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DEPARTMENT OF STATISTICS

SURVIVAL ANALYSIS OF TIME-TO-DEATH OF HEMODIALYSIS PATIENTS: THE CASE OF ICMC GENERAL HOSPITAL

A thesis submitted to the Department of Statistics in partial fulfillment of the requirements for the Degree of Master of Science in Statistics (Biostatistics)

BY

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ADDIS ABABA, ETHIOPIA

DECLARATION

I hereby, declare that this thesis is for the Degree of Master of science entitled "SURVIVAL ANALYSIS OF TIME-TO-DEATH OF HEMODIALYSIS PATIENTS: THE CASE OF ICMC GENERAL HOSPITAL" is an original piece of work, has not been submitted for review at any other academic institution, and all references utilized in the thesis have been properly cited.

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Abstract

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DEPARTMENT OF STATISTICS, ADDIS ABABA UNIVERSITY

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ENDALE YEHUALASHET

Hemodialysis (HD) is a life-saving treatments for those with end-stage kidney disease. The main goal of this research is to identify the effect of covariates that affect the survival analysis of time – to – death of hemodialysis patients in ICMC General Hospital. The research is based on a retrospective cohort study. The data were extracted from a secondary source obtained from the records of 149 hemodialysis patients who were registered between March 1, 2019, and March 1, 2024, at ICMC General Hospital, Addis Ababa, Ethiopia. Among the total of 149 patient, 98 patients (65.77%) were still alive at the end of the study period, while the remaining 51 patients (34.23%) died during the study period. The total risk time for these patients was 15,693 person-weeks and the overall incidence rate of death is 32 per 10,000 person-weeks with median survival time of 207 weeks. Kaplan-Meier survival curves and the log-rank test were used to compare the survival experiences of different categories of patients. The semi-parametric Cox proportional hazards model was fitted to identify survival analysis of time–to–death of the hemodialysis patients by using statistical software STATA-16. The model considered provided good fit for the data. The results of Cox model analysis showed that age, types of vascular access, frequency of dialysis, hemoglobin level, creatinine, white blood cell count, red blood cell count and oxygen saturation showed significant effect on the survival time-to-death of patients undergoing hemodialysis within the study area. However, gender, hematocrit, calcium, adequacy of dialysis, iron and erythropoietin did not have significant effect. The study suggests that healthcare providers and clinicians should consider the identified statistically significant factors when assessing and managing hemodialysis patients in order to improve survival outcomes.

ACRONYMS

CKD	Chronic kidney disease
CRRT	Continuous renal replacement therapy
ESRD	End-stage renal disease
GFR	Glomerular filtration rate
HD	Hemodialysis
HR	Hazard ratio
KM curve	Kaplan-Meir curve
PD	peritoneal dialysis
PH model	Proportional Hazards model
RBC	Red blood cell
RRT	renal replacement therapy
SSA	Sub–Sahara Africa
SPMMC	St. Paul Millennium Medical College
USRDS	United States Renal Data System's
WBC	White blood cell

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Chapter One

1. INTRODUCTION

1.1 Background of the study

The ultimate stage of chronic kidney disease (CKD), known as end-stage renal disease (ESRD), is a condition in which the kidneys have almost completely stopped functioning (Alam & Newport, 2022). This can cause various symptoms and complications, such as fluid retention, high blood pressure, anemia, and heart disease. Worldwide, the survival rate of Hemodialysis (HD) patients with end-stage kidney disease (ESKD) is increasing. People with CKD and ESRD to survive, have a kidney transplant or dialysis (Jin et al., 2015). Dialysis is a process that removes waste products and excess fluid from the blood using an artificial device.

Chronic kidney disease is a serious health issue that affects about 10%–13% of people worldwide. Chronic kidney disease can worsen over time and lead to ESKD. This is when the kidneys are permanently damaged, cannot function properly, and have a very low glomerular filtration rate (GFR) of less than 15 mL/min/1.73 m2. ESKD is the most severe form of chronic kidney disease (Vaidya & Aeddula, 2022).

According to Bello et al. (2022) around 69% of all kidney replacement therapy and 89% of all dialysis treatments worldwide are provided by hemodialysis (HD), making it the most widely used kind of kidney replacement therapy. Particularly in high-income nations, dialysis technology and patient access have significantly evolved during the past 60 years since the beginning of HD. The availability, affordability, results, and accessibility of HD, however, differ greatly worldwide, and generally, rates of morbidity, death, and reduced quality of life are high. HD involves pumping the blood through a machine that contains a dialyzer, a filter that mimics the renal function. After being cleaned, the blood is then put back into the body. There are three main kinds of dialysis: Hemodialysis (HD), peritoneal dialysis (PD) and Continuous renal replacement therapy (CRRT).

Different countries have different ways of doing renal replacement therapy (RRT), with Japan having longer and slower dialysis sessions. HD is usually performed three times a week, each session lasting about four hours, in a dialysis center or at home (Murdeshwar HN & Anjum, 2023).

A large number of individuals in Africa suffer from ESKD, but many are unaware of it and do not seek treatment, which increases their risk of death (Ashuntantang et al., 2017). In Sub-Saharan Africa (SSA), the most common way to treat ESKD is dialysis, which filters the blood using a machine. But dialysis is hard to get in many poor and middle-income countries. Some reasons for this are scarcity of enough healthcare workers and limited skills to diagnose and treat ESKD (Ashuntantang et al., 2017).

Many studies have shown how big the problem of ESRD is in sub-Sahara Africa (SSA). In Senegal, only a small fraction (8.23%) of ESRD patients gets RRT (Diouf et al., 2003). In Ghana, 5% of all hospital admissions are because of kidney problems, and most patients (27.1%) die from ESRD. High blood pressure and chronic kidney inflammation are the main reasons for ESRD in different African countries (Naicker, 2013).

Many people in Ethiopia and other poor countries have ESRD, which is the worst kind of kidney disease. They cannot afford dialysis, which is a treatment that cleans their blood. In Ethiopia, dialysis is very expensive and hard to find easily. It is seen as a luxury care that only rich people can afford (Shibiru et al., 2013).

The main problem in hemodialysis (HD) is that many patients die soon after starting the treatment. Therefore, many studies have tried to find out what factors affect how long HD patients live. Some HD patients do not die during the study period, so their data cannot be used in the usual statistical methods, like logistic or multiple linear regressions. These methods are not good for studying how long HD patients live. Instead, we need to use survival analysis methods that take into account the data of patients who are still alive at the end of the study, which is called censoring. One of the most popular survival analysis methods that is appropriate is the multivariable semi-parametric Cox proportional hazards (PH) model. The PH assumption requires that the risk of death does not change over time for each factor. However, a systematic review found that most studies using this method did not meet the PH assumption (Klein and Moeschberger, 2003).

The survival outcomes of HD patients are influenced by covariates such as age, sex, dialysis adequacy, vascular access, infection, inflammation, and cardiovascular disease (Montaseri et al., 2022).

Despite the advances in dialysis technology and care, the survival of HD patients remains low and has not improved significantly over the years. Therefore, there is a need to explore the survival of HD patients in different regions, settings, and populations, and to identify the factors that affect their survival outcomes. This study aims to identify the factors that affect survival analysis of time-to-death of HD patients in ICMC General Hospital.

1.2 Statement of the problem

Hemodialysis (HD) is a life-saving treatment for patients with end-stage kidney disease, but it is also related with high mortality rates and a lower standard of living. Based on the findings of (Mohtashami et al., 2022), it can be inferred that in Iran, the survival rate of Hemodialysis for the first, second, third, fourth, and fifth years is estimated to be 81.7%, 68.3%, 58.4%, 50.1%, and 39.1% respectively. According to a study conducted in Ghana, it was found that within ninety days of beginning dialysis, 32 percent of patients died (Eghan et al., 2009). Conversely, in a comparable study carried out in Ethiopia, only forty-two percent of patients survived after a year, with a 23% death rate after 90 days. (Shibiru et al., 2013). In Sudan, the 1-year mortality rate was 7.4% (Elsharif, 2011).

Demographic characteristics, comorbidities, dialysis adequacy, nutritional status, anemia, inflammation, mineral and bone disorders, and dialysis modality influence the survival of HD patients (Hong and Lee, 2019). However, the relative importance and the causal mechanisms of these factors are not well understood. Furthermore, there may be regional and temporal variations in the survival patterns and the prognostic factors of HD patients, depending on the availability and quality of healthcare services, the prevalence and management of risk covariates, and socio-economic and cultural variables in Adama Hospital, Ethiopia (Hussein et al., 2017).

Therefore, there is a need for more studies to identify and analyze covariates affecting the survival of HD patients in different settings and contexts. Such studies can provide valuable information for improving the clinical management and the health outcomes of HD patients, as well as for developing and evaluating preventive and therapeutic interventions.

This study aims to determine the effect of covariates that affect the survival analysis of time-to-death of hemodialysis patients in ICMC general hospital in Addis Ababa, Ethiopia. Ethiopia is a low-income country in SSA, where the burden of ESRD and the demand for HD are increasing, but the resources and the infrastructure for HD are limited (Shibiru et al., 2013).

1.3 The general objective of the study

The general objective of this study is to determine the effect of covariates on the survival time-to-death of hemodialysis patients in the specific context of ICMC General Hospital, Addis Ababa.

1.3.1 Specific objectives

1. To evaluate the HD patients' median survival time at ICMC General Hospital.
2. To identify factors associated with time-to-death of HD patients in ICMC General Hospital.

1.4 Significance of the study

The significance of this study is that it provides valuable information about the epidemiology and prognosis of hemodialysis patients in Ethiopia. This study could also contribute to the literature on the factors affecting survival rate of hemodialysis patients, which has been the subject of many studies in different contexts. The study provides information about the clinical decision making and policy making regarding the caregiver, management and allocation of resources for ESRD patients in Ethiopia.

Overall, the significance of this study lies in its potential to enhance the understanding and management of hemodialysis patients, ultimately leading to better survival status and improved quality of life for HD patients in the context of ICMC General Hospital.

Chapter Two

2. LITERATURE REVIEW

2.1 Introduction

The survival analysis of hemodialysis patients can vary depending on numerous factors. According to Hazara and Bhandari (2020), the death rate for patients who started hemodialysis was 8.8 times greater than that of the whole population. The primary causes include hypertension, diabetes mellitus, and cardiovascular disease; interstitial nephritis, renal vascular disease, and chronic glomerulonephritis are other reasons (Sowers et al., 2001).

An alternative to the kidneys' natural blood-filtering function is renal replacement therapy, or RRT. Individuals with ESKD may live longer and have better quality of life as a result of RRT. However, due to a number of obstacles, including lack of availability, price, knowledge, or acceptability of the treatment, not all ESKD patients can receive RRT. A recent research by Pecoits-Filho et al., (2020) who found that there is a significant gap between the population that need RRT and those which actually receive it. According to the report, only 10.4 million of the 15.9 million ESKD patients in 2017 underwent RRT; the other patients passed away before their time. The study also discovered that the availability of RRT differed significantly between nations and regions based on factors such as governmental priorities, health system capability, and economic growth.

End-stage renal disease (ESRD) is a severe form of chronic kidney disease (CKD) that requires dialysis or kidney transplant to stay alive. The most popular type of dialysis is hemodialysis, but it is difficult to access dialysis in many poor and middle-income countries. The survival rate of HD patients is a major concern, and variables that influence survival outcomes need to be identified (Ashuntantang et al., 2017).

Previous studies have shown that ESRD is a growing problem in SSA. In Ethiopia, due to the high cost of dialysis, many patients find it difficult to finance frequent treatments. Dialysis facilities are not easily accessible, particularly in rural locations. Long distances are frequently required for patients to obtain treatment. The facilities, experienced staff, and equipment that make up the dialysis service infrastructure are insufficient. It's still difficult to guarantee excellent dialysis treatment. Due to these difficulties, ESRD patients in Ethiopia have high rates of illness and mortality (Gebrie et al., 2023).

One reason that discourages people from starting dialysis is the difficulty in getting to dialysis centers, which are mostly found in cities or other urban regions. With just half of the areas having access to any type of dialysis facility, the majority of Ghana's 65 hemodialysis machines (63.1%) are located in the Greater Accra region (Tannor and Calice-Silva, 2022). Access to additional medical appointments is hindered in SSA by inadequate health infrastructure and challenges in reaching dialysis clinics (Ashuntantang et al., 2017).

2.2. Factors affecting the survival of hemodialysis patients

A study by Ardianto et al. (2016) used the Kaplan-Meier survival analysis technique to determine the survival rates of hemodialysis patients. The study was conducted retrospectively, using a non-reactive research design with a retrospective cohort. A random sample of 155 patients was taken, and data was collected using a checklist. The analysis revealed that certain factors, such as being female, an adult, having further education, being employed, not having insurance, having normal nutritional status, having a history of the disease, having hypertension, and having diabetes, were associated with better survival rates. The researchers also found that the insurance status, nutritional status, hypertension, and diabetes were significant factors influencing survival time, with a p-value of less than 0.05.

The majority of Congolese citizens, who make less than USD 1.25 per day, cannot afford the average quarterly direct cost of chronic hemodialysis in Kinshasa, the Democratic Republic of the Congo, which is USD 7070 per patient, according to research by (Izeidi et al., 2020). Included in the direct cost are the expenses for the hemodialysis session (USD 237) and the medication (USD 33), which make up 82.5% and 11.3% of the total cost, respectively. Infection and the existence of at least four comorbidities both independently predict increased direct costs. To enhance the accessibility and caliber of care for patients with end-stage renal illness, the study proposed creating more inexpensive and economical renal replacement therapy and hiring additional nephrology personnel.

Also a study by Mbabazi et al. (2022) investigated the barriers and facilitators to dialysis for patients suffering from end-stage renal disease (ESKD) in Rwanda, a country with limited resources. According to the study, social support, lack of information, financial limitations, and the scarcity of dialysis services were the primary variables affecting access to the treatment. The report suggested that in order to enhance dialysis access for ESKD patients in Rwanda, public money should be increased, health insurance coverage should be expanded, awareness should be raised, dialysis services should be decentralized, and referral networks should be strengthened.

