone successful renal transplants is superior to that of those on dialysis (Foster et al. 2002).

2.4 Renal Allograft Survival

Graft survival is defined as time from transplant to graft failure, censoring for death with a functioning graft and grafts still functioning at time of analysis.

In a retrospective study of 589 recipients of first deceased-donor allografts, mortality was significantly increased patients with primary non-function compared to those with less severe graft dysfunction (45 v/s 20% at years); however there were no significant difference in survival among patients with delayed graft function versus immediate graft function (Tapiawala et. al. 2010). Death can occur while the graft is functioning or after kidney allograft failure. Death with graft function (DWGF) has been reported to occur in 10 to 30% of patients. In an analysis of the US Renal Data System (USRDS) by Ojo *et al. (*2000), 86,502 patients were studied, 18,482 of whom died during a 10-yr period (7040 (38%) with graft function). Survival at 1, 5, and 10 yr was 97, 91, and 86%, respectively. The median time from transplantation to death with function was twenty three months.

According to Ojo et al. (2000) patients with a functioning graft have a high long term survival. Although death with graft function is the major cause of graft loss, the risk has declined substantially since 1990. Cardiovascular disease was the predominant reported cause of DWGF. Other causes vary by post-transplant time period. Furthermore, the transplant operation, graft loss, return to dialysis, and repeat transplantation are associated with variable time-dependent mortality risks that may not be fully accounted for when overall post-transplant patient survival is studied. The results of the observational study showed a marked and significant improvement over time in the survival of renal transplant recipients with functioning grafts.

Singapore witnessed marked improvements in graft survival over a ten year period starting from year 2000 to 2010 due to pharmacological and surgical advances (Mok et al 2012). The

number of patients who received deceased donor transplantation in the 2000s compared to the 1980s had also increased following amendments to the Human Organ Transplant Act. In this study the overall 10 year graft survival rate was 69.4%. The excellent overall graft survival was helped by government subsidies for immunosuppressant drugs, which contributed to increased patient compliance with medications. All patients in Singapore have lifelong follow up in a tertiary hospital with a nephrologist. This could be another factor which contributed to good long term outcomes. The results of the study also showed that live donors kidney transplants have better short and long-term survival rates compared to deceased donor kidney transplants (Mok et al 2012). Terasaki &, Ozawa (2004) have shown that ant-HLA antibodies, especially those that develop post transplant, are an important cause of decreased long term graft survival.

Treatment of ESRD in South Africa has been an important public health issue (Rayner 2003). Prevalence of ESRD in South Africa as estimated by data from Europe and USA is 790 and 1400 per million populations respectively. The prevalence figures from the USA indicate a marked increase of chronic renal failure in the African American population approximately fourfold greater than the Caucasians American population. The South African figures are likely to approximately exceed the US data. The Southern Africa dialysis and transplantation registry estimate that only 99 cases per million populations receive treatment. Transplantation is cost effective in the long term, offers the chance of full rehabilitation and can be offered to a greater number of patients provided that there is sufficient supply of organs. The results of transplantation are not properly documented. Most studies have originated from Europe or USA. The Southern Africa Dialysis and Transplantation Registry have documented dialysis and transplant outcomes in South Africa, but the last reliable report was issued in 1994. There is

currently no central data collection system that tracks long-term survival rates for all the transplant recipients in South Africa.

According to Arend et al (1997); Briggs (2001) some of the negative determinants of patient survival are suggested to be; older age of recipients; male gender, presence of diabetes, hypertension and cigarette smoking

CHAPTER THREE: METHODOLOGY

3.1 Introduction

This chapter presents the statistical techniques used to analyze data. It also describes the key aspects of survival models used in the study.

3.2 Study Area Description

This study was conducted at the Kenyatta National Hospital (KNH) Renal Unit records department. KNH is a major teaching and national referral hospitals in Kenya, East and Central Africa. It was established in the year 1901 and became a corporate in 1987. It has a bed capacity of 1800 patients. It is situated in Dagoretti constituency, Nairobi County, about 3 km from the city centre, off Ngong Road on Hospital road and borders Mbagathi way to the south. The renal Unit is situated on the first floor of the old hospital wing, opposite Critical Care Unit. Approximately one hundred and fifty (150) patients undergo hemodialysis every week. Renal transplantation is performed once a week. The unit also offers peritoneal dialysis.

3.3 Sampling

There was no sampling since the number of patients who underwent transplant during the period was ninety four (94). The whole population was included in the study. The whole population was eligible for the study. Initially the population was thought to be one hundred and seven but on close scrutiny we found out that there was one who was done on 2009 and twelve in 2014.

3.4 Data Collection

Data collection was undertaken by trained staff that looked at the patients' files and collected the required information. The trained staff was the registered nurse who has specialized in renal nursing and co-ordinates renal transplantation in the unit. The role of the research assistant was to collect data using a prepared check list. The data was entered in a database to facilitate editing, coding and classification before analysis. The computer in which the data was stored had a pass word of which not everybody could assess the data.

3.5 Ethical Consideration

Authority to conduct the study was sought from the Kenyatta National Hospital/ University of Nairobi Ethical and Research committee. Permission was also sought from the head of department renal unit Kenyatta National Hospital and the Head of medical records department. Privacy and confidentiality was maintained by ensuring the information gathered was not communicated to anyone, but was used for this study only. Patients' names were not included in the information as we used the patients' identification number. No risks were subjected to the patient. There may not be a direct benefit to the study population but the study may be useful in terms of policy formulation. Raw data collected will be kept under key and lock for a period of five years then destroyed by burning. Dissemination for the study results will be done through the Head of Department (HOD) Kenyatta National Hospital research department and the HOD Renal unit.

3.6 Analytical Methods (Data Analysis and Methods)

3.6.1 Survival Analysis

Survival analysis models factors that influence the time to an event. Ordinary least squares regression methods fall short because the time to event is typically not normally distributed, and the model cannot handle censoring, very common in survival data, without modification. Nonparametric methods provide simple and quick looks at the survival experience, and the Cox proportional hazards regression model remains the dominant analysis method.

3.6.2 Distribution of Time to Event

In analyzing survival data we estimated the underlying true distribution (either parametric or non parametric), then we were able to estimate other measures of interest such as measures of location (central tendencies) of the survival times.

3.6.3 Using the Kaplan-Meier Method to Estimate Survival Curve

Kaplan-Meier estimate is one of the best options to be used to measure the fraction of subjects living for a certain amount of time after treatment. In clinical trials or community trials, the effect of an intervention is assessed by measuring the number of subjects survived or saved after that intervention over a period of time. The time starting from a defined point to the occurrence of a given event, for example death is called as survival time and the analysis of group data as survival analysis. This can be affected by subjects under study that are uncooperative and refused to be remained in the study or when some of the subjects may not experience the event or death before the end of the study, although they would have experienced or died if observation continued, or we lose touch with them midway in the study. We label these situations as censored observations. The Kaplan-Meier estimate is the simplest way of

computing the survival over time in spite of all these difficulties associated with subjects or situations. The survival curve can be created assuming various situations. It involves computing of probabilities of occurrence of event at a certain point of time and multiplying these successive probabilities by any earlier computed probabilities to get the final estimate. This can be calculated for two groups of subjects and also their statistical difference in the survivals.

In survival analysis there are two functions that are dependent on time and are of a particular interest. These functions are the survival function *S (t)* and the hazard function *h (t).* Survival function is defined as the probability of surviving to time *t.* The hazard function is the conditional probability of dying at time *t* having survived to that time. Kaplan-Meier method was used to estimate the survival curve without the assumption of the underlying probability distribution. The method is based on the fact that the probability of surviving *k* or more time periods from joining the study is a product of the observed survival rates for each period.

$$S(k) = P_1 * \ldots * P_k \qquad (3.1)$$ $^{*}P_2$

Here P_1 is the proportion surviving the first period; P_2 is the proportion surviving beyond the second period having survived up to the second period as a condition and so on. The proportion surviving period *j* conditional on having survived up to period *j* is;

$$Pi = \frac{nj - dj}{nj} \qquad (3.2)$$

Where n_j is the number alive at the beginning of the period and d_j is the number of deaths within the period.

3.6.3.1 The Hazard and Survival Functions

Let T be a random variable representing the waiting time until the occurrence of the event. The random variable is non-negative. One of the events of interest is rejection of allograft and the other is death due to renal causes or renal complications. The survival time is the waiting time.

The survival function

With the assumption that T is a continuous random variable with probability density function (p.d.f) f (t) and cumulative function (c.d.f) F (t) = Pr [$T \leq t$], giving the probability that the probability that the event has occurred during time *t.*

$$S(t) = \Pr[T>t] = 1 - F(t) = \int f(x)dx \qquad (3.3)$$

This gives the probability that the event of interest did not occur by duration *t.* In our case it means the probability the allograft was not rejected by duration *t.*

The Hazard Function

Distribution of T is also given by the hazard function. Hazard function h(t) is the instantaneous rate of occurrence of the event;

$$h(t) = \lim_{dt \to 0} \frac{\Pr(t < T \leq t + dt / T > t)}{dt} \qquad (3.4)$$

The numerator of the above equation is the conditional probability that the event will occur in the interval (*t, t+dt)* given that the event has not occurred before. The denominator represents the interval width. With this we obtain a rate of event occurrence per unit time. Taking the limit down to zero, we obtain an instantaneous rate of occurrence.

The conditional probability in the numerator may be written as the ratio of the joint probability that T is in the interval (t, t + dt) and T >t. The former may be written as *f (t)dt* for small *dt*, while the later is *S (t)* by definition. Dividing by *dt* and passing to the limit gives the following;

$$h(t) = \frac{f(t)}{S(t)} \tag{3.5}$$

Where f(t) is the density function and S(t) is the survival function Collet (2003).

A closely related function to the hazard function is the cumulative hazard function H(t);

$$H(t) = - \ln(S(t)) \tag{3.6}$$

3.6.4 Comparing the survival of two groups (Log-rank test)

The log-rank test is used to compare two or more groups of survival times. It tests the null hypothesis that the groups are from the same population. The log-rank test compares the observed number of events in each group with the corresponding expected numbers for each.

Survival times from two groups can be obtained by plotting the corresponding estimates of the two survival functions on the same axes. The summary statistics which will be obtained across the two groups can be compared. Log-rank test is used to compare the statistics. It is used to test the null hypothesis. The null hypothesis of no difference can be obtained between groups can be expressed by stating that the median survival of the two groups are equal.

3.6.4.1 Procedure for calculating the log-rank test two groups A & B (Machin, Campbell &Walters 2013)

i. The total number of events observed in groups A& B are O_A and O_B

ii. Under the null hypothesis, the expected number of events receiving treatment A at time t_i is $e_{Ai} = (d_i n_{Ai})/n_i$ (3.7)

t_i = ordered survival time

e_{Ai} = Expected number of events in A

d_i = number of events at t_i

n_{Ai} = number at risk in A

iii. the expected number of events should not be calculated beyond the last event

iv. the total number of events expected on A, assuming the null hypothesis of no difference between treatments, is $E_A = \sum e_{Ai}$ (3.8)

v. The number expected on B is $E_B = \sum d_i - E_A$. (3.9)

vi. Calculate X^2 Log-rank = $\frac{(O_A - E_A)2}{E_A} + \frac{(O_B - E_B)2}{E_B}$ (3.10)

vii. This has a X^2 distribution with degree of freedom df=1 as two groups are being compared

3.6.5 Multivariate Survival Analysis

3.6.5.1 Cox Proportional – Hazards Model

Proportional Hazards Regression using a partial maximum likelihood function to estimate the covariate parameters in the presence of censored time to failure data (Cox, 1972) has become widely used for conducting survival analysis. The Cox model is based on a modeling approach to

the analysis of survival data. The purpose of the model is to simultaneously explore the effects of several variables on survival.

It deals with the analysis of data which have the following characteristics:

1. The dependent variable is the waiting time until the occurrence of a well defined event
2. The observations are censored (some units the event of interest has not occurred at time of data analysis)
3. There are predictor variables whose effect on the waiting time needs to be assessed.

According to Wilson (2013), Model adequacy focuses on overall fitness, validity of the linearity assumption, inclusion (or exclusion) of a correct (or an incorrect) covariate, and identification of outlier and highly-influential observations. Due to the presence of censored data and the use of the partial maximum likelihood function, diagnostics to assess these elements in proportional hazards regression compared to most modeling exercises can be slightly more complicated.

The proportional hazards (PH) regression model has two kinds of assumptions, that when satisfied ordinarily allow one to rely on the statistical inferences and predictions the model yields. The first assumption is that the time independence of the covariates in the hazard function, that is, the ratio of the hazard function for two individuals with different regression covariates, does not vary with time, which is also known as the PH assumption. The second assumption is that the relationship between log cumulative hazard and a covariate is linear.

3.6.5.2 Fitting the Cox Proportional Hazard Model

A Cox regression analysis yields an equation for the hazard as a function of several explanatory variables. This entails obtaining parameter estimates for the unknown beta (β)

coefficients. The baseline hazard h_0 (t) may also be estimated. These two components were estimated separately by first estimating the beta (β) using the Maximum Likelihood Estimator methods and then h_0 (t) non-parametrically. According to Cox (1972), one can obtain consistent and highly efficient estimators of betas (β) by maximizing a partial likelihood independently of h_0 (t).

The multivariable Cox model links the hazard to an individual *i* at time *t*, h_i *(t)* to a baseline hazard h_0 (t) by;

$$log\ [hi\ (t)] = \log[h_0(t)] + \beta_1 x_1 + \beta_2 x_2 + \ldots + \beta_k x_k \qquad (3.11)$$

Where x_1, $x_{2\ldots}x_k$ are covariates associated with individual *i*. The baseline log hazard, log [h_0 *(t)*], serves as a reference point, and can be thought of as the intercept, α, of a multiple regression equation.

The coefficients in a Cox regression relate to hazard; a positive coefficient indicates a worse prognosis and a negative coefficient indicates a protective effect of the variable with which it is associated. The interpretation of the hazards ratio depends upon the measurement scale of the predictor variable in question.

3.6.5.3 Time-dependent and fixed covariates

In prospective studies, when individuals are followed over time, the values of covariates may change with time. Covariates can thus be divided into fixed and time-dependent. A covariate is time dependent if the difference between its values for two different subjects changes with time; e.g. serum cholesterol. A covariate is fixed if its values cannot change with time, e.g. sex or race. Lifestyle factors and physiological measurements such as blood pressure are usually time-dependent. Cumulative exposures such as smoking are also time-dependent but are often

forced into an imprecise dichotomy, i.e. "exposed" vs. "not-exposed" instead of the more meaningful "time of exposure". There are no hard and fast rules about the handling of time dependent covariates.

3.6.5.4 Model analysis and deviance

A test of the overall statistical significance of the model is given under the "model analysis" option. Here the likelihood chi-square statistic is calculated by comparing the deviance (- 2 * log likelihood) of the model, with all of the covariates you have specified, against the model with all covariates dropped. The individual contribution of covariates to the model can be assessed from the significance test given with each coefficient in the main output; this assumes a reasonably large sample size. Deviance is minus twice the log of the likelihood ratio for models fitted by maximum likelihood (Cox 1972).The value of adding a parameter to a Cox model is tested by subtracting the deviance of the model with the new parameter from the deviance of the model without the new parameter, the difference is then tested against a chi-square distribution with degrees of freedom equal to the difference between the degrees of freedom of the old and new models. The model analysis option tests the model you specify against a model with only one parameter, the intercept; this tests the combined value of the specified predictors/covariates in the model.

CHAPTER FOUR: RESULTS AND ANALYSIS

4.0 Introduction

This chapter describes the analysis of data and the findings of the study.

4.0.1 Study Design

The study design was a retrospective cohort of patients who underwent renal transplant for the four year period between January 2010 and February 2014. Patient's demographic data, history of investigations, Comorbidity, and health history during the transplant period were obtained.

4.0.2 Study population.

Target population in a study is the whole population in which the researcher has interest and to which the researcher will postulate the findings. The study population comprised of all chronic renal failure patients who underwent kidney transplant for the four year period between January 2010 and February 2014.

4.0.3. Inclusion and Exclusion Criteria

4.0.3.1 Inclusion Criteria

All patients who underwent renal transplant at Kenyatta National Hospital renal Unit between year January 2010 and February 2014 were included in the study.

4.0.3.2 Exclusion Criteria

All patients who underwent renal transplant outside Kenyatta Hospital and were attending clinic at the Renal Unit Clinic were excluded from the study.

4.0.4 Key variables in survival analysis are;

4.0.4.1 Time to event: The variable measures the duration to the event defined by the status variable. In this case it is the time taken for the patient to reject a kidney allograft and also the time taken by the patient from time of transplant to death. The time of enrollment was the month of transplant. Time was measured in months.

4.0.4.2 Status variable (outcome variables): Also called the event or censoring variable. It is the response or the dependent variable in Cox regression. In this study event variables are the rejection of the allograft and death of the patient. Graft survival is defined as time from transplant to graft failure, censoring for death with a functioning graft and grafts still functioning at time of analysis. The rejection was considered to have taken place if the patient went back to hemodialysis or undergoes another transplant. Those who rejected the allograft were considered to experience the event in the case of allograft survival while others were censored. Those who died with a working allograft were said to have survived in the case of allograft survival. Patients who died due to kidney related causes and complications were said to have experienced the event in the case of patient survival while others were censored. Events were coded as 1 and censored as 0. The outcomes were obtained from the file using a check list whereby we read through the file and charted all the outcomes.

4.0.4.3 Covariates*:* these are independent variables which were tested for their association with the events of interest. Some covariates were tested for their association with time to allograft rejection and patient's death.

The following are required for survival analysis to be successful;

- Date of entry (date of transplantation): the date when the transplant was done
- Well defined scale of measurement: the scale of measurement was the number of months since transplantation to the event or to exit.
- Well defined event of interest (allograft rejection or death due to kidney complications)

  Definition:

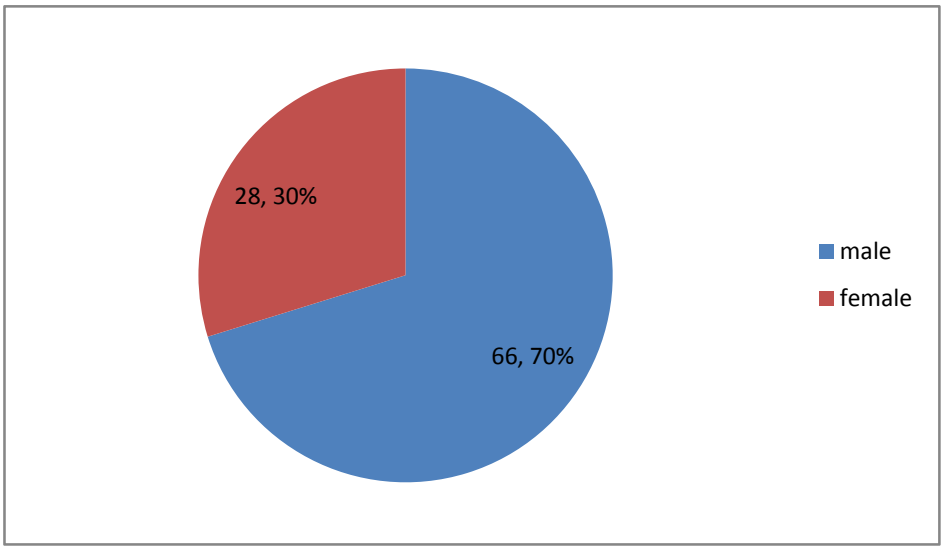
  - Age – the number of years the patient lived from birth to date of transplantation.
  - Gender- the qualitative measure of whether the patient is male of female
  - Smoking status:- the qualitative measure of whether the patient was smoking or not during the period after transplantation
  - Hypertension: - this was defined as the patient having a blood pressure of above 140/90 mmHg during the period after transplantation of the allograft.
  - Diabetes mellitus: - this was defined as a patient who had been diagnosed by a medical specialist to have diabetes mellitus and was on treatment for the same.

4.1 Baseline Enrollment Characteristics

A total of ninety four (94) clients were enrolled into the study. The study included all the patients who underwent renal transplant at Kenyatta National Hospital between the months of February 2010 to the month of February 2014. 70.2% were male while 29.8% were female. All the subjects who were transplanted at Kenyatta National Hospital were hypertensive. Among those enrolled in the study, twenty six (26) were diabetic & two (2) smokers. Eight (8) kidney allografts failed post transplant while eighty six (86) survived. Twelve (12) patients died while eighty two (82) survived. All the kidney donors were life donors. They were all relatives to the patients. Majority of the donors were female. Only two patients had Systemic Lupus Erythematosus (SLE).

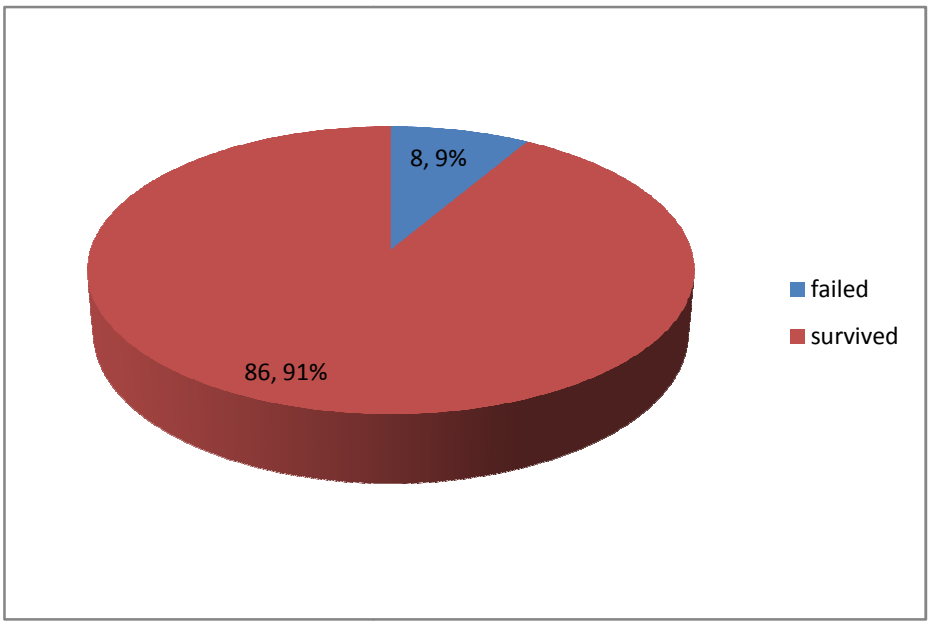
Out of 94 subjects 66 were male while 28 were female. Figure 4.1.1 (a) illustrates composition of gender.

Figure 4.1.1(a) Gender



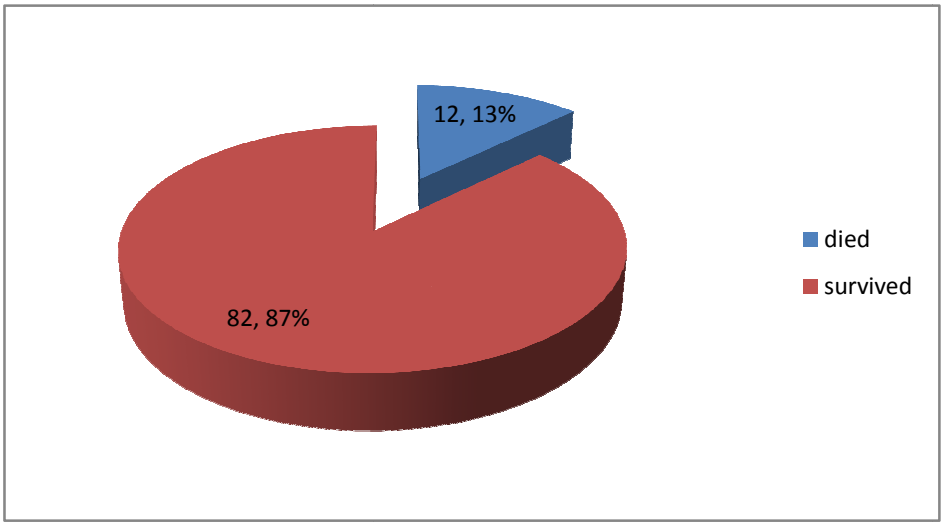
Among the 94 patients who were transplanted 8 lost the graft while 86 grafts survived. Figure 4.1.1(b) illustrates the status of the kidney graft.

Figure 4.1.1 (b) Kidney Graft Status



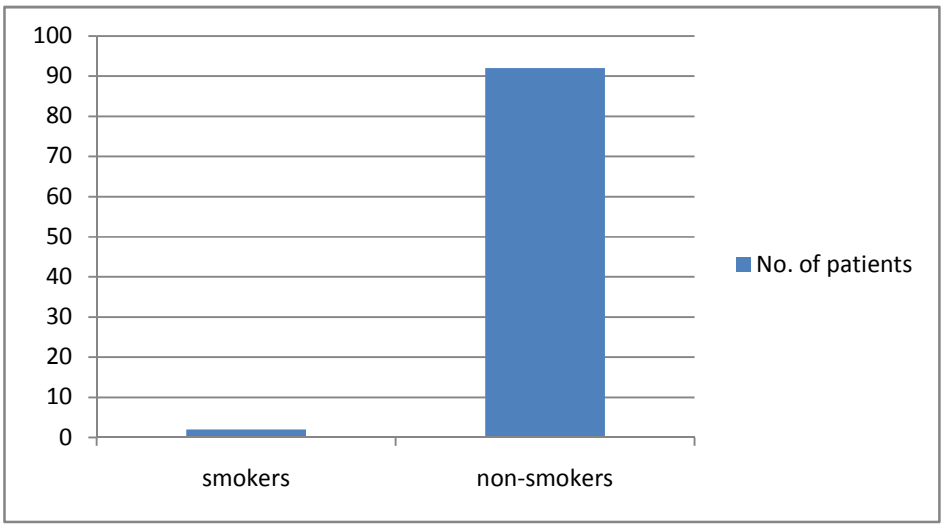
Among the patients who underwent kidney transplant 12 died while 82 survived. Figure 4.1.1.(c) illustrates the patient status

Figure 4.1.1 (c) Patient Status



Among the subjects there were only two smokers. Figure 4.1.1 (d) illustrates the smoking status.

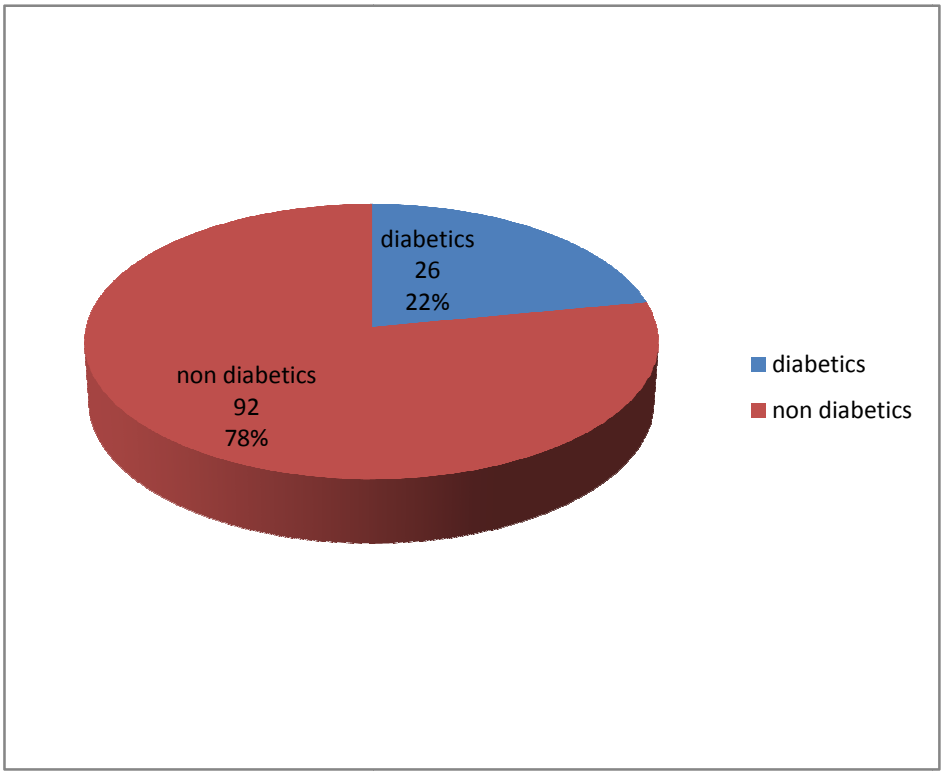
Figure 4.1.1 (d) Smoking Status



All the patients who were enrolled in the study were hypertensive.

Minority of the subjects enrolled in the study had diabetes mellitus. Figure 4.1.1 (e) shows the diabetic status.

Figure 4.1.1 (e) Status of Diabetes Mellitus



Majority of the kidney donors were female. Figure 4.1.1 (f) below illustrates the donor and relationships.