A study by Ferreira et al. (2020) found that leukocyte count, serum iron, serum calcium, serum protein, chronic obstructive pyelonephritis, ferritin, serum phosphorus, and serum albumin were found to be significant factors with the survival time of 422 hemodialysis patients in Brazil. They used Kaplan-Meier method and Cox PH model to perform survival analysis.

Susanto and Asiandi (2020) studied the survival time of CKD patients undergoing hemodialysis based on various covariates such as age, sex, marital status, educational level, payment status, and diabetes status. The mean age of the patients was 55.9 years, and most of them were married, hypertensive, non-diabetic, normal-nutrition, and used femoral access for hemodialysis. The estimated median survival time of the patients was 462 days, and it did not vary significantly by any of the factors. The study employed the Kaplan-Meier method and the log rank test to analyze the survival curves and compare the groups. Cox regression analysis showed that the survival time of CKD patients undergoing hemodialysis does not have effect on diabetes status, hypertension status and nutritional status. But the type of work and the vascular access are significant factors affecting the survival of CKD patients undergoing hemodialysis. Patients with private employment and AV shunt vascular access have higher risks of death than those who do not work and have femoral vascular access.

According to a study by Ebrahimi et al. (2019) in Iran, some of the variables that influence the survival time of HD patients are: ultrafiltration volume, white blood cell count, red blood cell count, mean corpuscular hemoglobin concentration, and serum albumin. They used an accelerated failure time namely log-normal model, to analyze the data of 428 hemodialysis patients.

The study by Rafati et al. (2019) in Bandar Abbas, Iran observed 252 HD patients by Cox regression model., of these 13.9% died and 86.1% were censored. The average survival time was 10.93 years, with a median survival time of ten years. The average age of the patients was 53.39 years, and the average age of dialysis initiation was 42.88 years. The average BMI score was 22.87. Most of the women in the study were housewives, while most of the men were unemployed or retired. None of the patients had HIV infection. The majority of patients underwent a 4-hour dialysis session three times a week. The Cox model results showed that patients with a diploma had a 49% reduced chance of death than the uneducated group (HR = 0.51). Patients without a job had a mortality risk that was 0.66 (HR = 1.66) and 0.29 (HR = 1.29), respectively, more than that of workers. The length of each dialysis session is an additional important component in this research. For every increment during dialysis, there is a 0.34 (HR = 0.66) reduction in the chance of death.

Hussein et al. (2017) carried out a retrospective cohort research at Adama Hospital, Ethiopia. The study included 500 HD patients with end-stage renal illness. At the end of the study, 72.40% of participants were still living, while 27.40% had passed away. Cox PH regression model, Kaplan-Meier technique, the log-rank test, and nonparametric survival analysis were used to estimate and analyze the hazard and survival functions of various covariate groups. Early in the therapy, there appeared to be more fatalities. Age, sex, and a family history of renal disease contributed to a considerable rise of mortality risk of ESRD patients. Comparatively speaking, females, elder and those a family history of renal disease had greater hazard ratios.

The study by Kore and Yohannes (2018) conducted in Addis Ababa, Ethiopia used demographic data of respondents, including their age, sex, education, and marital status to study survival of HD patients. The average age of participants was 43.95 years, with almost half of them aged between 18 and 39. About a quarter of participants were between 40 and 49, and a similar percentage were 58 and above. Males made 54.7% of the participants, while females accounted for 45.3%. In terms of education, a small percentage attended non-formal education, while the majority had primary or secondary education. About 28.4% had attended college or university. With regard to marital status, 21.3% were single, 67.3% were married, and 11.4% were divorced or widowed. Of the total population, 43.6% had started dialysis, with a majority of them starting within the past three years. The majority of patients had dialysis three times each week. A large number of patients complained about how long it took them to start dialysis. Certain individuals saw notable variations in their dialysis costs between private medical facilities and public hospitals.

By reviewing the medical records of 436 patients from 2016 to 2020, Workie et al. (2022) evaluated the survival and mortality predictors of patients with chronic renal disease receiving hemodialysis in the Amhara region, Ethiopia. The median survival period was 345 days, with a 5-year survival probability of 65% and a death rate of 1.89 per 1000 person-days. Living in rural part of the region, high blood pressure, HIV as CKD causes, and central venous catheter as vascular access were risk variables of mortality.

According to a study by Betiru et al. (2023) in Addis Ababa, Ethiopia, out of 128 hemodialysis patients, 37% were female and 63% were male. The age range of 15–47 years comprised the bulk of the patients. Diabetes plus hypertension were the most prevalent comorbid condition, followed by diabetes alone and hypertension alone. Males were more likely to have all three comorbidities than girls. Arteriovenous fistulas (AVF) were the most often utilized vascular access, whereas arteriovenous grafts (AVG) were least frequently used. The majority of patients had dialysis three times a week for three hours. About 33% of the patients passed away and 67% were censored. The mortality rate per 10,000 person years was 2.9 overall. The mortality rate was somewhat lower in men than in females. Over-64-year-olds had the greatest rate of mortality. Death rates were greater in those who experienced bloodstream infections. The median survival time was 1,955 days. Presence of infection, vascular access type, age, and treatment institution all significantly affected survival. When comparing older age groups to younger age groups, the older age showed shorter survival periods. Comparing AVF to central venous catheterization (CVC), a longer survival rate was linked to its usage. Compared to patients with infections, those without bloodstream infections had longer lifetimes. Cox regression analysis found bloodstream infection, vascular access type, and treatment facility to be significant variables of mortality. The risk of mortality decreased for patients receiving care at the government hospital and utilizing AVF, but it was still nearly three times higher for those with bloodstream infections. The study also discovered that bloodstream infections, treatment facilities, and vascular access type all significantly impacted hemodialysis patients' longevity. Males, younger patients, and AVF users survived longer.

The study by Belachew et al. (2018) in Tigray, Ethiopia was based on 130 HD patients showed that the median survival length was 12.6 months. The patients were mostly male, middle-aged, and had hypertension as a prior condition. The study used a lognormal model to predict the survival of HD patients, and found that HIV associated with nephropathy (HIVAN) had a significant negative effect on survival. The study also revealed that lower frequency of dialysis, fluid overload, hyperkalemia, and diabetes mellitus were significant effect with lower survival rates. It was observed that HD significantly reduced blood urea nitrogen, serum creatinine, and serum potassium levels, but also lowered hemoglobin levels.

A study by Montaseri et al. (2022) in Mazandaran University Iran, conducted a retrospective cohort study including 335 patients on HD in Imam Khomeini and Fatima Zahra Hospitals. The study employed two models: one called frailty, which takes into account the unobserved variability across patients, and the other called Cox proportional hazards model. The frailty model fit the data better and identified several factors, including age, marital status, diabetes, kidney stones, serum albumin, urea, and clinic, that affected the longevity of hemodialysis patients. The frailty model fits the data better, according to the study's comparison of the models' fits using the Akaike criteria and Cox-Snell residuals.

2.3 Conceptual framework

Various empirical evidences indicate that the survival status of patients receiving hemodialysis is influenced by: age, gender, erythropoietin (EPO) medication, adequacy of dialysis, hematocrit, hemoglobin level, creatinine, vascular access, frequency of dialysis, hypertension, WBC count, RBC counts, oxygen saturation, serum iron, serum calcium, serum phosphor. The conceptual framework was constructed with minor modifications from several literary works (Ardianto et al., 2016; Belachew et al., 2018; Betiru et al., 2023; Desta et al., 2023; Ebrahimi et al., 2019; Ferreira et al., 2020; Gebrie et al., 2023; Hussein et al., 2017; Izeidi et al., 2020; Kore C & Yohannes HM, 2018; Mohtashami et al., 2022; Montaseri et al., 2022; Rafati et al., 2019; Shibiru et al., 2013; Workie et al., 2022).

The study has seen how these variables determine survival analysis of time-to-death of hemodialysis patient in case of ICMC general hospital using data from 2019 to 2024.

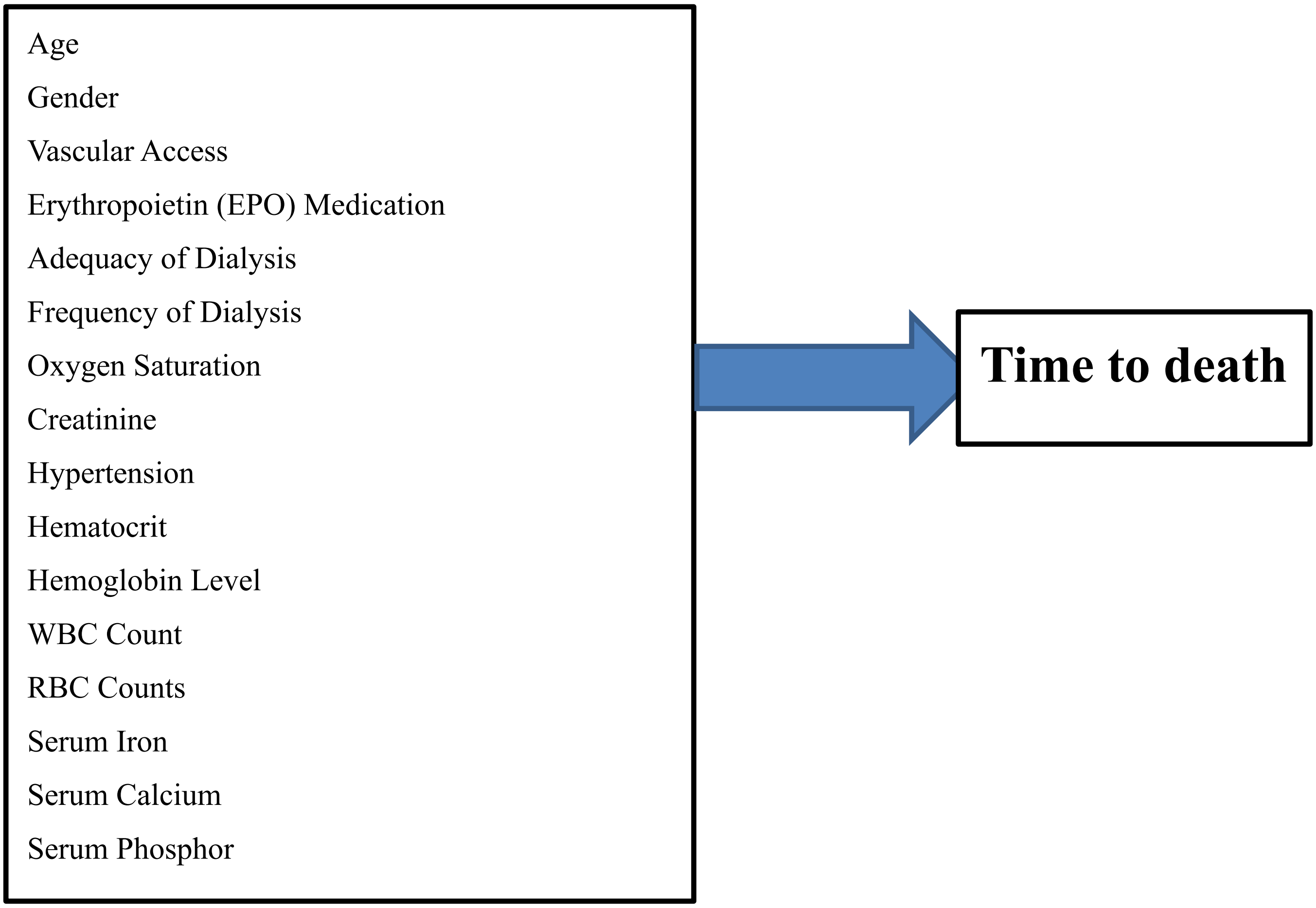


Figure 2. 1 Conceptual framework on survival analysis of HD patient.

2.4 Operational Definition of Variables

- **The adequacy of dialysis: -** The effectiveness of dialysis in removing waste products from the blood is often assessed using a measure known as Kt/V. This measure categorizes the adequacy of dialysis into different levels. When the Kt/V value is less than 1.2, it indicates inadequate dialysis, which can result in the accumulation of waste products in the blood. On the other hand, a Kt/V value ranging from 1.2 to 1.4 is considered adequate for most dialysis patients as it helps maintain proper levels of waste removal. Values above 1.4 are classified as optimal dialysis, indicating excellent clearance of waste products during the dialysis process (Hong and Lee, 2019).
- **Oxygen saturation: -** is a metric indicating the proportion of hemoglobin molecules in the bloodstream that are bound to oxygen. The body carefully controls oxygen levels as hypoxemia can result in various immediate negative impacts on specific organ

functions, such as the brain, heart, and kidneys (Hafen & Sharma, 2022). Normal oxygen saturation levels generally fall within the range of 95% to 100%. When oxygen saturation levels are within this range, it signifies that the blood is sufficiently oxygenated. On the other hand, moderate hypoxemia is characterized by oxygen saturation levels ranging from 86% to 94%. This level of hypoxemia indicates moderate and early indications of oxygen deficiency in the blood. Conversely, severe hypoxemia is identified by oxygen saturation levels below 85%. This severe level of hypoxemia signifies a critical oxygen deficiency in the blood, necessitating prompt medical intervention (Beasley et al., 2015).

- **Hematocrit levels**: - The hematocrit levels provide an indication of the proportion of red blood cells present in the bloodstream.

  High hematocrit levels, also referred to as polycythemia, are characterized by values that exceed the normal range. In the case of adults, this typically entails values surpassing 50% for men and 44% for women. Various factors can contribute to high hematocrit levels, including dehydration, lung disease, kidney disease, or disorders affecting the bone marrow. On the other hand, normal hematocrit levels vary depending on age and gender. For adults, the acceptable range for men generally falls between 41% and 50%, while for women, it typically ranges from 36% to 44%.