Figure 4.1.1 (f) Donor Relationships

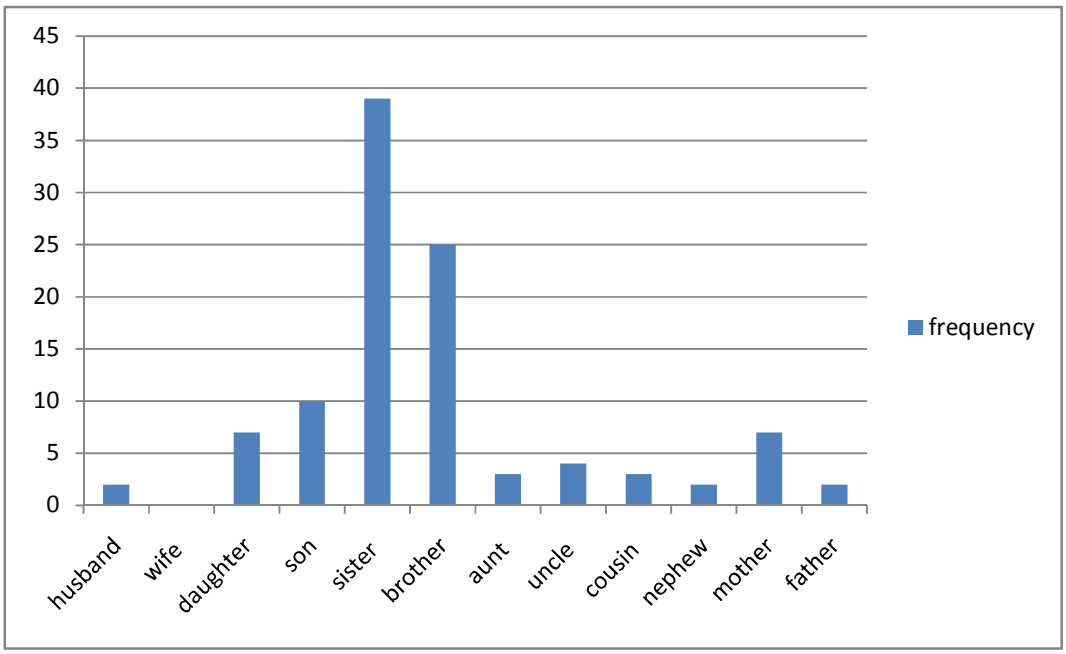
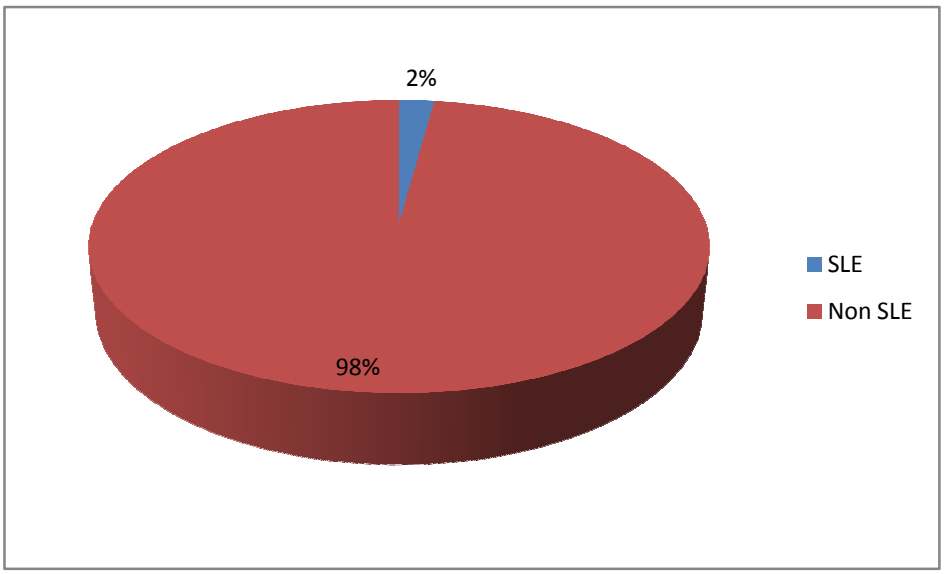


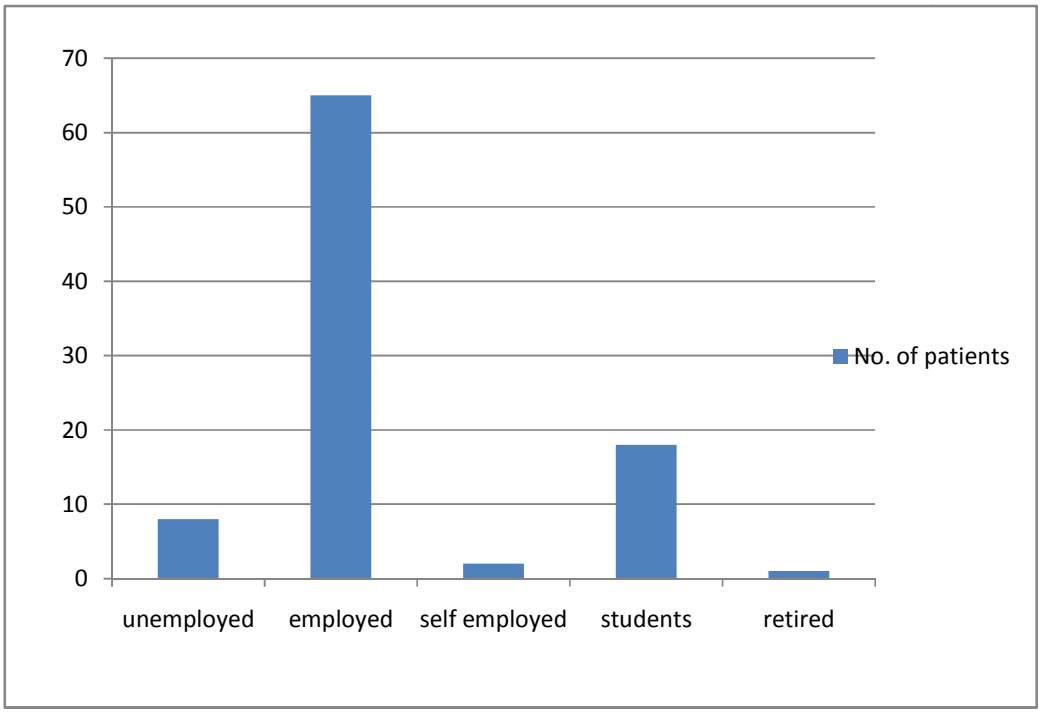
Table 4.1.1 HLA Missmatch

	No.	**Percentage**
0	4	4.3%
1	1	1.1%
2	20	21.1%
3	39	41.5%
4	22	23.4%
5	0	0
6	7	7.4%

Figure 4.1.1 (g) SLE Status



Only two kidney recipients were having SLE as shown in figure 4.1.1 (h) above. Figure 4.1.1 (h) presents the occupation status



Age at transplant

The mean age at transplant for the patients at Kenyatta National Hospital was 37.73 years with a standard deviation of 1.4 years. The 95% confidence interval was [34.95- 40.51]. The confidence interval is narrow,which gives a good precision. This means there is less uncertainity about the effect size.

Mean Donors Age

The mean age of the donor at Kenyatta National Hospital was 34.44 years with a standard deviation of 0.91years. The 95% confidence interval was [32.62- 36.25]. The confidence interval is narrow,which gives a good precision. This means there is less uncertainity about the effect size.

4.2 Renal Transplant Patients' Survival

A total of ninety four clients were enrolled in the study. Four clients died between day zero and the fourteenth day post kidney transplant. There were eight failures among the ninety subjects who survived the first two weeks post kidney transplant. Total time at risk was 2190 months. The Median was twenty five (25) months. All the subjects were hypertensive. The incidence rate was 0.003653. Table 4.2.1 below illustrates patient survival observations.

There were ninety four (94) observations in the study. Four (4) of the subjects died on or before they entered the study. This is to mean that they died on the day of transplant or within the first two weeks post transplant. These are the patients who did not leave the hospital alive post transplant. Ninety subjects remained in the study. Among the ninety subjects there were eight (8) failures. By failure we mean deaths. The total analysis time at time zero (t=0) at risk was 2190 months. The last observed exit was at forty nine (49) months.

The four subjects who died between the zero days and the fourteenth day being not included in the survival summary give an incidence rate of 0.003653.

Table 4.2.1 Patients' Survival Data Description

Category	Total	Mean	Minimum	Median	Maximum
No. of subjects	90				
No. of records	90	1	1	1	1
First entry time		0	0	0	0
Final exit time		24.33333	1	25	49
Subject with gap	0				
Time on gap if gap	0	.	.	.	.
Time at risk	2190	24.33333	1	25	49
Failures	8	0.0888889	0	0	1

Table 4.2.1 above illustrates patients, survival descriptions. The median time was twenty five (25) months.

The patients' survival for the first year while including the subjects who died on or before entry to the study was 88.7%, second year 88.7%, third year 88.7% and 82.6% for the fourth year. Survival for the first month was 95.74%, second month 94.68%, third month 93.62% and 91.48% for the fourth to the nineth month. Figure 4.2.1 below illustrates the Kaplan-Meier survival graph for the patients survival post renal transplant.

Figure 4.2.1 Survival Graph

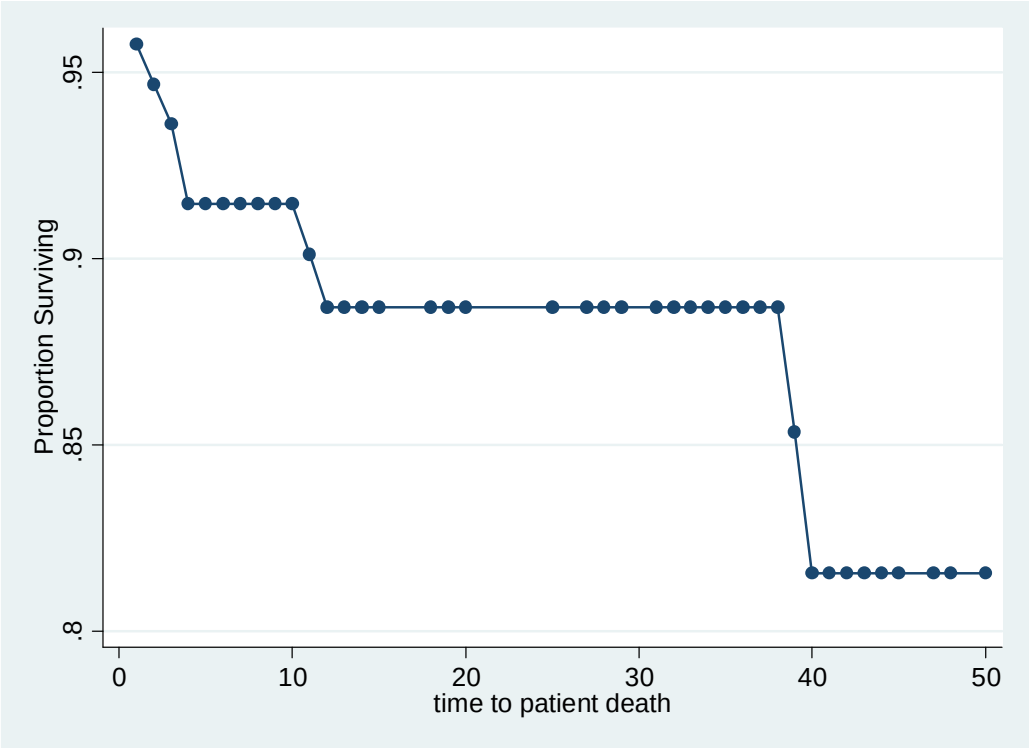


Table **4.2.2** below illustrates the survival of patients post renal transplant. It includes patients who died on or before entry (subjects who died immediately after they were transplanted). The survival time proportions in the table are cumulative.

Table 4.2.2: Patients' Survival Table

Interval	Beginning total	Deaths	Lost	Survival	Std. error	95% confidence interval
< 1	94	4	0	0.9574	0.0208	0.8906 0.9838
1 - 2	90	1	0	0.9468	0.0231	0.8769 0.9775
2 - 3	89	1	0	0.9362	0.0252	0.8634 0.9708
3 - 4	88	2	1	0.9148	0.0288	0.8368 0.9564
4 - 5	85	0	6	0.9148	0.0288	0.8368 0.9564
5 - 6	79	0	3	0.9148	0.0288	0.8368 0.9564
6 - 7	76	0	2	0.9148	0.0288	0.8368 0.9564
7 - 8	74	0	1	0.9148	0.0288	0.8368 0.9564
8 - 9	73	0	3	0.9148	0.0288	0.8368 0.9564
9 – 10	70	0	1	0.9148	0.0288	0.8368 0.9564
10 - 11	69	1	4	0.9011	0.0315	0.8180 0.9475
11 - 12	64	1	1	0.8869	0.0340	0.7989 0.9379
12 - 13	62	0	1	0.8869	0.0340	0.7989 0.9379
13 -14	61	0	4	0.8869	0.0340	0.7989 0.9379
14 -15	57	0	4	0.8869	0.0340	0.7989 0.9379
17 -18	53	0	1	0.8869	0.0340	0.7989 0.9379
18 - 19	52	0	1	0.8869	0.0340	0.7989 0.9379
19 - 20	51	0	2	0.8869	0.0340	0.7989 0.9379
24 - 25	49	0	4	0.8869	0.0340	0.7989 0.9379
26 - 27	45	0	2	0.8869	0.0340	0.7989 0.9379
27 - 28	43	0	1	0.8869	0.0340	0.7989 0.9379

28 -29	42	0	1	0.8869	0.0340	0.7989	0.9379
30 - 31	41	0	3	0.8869	0.0340	0.7989	0.9379
31 - 32	38	0	2	0.8869	0.0340	0.7989	0.9379
32 - 33	36	0	3	0.8869	0.0340	0.7989	0.9379
33 - 34	33	0	1	0.8869	0.0340	0.7989	0.9379
34 - 35	32	0	1	0.8869	0.0340	0.7989	0.9379
35 - 36	31	0	2	0.8869	0.0340	0.7989	0.9379
36 - 37	29	0	1	0.8869	0.0340	0.7989	0.9379
37 - 38	28	0	1	0.8869	0.0340	0.7989	0.9379
38 - 39	27	1	1	0.8535	0.0464	0.7333	0.9223
39 - 40	25	1	5	0.8155	0.0578	0.6684	0.9019
40 - 41	19	0	2	0.8155	0.0578	0.6684	0.9019
41 - 42	17	0	2	0.8155	0.0578	0.6684	0.9019
42 - 43	15	0	2	0.8155	0.0578	0.6684	0.9019
43 - 44	13	0	1	0.8155	0.0578	0.6684	0.9019
44 - 45	12	0	1	0.8155	0.0578	0.6684	0.9019
46 - 47	11	0	1	0.8155	0.0578	0.6684	0.9019
47 - 48	10	0	9	0.8155	0.0578	0.6684	0.9019
49 - 50	1	0	1	0.8155	0.0578	0.6684	0.9019

The **table 4.2.3**, below includes the patients' survival while excluding the four subjects who died in the first two weeks post transplant. This was the survival of the patients who survived the transplant. The survival after the initial two weeks post transplant is higher. The one year, two

years, three years and four years survival rate in this group is 92.7%, 92.7%, 92.7% & 85.7 % respectively.

Table 4.2.3

Time	Beginning total	Fail	Net lost	Survivor function	Std. error	95% Confidence interval
1	90	1	0	0.9889	0.0110	0.9237 0.9984
2	89	1	0	0.9778	0.0155	0.9141 0.9944
3	88	2	1	0.9556	0.0217	0.8859 0.9831
4	85	0	6	0.9556	0.0217	0.8859 0.9831
5	79	0	3	0.9556	0.0217	0.8859 0.9831
6	76	0	2	0.9556	0.0217	0.8859 0.9831
7	74	0	1	0.9556	0.0217	0.8859 0.9831
8	73	0	3	0.9556	0.0217	0.8859 0.9831
9	70	0	1	0.9556	0.0217	0.8859 0.9831
10	69	1	4	0.9417	0.0254	0.8650 0.9754
11	64	1	1	0.9270	0.0290	0.8435 0.9668
12	62	0	1	0.9270	0.0290	0.8435 0.9668
13	61	0	4	0.9270	0.0290	0.8435 0.9668
14	57	0	4	0.9270	0.0290	0.8435 0.9668
17	53	0	1	0.9270	0.0290	0.8435 0.9668
18	52	0	1	0.9270	0.0290	0.8435 0.9668
19	51	0	2	0.9270	0.0290	0.8435 0.9668
24	49	0	4	0.9270	0.0290	0.8435 0.9668
26	45	0	2	0.9270	0.0290	0.8435 0.9668

27	43	0	1	0.9270	0.0290	0.8435	0.9668
28	42	0	1	0.9270	0.0290	0.8435	0.9668
30	41	0	3	0.9270	0.0290	0.8435	0.9668
31	38	0	2	0.9270	0.0290	0.8435	0.9668
32	36	0	3	0.9270	0.0290	0.8435	0.9668
33	33	0	1	0.9270	0.0290	0.8435	0.9668
34	32	0	1	0.9270	0.0290	0.8435	0.9668
35	31	0	2	0.9270	0.0290	0.8435	0.9668
36	29	0	1	0.9270	0.0290	0.8435	0.9668
37	28	0	1	0.9270	0.0290	0.8435	0.9668
38	27	1	1	0.8927	0.0438	0.7675	0.9524
39	25	1	5	0.8570	0.0547	0.7078	0.9336
40	19	0	2	0.8570	0.0547	0.7078	0.9336
41	17	0	2	0.8570	0.0547	0.7078	0.9336
42	15	0	2	0.8570	0.0547	0.7078	0.9336
43	13	0	1	0.8570	0.0547	0.7078	0.9336
44	12	0	1	0.8570	0.0547	0.7078	0.9336
46	11	0	1	0.8570	0.0547	0.7078	0.9336
47	10	0	9	0.8570	0.0547	0.7078	0.9336
49	1	0	1	0.8570	0.0547	0.7078	0.9336

Table 4.2.4 Failure Rates as Per Gender

Total observations included in the analysis = 90 subjects

Gender	Died	Estimated Rate	95% confidence intervals	
			Lower	Upper
Female	3	0.0041265	0.0013309	0.0127946
Male	5	0.0034176	0.0014225	0.0082110

Five (5) male patients died after they survived the first two weeks post-transplant, while three (3) female patients died at the same period. The failure rate for the female was higher than that for the male patients.

4.2.1 Non Parametric Test for Categorical Variables

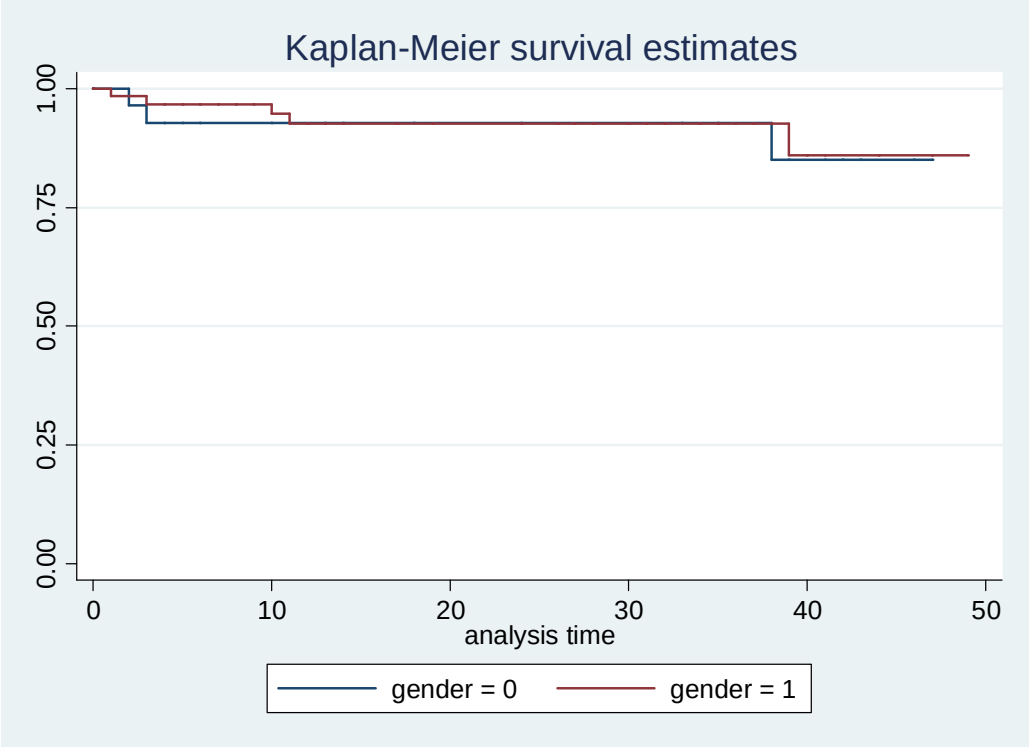
Kaplan-Meier survival curve was used to analyze survival at fixed time points and then comparisons were made of the patients survival times exceeding the period. The periods are in months. Logrank test was used to compare the survival times of the two groups.

Table 4.2.5 Logrank Test for Gender

Gender	Events observed	Events expected
Female	3	2.74
Male	5	5.26
Total	8	8.00

Chi2 (1) = 0.04; p-value = 0.8455

Figure 4.2.2 Kaplan-Meier survival Estimates for Gender



Key: analysis time = time to patients' death.

Gender: female = 0; Male = 1

The test P-value is higher than 0.05. This meant that gender was not to be considered as a predictor in the final model. Through the Logrank test we considered to eliminate gender. The Kaplan-Meier survival curve suggests that there was no difference in terms of survival for both gender.

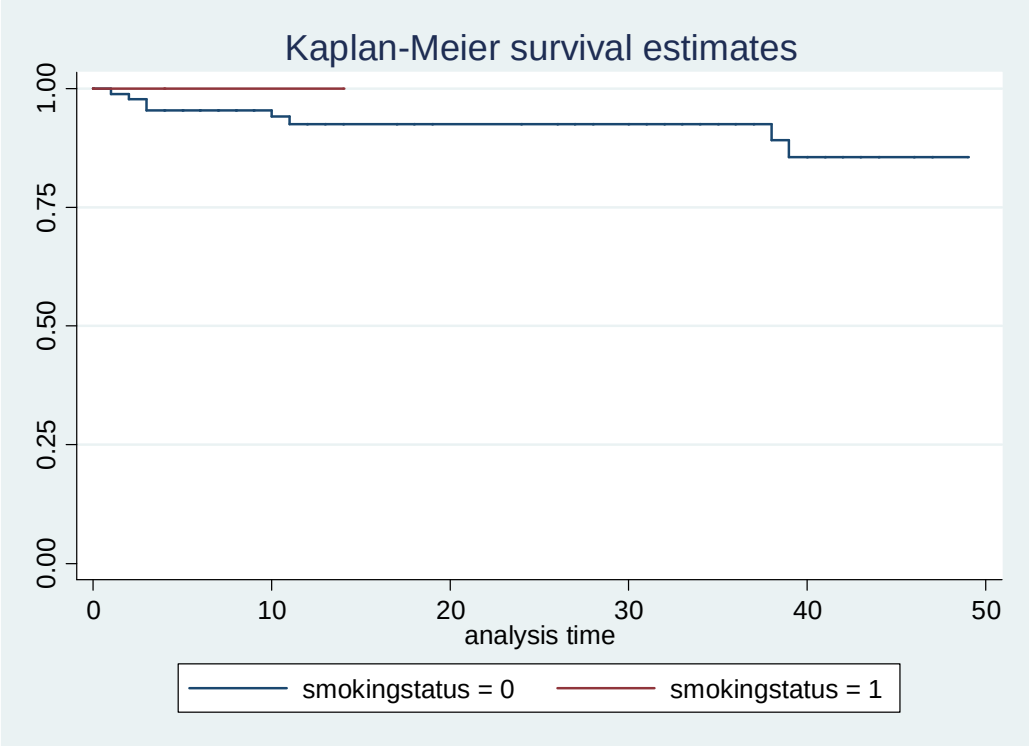
Table 4.2.6: Logrank Test for Smoking Status

Smoking status	Events observed	Events expected
Non-smoker	8	7.88
Smoker	0	0.12
total	8	8.00

Chi2 (1) = 0.12, p-value = 0.7254

Since the P-value was above 0.05, we considered eliminating smoking status from the final model. The number of the smokers was only two against ninety two non-smokers. This may have affected the significance of the results.

Figure 4.2.3 Kaplan Meier Survival Graph for smoking status



Key: Non-Smoker = 0; Smoker =1; Analysis Time = time to patient's death

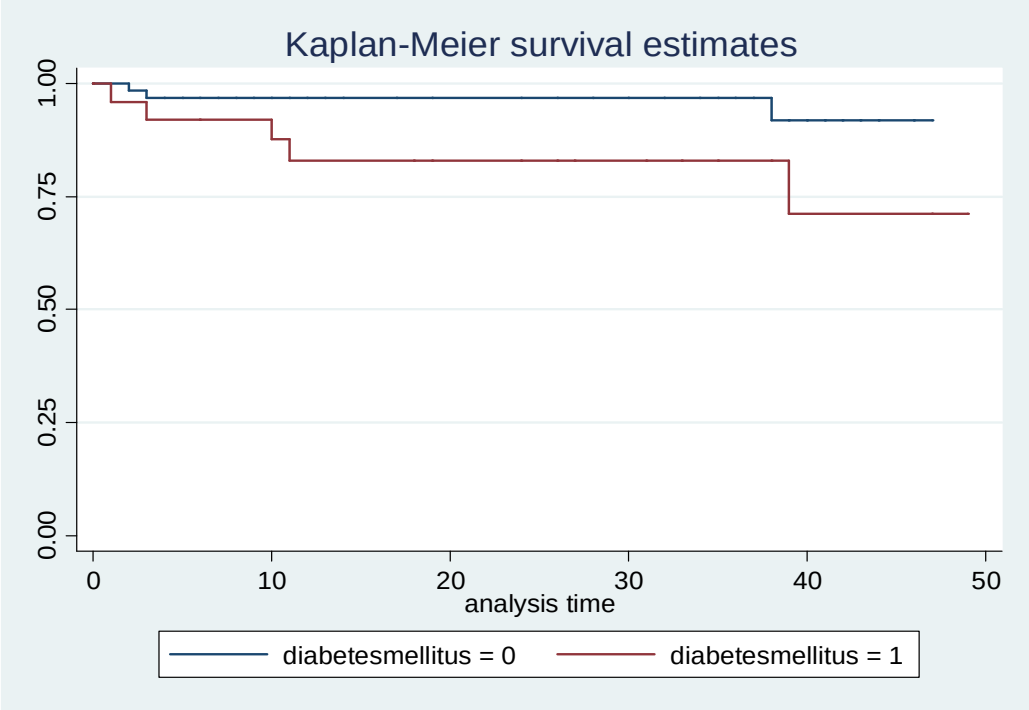
Table 4.2.7 Logrank Test for Diabetes Mellitus

Diabetes Mellitus	Events observed	Events Expected
Non- Diabetic	3	5.73
Diabetic	5	2.27
Total	8	8.00

Chi2 (1) = 4.60, p-value = 0.032

Diabetes mellitus was considered for inclusion in the final model because of the P-value of 0.0320. Diabetic patients had a lower probability of surviving compared to non diabetic patients. This meant that diabetic status affected survival of the patients post transplant.

Figure 4.2.4 Kaplan Meier Survival Graph for Diabetes Mellitus



Key: Non-Diabetic = 0; Diabetic = 1

Table 4.2.8 Logrank Test for Donor Relationship

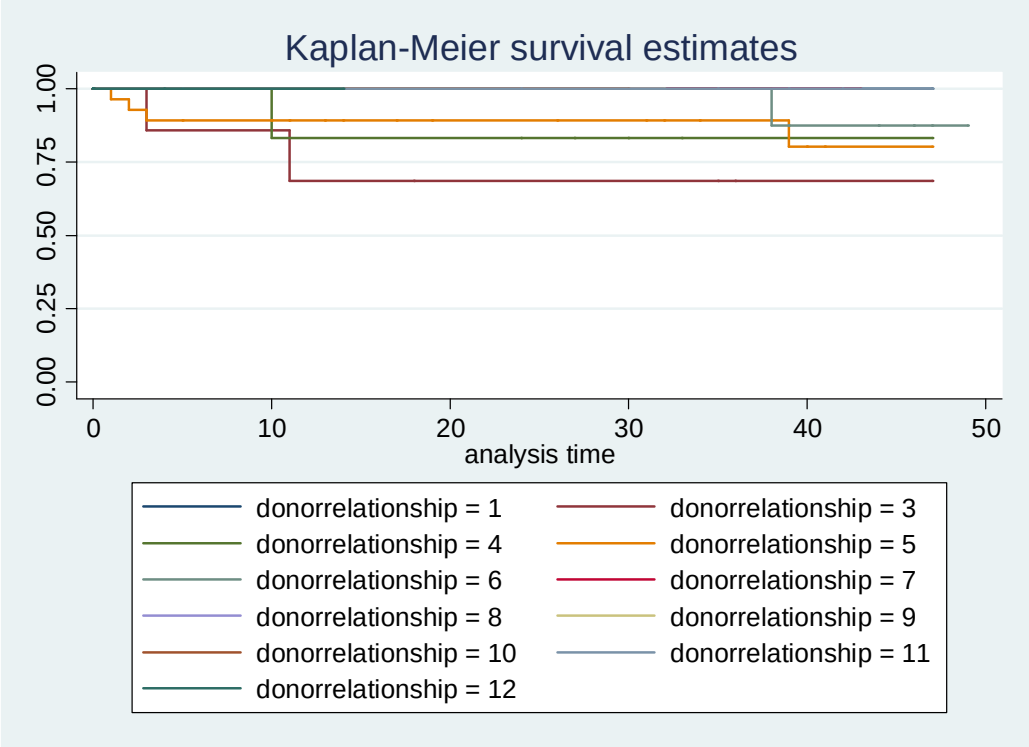
Donor relationship	Events observed	Events expected
1	0	0.21
3	2	0.54
4	1	0.64
5	4	2.72
6	1	2.27
7	0	0.24
8	0	0.17
9	0	0.20
10	0	0.12
11	0	0.80
12	0	0.12
Total	8	8.00

Chi2 (10) = 7.39,

P-value =0.6883

The P- value in the Logrank test suggested that the donor relationship to be considered for elimination in the final model.

Figure 4.2.5 Survival Graph for Donor Relationship



Key: Husband=1; Wife=2; Daughter = 3; Son = 4; Sister = 5; Brother = 6; Aunt = 7; Uncle =8; Cousin =9; Nephew = 10; Mother =11; Father =12.

All the donors in the study were relatives to the patients. They were live donors. The Kaplan-Meier survival curves shows that different donor relationships had a difference in survival of patients post transplant.