  Conversely, low hematocrit levels, known as anemia, indicate values that fall below the normal range. In adults, this typically means values below 36% for women and below 41% for men. Several factors can lead to low hematocrit levels, including nutritional deficiencies such as iron deficiency anemia, chronic diseases, blood loss, or disorders affecting the bone marrow (Walker HK, Hall WD, 1990).

- **Hypertension: -** Hypertension among individuals undergoing hemodialysis has emerged as a significant concern due to the rise in blood pressure levels observed before and after the procedure. Diagnosis of hypertension in hemodialysis patients is typically made when pre-dialysis blood pressure readings exceed 140/90 mmHg or post-dialysis blood pressure readings above 130/80 mmHg (Fuchs & Whelton, 2020).

- **Creatinine**: - is a byproduct generated by muscle metabolism through the degradation of creatine. The kidneys are responsible for filtering it from the bloodstream and eliminating it through urine. Healthy kidney function is indicated by normal creatinine levels, which typically range from 0.6 to 1.2 mg/dL in adult males and from 0.5 to 1.1 mg/dL in adult females, indicating healthy kidney function. Creatinine levels below this range are considered low and may be attributed to factors like muscle loss, liver disease, or pregnancy. Conversely, creatinine levels above the normal range can signal kidney disease, dehydration, muscle breakdown, or other health issues impacting kidney function. Healthcare professionals utilize creatinine levels in conjunction with other kidney function assessments to evaluate overall health and kidney function (Katayev et al., 2010).

- **Hemoglobin (Hb)**: - is the protein found in red blood cells, which is crucial in delivering oxygen to the tissues. Sufficient oxygenation of the tissues depends on maintaining an appropriate amount of hemoglobin levels. Hemoglobin levels in men typically vary from 14 to 18 g/dl, but in females, they are typically between 12 and 16 g/dl. Patients are diagnosed with anemia when their hemoglobin level is below the normal range (Thomas et al., 2013).
- **White blood cells**: - are an essential part of the immune system and help protect the body from illnesses. These cells move through the blood and different tissues, quickly responding to wounds or diseases by attacking any foreign organisms that enter the body. The normal white blood cell levels generally fall within the range of 4,500 to 11,000 cells per microliter (Vesper et al., 2016).
- **The red blood cell count (RBC count)**: - is a diagnostic test that measures the amount of oxygen-carrying red blood cells in the blood. Often, the first sign of an underlying medical disease is an abnormal result on an RBC test. A medical condition that prevents the body from absorbing enough oxygen may be indicated by elevated red blood cell numbers. For men, anything above 6.1 million cells per microliter (mcL) is considered high, while anything over 5.4 million cells/mcL is considered high for females. A lower RBC count, on the other hand, may indicate an infection or a health condition linked to anemia. Male RBC levels below 4.7 and female RBC levels below 4.2 are considered low (Vesper et al., 2016).
- **Serum iron: -** is a measurement of the iron content in serum, the liquid portion of blood left over after clotting factors and red blood cells have been eliminated. The normal

ranges for serum iron in adults are usually thought to be 26–170 mcg/dL for women and 76–198 mcg/dL for men (O'Connor, 2009).

- **Serum calcium levels**: - are commonly examined to evaluate the calcium balance and identify disorders pertaining to calcium control or bone metabolism. Adults' blood calcium levels typically vary from 8.5 to 10.2 mg/dL (Katayev et al., 2010).
- **Serum phosphorus levels**: - are measured to determine the amount of phosphorus in the blood, which is essential for energy storage and bone health maintenance. Adults may usually tolerate levels between 2.5 and 4.5 mg/dL. Disturbances from this spectrum may suggest various medical issues. Chronic alcohol use, vitamin D insufficiency, and malnutrition can all be causes of low blood phosphorus levels. On the other hand, increased levels of serum phosphorus are frequently associated with renal issues or significant challenges with the absorption of calcium (Thomas et al., 2013).

Chapter Three

3. DATA AND METHODOLOGY

3.1 Introduction

The research methodology and design used in this study are described in this chapter. Discussion topics include: research design and methodology, target population, study area description, data source, data collecting and analysis techniques, the study variables, and ethical issues.

The approach used by researchers to do their work is known as research methodology. It displays how these researchers design their problem and goal, as well as how they present their conclusions based on the data obtained throughout the study period (Jilcha Sileyew, 2020). The ultimate research outcome will be attained in compliance with the study's purpose, as this chapter on research design and procedure describes.

3.2 Study Area

The research took place at the ICMC general hospital's dialysis center, a private hospital in Ethiopia's capital, Addis Ababa. The city has 11 sub-cities and lies at an altitude of 7,546 feet (2300 meters). The city has 23 dialysis centers, of which 20 are non-governmental and three are governmental (Mengistu & Ejigu, 2022). ICMC is a tertiary private hospital in Ethiopia that specializes in cardiology.

It was founded in 2008 as the private specialty hospital in the country to serve cardiac patients from Ethiopia and abroad. The hospital offers various medical services, such as emergency care, surgery and dialysis. It has 14 dialysis machines that serve more than 80 patients weekly and a team of experienced nephrologists and nurses. The hospital offers round-the-clock medical services for both inpatients and outpatients. It delivers high-quality emergency services by competent and dedicated staff.

3.2.2 Study Population and Data source

All hemodialysis patients who visited the ICMC General Hospital's dialysis center between March 1, 2019 and March 1, 2024 was the research population. All patients receiving maintenance hemodialysis for end-stage renal disease (ESRD) throughout the designated timeframe was included in the research. But medical records with less than a month's worth of HD information, or incomplete medical records was not included in the research.

3.2.3 Ethical consideration

Ethical clearance was obtained from Addis Ababa University College of Natural and Computational Sciences Department of Statistics. The cooperation letter was written to the concerned bodies ICMC general hospital management with reference number stat/33/2023. Since names and patient card numbers were not included in the data extraction form and the data were just used for the study, the confidentiality of the information was kept throughout the investigation.

3.3 Research Design

The general approach or plan for carrying out a research study is known as the research design. It involves making decisions about the objectives, methods, and procedures of the study. This research was employed a retrospective cohort analysis on hemodialysis patients who visited ICMC General Hospital. The recorded data cover the period between March 1, 2019 up to March 1, 2024.

3.4 Study variables

3.4.1 The dependent variable

The dependent variable in a research study is one whose value is determined by the independent variable(s). The dependent variable of this study is time to death of HD patient time measured in week.

3.4.2 Independent Covariates

The study included independent variables, which were sociodemographic and clinical covariates gathered from the patient card. These variables were recorded as secondary data and were chosen based on relevant literature. The following table contains a list of those independent covariates for their respective categories.

Table 3. 1 Independent variables of the study

Independent variables	Categories
Age	
Hypertension	1 = Yes, 0 = No
Erythropoietin (EPO) Medication	1 = Yes, 0 = No
Gender	1 = Male, 0= Female
Vascular Access	0 = catheter, 1 = fistula, 2 = graft
Adequacy of Dialysis	0 = in adequate, 1 = Adequate, 2 = Optimal
Frequency of Dialysis per week	0 = one time, 1 = two times, 2 = three times per weak
Oxygen Saturation	0 = Normal, 1 = moderate hypoxemia, 2 = severe hypoxemia
Creatinine	1 = High, 2 = Normal, 3 = Low
Hematocrit	1 = High, 2 = Normal, 3 = Low
Hemoglobin Level	1 = High, 2 = Normal, 3 = Low
WBC Count	1 = High, 2 = Normal, 3 = Low
RBC Counts	1 = High, 2 = Normal, 3 = Low
Serum Iron	1 = High, 2 = Normal, 3 = Low
Serum Calcium	1 = High, 2 = Normal, 3 = Low
Serum Phosphor	1 = High, 2 = Normal, 3 = Low

3.5 Methods of Data Analysis

The data was analyzed using both inferential and descriptive statistical methods in this study. Descriptive statistics includes transforming data into a meaningful format through frequency distribution, graphs, and diagrams to illustrate data patterns and structures. In survival analysis, the descriptive component typically utilizes survival functions to summarize time-to-event data patterns. The application of Kaplan-Meier techniques allows for obtaining descriptive statistics on survival times, such as median survival time or the proportion surviving at specific time points post-treatment or diagnosis.

These methodologies play a crucial role in comprehending the distribution of survival times and are essential for the initial descriptive examination in survival research. They establish a basis for further analysis, including comparison of survival rates among different groups or evaluating the impact of explanatory variables on survival time.

Statistical inference focuses on drawing conclusions about population based on sample data. In the context of survival analysis, inferential statistics employ statistical methods to make inferences about the survival probabilities of a population using sampled data.

3.6 Survival Data Analysis

Survival analysis involves a set of statistical techniques used to analyze data where the main variable of interest is the time until a specific event takes place. Time frame can be measured in years, months, weeks, or days from the start of observation until the event occurs, or it can be the age of the individual at the time of the event. The event itself can be death, disease onset, relapse, recovery, or any other significant occurrence. Survival analysis is particularly valuable when some participants are lost to follow-up or when the observation period is limited, leading to incomplete data for certain individuals. These cases are known as censored observations, where the exact survival time is unknown despite having some information available. The issue of censoring is a central challenge in most survival analyses. The occurrence of such an event in reality can be attributed to several factors (Cox & Oakes, 2018):

3.6.1 The survival function

The probability that a randomly selected subject's survival time will be equal to or longer than a certain duration is known as the survivor function. As such, it gives the likelihood that a person will live past a given point in time. Let T denotes a continuous random variable that is related to the survival times, t represents the random variable's designated value, and f(t) be the survival time T's underlying probability density function. According to (Collett, 2015), the likelihood that a randomly chosen subject would survive for a shorter period of time than a given value t is represented by the cumulative distribution function F(t).

$$F(t) = P(T \leq t) = \int_0^t f(u)du, \text{ where; } t \geq 0 \quad (1)$$

where $F(t) =$ P (a patient has died before time t).

The basic quantity employed to describe time-to-event phenomena is the survival function, the probability of an individual surviving beyond time t (experiencing the event after time t). It is defined as

$$S(t) = P(T > t) = 1 - F(t),\ t \geq 0 \tag{2}$$

where $S(t) = 1 - \text{P(a patient has died before time t)}$.

Equations (1) and (2) then allow for the derivation of the link between f(t) and S(t).

$$f(t) = \frac{d}{dt}F(t) = \frac{d}{dt}\left(1 - s(t)\right) = \frac{-d}{dt}s(t),\ t \geq 0 \tag{3}$$

The survivor function can be represented as a smooth curve when t ranges from 0 to infinity. According to (Collett, 2015) survivor functions possess the following characteristics:

1. They exhibit a non-increasing pattern.
2. At the beginning of the study, when t=0, the probability of surviving beyond time 0, denoted as S (0), is equal to 1. This implies that since no individual has encountered the event yet, the likelihood of survival is certain.
3. As time approaches infinity, denoted as t→∞, the survivor function, S (∞), tends towards 0.

3.6.2 Median Survival Time

The estimated median survival time m is defined as the value for which $S(m) = 0.5$. Sometimes represented by $t_{0.5}$. If $S(t)$ is not strictly decreasing, m is the smallest number such that $S(m) \leq 0.5$ or

$$t_{med} = S^{-1}(0.5) \tag{4}$$

3.6.3 Non-parametric Survival Methods

Survival data are conveniently summarized through estimates of the survival function and hazard function. Methods of estimating these functions from a sample of survival data are nonparametric or distribution-free. Regarding the underlying distribution of the survival times, no particular assumptions were made. This method is used to present numerical or graphical summaries of the survival times for individuals in a particular group (Collett, 2015).

For estimating the survival and hazard functions, the Kaplan-Meier, Nelson-Aalen, and Life Tables are the most commonly used methods. Since these techniques don't need a particular assumption about the underlying distribution of the survival times, they are referred to as non-parametric or distribution-free techniques. The two most often used statistical techniques in medical reporting on survival data are the log-rank test for comparing two estimated survival curves and the Kaplan-Meier method for calculating survival curves (Cox & Oakes, 2018).

3.6.3.1 Kaplan-Meier (KM) estimator

The Kaplan-Meier estimator, also known as the Product Limit estimator, was introduced by (Kaplan and Meier, 1958) as the standard non-parametric estimator for survival functions. This estimator takes into account all available observations, whether censored or uncensored, by representing survival up to any given time as a sequence of steps determined by the observed survival and censored times. Being non-parametric or distribution-free, this method does not rely on making assumptions about the underlying distribution of survival times, as highlighted by (Collett, 2015).

The Kaplan-Meier estimator of the survival function at time t is obtained from the equation,

$\hat{S}_{KM}(t) = \prod_{t_{(i)} \leq t} \left(\frac{n_i - d_i}{n_i} \right) = \prod_{t_{(i)} \leq t} \hat{p}_i$ with the convention that $\hat{S}_{KM}(t) = 1$ if $t < t_1$. Thus,

The variance of the Kaplan-Meier estimators which is referred to as Greenwood's formula is given as (Collett, 2015):

$$\hat{\mathrm{Var}}\left(\hat{S}_{KM}(t)\right) = \left[\hat{S}_{KM}(t)\right]^2 \sum_{t_{(i)} \leq t} \frac{d_i}{n_i(n_i - d_i)} \qquad (5)$$

Where; $t_{(i)}$ = i-ordered failure time, n_i = number of failures at $t_{(i)}$ and n_i = number in the risk set at $t_{(i)}$.

3.6.3.2 Log-rank test

The log rank test, created by Mantel and Haenszel, is a non-parametric method used to compare two or more independent survival curves. This test does not require any assumptions about the data distribution due to its non-parametric nature.

In this research, log-rank test is used to compare the survival outcomes of hemodialysis patients among various groups including gender, frequency of dialysis per week, and vascular access. The idea being tested is that there are no variations in the groups' respective probabilities of an event happening at any given time.