Table 4.2.9 Logrank Test for HLA Mismatch

HLA Mismatch	Events Observed	Events Expected
0	0	0.32
1	1	0.10
2	1	1.05
3	5	3.81
4	1	2.23
6	0	0.50
Total	8	8.00

Chi2 (5) = 10.27, P- value = 0.0681

The antigens of the human leukocyte antigen (HLA) system were considered for the model. The HLA mismatch of zero (0) meant that there was perfect match. HLA mismatch played a role in the survival of the patient depending on the level. Figure 4.2.6 below illustrates the Kaplan-Meier survival curves for HLA mismatch.

Figure 4.2.6 Survival Graph for HLA Missmatch

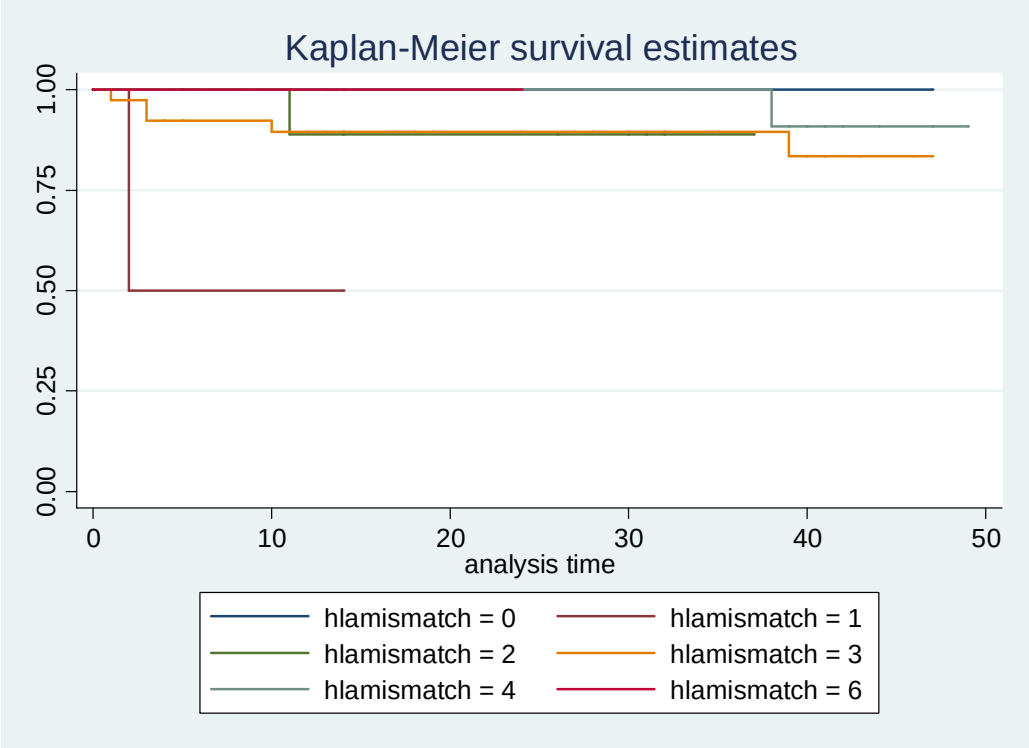


Table 4.2.10 Logrank Test for Systemic Lupus Erythematosus

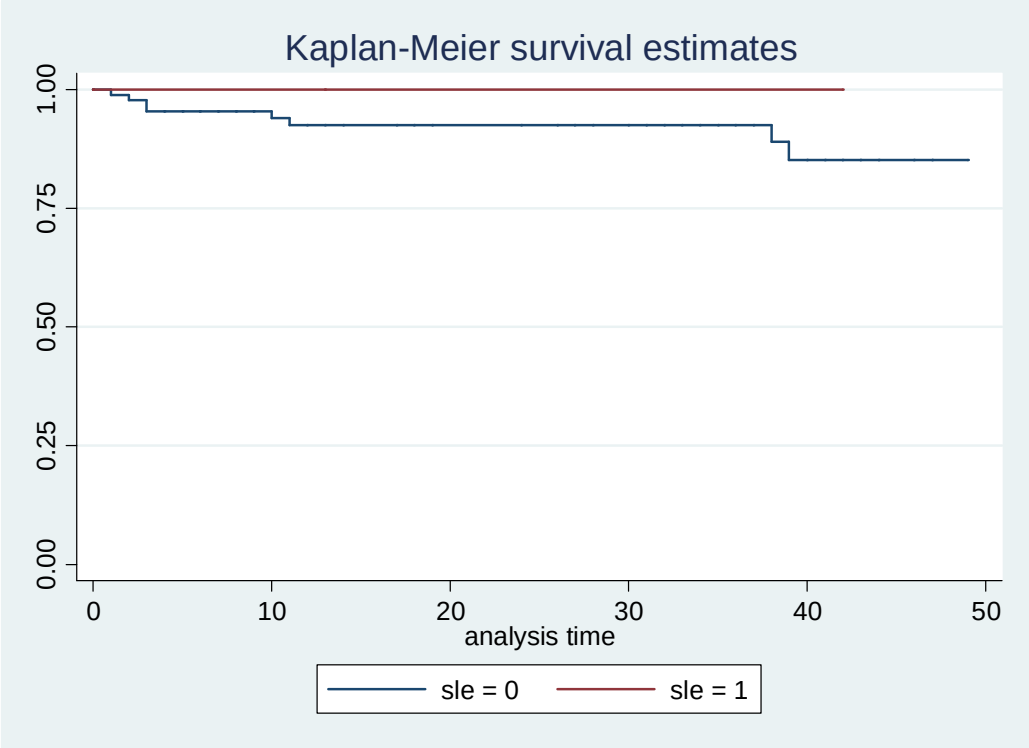
SLE	Events Observed	Events Expected
Non SLE patient	8	7.77
SLE patient	0	0.23
Total	8	8.00

Chi2 (1) = 0.23; P- value = 0.6278

SLE was considered for elimination from the final model. The survival curves were not different.

The number of patients who had SLE was few compared to those who did not have SLE.

Figure 4.2.7 Survival Graph for SLE



Key: Patients with SLE = 1 Patients without SLE =0

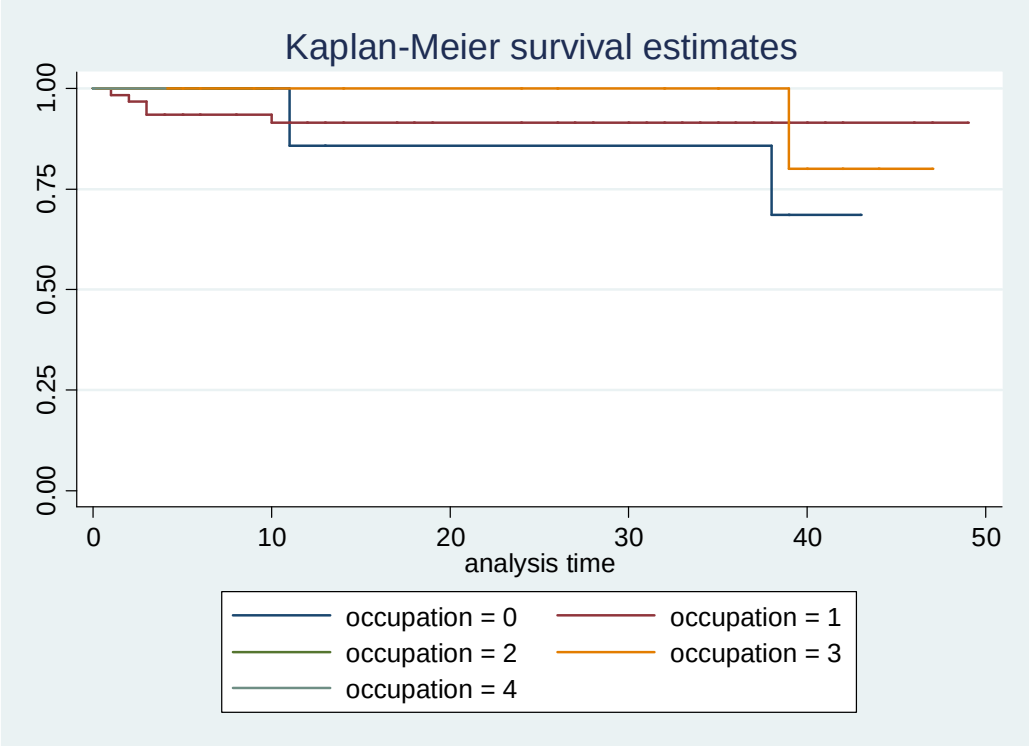
Table 4.2.11 Logrank Test for Occupation

Occupation	**Events Observed**	**Events Expected**
Unemployed	2	0.98
Employed	5	5.36
Self employed	0	0.10
Students	1	1.51
Retired	0	0.05
Total	8	8.00

Chi2 (4) = 1.44; P-value=0.8367

Occupation was considered for elimination from the final model. The survival curves for occupation had no difference. The survival curves in the figure 4.2.8 below shows that patient survival was different among the different occupations.

Figure 4.2.8 Survival Graph for Occupation



Key: Unemployed = 0

Employed = 1

Self employed = 2

Student = 3

Retired = 4

4.2.2 Tests for Continuous Variables

Table 4.2.12 Cox PH Regression for Age at Transplant
Cox regression – Breslow method for ties

Log likelihood = -31.542621 LR chi2 (1) = 2.62; Prob. > chi2 =0.1058

_t	Coefficient	Std. error	Z	P>Z	[95% Confidence interval
Age at transplant	0.045442	0.0286892	1.58	0.113	- 0.0107877 0.1016718

The P-value was greater than 0.05 which meant that the model was not a potential candidate for the final model. This meant that age at transplant may have contributed to the survival of the patient.

Table 4.2.13 Cox PH Regression for Age of the Donor
Cox regression – Breslow method for ties

Log likelihood = - 32.6821 LR chi2 (1) = 0.34 Prob. >chi2 = 0.5613

_t	Coefficient	Std. Error	Z	P > Z	[95% Confidence interval]
Donors' age	0.024085	0.0410284	0.59	0.557	-0.0563291 0.1044991

The Chi-squared test of age of the donor had a p-value of more than 0.05 and so it was not a potential candidate for the final model.

Model Building

For the model building, we first considered the model which included all the predictors that had a p-value of less than 0.2 - 0.25 in the univariate analyses. Categorical variables considered were, diabetes mellitus, and HLA mismatch. The continuous variable considered was age at transplant. The categorical predictor HLA mismatch has seven levels and therefore we included this predictor using dummy variable with the group HLA mismatch =0 as the reference group.

Table 4.2.14 Cox regression – Breslow for ties
Log likelihood = -27.004323, LR Chi2 (6) = 11.69; Prob. > chi2 =0.0692

_t	**Coefficient**	**Std. error**	**Z**	**P > Z**	**[95% Confidence interval]**
Age at transplant	0.0220069	0.0372266	0.59	0.554	-0.0509559 0.0949698
Diabetes Mellitus	1.542578	0.9916366	1.56	0.120	-0.400994 3.48615
HLA mismatch **1**	24.48769	.	.	.	.
2	21.1603	1.545323	13.68	0.000	18.13152 24.18908
3	21.42517	1.288839	16.62	0.000	18.89909 23.95124
4	20.36073	1.584286	12.85	0.000	17.25559 23.461587
6	-21.37695	3.10e+09	-0.00	1.000	-6.08e+09 6.08e+09

The results were not statistically significant for age at transplant and diabetes mellitus. There were significant results for HLA mismatch. As the level of mismatch increases the patient was more likely to experience the event which was death.

P< 0.05 shows there is statistical significance.

Table 4.2.15 hazard ratio model

Log likelihood = -27.004323, LR Chi2 (6) = 11.69; Prob. > chi2 =0.0692

_t	**Hazard ratio**	**Std. error**	**Z**	**P > Z**	**[95% Confidence interval]**
Age at transplant	1.022251	0.038055	0.59	0.554	0.9503205 1.099626
Diabetes Mellitus	4.676632	4.637519	1.56	0.120	0.6696541 32.65997
HLA mismatch 1	4.31e+10	.	.	.	.
2	1.55e+09	2.39e+09	13.68	0.000	7.49e+07 3.2e+10
3	2.02e+09	2.60e+09	16.62	0.000	1.61e+08 2.52e+10
4	6.96e+08	1.10e+09	12.85	0.000	3.12e+07 1.55e+10
6	5.20e-10	1.614521	-0.00	1.000	.

4.3 Renal Graft Survival

A total of ninety four patients were done kidney transplant during the four years study period. Eight subjects rejected their kidney immediately. By immediately we mean before two weeks erupts after the transplant. This then left eighty six patients in the study. The total analysis time was 2152 months. There were five failures of the patients who survived the first two weeks. In total the failures were thirteen.

Figure 4.3.1 Renal Graft Survival Graph

The first and second year graft survival was 92.01%. the third and fourth year survival went down to 83.01%.

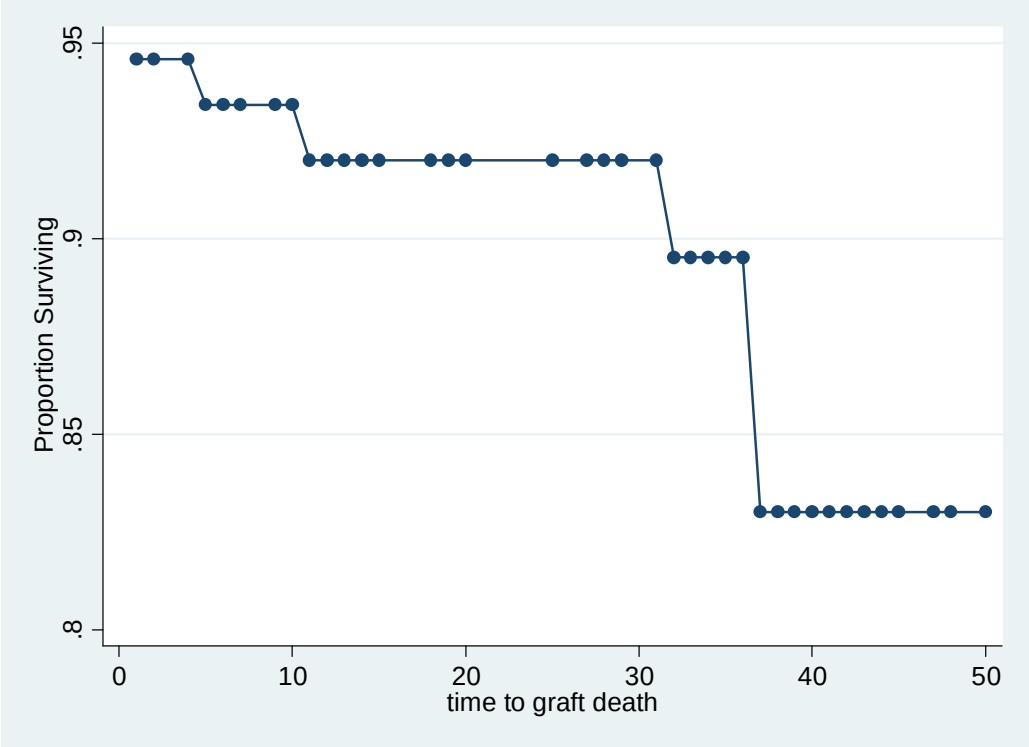


Table **4.3.1** below illustrates the renal graft survival for all the ninety four subjects in the study. Interval 0 -1 indicates that five kidneys were rejected while three patients were censored. The survival times is in months.

Table 4.3.1 Renal Graft Survival Life Table

Interval	Beginning total	Deaths	Lost	Survival	Std. error	95% confidence interval	
O - 1	94	5	3	0.9459	0.0235	0.8750	0.9771
1 - 2	86	0	1	0.9459	0.0235	0.8750	0.9771
3 - 4	85	0	1	0.9459	0.0235	0.8750	0.9771

4 - 5	84	1	6	0.9343	0.0260	0.8594	0.9699
5 - 6	77	0	3	0.9343	0.0260	0.8594	0.9699
6 - 7	74	0	2	0.9343	0.0260	0.8594	0.9699
8 - 9	72	0	3	0.9343	0.0260	0.8594	0.9699
9 – 10	69	0	1	0.9343	0.0260	0.8594	0.9699
10 - 11	68	1	4	0.9201	0.0292	0.8389	0.9613
11 - 12	63	0	1	0.9201	0.0292	0.8389	0.9613
12 - 13	62	0	1	0.9201	0.0292	0.8389	0.9613
13 -14	61	0	4	0.9201	0.0292	0.8389	0.9613
14 -15	57	0	4	0.9201	0.0292	0.8389	0.9613
17 -18	53	0	1	0.9201	0.0292	0.8389	0.9613
18 - 19	52	0	1	0.9201	0.0292	0.8389	0.9613
19 - 20	51	0	2	0.9201	0.0292	0.8389	0.9613
24 - 25	49	0	4	0.9201	0.0292	0.8389	0.9613
26 - 27	45	0	2	0.9201	0.0292	0.8389	0.9613
27 - 28	43	0	1	0.9201	0.0292	0.8389	0.9613
28 -29	42	0	1	0.9201	0.0292	0.8389	0.9613
30 - 31	41	0	3	0.9201	0.0292	0.8389	0.9613
31 - 32	38	1	2	0.8952	0.0375	0.7926	0.9487
32 - 33	35	0	3	0.8952	0.0375	0.7926	0.9487
33 - 34	32	0	1	0.8952	0.0375	0.7926	0.9487
34 - 35	31	0	1	0.8952	0.0375	0.7926	0.9487
35 - 36	30	0	2	0.8952	0.0375	0.7926	0.9487
36 - 37	28	2	1	0.8301	0.0564	0.6836	0.9129

37 - 38	25	0	1	0.8301	0.0564	0.6836	0.9129
38 - 39	24	0	1	0.8301	0.0564	0.6836	0.9129
39 - 40	23	0	5	0.8301	0.0564	0.6836	0.9129
40 - 41	18	0	2	0.8301	0.0564	0.6836	0.9129
41 - 42	16	0	2	0.8301	0.0564	0.6836	0.9129
42 - 43	14	0	1	0.8301	0.0564	0.6836	0.9129
43 - 44	13	0	1	0.8301	0.0564	0.6836	0.9129
44 - 45	12	0	1	0.8301	0.0564	0.6836	0.9129
46 - 47	11	0	1	0.8301	0.0564	0.6836	0.9129
47 - 48	10	0	9	0.8301	0.0564	0.6836	0.9129
49 - 50	1	0	1	0.8301	0.0564	0.6836	0.9129

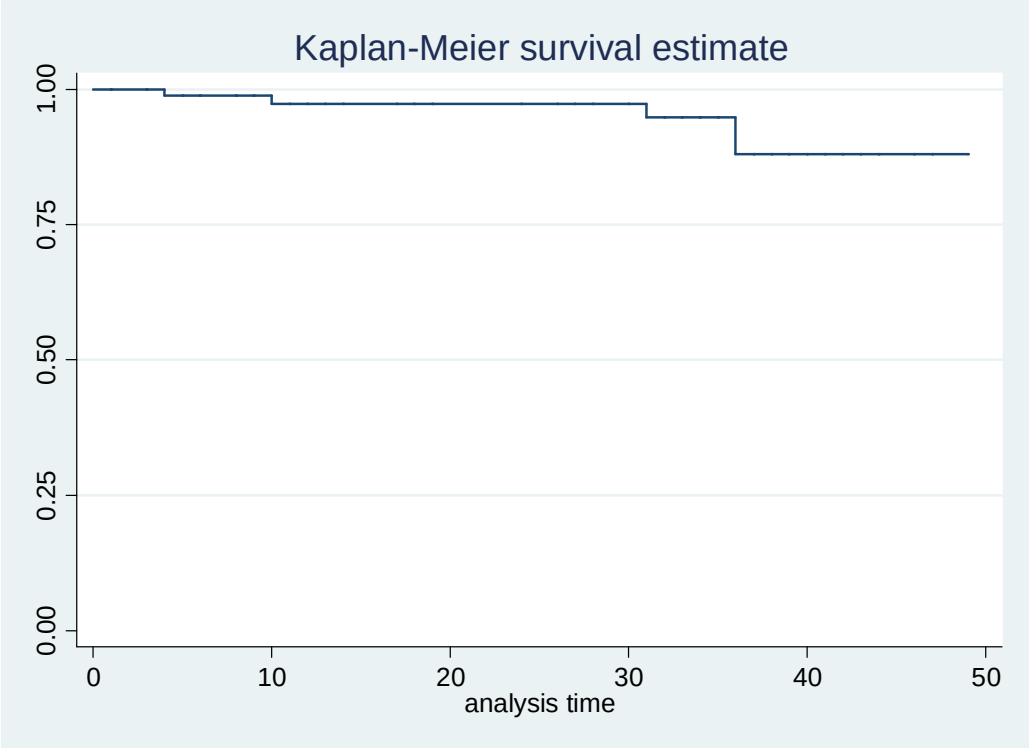
The life table below **(table 4.3.2)** excludes the eight subjects who lost their kidney allografts between the zero day and fourteenth day post transplant.

Table 4.3.2 Renal Graft Survival Life Table

Time	Beginning total	Fail	Net lost	Survivor function	Std. error	95% Confidence interval	
1	86	0	1	1.000	.	.	.
3	85	0	1	1.000	.	.	.
4	84	1	6	0.9881	0.118	0.9185	0.9983
5	77	0	3	0.9881	0.118	0.9185	0.9983
6	74	0	2	0.9881	0.118	0.9185	0.9983
8	72	0	3	0.9881	0.118	0.9185	0.9983
9	69	0	1	0.9881	0.118	0.9185	0.9983
10	68	1	4	0.9736	0.185	0.8977	0.9934
11	63	0	1	0.9736	0.185	0.8977	0.9934
12	62	0	1	0.9736	0.185	0.8977	0.9934
13	61	0	4	0.9736	0.185	0.8977	0.9934
14	57	0	4	0.9736	0.185	0.8977	0.9934
17	53	0	1	0.9736	0.185	0.8977	0.9934
18	52	0	1	0.9736	0.185	0.8977	0.9934
19	51	0	2	0.9736	0.185	0.8977	0.9934
24	49	0	4	0.9736	0.185	0.8977	0.9934
26	45	0	2	0.9736	0.185	0.8977	0.9934
27	43	0	1	0.9736	0.185	0.8977	0.9934
28	42	0	1	0.9736	0.185	0.8977	0.9934

30	41	0	3	0.9736	0.185	0.8977	0.9934
31	38	1	2	0.9479	0.0311	0.8371	0.9841
32	35	0	3	0.9479	0.0311	0.8371	0.9841
33	32	0	1	0.9479	0.0311	0.8371	0.9841
34	31	0	1	0.9479	0.0311	0.8371	0.9841
35	30	0	2	0.9479	0.0311	0.8371	0.9841
36	28	2	1	0.8802	0.0544	0.7191	0.9519
37	25	0	1	0.8802	0.0544	0.7191	0.9519
38	24	0	1	0.8802	0.0544	0.7191	0.9519
39	23	0	5	0.8802	0.0544	0.7191	0.9519
40	18	0	2	0.8802	0.0544	0.7191	0.9519
41	16	0	2	0.8802	0.0544	0.7191	0.9519
42	14	0	1	0.8802	0.0544	0.7191	0.9519
43	13	0	1	0.8802	0.0544	0.7191	0.9519
44	12	0	1	0.8802	0.0544	0.7191	0.9519
46	11	0	1	0.8802	0.0544	0.7191	0.9519
47	10	0	9	0.8802	0.0544	0.7191	0.9519
49	1	0	1	0.8802	0.0544	0.7191	0.9519

Figure 4.3.2 Renal Graft Survival Graph



Key: analysis time = time to rejection

Table 4.3.3 Logrank Test for Gender

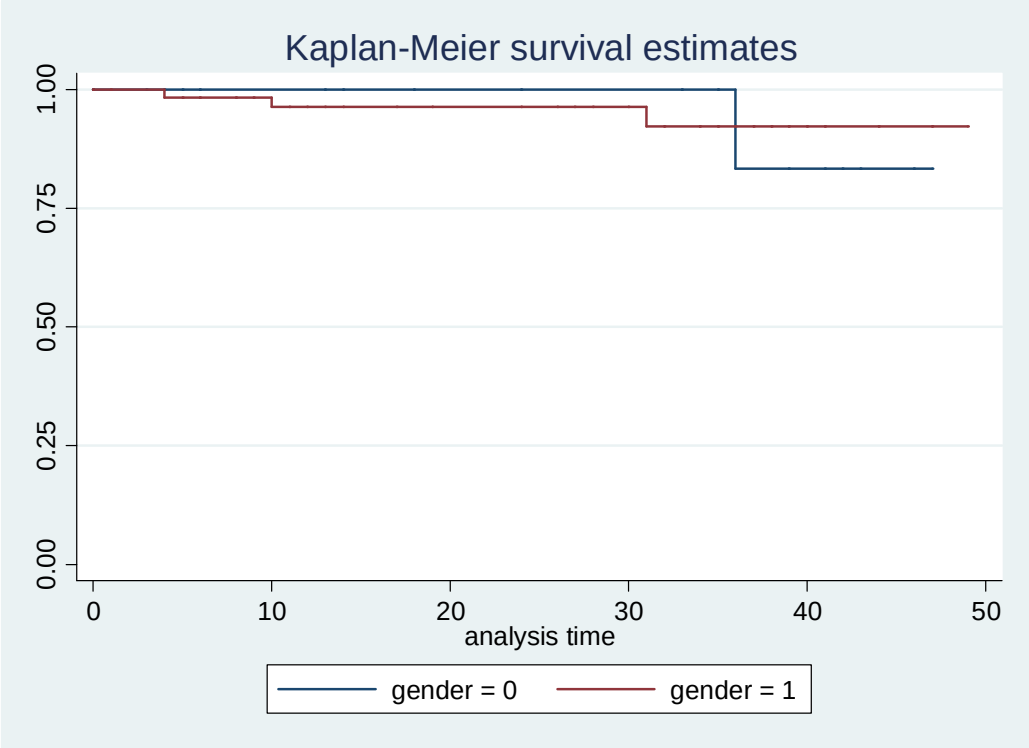
Gender	**Events Observed**	**Events Expected**
Female	2	1.81
Male	3	3.19
Total	5	5.00

Chi2 (1) = 0.03; P-value = 0.8538

The p-value for the test is more 0.05, so it was considered for elimination from the final model.

The Kaplan-Meier survival curves were not different for either gender.

Figure 4.3.3 Renal Graft Survival Graph for Gender



Key: 0 = Female; 1=Male

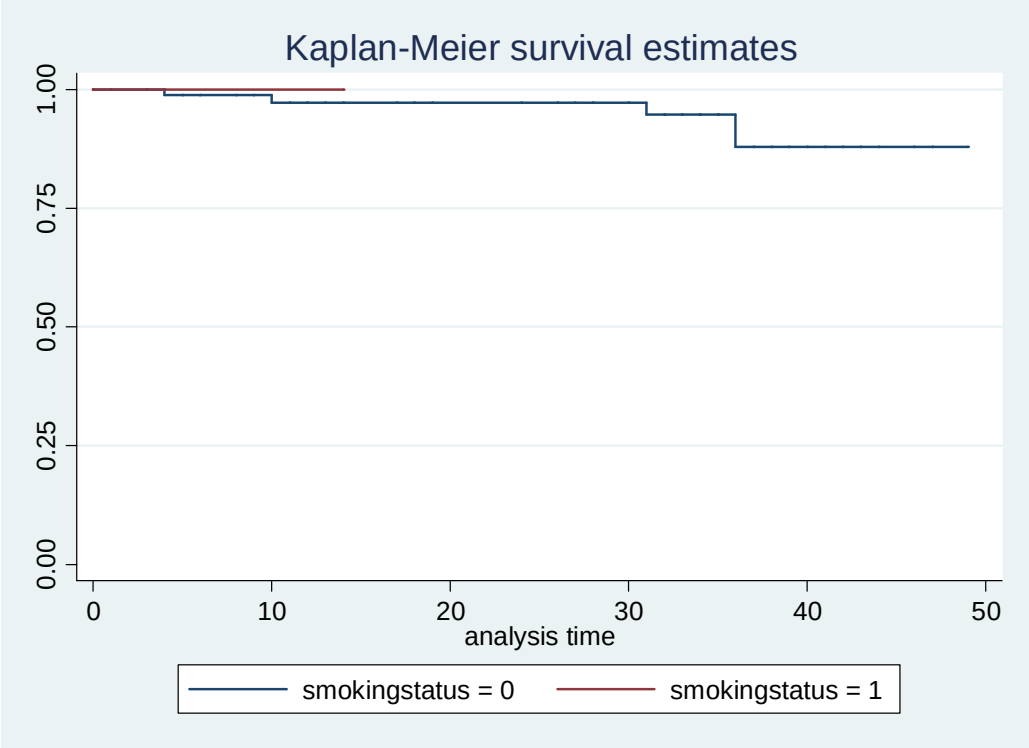
Table 4.3.4 Logrank Test for Smoking Status

Smoking status	**Events Observed**	**Events Expected**
Non-smoker	5	4.96
Smoker	0	0.04
Total	5	5.00

Chi2 (1) = 0.04; P-value= 0.8428

Smoking status considered for elimination in the final model because the P-value is above 0.05.