3.6.4 Regression Models for Survival Data

There are different models and methods available for conducting this type of survival analysis, including parametric and semi-parametric approaches. Semi-parametric models parametrically specify the functional relationship between an individual's lifetime and their characteristics, while leaving the actual distribution of lifetimes arbitrary. The proportional hazards model is the most popular semi-parametric model (Hosmer & Lemeshow, 1999).

3.6.4.1 The Cox Proportional Hazards Model

The non-parametric approach does not account for covariates and necessitates the use of categorical predictors. In situations where we have multiple prognostic variables, it is imperative to employ multivariate techniques. However, multiple linear regression or logistic regression cannot be utilized due to their inability to handle censored observations. Therefore, an alternative method is required to effectively model survival data in the presence of censoring. The Cox proportional hazards (PH) regression model is the most popular and commonly applied technique for survival analysis. It was first presented in a seminal work by (Cox, 1972). Survival models are employed to measure the impact of one or multiple independent covariates on failure time. This requires defining a linear-type model for the log hazard. A parametric model utilizing the exponential distribution can be expressed in the following manner:

$$\log h_i(t \mid x) = \alpha + \beta_1 x_{i1} + \beta_2 x_{i2} + \cdots + \beta_k x_{ik}$$

Equivalently;

$$h_i(t \mid x) = \exp\left(\alpha + \beta_1 x_{i1} + \beta_2 x_{i2} + \cdots + \beta_k x_{ik}\right) = \exp(\alpha)\exp\left(\beta' X\right)$$

In this instance, the log-baseline hazard is represented by the constant α since, at zero x, $\log h_i(t) = \alpha$.

$$log h_i(t \mid x) = \alpha + \beta_1 x_{i1} + \beta_2 x_{i2} + \cdots + \beta_k x_{ik}$$
$$h_i(t \mid x) = h_o(t)\exp(\beta_1 x_{i1} + \beta_2 x_{i2} + \cdots + \beta_k x_{ik}), \quad (6)$$

When the baseline hazard function is represented by $h_o(t)$, explanatory variable vectors are represented by $\mathbf{X}_i$, and fixed effect vectors are represented by $\boldsymbol{\beta}$. The following is the fitting survival function for the Cox-PH model:

$$S(t,X) = [S_o(t)]^{\exp\{\sum_{i=1}^{p} \beta_i X_i\}}$$

where, $S_o(t)$ is the baseline survival function.

This model is sometimes known as a semi-parametric model since it does not make any distributional assumptions about the survival time; instead, it just makes the assumption that the hazards ratio remains constant over time, or proportional hazards. Regression coefficients β, hazard ratios, and adjusted hazard curves may all be estimated well, even in the absence of the baseline hazard. If all of the x's are zero the second part of equation (6) equals 1 so, $h_i(t) = h_o(t)$.

3.6.4.2 Assumption of Cox proportional hazard model

1. The baseline hazard $h_0(t)$ depends on t, but not on covariates $x_1, x_2, \dots, x_p$, the
2. The hazard ratio $e^{\beta\chi}$ depends on the covariates $x = (x_1, x_2, \dots, x_p)'$ but not on time t.
3. The covariate x_i does not depend on time t.

$$h(t, x_i, \beta) = h_0(t)e^{\beta'\chi}$$

Then the hazard ratio becomes

$$H(t, x_2, x_1) = \frac{h(t, x_2, \beta)}{h(t, x_1, \beta)} = \frac{h_0(t)e^{\beta\chi_2}}{h_0(t)e^{\beta'\chi_1}} = \frac{e^{\beta'\chi_2}}{e^{\beta'\chi_1}} = e^{\beta'(x_2-\chi_1)}. \quad (7)$$

The hazard function ratio for two individuals with differing covariate values does not change over time, as demonstrated by the fact that $e^{\beta(x_1-x_2)}$ is time-independent.

3.6.5 Testing of Regression Coefficients

The partial likelihood ratio test and the Wald test are the test used to evaluate the significance of the coefficient.

3.6.5.1 The Partial Likelihood Ratio Test (LR)

The partial likelihood ratio test, symbolized as G, is computed by twice the difference between the log partial likelihood of the model with the covariate and the log partial likelihood of the model without the covariate (Collett, 2015). Specifically,

$$G = 2\{L_p(\hat{\beta}) - L_p(0)\} \tag{8}$$

$$L_p(0) = -\sum_{i=1}^{m} \ln(n_i), \ldots. \tag{9}$$

and n_i denotes the number of subjects in the risk set at observed survival time $t_{(i)}$. This statistic will have a 1 degree of freedom chi-square distribution under the null hypothesis that the coefficient is equal to zero. P-values for assessing the significance of the coefficient may be obtained using this distribution. In this instance, a "sufficiently" big sample size corresponds to a high number of observed non-censored survival times (Cox, 1972).

3.6.5.2 The Wald Test

To test $H_0: \beta_q = (0,0,\ldots,0)^t$, the multivariable Wald statistic is used.

$$Q_W = \hat{\beta}_q{}'\left[I_q(\hat{\beta})\right]^{-1}\hat{\beta}_q \tag{10}$$

Where: -

$\hat{\beta}_q$ represents the estimated coefficient vector for the q parameters you're testing simultaneously.

$I_q(\hat{\beta})$ represents the inverse of the Fisher Information matrix evaluated at the estimated coefficients β̂.

Q_w represents the test statistic, which quantifies how far away your sample estimate (β̂) is from the hypothesized population parameter (usually zero). Under H_0 and for large sample the statistics $Q_w \sim X^2(q)$ at α level of significance follows a chi-squared distribution with q degrees of freedom.

The Wald test can also be used to test the significance of individual variables. The test statistic then becomes

$$Z = \frac{\hat{\beta}_j}{S\hat{E}(\hat{\beta}_j)}$$

Under the null hypothesis $H_0: \beta_j = 0$ the statistic $Z \sim N(0,1)$ at a significance level α, consequently the $100(1-\alpha)\%$ Wald statistic-based confidence interval for β_j is

$$\hat{\beta}_j \pm Z_{\alpha/2} \text{se}\left(\hat{\beta}_j\right)$$

where $Z_{\alpha/2}$ is the upper $\alpha/2$ percentile of the standard normal distribution.

3.6.7 Checking the assumption of proportional hazards

The evaluation of a model's conformity to its assumptions is an essential step in the model building process. In the case of the Cox model, a crucial assumption is the consistency of the covariate's effect on the outcome variable throughout the study period. In other words, it is necessary to examine the extent to which the coefficients of a covariate vary over time. While there are multiple approaches to assess the proportionality of hazard ratios over time, research by (Grambsch & Therneau, 1994) have demonstrated that a numerical test and graph are effective method to verify this assumption.

As an alternative to the proportional hazard's regression model, $h(t, x, \beta) = h_0(t)e^{\beta x}$, consider a model with time varying coefficient β as $h(t, x, \beta) = h(t, x, \beta)e^{\beta(t)X}$. Let the j^{th} covariate coefficient β_j vary over time as $\beta_j(t) = \beta_j + \gamma_j g_j(t)$ where $j = 1,2,3, \dots, p$. β_j is constant, $g_j(t)$ is some specified function of time (usually $g_j(t)$ is specified as $\ln(t)$) and γ_j is coefficient of $g_j(t)$. Then the hazard function becomes: $h(t, x, \beta) = h_0(t)e^{(\beta+\gamma \ln t)X} = h_0(t)e^{(\beta X+\gamma X \ln(t))}$.

The underlying principle of this model is based on the notion that the impact of a covariate might vary throughout the follow-up period. In order to assess this, the coefficient γ_j is tested to determine whether it is equal to zero or not. If the coefficient is found to be different from zero, it suggests that the proportional hazard assumption is not met. Conversely, if the coefficient is zero, the model simplifies to the proportional hazard model with a fulfilled assumption.

To evaluate the assumption, one can examine the plots of the scaled Schoenfeld residuals against the logarithm of time. If these plots exhibit a random distribution around the reference line at zero, it indicates that the assumption is satisfied. However, if a discernible pattern emerges from the plot, it suggests a violation of the proportional hazard assumption.

The test procedure to check whether the coefficient is really time varying or not is

$$\text{H}_0: \gamma_j = 0 \text{ Vs } H_1 = \gamma_j \neq 0 \text{ j} = 1,2,\dots,p$$

The test statistic to be used is the Wald test statistic which is given as:

$$Z = \frac{\gamma_j}{S.E(\gamma_j)}, \text{ which follows a standard normal distribution.}$$

Where Z : represents the test statistics.

γ_j: refers to the estimated parameter (often a regression coefficient) associated with a specific covariate or predictor.

$S.E(\gamma_j)$: refers to the standard error of the estimate for γ_j.

The test rule used is:

The coefficient of the j^{th} covariate is not time dependent if $Z < Z_{(\alpha/2)}$, then don't reject H_0, that is model assumption is satisfied. The coefficient of the j^{th} covariate is time dependent if $Z > Z_{(\alpha/2)}$, then reject H_0, that is model assumption is not met.

3.7 Overall goodness of fit

If the fitted model is satisfactory (appropriate), the final step in assessing the model's goodness of fit involves using Cox-Snell residuals. These residuals are derived from the Cox regression model and provide insights into how well the model fits the data. The plot of Nelson-Aalen estimates of the cumulative hazard function against these residuals shows that the model aligns fairly well with a straight line at a 45^{O} straight from the origin.

Additionally, statistical tests (such as Likelihood ratio, Score, and Wald tests) confirm that the model is a good fit, significant at the 5% level of significance.

Chapter Four

4. RESULTS

4.1 Introduction

The results of the data analysis, discussion, and interpretation are provided in this part in the following format. The first section gives an overview of descriptive statistics of status of patient with all independent variables, while the second is descriptive survival time for different groups. The model's fitting and appropriateness evaluation are the main topics of the third section. STATA 16 are the statistical software programs utilized in this study for data analysis.

4.2 Results of Descriptive Statistics

A cohort of 149 kidney failure patients undergoing Hemodialysis were part of the study during data collection. Among the total, 98 patients (65.77%) were censored and the remaining 51 patients (34.23%) died during the study period.

The data reveals that the percentage of female patients who were censored (24.16%) is lower than the percentage of male patients who were censored (41.61%). The proportion of female patients who experienced death (20.81%) is higher than the proportion of male patients who experienced death (13.42%). This suggests that female patients exhibit a higher mortality rate in comparison to male patients.

Patients who do not have hypertension exhibit a slightly higher rate of censorship (34.23%) and lower death (11.41%) in contrast to individuals with higher hypertension of censored (31.54%) and death (22.82%). The findings indicate that patients without hypertension experience superior survival rates when compared to those with higher hypertension. The mortality rate among patients with higher hypertension is approximately twice that of patients without hypertension, suggesting that hypertension could be a notable risk factor impacting the survival of time-to-death of hemodialysis patients.

Based on the data presented in Table 4.1, it can be observed that patients with normal hemoglobin levels exhibit the highest percentage of being censored (34.23%), implying more favorable survival outcomes, along with a relatively lower death rate (8.05%). Conversely, individuals with higher hemoglobin levels display a lower rate of being censored (9.40%) and a death rate that is comparable (10.07%). On the other hand, those with low hemoglobin levels demonstrate a notable censored rate (22.15%) but also a higher death rate (16.11%).

Compared to patients who do not get erythropoietin treatment (18.12%), those who receive it have a greater rate of censoring (47.65%). The mortality rate among patients receiving erythropoietin medication (11.41%) is lower than that of patients not receiving it (22.82%), suggesting that patients under erythropoietin medication experience improved survival outcomes (reduced risk of mortality throughout the study duration). Patients who are not prescribed erythropoietin have a higher chance of dying.

Out of the 149 participants involved in the study, 42 individuals (28.19%) received inadequate dialysis services, while 63 individuals (42.28%) received adequate dialysis services. Additionally, 44 individuals (29.53%) were enough to receive optimal dialysis services within the study area. In terms of frequency of dialysis, 44 patients (29.53%) underwent dialysis once a week, 54 patients (36.24%) underwent dialysis twice a week, and 51 patients (34.23%) underwent dialysis three or more times per week. Out of the total 149 patients included in the study, 68 individuals (45.64%) access for fistulas as their vascular access for hemodialysis, while 55 patients (36.91%) access on catheters, and 26 patients (17.45%) utilized grafts. Fistulas emerge as the most favorable choice for hemodialysis due to their lower mortality rate and the highest rate of survival.

Based on the data presented in Table 4.1, it is evident that patients who exhibit normal oxygen saturation levels tend to have the most favorable survival outcomes. This is supported by a notably high censored rate of 34.23% and a low death rate of 8.05%. Conversely, individuals with moderate hypoxemia display lower survival rates, as indicated by a censored rate of 16.78% and a death rate of 5.37%. Patients suffering from severe hypoxemia experience the poorest outcomes, with higher death rate of 20.81% in comparison to a censored rate of 14.77%. These findings underscore the critical importance of maintaining adequate oxygen level in order to enhance patient survival.

Table 4. 1 Descriptive Statistics

Covariates	Category	Status of Patient		
		Censored	Death	Total
Gender	Female	36 (24.16)	31 (20.81)	67 (44.97)
	Male	62(41.61)	20(13.42)	82(55.03)
Hypertension	Yes	47(31.54)	34(22.82)	81(54.36)
	No	51(34.23)	17(11.41)	68(45.64)
Erythropoietin Medication	Yes	71(47.65)	17(11.41)	88(59.06)
	No	27(18.12)	34(22.82)	61 (40.94)
Vascular Access	Fistula	53(35.57)	15(10.07)	68(45.64)
	Catheter	27(18.12)	28(18.79)	55(36.91)
	Graft	18(12.08)	8(5.37)	26(17.45)
Adequacy of Dialysis	In adequate	12 (8.05)	30 (20.13)	42 (28.19)
	Adequate	54 (36.24)	9 (6.04)	63 (42.28)
	Optimal	32 (21.48)	12 (8.05)	44 (29.53)
Frequency of Dialysis per week	One times per week	15(10.06)	29(19.46)	44(29.53)
	Two times per week	42(28.19)	12(8.05)	54(36.24)
	Three times per weak	41(27.52)	10(6.71)	51(34.23)
Oxygen Saturation	Normal	51(34.23)	12(8.05)	63 (42.28)
	Moderate hypoxemia	25(16.78)	8(5.37)	33(22.15)
	Severe hypoxemia	22(14.77)	31(20.81)	53(35.57)
Creatinine	High	23(15.44)	29(19.46)	52(34.90)
	Normal	48(32.21)	8(5.37)	56(37.58)
	Low	27(18.12)	14(9.40)	41(27.52)
Hematocrit	High	26(17.45)	23 (15.44)	49 (32.89)
	Normal	51 (34.23)	9 (6.04)	60 (40.27)
	Low	21 (14.09)	19(12.75)	40 (26.84)
Hemoglobin Level	High	14(9.40)	15(10.07)	29(19.46)
	Normal	51(34.23)	12(8.05)	63(42.28)
	Low	33(22.15)	24(16.11)	57(38.26)
WBC Count	High	20(13.42)	20(13.42)	40(26.84)
	Normal	51(34.23)	8(5.37)	59(39.60)
	Low	27(18.12)	23(15.44)	50(33.56)
RBC Counts	High	19(12.75)	25(16.78)	44(29.53)
	Normal	54(36.24)	11(7.38)	65(43.62)
	Low	25(16.78)	15(10.07)	40(26.85)
Serum Phosphor	High	19(12.75)	20(13.42)	39(26.17)
	Normal	48(32.21)	15(10.07)	63(42.28)
	Low	31(20.81)	16(10.74)	47(31.54)

4.3 Non parametric Survival Analysis

4.3.1 Median Survival time and Kaplan-Meier Survival estimate

A total of 149 patients were followed during the study period of which 51 (34.23%) HD patients died during the study period and 98 (65.77%) were censored. Among these censored patients, six of them had a kidney transplant, eight patients transferred out, and for the rest of the patients the study ended. The total risk time for these patients was 15,693-person weeks. Fifty-one deaths occurred within this time period, which gives an overall incidence rate of death as 32 per 10,000-person weeks with median survival time 207 weeks. A follow-up period of 13 weeks was the least and 231 weeks the highest.

The median survival time of hemodialysis patients and different background characteristics of patients are summarized in Table 4.2. Accordingly, the median survival time of male patients to death was 231 weeks with incidence rate 23 per 10,000 persons week, which is lower than female patients' median survival time 195 weeks with incidence rate 46 per 10,000 persons week.

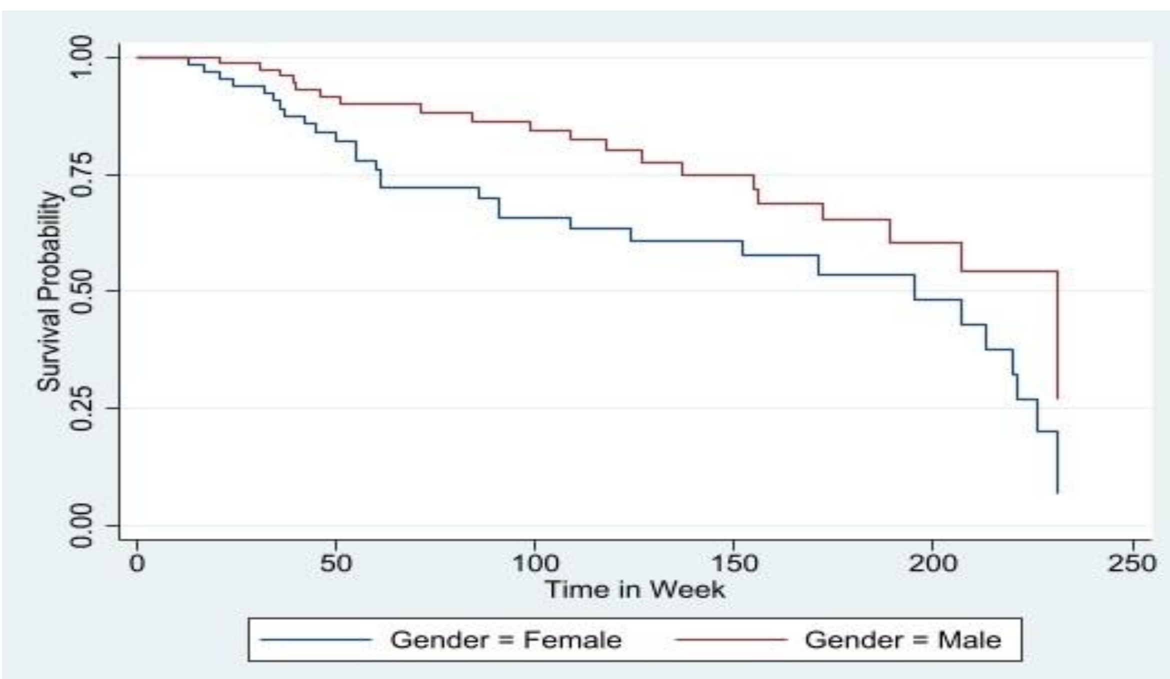


Figure 4. 1 Kaplan-Meier Survival estimate by Gender

The Kaplan Meier graph of survival estimate show that the survival time of hemodialysis patients of male was longer survival than that of female.

Table 4. 2 Median survival Time and Incidence rate

Variables	**Categories**	**Time at risk**	**Incidence rate**	**Median Survival**
Gender	Female	6804	0.0045	195
	Male	8889	0.0022	231
Erythropoietin Medication (EPO)	Yes	8628	0.0019	220
	No	7065	0.0047	171
Vascular Access	Catheter	4848	0.0057	127
	Fistula	7635	0.002	221
	Graft	3210	0.0024	231
Frequency Of Dialysis Per Week	One Times Per Week	4920	0.0059	172
	Two Times Per Week	5242	0.0023	226
	Three and more Times Per Weak	5531	0.0018	220
Hematocrit	High	4725	0.0048	152
	Normal	6655	0.0013	226
	Low	4313	0.0044	189
Hemoglobin Level	High	1869	0.008	71
	Normal	6532	0.0018	226
	Low	7292	0.0033	213
WBC Count	High	3701	0.0054	152
	Normal	6606	0.0012	231
	Low	5386	0.0043	172
Serum Iron	High	3976	0.0045	172
	Normal	7049	0.0027	221
	Low	4668	0.003	195
Serum Calcium	High	3246	0.005	189
	Normal	6590	0.0027	231
	Low	5857	0.0029	220
Serum Phosphor	High	4146	0.0048	207
	Normal	6808	0.0022	221
	Low	4739	0.0034	171
Total		**15693**	**0.0032**	**207**

As shown in the above Table 4.2, the median survival time of patients who received erythropoietin treatment is 220 weeks. The incidence rate was 19 per 10,000 persons week, which is lower than that of those who had never received it median survival time of 171 weeks and incidence rate of 47 per 10,000 persons week.

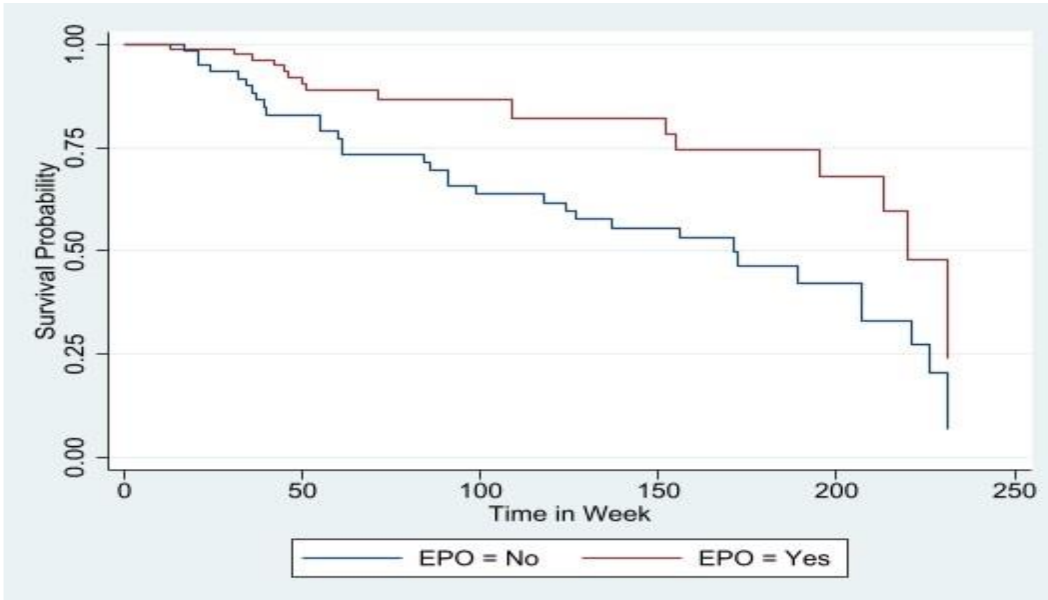


Figure 4. 2 Kaplan-Meier Survival estimate by EPO

According to the Kaplan-Meier graph, hemodialysis patients who got erythropoietin therapy had a longer survival period than those who did not.

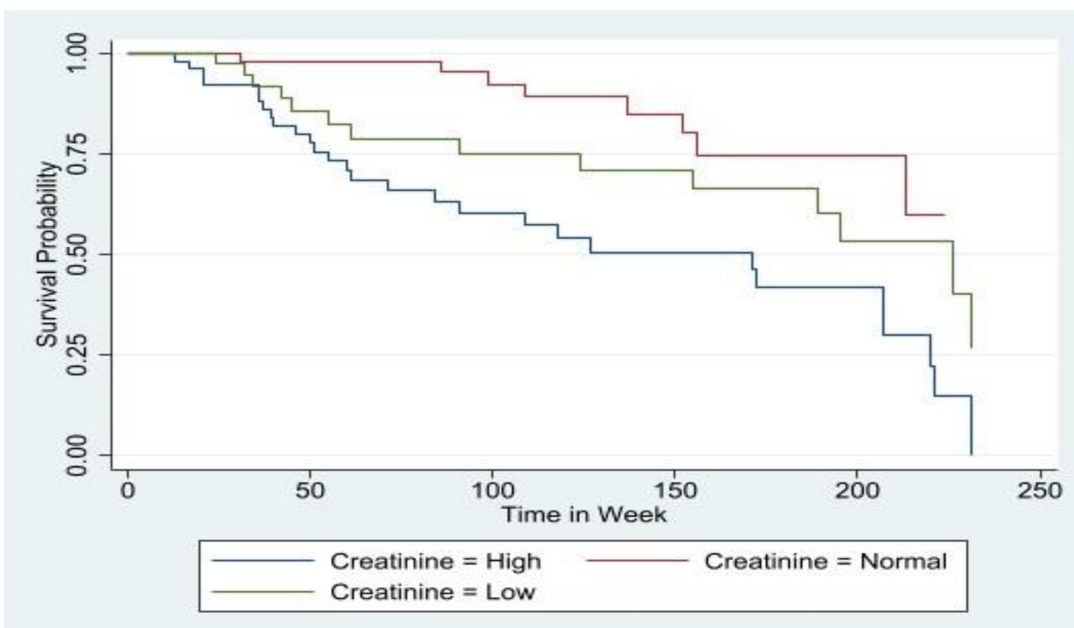


Figure 4. 3 Kaplan-Meier Survival estimate by Creatinine Level

The Kaplan-Meier graph revealed that the median survival of patients with a high creatinine level was lower than the median survival time of patients with a normal creatinine level. Additionally, patients with a low creatinine level had a lower median survival time compared to those with a normal creatinine level.

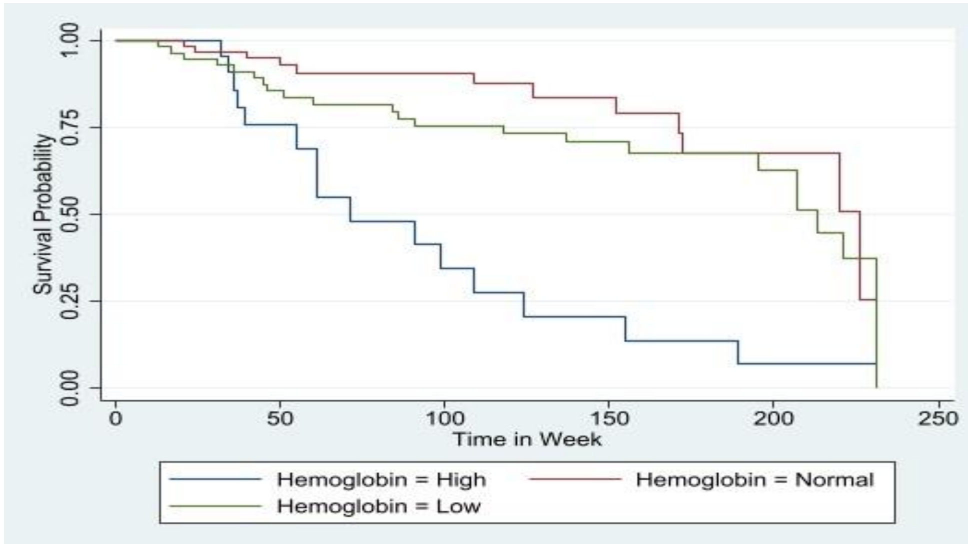


Figure 4. 4 Kaplan-Meier Survival estimate by Hemoglobin Level

The Kaplan Meier graph revealed that the median survival of patients with a high hemoglobin level was lower than the median survival time of patients with a normal hemoglobin level. Additionally, patients with a low hemoglobin level had a lower median survival time compared to those with a normal Hemoglobin level.