Figure 4.3.4 Renal Graft Survival Graph for Smoking Status



Key; Non-smoker = 0; Smoker = 1

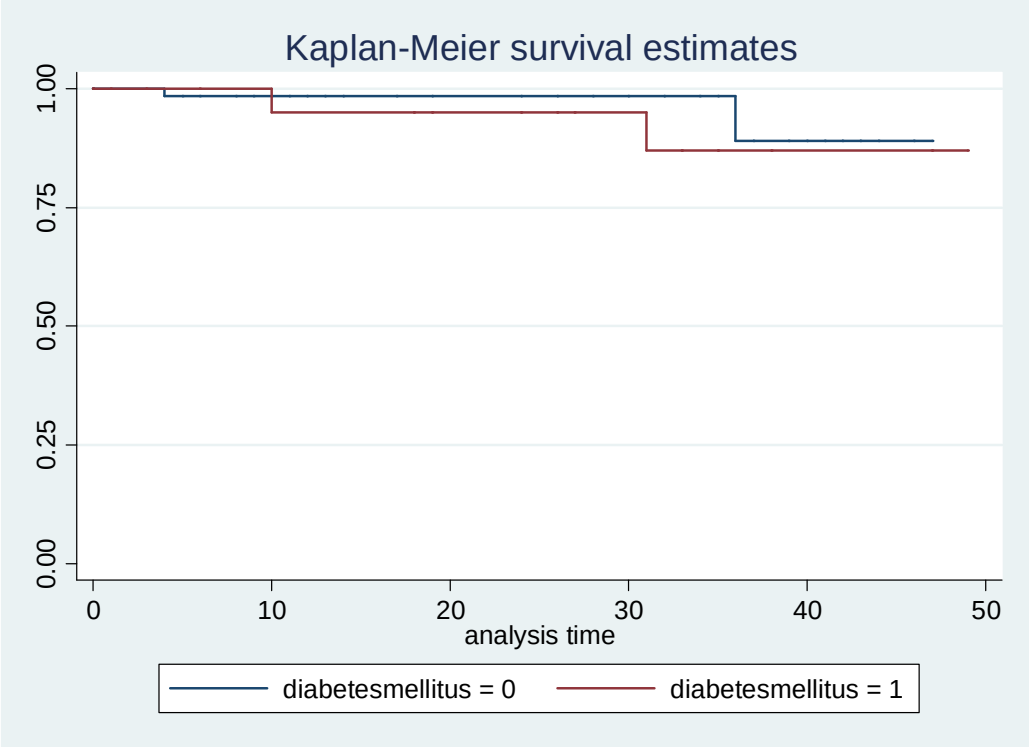
Table 4.3.5 Logrank Test for Diabetes Mellitus

Diabetes mellitus	**Events Observed**	**Events Expected**
Non-diabetic	3	3.64
Diabetic	2	1.36
Total	5	5.00

Chi2 (1) = 0.42; P-value= 0.5162

Diabetes mellitus was considered for elimination.

Figure 4.3.5 Renal Graft Survival Graph for Diabetes Mellitus



Key; Non-Diabetic = 0; Diabetic = 1

There was no difference in the allograft survival for the diabetic and non diabetic patients in the study.

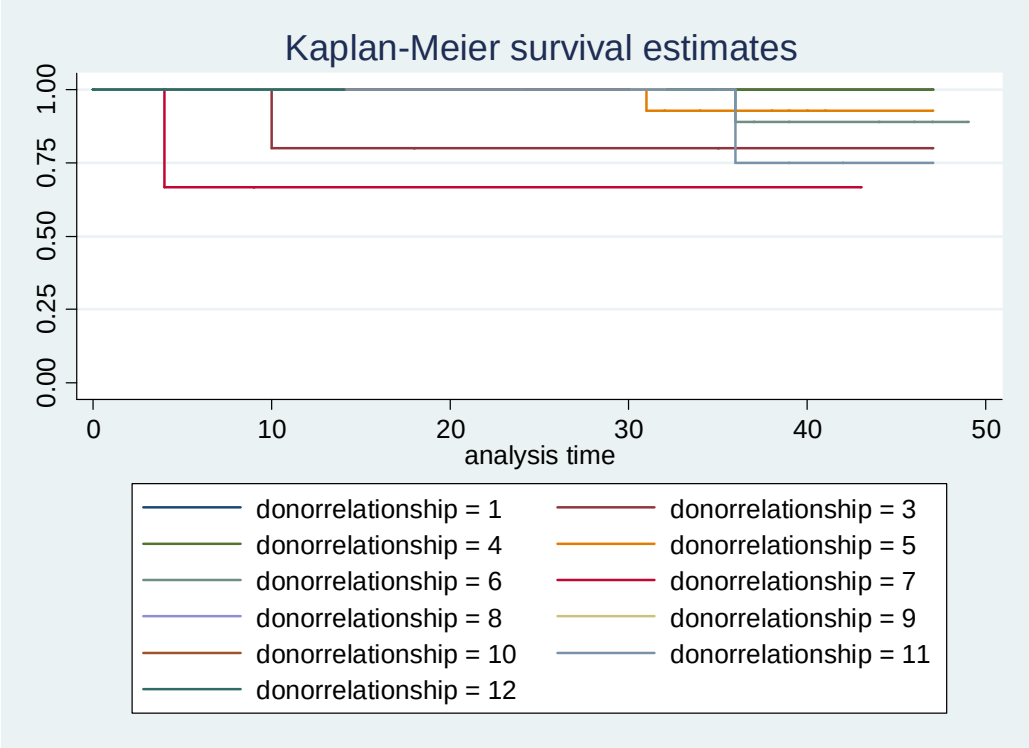
Table 4.3.6 Logrank Test for Donor Relationship

Donor relationships	Events Observed	Events Expected
Husband	0	0.12
Daughter	1	0.35
Son	0	0.31
Sister	1	1.73
Brother	1	1.50
Aunt	1	0.15
Uncle	0	0.08
Cousin	0	0.09
Nephew	0	0.04
Mother	1	0.59
Father	0	0.04
Total	**5**	**5.00**

Chi2 (10) = 7.69; P-value = 0.6594

Donor relationship was considered for elimination since the P-value was above 0.05.

Figure 4.3.6 Renal Graft Survival Graph for Donor Relationship



Key = husband=1; wife=2; daughter = 3; son = 4; sister = 5; brother = 6; aunt = 7; uncle =8;

Cousin =9; nephew = 10; mother =11; father =12.

The Kaplan-Meier survival curves for the donor relationships showed no difference in regard to allograft survival.

Table 4.3.7 Logrank Test for HLA Mismatch

HLA Mismatch	Events Observed	Events Expected
0	0	0.16
1	0	0.03
2	2	0.51
3	1	2.37
4	2	1.75
6	0	0.17
Total	**5**	**5.00**

Chi2 (5) = 5.63; P-value=0.3438

The hla Mismatch was considered for elimination in the final model due to the P-value.

Figure 4.3.7 Renal Graft Survival Graph for HLA Mismatch

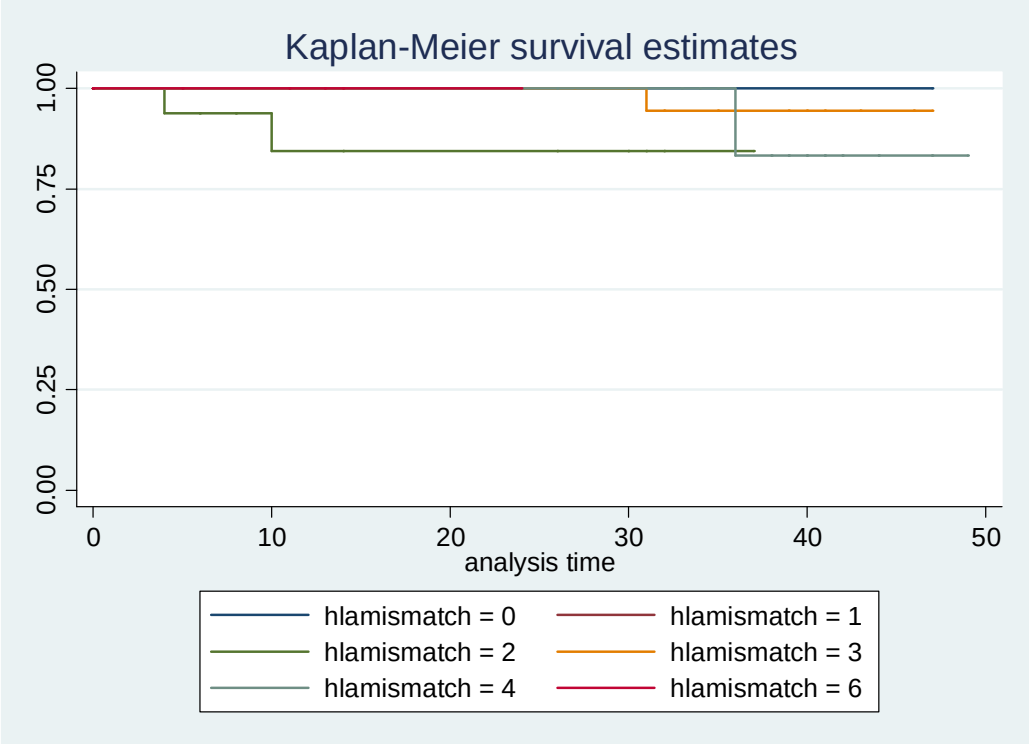


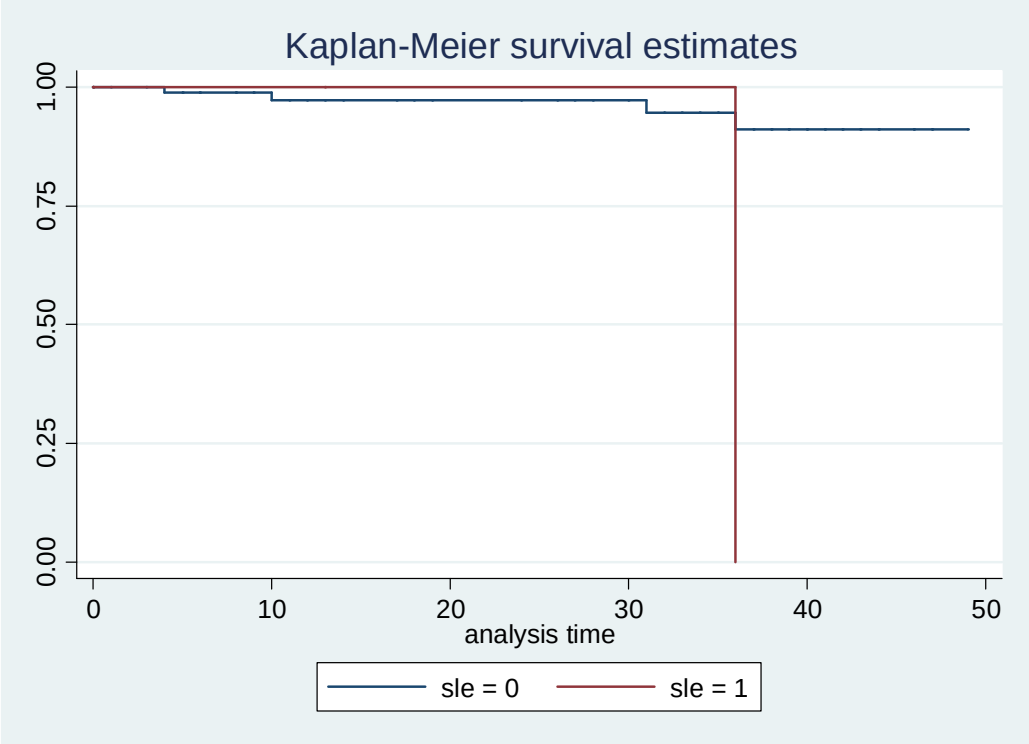
Table 4.3.8 Logrank Test for SLE

SLE	Events Observed	Events Expected
Non- SLE Patient	4	4.85
SLE Patient	1	0.15
Total	5	5.00

Chi2 (1) =5.02; P-value=0.0251

SLE was considered for the final model. The graft survival for those with SLE and those without as shown by the Kaplan-Meier survival graph below was different. So SLE may have an effect in the survival of the kidney allograft.

Figure 4.3.8 Renal Graft Survival Graph for SLE



Key; SLE Patients = 1, Non SLE Patient = 0; analysis time = time in months

Table 4.3.9 Logrank Test for Occupation

Occupation	Events Observed	Events Expected
Unemployed	2	0.69
Employed	1	3.41
Self employed	1	0.04
Student	1	0.85
Retired	0	0.01
Total	5	5.00

Chi2 (4) = 28.52; Pr <0.0001

Occupation was considered for the final model. The survival of the graft for the employed was better than for the rest.

Figure 4.3.9 Renal Graft Survival Graph for Occupation

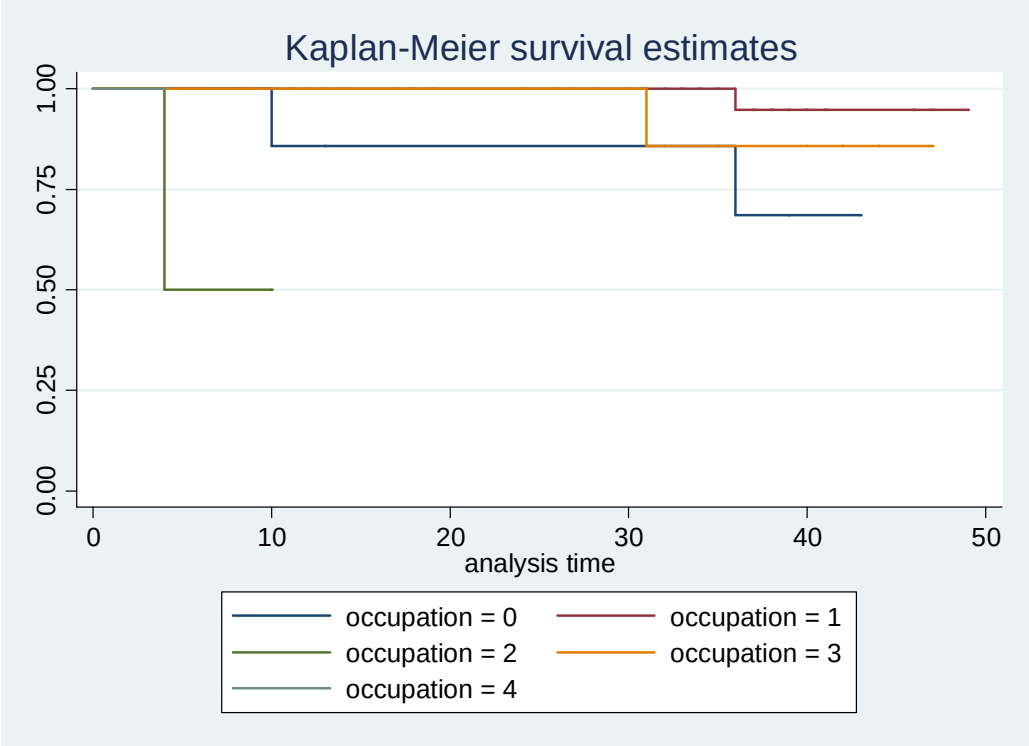


Table 4.3.10 Cox PH for Age at Transplant

Cox regression – Breslow method for ties

Log likelihood = -18.931239 LR Chi2 (1) = 0.04; Prob. > chi2 =0.8373

_t	Coefficient	Std. error	Z	P > Z	[95% Confidence interval]
Age at transplant	-0.0077555	0.037992	-0.20	0.838	0.0667074

Age at transplant was not considered for the final model since the p-value was above 0.05. It also indicates that age at transplant was not statistically significant in the survival of the allograft.

Table 4.3.11 Cox PH for Age of the Donor

Cox regression – Breslow method for ties

Log likelihood = -18.888923 LR Chi2 (1) = 0.13; Prob. > chi2 =0.7218

_t	Coefficient	Std. error	Z	P > Z	[95% Confidence interval]
Donors' age	-0.0202563	0.0577782	-0.35	0.726	-0.1334994 0.0929868

Model building

SLE and Occupation were the categorical variable which were considered for the model. All the continous variables were not considered for the final model.