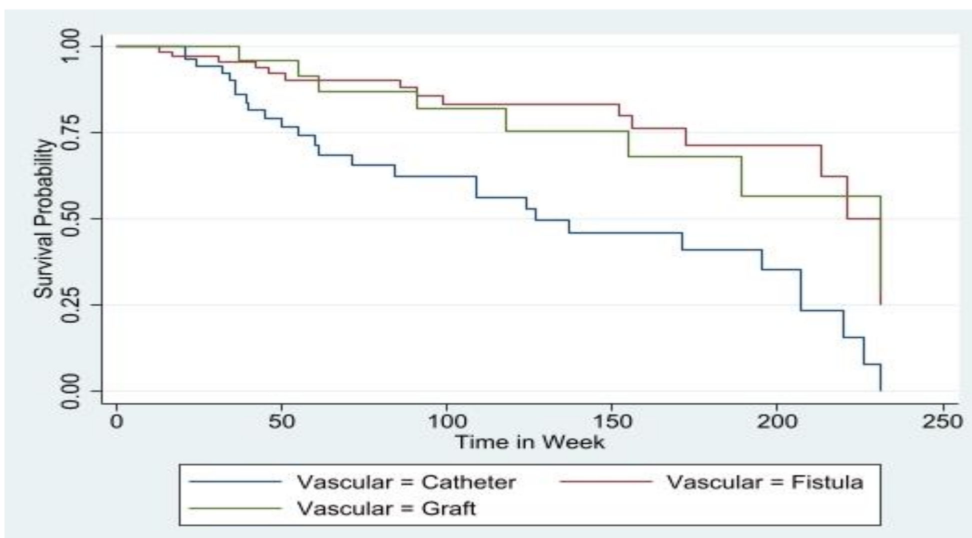


Figure 4. 5 Kaplan-Meier Survival estimate by Vascular Accesses

The Kaplan-Meier graph showed that the survival time of hemodialysis patients who had catheter is lower than median survival time of those who had a fistula with median survival time of catheter 127 weeks with 57 per 10,000 person weeks incidence rate, the median survival time of fistula 221 weeks with 20 per 10,000 person weeks incidence rate and the median survival time of graft was 231 weeks and 24 per 10,000 person weeks incidence rate.

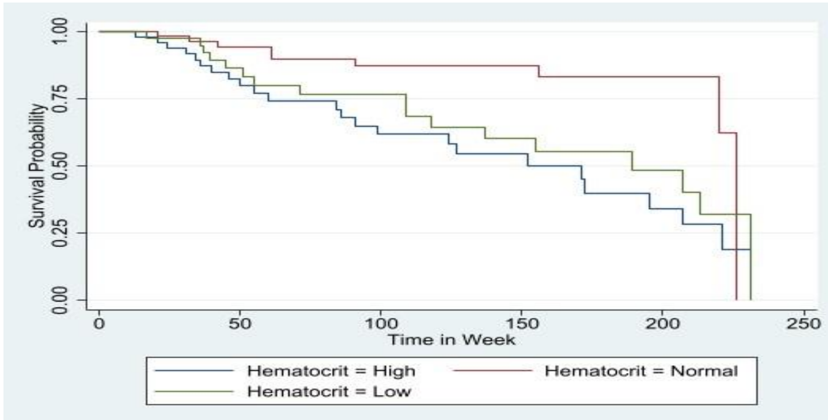


Figure 4. 6 Kaplan-Meier Survival estimate by Hematocrit level

The Kaplan-Meier graph revealed that the median survival of patients with a high hematocrit level was lower than the median survival time of patients with a normal hematocrit level. Additionally, patients with a low hematocrit level had a lower median survival time compared to those with a normal hematocrit level. As shown in Table 4.2 the median survival time of high hematocrit level was 152 weeks with 48 per 10,000 person weeks incidence rate, the median survival time of normal hematocrit level was 226 weeks with 13 per 10,000 person weeks incidence rate and the median survival time of low hematocrit level was 189 weeks and 44 per 10,000 person weeks incidence rate.

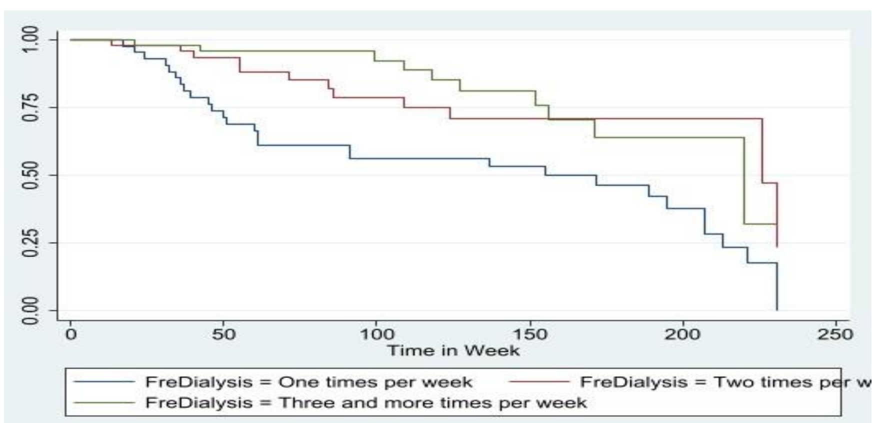


Figure 4. 7 Kaplan-Meier Survival estimate by Frequency of Dialysis per week

In the above Figure 4.7 Kaplan-Meier graph revealed that the median survival of patients with frequency of dialysis one times per week was lower than the median survival time of patients with frequency of dialysis three and more times per week. Additionally, as shown in Table 4.2 the median survival time of frequency of dialysis one times per week was 172 weeks with 59 per 10,000 person weeks incidence rate, the median survival time of frequency of dialysis two times per week was 226 weeks with 23 per 10,000 person weeks incidence rate and the median survival time of frequency of dialysis three and more times per week was 220 weeks and 18 per 10,000 person weeks incidence rate.

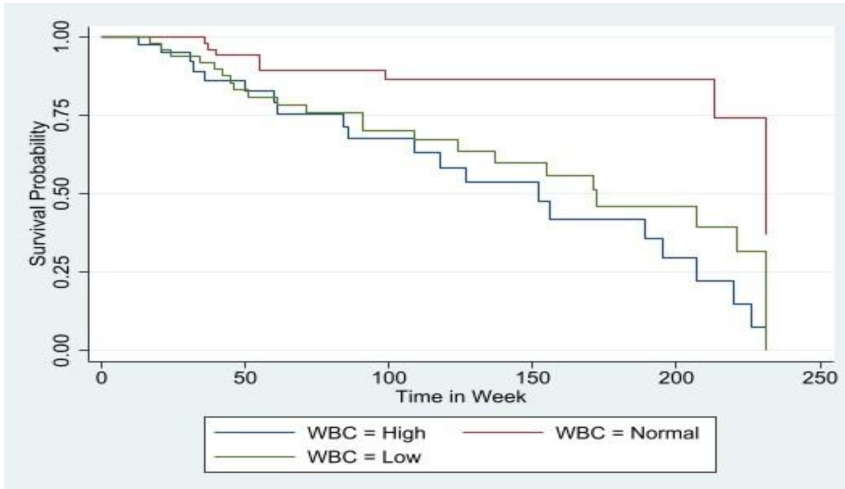


Figure 4. 8 Kaplan-Meier Survival Estimate by WBC Saturation

The Kaplan-Meier graph revealed that the median survival of patients with a high white blood cell level was lower than the median survival time of patients with a normal white blood cell level. Additionally, patients with a low white blood cell levels had a lower median survival time compared to those with a normal white blood cell level. As shown in Table 4.2 the median survival time of high white blood cell levels was 152 weeks with 48 per 10,000 person weeks incidence rate, the median survival time of normal white blood cell levels was 226 weeks with 13 per 10,000 person weeks incidence rate and the median survival time of low white blood cell levels was 189 weeks and 44 per 10,000 person weeks incidence rate.

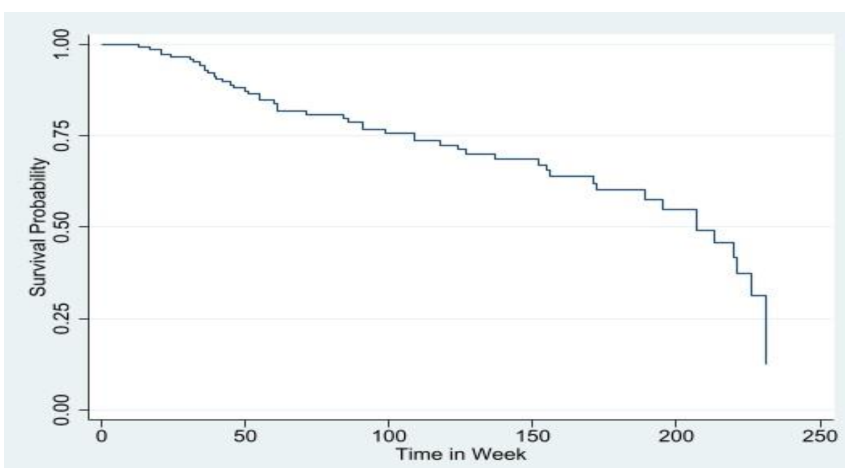


Figure 4. 9 Kaplan-Meier Survival Estimate of Hemodialysis patient

Figure 4.9 displays the KM curves illustrating the relationship between survival time and death. The survival plot exhibits a rapid decline initially, followed by a gradual decrease. The study's findings reveal the overall patients' survival rates for different time intervals: one-year (88.15%), two-year (77.01%), three-year (68.52%), four-year (57.56%), and five-year (21.59%).

4.3.2 Log rank test

The log-rank statistical test is utilized to investigate potential significant differences between several sets of categorical variables. There is no difference in the survival curves, which is the null hypothesis under test.

Table 4. 3 Log-rank test for each category variable

Covariates	DF	Chi-square	p-value
Gender	1	4.92	0.0265
Hypertension	1	0.48	0.4866
Erythropoietin Medication	1	8.35	0.0039
Vascular Access	2	16.43	0.0003
Adequacy of Dialysis	2	13.93	0.0009
Frequency of Dialysis per week	2	15.30	0.0005
Oxygen Saturation	2	15.33	0.0005
Creatinine	2	15.14	0.0005
Hematocrit	2	10.84	0.0044
Hemoglobin Level	2	19.15	0.0001
WBC Count	2	15.64	0.0004
RBC Counts	2	4.47	0.1069
Serum Iron	2	1.78	0.4107
Serum Calcium	2	2.96	0.2280
Serum Phosphor	2	4.81	0.0901

Table 4.3 indicates that the survival difference log-rank test of gender, erythropoietin medication (EPO), vascular access, adequacy of dialysis, frequency of dialysis per week, oxygen saturation, creatinine, hematocrit, hemoglobin level, and WBC count are statistically

significant independent variables in survival experience at 5% level of significance. The remaining categorical factors, however, including hypertension, RBC counts, serum iron, serum calcium, and serum phosphorus, do not statistically significantly differ in terms of survival or death experiences across the groups.

4.4 Results of the Cox proportional hazards model

It is essential to evaluate the relationship between the dependent variables and explanatory variables in order to construct the model.

4.4.1 Multivariable Analyses

The multivariable Cox PH model was constructed through a backward elimination variable selection process. Initially, all variables along with the survival outcome were included in the model. Subsequently, non-significant variables, which contributed minimally to the model, were removed in a stepwise manner to achieve model simplicity.

During the backward elimination process, certain variables were retained while others were eliminated. Variable elimination continued until all remaining variables in the model had p-values below 0.25. Following this approach, covariates that increased the -2Log likelihood value and higher p – value were removed.

Upon reviewing the results, it is evident that covariates, including age, vascular accesses, adequacy of dialysis, frequency of dialysis, oxygen, Creatinine, hemoglobin, WBC and RBC are statistically significant at a 5% level of significance and small AIC. Therefore, this model is regarded as a preliminary final model, which may potentially serve as the final model after checking of proportionality assumptions.

Table 4. 4 Multivariable Analysis of Cox PH model variable selection

Include variable	Eliminated variable	p-value	**AIC**
Age, EPO, vascular, adequacy of dialysis, frequency of dialysis, oxygen, creatinine, hemoglobin, WBC, RBC, phosphors, hematocrit, hypertension, gender, iron, calcium	Calcium	0.789 2	366.97
Age, EPO, vascular, adequacy of dialysis, frequency of dialysis, oxygen, creatinine, hemoglobin, WBC, RBC, phosphors, hematocrit, hypertension, gender, iron	Iron	0.7277	365.04
Age, EPO, vascular, adequacy of dialysis, frequency of dialysis, oxygen, creatinine, hemoglobin, WBC, RBC, phosphors, hematocrit, hypertension, gender	Gender	0.6802	363.16
Age, EPO, vascular, adequacy of dialysis, frequency of dialysis, oxygen, creatinine, hemoglobin, WBC, RBC, phosphors, hematocrit, hypertension	Phosphors	0.6458	361.33
Age, EPO, vascular, adequacy of dialysis, frequency of dialysis, oxygen, creatinine, hemoglobin, WBC, RBC, hematocrit, hypertension	Hypertension	0.5964	359.63
Age, EPO, vascular, adequacy of dialysis, frequency of dialysis, oxygen, creatinine, hemoglobin, WBC, RBC, hematocrit	Hematocrit	0.3565	357.83
Age, EPO, vascular, adequacy of dialysis, frequency of dialysis, oxygen, creatinine, hemoglobin, WBC, RBC	EPO	0.195	356.68
Age, vascular, adequacy of dialysis, frequency of dialysis, oxygen, creatinine, hemoglobin, WBC, RBC	-	-	**356.39**

4.5. Assessment of Model Adequacy

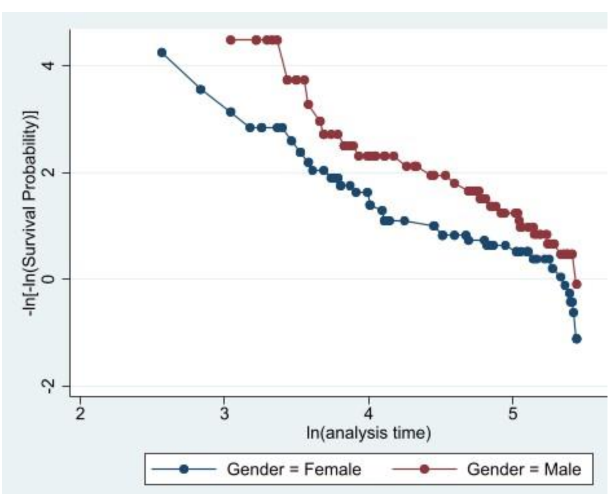
The next and most crucial phase in the statistical analysis is to determine the model's fit once the preliminary final model has been found. An assessment of the fitted model's appropriateness is necessary once it has been fitted to an observed set of survival data. As part of the model-in-process, diagnostic methods are used for model checking. Part of the model-in-process is the use of diagnostic techniques for model checking.

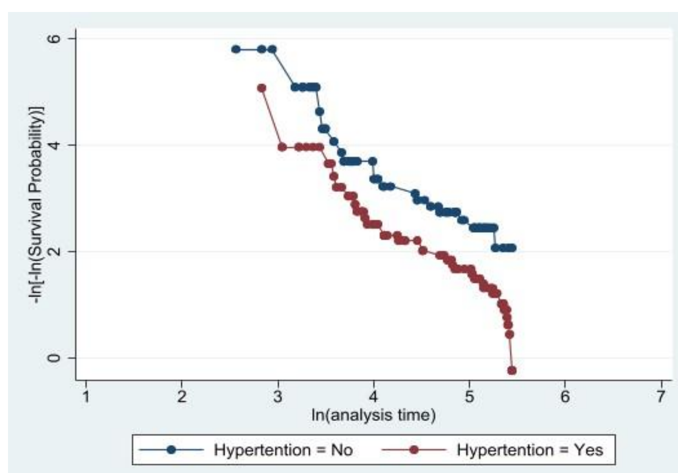
4.5.1 Test of proportional hazard assumption by Schoenfeld residuals

Table 4. 5 Goodness-of-fit test assessing proportional hazards Assumption.

	Rho	chi2	Df	Prob>chi2
Age	-0.060	0.230	1	0.632
Gender	0.051	0.180	1	0.676
Hypertension	0.097	0.600	1	0.439
EPO	-0.009	0.010	1	0.936
Vascular	-0.143	1.330	1	0.248
Adequacy of Dialysis	-0.013	0.010	1	0.914
Frequency of Dialysis	0.028	0.060	1	0.804
Oxygen	0.146	1.730	1	0.188
Creatinine	-0.077	0.460	1	0.497
Hematocrit	0.094	0.550	1	0.458
Hemoglobin	-0.164	2.240	1	0.135
WBC	-0.100	0.720	1	0.396
RBC	-0.051	0.210	1	0.647
Iron	0.076	0.380	1	0.539
Calcium	-0.112	1.020	1	0.313
Phosphors	0.010	0.010	1	0.932
Global test		**12.03**	**16**	**0.7419**

4.5.2 Test of proportional hazard assumption by graph





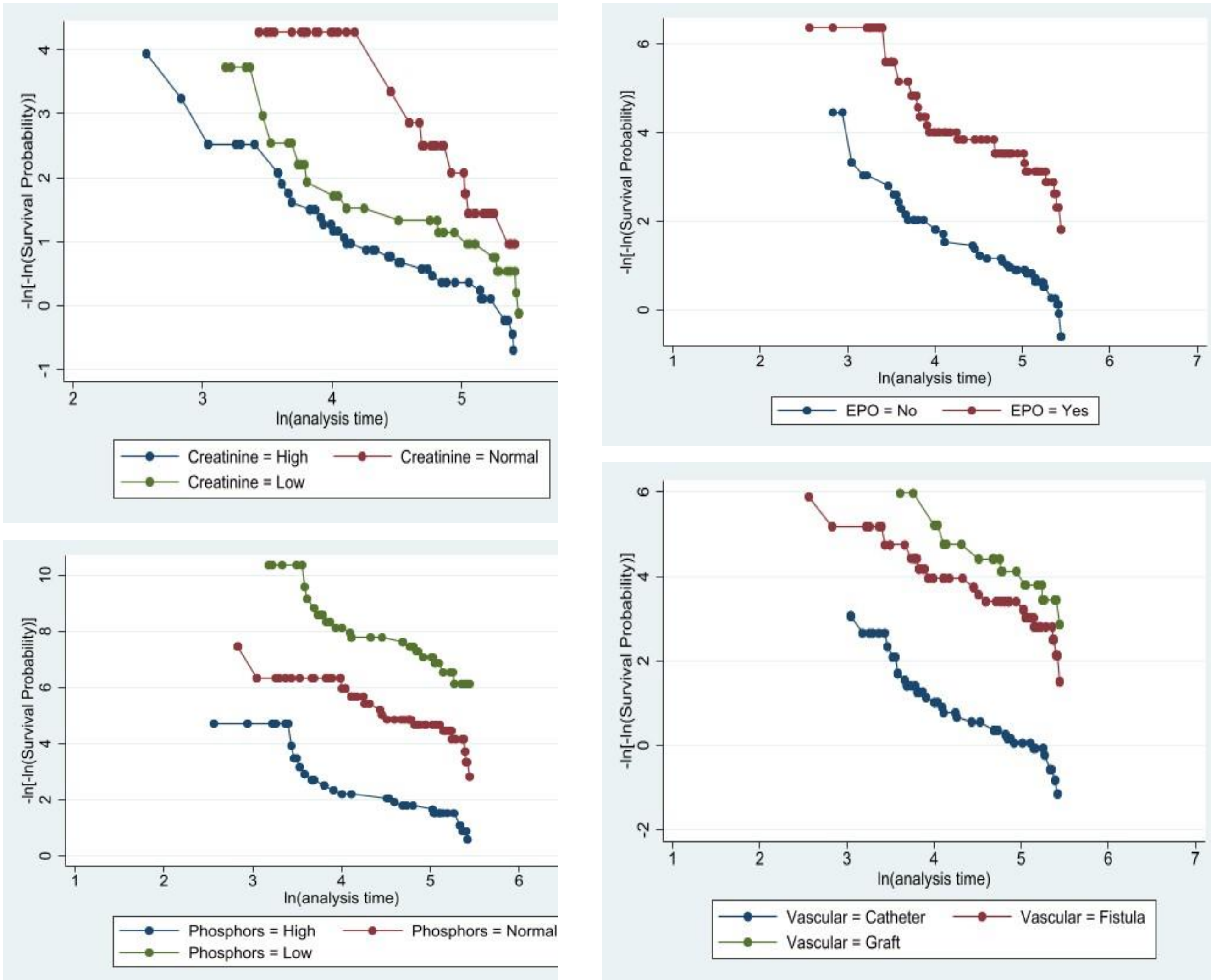


Figure 4. 10 Checking proportional for hazard assumption by graphical method

When modeling a Cox PH model, a key assumption is the proportional hazards. As shown in Figure 4.10, the graph of the log(-log(survival)) versus log of survival time graph for the predictor variable can be taken as parallel, implying that the proportional hazards assumption has not been violated.

4.5.3 Checking for the linearity of covariates in the model

The next step involves assessing the magnitude of continuous covariates in the initial main effects model. Various methodologies exist, all of which aim to ascertain whether the data substantiate the proposition that the impact of the covariate is linear in the logarithm of the hazard. If this is not the case, these techniques also help identify the transformation of the covariate that exhibits linearity in the logarithm of the hazard. Hence, we employ the graphical approach to examine linearity in continuous covariates.

Martingale residuals help assess the nonlinearity of the relationship between the continuous covariate and the log hazard in survival models. The following STATA output shows the resulting graph for the continuous covariate age.

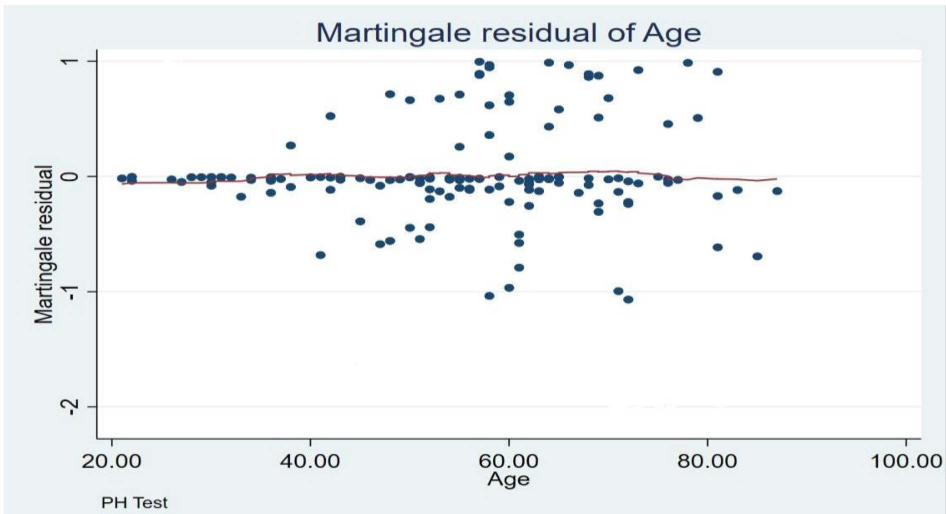


Figure 4. 11 Martingale residual of Age

Figure 4.11 illustrates the relationship between martingale residuals and the age variable. The absence of discernible patterns or trends in the plots, along with the LOWESS smoothed plots forming a nearly horizontal line, supporting the conclusion that there is an approximately linear relationship between age and survival time.

4.5.5 Checking for overall goodness of fit

The final step in assessing the model's goodness of fit involves using Cox-Snell residuals. These residuals are derived from the Cox regression model and provide insights into how well the model fits the data. The plot of Nelson-Aalen estimates of the cumulative hazard function against these residuals shows that the model aligns fairly well with a straight line at a 45^{o} straight from the origin.

In addition, statistical tests (such as Likelihood ratio, Score, and Wald tests) confirm that the model is a good fit, significant at the 5% level of significance. Consequently, the model with the parameter estimates from Table 4.6 is considered the final model.

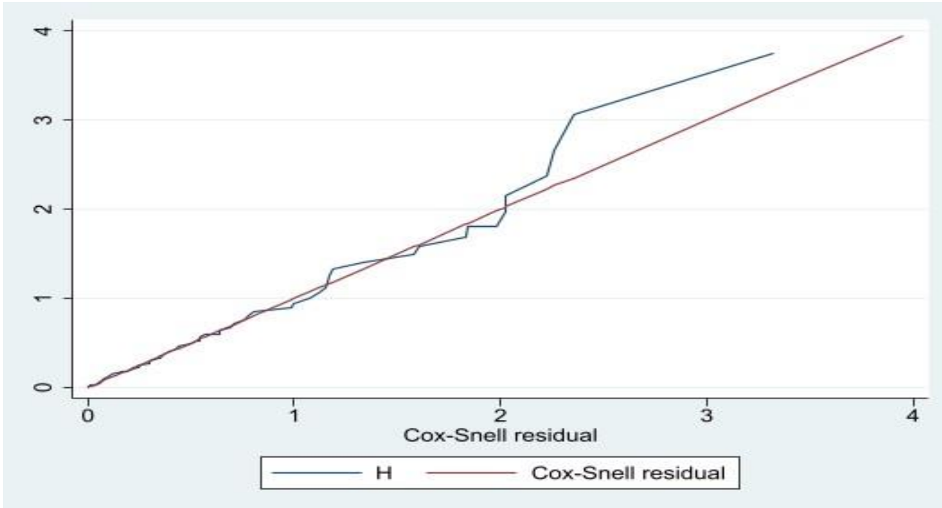


Figure 4. 12 Cox-Snell residuals

4.5.6 Interpretation of Cox PH regression

From the previous section graphical and hypothetical tests of the assumption of Cox PH model are satisfied. The hazard ratios are interpreted from the fitted final model as the log of the ratio of the hazard of death of a level of a categorical covariate to the baseline hazard. Stated in simpler terms, they are interpreted by comparing the reference group with others.

- **Age**

As shown in Table 4.6 below, the hazard ratio (HR) for a five-year increase in age is 1.174 = exp (0.032x5). This means that for each five-year increment in age, the risk of death increases by approximately 17.4%. Additionally, the p-value associated with this relationship is 0.026. Since 0.026 is less than the commonly used significance level of 0.05, we can conclude that the relationship between age and the risk of death is statistically significant, keeping other variables constant.

- **Vascular access**

The hazard ratio (HR) for patients with types of vascular access' fistula is 4.2, with a corresponding p-value of 0.009. This HR value implies that the risk of death for patients with types of vascular access' a fistula is 4.2 times higher than for those with a vascular access' graft keeping other variables constant. Hence, the p-value of 0.009 indicates that this observed difference is statistically significant, as the generally accepted threshold for statistical significance is a p-value less than 0.05. Therefore, based on this data, we can confidently conclude that the presence of a types of vascular access fistula increases the risk of death compared to types of vascular access graft.

On the other hand, the hazard ratio (HR) for patients with types of vascular accesses catheter is 6.57, with a p-value of 0.0001. This HR value suggests that the risk of death for patients with a types of vascular accesses catheter is 6.57 times higher than for those patients with types of vascular accesses a graft. The p-value of 0.000 is less than 0.05, indicating that this result is statistically significant. This means that there is strong evidence to suggest that a patient with types of vascular accesses catheter is associated with a substantially higher risk of death compared to types of vascular access graft.

- **Creatinine level**

The low creatinine level shows a hazard ratio of 0.191 and a p-value of 0.001, where it concluded that patients with low creatinine level have 80.9% lower hazard of dying compared to those with high creatinine level keeping other variables constant. The p-value is less than 0.05 this shows that low creatinine level is statistically significant.

- **Red Blood Cell count**

The hazard ratio of low RBC count is 2.29 with a p-value of 0.042, we concluded that patients with low RBC count have 2.29 times higher hazard of dying compared to those with high RBC count keeping other variables constant. And also, p-value (0.001) is less than 0.05 indicates that the relationship between low RBC count and the risk of death is statistically significant at 5% level of significance (since 0.019 < 0.05).