Table 4.3.12 Cox PH model

Cox regression—Breslow method for ties

Log likelihood= -11.397858; LR Chi2(3) =15.11; Prob.> Chi2 = 0.0017

_t	Coefficient	Std.error	Z	P> Z	[95%Confidence interval]	
SLE	24.99801	.	.	.	.	
OCCUPATION						
Employed	-24.15149	1.226395	-19.69	0.000	-26.55518	-21.7478
Self employed	2.560336	1.546747	1.66	0.098	-0.4712332	5.591905
Student	-0.8489008	1.238883	-0.69	0.493	-3.277068	1.579266
Retired	-39.06484	.	.	.	.	

Patients who had SLE had a lower risk of kidney allograft survival compared to those who did not have SLE.

Patients who were employed had a higher chance of survival compared to those who were unemployed. This results were significant as the P-value was 0.000. The results were not significant for those who were self employed,and students. This insignificant results had shown that those who were self employed had lower chance of survival compared to the unemployed; and students had a higer chance of survival compared to the unemployed. The retired also had a highe chance of survival as compared to those who were unemployed.

Table 4.3.13 Cox PHmodel With Hazard Ratio

_t	Haz. Ratio	Std.error	Z	P> Z	[95%Confidence interval]
SLE	7.19e+10	.	.	.	.
OCCUPATION					
Employed	3.24e-11	3.98e-11	-19.69	0.000	-2.93e-12 3.59e-10
Self employed	12.94016	20.01516	1.66	0.098	0.624232 268.2461
Student	0.427885	0.5300997	-0.69	0.493	0.0377388 4.851394
Retired	4.40e-18	.	.	.	.

The hazard ratios show similar results as indicated by the coefficients above. That is those with SLE Had a higher chance of rejecting the kidney graft. Those who were employed had a lower chance of rejecting the kidney graft.

CHAPTER FIVE: DISCUSSION

By summarizing results from this study and conducting some comparative analyses, key results were obtained. The selected demographic characteristics showed that 70.2% of the graft recipients were male compared to 29.8%. Women constituted the highest proportion when it came to donors. According Jindal et al. (2005), Gender inequity in access to hemodialysis and kidney transplantation created a public health crisis in the US. Women had lower chance of receiving hemodialysis and kidney transplant than men, but they constituted the majority of living kidney donors. The US study showed that economic factors such as greater income of men may encourage females to be donors; while gender-bias on part of physicians or institutions, lack of social support networks and differences in health-seeking behaviors compared to men were cited as reasons for this imbalance.

All the patients who underwent renal transplant were hypertensive thus eliminating hypertension as a variable determining both patient and allograft survivals due to co linearity. The patients' survival for the first year was 88.7%, second year 88.7%, third year 88.7% and 82.6% for the fourth year. The survival rate was affected by the four patients who died in between the day of transplant and the fourteenth day post transplant. The patients' survival for the patients who survived the operation was 92.7% for the first, second and third year post transplant. The fouth year survival was 85.7%. No much information about patients survival in sub saharan Africa due to poor record keeping in the registrys. The national living donor kidney transplant statistics shows a six month kidney transplant survival rate of 97.7% in 2009. According to the scientific registry of transplant recipients (2013), the United States Kidney transplant, the one year survival rate for the year 2008 was 96.5% while three year survival rate was 90.9 % in the year 2006. This shows that the patient survival rates in KNH are lower but in

consideration to the advancement in technology they are impressive. The median for the patient survival was twenty five (25) months.

The renal allograft survival was 92.01% for the first year, 92.01% for the second year, and 83.01% for the third and fourth year. The graft survival for those who survived the transplant was 97.36 for the first and the second year and 88.02% for the third and fourth year. In comparison the US as per the US Renal Data System (USRDS), Ojo *et al. (*2000), Survival at 1, 5, and 10 yr was 97, 91, and 86%, respectively. The median time from transplantation to death with function was twenty three (23) months. With difference in technological advancement the survival rates are good. There is no data from the sub-Saharan Africa for comparison.

Different factors were studied on how they impact on the survival of the patient. Hypertension caused co linearity as every patient in the study had hypertension. According to Ojo *et al. (*2000), cardiovascular conditions increase the incidences of death and rejection post kidney transplant. In this study gender had no impact on the patient survival. Smoking status also did not have an impact on the patients' survival in this study. This may be attributed to the fact that only two smokers were enrolled in the study comparing to ninety two non smokers. The relationship of the donor and the recipients did not show a significant difference. This may be attributed to the fact that all the donors were close relatives to the recipients. HLA mismatch played a role in the survival of the patient depending on the level. The hazard ratios seem to increase as the level of mismatch increases. In comparison with zero (0) mismatch, the patient had a higher probability of dying if the mismatch was higher. The results were significant with a P-value of <0.0001. Age of the donor did not show any statistical significance in relation to the patient survival. The ages of the donors in this study was between twenty one (1) and fifty three (53) years. The selection of the donor also included the age factor. A study done in United

Kingdom showed that increasing donor age (but not recipient age), recipient diabetes, and grafts from adult offspring were independently associated with poorer patient survival in the first three (3) years after transplantation (Fuggle, Allen, Johnson, Collett, Mason, Dudley, Rudge, Bradly & Watson 2010). The age of the recipient showed no statistical significance. This may be due to the fact that the patient recruitment for the transplant was considering age and very few people were above sixty years. According to studies done age at transplant affects the patients' survival negatively. SLE also seems not to affect patient survival in this study. This may be due to the low number of patients who were included in the study. Diabetic patients were more likely to die compared to non diabetic patients. This meant that diabetic status affected survival of the patients post transplant. The results were significant as the P-value was 0.032.

Different factors were studied on how they impacted on the survival of the kidney allograft. The results for Gender, smoking status, diabetes mellitus, donor relationship, HLA mismatch, and age at transplant and age of the donor were not significant. The results for SLE, and occupation showed significant results. Patients who had SLE had a lower risk of kidney allograft survival compared to those who did not have SLE. The p-value was 0.025. Stone, Amend and Criswell (1997) found that, despite the fact that many lupus patients have excellent renal transplantation outcomes, substantial evidence indicates that renal transplant patients with lupus do not fare as well as patients with other causes of end-stage renal disease. Lupus patients may be particularly susceptible to adverse events occurring in the first year after transplantation. Our results show similar results.

Patients who were employed had a higher chance of survival compared to those who were unemployed. This results were significant as the P-value was <0.0001. According to Gordon et al. (2010), studies show that graft survival is lower in patients with: lower income, less insurance

coverage, or Medicare or Medicaid versus private insurance. Recent research found that the duration of Medicare's coverage of immunosuppression affects graft survival differently by income level.

CHAPTER SIX: CONCLUSION

6.1 Conclusions

Patients transplant data at KNH is well maintained for the year 2010 to 2014.

Using Kaplan-Meier and Cox regression model we were able to come up with the following conclusions:

- Patient survival post renal transplant at Kenyatta National Hospital is good
- Renal allograft survival post renal transplant at Kenyatta National Hospital is better than the patients survival
- All patient who underwent kidney transplant had hypertension
- Selection for patient on the issue of age at transplant and age of the donor was well done thus having them not impacting on the survival of the patients.
- Patients with good HLA matching had a better survival comparing to the other patients. The better the matching the better the survival
- Diabetic patients had higher hazard rate than the non-diabetic.
- The hazard ratio was higher in cases of patients with SLE, in terms of kidney rejection.
- People in employment had a higher survival rate in terms of kidney allograft survival as compared to the rest.

6.2 Study Limitations

Some of the factors had insignificant results in the study because of the number of the people who were enrolled in the study. The study itself being a census had to be done with the people who were done transplant at that particular time. All the patients in the study had hypertension so it was not possible to study the impact of hypertension on the survival of both the patient and the allograft.

6.3 Recommendations

We would commend the renal department for good record keeping and they should keep up the spirit. All the files that were sought for the study were available. We would also commend them for a job well done considering the survival rates of both the patient and the allograft. Since the survival rates are good the patients undergoing hemodialysis should be counseled on the advantages of renal transplant. Renal transplant is known to be cheaper in the long run and patient does not have the inconveniencies of coming every week for dialysis thus wasting resources. Transplant will also reduce the hospital expenses and improve the patient machine ratio for those who will continue with dialysis. There need to be a law passed on the issue of cadaveric donors so that we can improve the number of people undergoing kidney transplant. There is need to consider how long a patient stays awaiting transplant. Establishment of a registry to follow up survival of patients who received transplant to determine mortality rates with time.

REFERENCES

Arend, S.M., Mallat, M.J., Westendorp, R.J., Van der Woude, F.J. & Van Es, L.A. (1997). Patient survival after renal transplantation; more than 25 years follow-up *Nephrol Dial Transplant; 12:1672-1 679*

Arogundade, F.A., & Barsoum, R.S (2008). CKD prevention in sub-Saharan Africa: a call for governmental, nongovernmental and communitysupport. *Am J Kidney Dis. 51:515–523.*

Briggs, J.D., (2001) Causes of death after renal transplantation *Nephrol dial Transplant 2001; 16: 1545-1549*

Collet, D. (2003). *Modeling survival data in Medical research, 2nd edition.* Chapman & Hall/CRC: Newyork.

Collins, B. H., & Kulkarn, S., (2013). Renal Transplantation. Downloaded from http://emedicine.medscape.com/article/430128-overview#aw2aab6b2b2 on 16th Jan. 2014

Cox, D.R. (1972) Regression models and life tables (with discussions). *J Royal Stat Society B34:187-220*

Foster, E.C., Philosophe, B., Schweitzer, E.J., Colonna, J.O., Farney, A.C, Jarrell, B., Anderson, L & Bartlett, S. (2002). A Decade of Experience With Renal Transplantation in African-Americans. *Ann Surg. 236(6): 794–805.* PMCID: PMC1422646

Fuggle, S.V., Allen, J.E., Johnson, R.J., Collett, D., Mason, P.D., Dudley, C., Rudge, C.J., Bradley, J.A.,& Watson, C.J. (2010). Factors affecting graft and patient survival after live donor kidney transplantation in the UK. Transplantation, 2010 Mar 27;89(6):694-701. doi: 10.1097/TP.0b013e3181c7dc99.

Gordon, E. J., Ladner, D.P., Caicedo, J. C., & Franklin, J., (2010). Disparities in Kidney Transplant Outcomes: A Review. Semin Nephrol. Jan 2010; 30(1): 81. doi: 10.1016/j.semnephrol.2009.10.009

Grassman, A., Gioberge, S., Moeller, S., & Brown, G. (2005). ESRD patients in 2004: global overview of patient numbers, treatment modalities and associated trends. *Nephrol Dial Transplant.20:2587–2593.*

Jindal, R.M., Ryan, J.J., Sajjad, I., Murthy, M.H., & Baines, L.S.,(2005) Kidney Transplantation And Gender Disparity. Am J Nephrol.: 474-83

Machin, D., Campbell, M.J., & Walters, S.J.(2013). *Medical Statistics; A Textbook for the Health Sciences 4th Ed.* CBS Publishers &Distributors: New Delhi

Mok, I.Y., Kee, T.,& Goh, A.,(2012). Ten Outcomes of Kidey Transplants at Singapore General Hospital. Downloaded from http://www.singhealthacademy.edu.sg/Pages/Proceedings Vol-21-1-2012.aspx on 16th January 2014

Naicker, S., (2009). End Renal Disease in Sub-Saharan Africa. *Ethnicity & Disease, Volume 19, Spring* downloaded from *http://www.ishib.org/journal/19-1s1/ethn-19-01s1-13.pdf* on16th January 2014

Ojo, A.O., Hanson, J.A., Wolfe, R.A., Leichtman, A.B., Agodoa, L.Y. & Port, F.K.(2000): Long-term survival in renal transplant recipients with graft function. *Kidney Int* , 57: 307–313

Rayner, B. (2003). Divisions of Nephrology and Hypertension Groote Schuur Hospital. *Vol. 93, No. 9* ***SAMJ****University of Cape Town*

Scientific registry of transplant receipients (2013) downloaded from http://www.srtr.org/csrcurrent/centres/centerdetail.aspx? On 16th Jan 2014

Singh, A. (2012). Kidney failure in Kenya downloaded from http://www.thekidneydoctor.org/?theisn.or on 16th Jan. 2014

Stone, J.H., Amend, W.J., & Criswell, L.A., (1997). Outcome of renal transplantation in systemic lupus erythematosus. Downloaded from http://www.ncbi.nlm.nih.gov/pubmed on 10th October 2014.

Tapiawala, S.N., Tinckam, K.J., Cardella, C. J., Schiff, J., Cattran, D.C., Cole, E.H & Kim, S. J. (2010) *Delayed Graft Function and Risk For Death with a Functioning Graft.* Division of Nephrology and Multi-Organ Transplant Program. University of Toronto; Ontario Canada

Terasaki, P., Ozawa, M.(2004). Predicting kidney graft failure by HLA antibodies : a prospective trial. *Am J Transplant 2004 Mar; 4(3):438–43.*

Wilson, M.G., (2013). Assessing Model Adequacy in proportional hazards regression. Paper *431-2013* Indianapolis: USA

World Health Organization (WHO) (2011). Downloaded from http://www.worldlifeexpectancy.com/world-healthranking on 16th Jan. 2014

Appendix 1: Time frame

Activities			**Period**				
	Jan-May	June	July	Aug	Sep	Oct	Nov
Development of the proposal							
UoN/KNH Ethical Review committee							
Implementation of the proposal							
Data analysis							
Report writing							
Project Submission							

Appendix II: budget

ITEM	TOTAL IN KSH.
Travelling allowance	45,000
Stationery	20,000
Subsistence allowance	20,000
Data processing	30,000
Research assistant (1)	30,000
ERC fee	2,000
Miscellaneous	25,000
TOTAL IN KSH.	172,000

Budget Justification

Travelling allowance: this will cater for travelling to KNH to collect data

Stationery: One ream of full scaps, a dozen of pencils and pens, three box files and other stationeries that will be used will be purchased.

Subsistence allowance: this allowance will be used for food, refreshments during data collection

Data processing: this amount will be used to purchase STATA software for quantitative data analysis.

Research assistant: this allowance will be used to pay the research assistant who will participate in data collection.

Miscellaneous: this amount will cater for the any emergences and unplanned activities which will incur some money

Appendix III; Check List

Coding;

Gender (male = 1; Female =0)

Smoking status (smoker =1; non smoker =0)

Hypertension (hypertensive =1; non hypertensive =0)

Diabetes mellitus (diabetic=1; non diabetic =0)

Current Graft Status (dead =1; alive=0)

Patient status (dead =1; alive=0)

Systemic Lupus Erythematosus (SLE) (Present =1; Absent=0)

serial no	patient ID	Age at transplant	gender	smoking status	Hypertension	diabetes Mellitus	current graft status	Graft Rejection date	patient status (alive/dead)	date of death	donors age	donor relationship	HLA Mismatch	SLE	OCCUPATION
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