- **Oxygen saturation**

The hazard ratio (HR) for patients with oxygen saturation severe hypoxemia is 0.288, with a p-value of 0.031. This HR value suggests that the risk of death for patients with oxygen saturation level sever hypoxemia is 71.2% lower than for those patients with normal oxygen saturation. The p-value of 0.031 is less than 0.05, indicating that this result is statistically significant. This means that there is strong evidence to suggest that a patient with oxygen saturation level sever hypoxemia is associated with a substantially lower risk of death compared to a normal oxygen saturation level.

Table 4. 6 Fitted final Cox PH model

		Haz. Ratio					95% C. I of exp (β)	
Variables	Categories	β	exp(β)	Std.Err. of exp(β)	Z	P-value	Lower	Upper
Age	Age	0.032	1.032	0.0147	2.22	**0.026**	1.004	1.061
Vascular Access	Graft (Ref)							
	Catheter	1.88	6.57	3.278	3.78	**0.0001**	2.475	17.467
	Fistula	1.43	4.2	2.313	2.60	**0.009**	1.425	12.36
Frequency of Dialysis Per Week	One Times Per Week (Ref)							
	Two Times Per Week	-1.933	0.145	0.067	-4.15	**0.0001**	0.058	0.361
	Three and more Times Per Weak	-2.13	0.119	0.06	-4.18	**0.0001**	0.044	0.322
Adequacy of Dialysis	Inadequate (Ref)							
	Adequate	-0.643	0.526	0.235	-1.44	0.150	0.219	1.26
	Optimal	-0.984	0.374	0.21	-1.75	0.081	0.124	1.127
Oxygen Saturation	Normal (Ref)							
	Moderate Hypoxemia	-0.84	0.432	0.213	-1.70	0.088	0.165	1.134
	Severe Hypoxemia	-1.25	0.288	0.166	-2.16	**0.031**	0.093	0.893
Creatinine	High (Ref)							
	Normal	-0.84	0.432	0.198	-1.83	0.067	0.176	1.061
	Low	-1.66	0.191	0.0924	-3.42	**0.001**	0.074	0.493
Hemoglobin Level	High (Ref)							
	Normal	-2.06	0.127	0.0685	-3.83	**0.0001**	0.044	0.366
	Low	-2.19	0.112	0.0583	-4.20	**0.0001**	0.04	0.311
WBC Count	High (Ref)							
	Normal	-1.13	0.322	0.1663	-2.19	**0.028**	0.117	0.886
	Low	-1.016	0.362	0.1387	-2.65	**0.008**	0.171	0.767
RBC Counts	High (Ref)							
	Normal	0.792	2.21	0.995	1.76	0.079	0.912	5.34
	Low	0.827	2.29	0.929	2.03	**0.042**	1.03	5.072

- **White Blood Cell count**

The hazard ratio of normal WBC count is 0.322 with a p-value of 0.028, indicates that patients with normal WBC count have 67.8% lower hazard of dying compared to those with high WBC count, holding all other variables constant. And also, p-value (0.028) is less than 0.05 indicates that the relationship between normal WBC count and the risk of death is statistically significant at 5% level of significance (since 0.028 < 0.05).

The hazard ratio of low WBC count is 0.362 with a p-value of 0.008, indicates that individuals with low WBC have a 63.8% lower hazard or risk of the event compared to individuals with high WBC count, holding all other variables constant. And also, p-value (0.008) is less than 0.05 indicates that the relationship between low WBC count and the risk of death is statistically significant at 5% level of significance (since 0.008 < 0.05). The result is unexpected those might be due to the sample includes specific patient groups (those on hemodialysis). A low WBC count might compromise the body's ability to fight off infections.

- **Frequency of Dialysis Per Week**

The estimated relative risk (hazard ratio) of death for hemodialysis patients taking dialysis two times per week, as compared to those who take one times per week, is 0.145 with p – value 0.0001. This indicates that the hazards of death are lesser by 85.5 % for those hemodialysis patients who are taking dialysis two times per week than those of hemodialysis patients taking dialysis one times per week.

The estimated hazard ratio of hemodialysis patient taking dialysis three and more times per week is 0.119 with a p-value of 0.0001, indicates that individuals with frequency of dialysis three and more times per week have 88.1% lower hazard or risk of the event compared to individuals with frequency of dialysis one times per week, holding all other variables constant. And also, p-value (0.008) is less than 0.05 indicates that the relationship between frequency of dialysis three and more times per week and one times per week is statistically significant at 5% level of significance (since 0.0001 < 0.05).

- **Hemoglobin level**

The estimated hazard ratio of hemodialysis patient with normal hemoglobin level is 0.127, indicates that individuals with normal hemoglobin levels have about 87.3% reduction in the hazard of death compared to those hemodialysis patients with high hemoglobin levels, holding all other variables constant. And also, p-value (0.0001) is less than 0.05 indicates that the relationship between normal hemoglobin level and high hemoglobin level is statistically significant at 5% level of significance (since 0.0001 < 0.05).

The estimated hazard ratio of hemodialysis patient with low hemoglobin level is 0.112, indicates that individuals with low hemoglobin levels have about 88.8% reduction in the hazard of death compared to those hemodialysis patients with high hemoglobin levels, holding all other variables constant. And also, p-value (0.0001) is less than 0.05 indicates that the relationship between normal hemoglobin level and high hemoglobin level is statistically significant at 5% level of significance (since 0.0001 < 0.05).

- **Adequacy of dialysis**

The hazard ratio of adequate dialysis is 0.526 with a p-value of 0.15, indicates that patients with adequate dialysis have 47.4% lower hazard of death compared to those with inadequate dialysis, holding all other variables constant. And also, p-value (0.15) is greater than 0.05 indicates that the relationship between adequate dialysis and the risk of death is statistically insignificant at 5% level of significance (since 0.15 > 0.05).

The hazard ratio of optimal adequacy of dialysis is 0.374 with a p-value of 0.081, indicates that individuals with optimal adequacy of dialysis have a 62.6% lower hazard or risk of death compared to individuals with inadequate dialysis, holding all other variables constant. And also, p-value (0.081) is greater than 0.05 indicates that the relationship between optimal adequacy of dialysis and the risk of death is statistically insignificant at 5% level of significance (since 0.081 > 0.05).

Chapter Five

5. DISCUSSION

The general objective of this study was to determine the effect of covariates that affect the survival analysis of hemodialysis patients in the specific context of ICMC General Hospital in Addis Ababa. We analyzed data from a 5-year retrospective cohort study for a total of 149 chronic kidney disease undergoing hemodialysis patient.

To identify significant covariates of hemodialysis patient in ICMC general hospital we used Cox PH model. The proportionality assumption in Cox PH model was checked and satisfied. The multivariable Cox proportional hazards regression analysis indicated that age, hemoglobin level, creatinine, white blood cell count, red blood cell count, vascular access, frequency of dialysis and oxygen saturation have a significant effect on the survival time of patients undergoing hemodialysis within the study area. However, gender, adequacy of dialysis, hematocrit, calcium, iron and erythropoietin did not have significant effect.

In this study a retrospective cohort study of 149 recorded hemodialysis patients were collected out of this 51 (34.23%) are death and 98 (65.77%) are censored. The median survival time was 207 weeks; the incidence rate is 3.2 per 1000 persons week. In contrast a study conducted based on data from Felege Hiwot, Gonder, and Gambi hospitals from a total of 436 medical records, 153 individuals (35.1%) died and 283 (64.9%) were censored. The median survival time was determined to be 345 days, and the mortality rate was calculated to be 1.89 per 1000 person-days or 13.23 per 1000-person week (Workie et al., 2022). That result was in line with the studies conducted in St. Paul Millennium Medical College, Zewditu Memorial Hospital, and Menelik II Hospital by (Desta et al., 2023). The incidence of mortality at the end of follow-up is estimated at 104 per 1000 person-years or 2.17 per 1000 person weeks.

Age is statistically significant at 5% level of significance with hazard ratio for a five-year increase in age is 1.174 = exp (0.032x5). This means for each five-year increment in age, the risk of death increases by approximately 17.4%. These result is similar to the finding in a study in Southwest Ethiopia (Kebede et al., 2022), in Adama hospital (Betiru et al., 2023) and in Imam Khomeini and Fatima Zahra hospitals in Sari, Iran (Montaseri et al., 2022) increasing age was significantly associated with chronic kidney disease undergoing hemodialysis.

The mortality rate among patients receiving erythropoietin medication (11.41%) is lower than that of patients not receiving it (22.82%), suggesting that patients under erythropoietin medication experience improved survival outcomes (reduced risk of mortality throughout the study duration). Patients who did not receive erythropoietin have a higher chance of dying. But in Cox PH model this result is not statistically significant at 5% level of significance. This result is contradicts a finding by a previous study conducted in Addis Ababa government dialysis center by (Mossie, 2021) and in Saint Gabriel general hospital by (Shibiru et al., 2013).

We found that patients with normal WBC count have 67.8% lower hazard of dying compared to those with high WBC count. And also, individuals with low WBC have a 63.8% lower hazard or risk of the event compared to individuals with high WBC count. In addition to that both normal WBC count and low WBC count p-value is less than 0.05 indicating that the relationship between WBC count and the risk of death is statistically significant at 5% level of significance. This finding is similar to a study in Iran by (Ebrahimi et al., 2019); WBC count had significant effects on survival time of hemodialysis patients (p-values< 0.05).

Patients with normal hemoglobin levels have about 87.3% lower hazard of death compared to those hemodialysis patients with high hemoglobin levels. And individuals with low hemoglobin levels have about 88.8% lower hazard of death compared to those hemodialysis patients with high hemoglobin levels. Consequently, both normal hemoglobin levels and low hemoglobin levels p-value (0.0001) is less than 0.05 indicating that the relationship between hemoglobin level and the risk of death is statistically significant at 5% level of significance (since 0.0001 < 0.05). This result is supported by a previous study conducted in Shiraz University of Medical Sciences, Iran by (Ebrahimi et al., 2019) hemoglobin concentration has statistically significant effect on survival time of HD patients (p-values < 0.05).

Low red blood cell count is found to have statistically significant effect on the survival analysis of time-to-death of hemodialysis patient at 5% level of significance with hazard ratio of 2.29. This means that patients with low RBC count have 2.29 times higher hazard of dying compared to those with high RBC count. This result is the same as a study in Shiraz university of medical sciences, Iran by (Ebrahimi et al., 2019) at 5 % level of significance. Low RBC count are factors significantly affects survival time of HD patients.

The Cox PH regression results indicated that types of vascular access are significant covariates of death in the study. Uses of vascular access fistula and catheter increase the risk of death compared to uses of vascular access graft. This result is supported by the result of (Mossie, 2021); (Susanto & Asiandi, 2020); (Shibiru et al., 2013); (Workie et al., 2022) and (Betiru et al., 2023) HD patients who were using vascular access fistula and catheter are statistically significant effect on the time to death of patients with the Chronic Kidney disease.

Low creatinine level is statistically significant at 5% level of significance with hazard ratio of 0.191 and a p-value of 0.001, this means that patients with low creatinine level have 80.9% lower hazard of dying compared to those with high creatinine level. Other findings contradict this result. A study in Imam Khomeini and Fatima Zahra hospitals in Sari, Iran (Montaseri et al., 2022) and in Saint Gabriel general hospital (Shibiru et al., 2013) at 5 % level of significance low creatinine level was not statistically significant effect on survival analysis of hemodialysis patients.

The current finding also revealed that frequency of dialysis per week had a significant effect on the survival analysis of time-to-death of HD patient. This study found that individuals with frequency of dialysis three and more times per week have 88.1% lower hazard or risk of the event compared to individuals with frequency of dialysis one times per week. This result contradicts the results in Saint Paul hospital Millennium medical college and Myungsung Christian medical center in Addis Ababa by (Betiru et al., 2023) and in Saint Geberial general hospital (Mekonen et al., 2020). Based on the Cox proportional hazards regression model results, there was no significant mortality difference between frequency of dialysis per week and survival of the HD patient.

5.1 Limitation of the study

Overall, the results are limited since several significant factors could not be included because this study is retrospective and uses secondary data. The primary drawback of this research is that socioeconomic variables, such as patient income, body mass index (BMI), and burdens on caregivers including emotional, physical, and social aspects should have been considered. These variables impact patient survival and potentially function as a confounding factor.

Chapter Six

6. CONCLUSION AND RECOMMENDATION

6.1 Conclusion

The main purpose of this study was to estimate the survival rate of hemodialysis patients and to identify the factors affecting the survival of time-to-death of hemodialysis patients. A retrospective cohort study was conducted on hemodialysis patients in ICMC General Hospital, covering a period of five years from 2019 to 2024 for a total of 149 chronic kidney diseases undergoing hemodialysis. Data analysis was based on Cox proportional hazards regression model. The study found that the total time at risk are 115,693 weeks and the median survival time was 207 weeks with the overall incidence rate in hemodialysis patient 32 per 10,000 person-weeks.

The study showed that age, hemoglobin level, creatinine, white blood cell count, red blood cell count, vascular access, frequency of dialysis and oxygen saturation have a significant effect on the survival time of hemodialysis patients. However, gender, adequacy of dialysis, hypertension, hematocrit, serum calcium, serum iron, serum phosphors and erythropoietin did not have significant effect.

6.2 Recommendations

Based on the findings of the study and the conclusions drawn above, the following recommendations are forwarded to government, to dialysis centers and health care providers.

- The medical staff at ICMC General Hospital pays particular attention to the important factors that influence the survival analysis of time-to-death of hemodialysis patients.
- Increase the frequency of dialysis per week for different patient groups while the dialysis center should reduce costs of the price to maximize treatment effectiveness.
- Future studies could investigate the impact of comorbidities, nutritional status, psychosocial factors, and genetic predispositions on survival outcomes.

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