# IMPACT OF IMMUNOSUPPRESSANT THERAPIES AND TRANSPLANTATION ON HEALTH-RELATED QUALITY OF LIFE AMONG RENAL TRANSPLANT RECIPIENTS AT KENYATTA NATIONAL HOSPITAL

Phaustine Adhiambo Onyango (B. Pharm)

U56/34534/2019

*A research dissertation submitted in partial fulfillment of the requirements for the award of the degree of master of pharmacy in clinical pharmacy*

Department of Pharmaceutics and Pharmacy Practice

University of Nairobi

**NOVEMBER, 2021**

**DECLARATION OF ORIGINALITY**

| | |
|---|---|
| **Name of student:** | Phaustine Adhiambo Onyango |
| **Registration number:** | U56/34534/2019 |
| **College:** | College of health science |
| **School:** | Pharmacy |
| **Department:** | Pharmaceutics and pharmacy practice |
| **Course name:** | Master of pharmacy in clinical pharmacy |
| **Title work:** | Impact of immunosuppressant therapies and transplantation on health related quality of life among renal transplant recipients at Kenyatta National Hospital. |

**Declaration**

1. I understand what plagiarism is, and I am aware of the University's policy in this regard.
2. I declare that this dissertation is my original work and has not been submitted anywhere for examination, award of degree or publication. Where other people's work has been used, it has been acknowledged and referenced in accordance with the University of Nairobi requirements.
3. I have not used the services of professional agencies to produce my work.
4. I have not allowed, and shall never allow anyone to copy my work with the intention of using it as his/her work.
5. I am aware that any false claim in respect of this work shall result in disciplinary action, in accordance with University Plagiarism Policy.

**Signature**  **Date** 18.11.2021

**APPROVAL BY SUPERVISORS**

This proposal has been submitted for research and examination with our approval as University

Supervisors:

1. Signature  Date 18/11/2021

   Dr. David G. Nyamu, PhD

   Senior Lecturer,

   Department of Pharmaceutics and Pharmacy Practice,

   University of Nairobi

2. Signature _____ Date 18.11.2021

   Dr. Sylvia A. Opanga, PhD

   Senior Lecturer,

   Department of Pharmaceutics and pharmaceutic practice,

   University of Nairobi

**DEDICATION**

I dedicate this work to my parents, Caren and Anthony. Your words of encouragement, support and prayers kept me going.

**ACKNOWLEDGEMENTS**

First and foremost, I thank the Almighty God for his grace and strength during the research period.

Secondly, I wish to express my sincere gratitude to my supervisors Dr. David Nyamu and Dr. Sylvia Opanga for their immense guidance, advice, suggestions and positive criticism throughout the research and dissertation writing. May God richly bless and increase you. May He perfect everything concerning you!

Thirdly, I am very grateful to nurse Nancy Wang'ombe and Grace Kwamboka for their unwavering support during data collection. I also wish to recognize the study participants who accepted to be part of this research. May God bless you.

Finally, I appreciate the School of Pharmacy, Department of Pharmaceutics and Pharmacy practice for providing training and a conducive environment that enabled the development and execution of this research. I will forever be grateful.

**LIST OF ABBREVIATIONS**

| | |
|---|---|
| CKD | Chronic kidney disease. |
| ESRD | End stage renal disease |
| ESRD-SCL | End-Stage Renal Disease Symptom Checklist |
| GI | Gastrointestinal |
| GODT | Global Observatory on Donation and Transplantation |
| HRQoL | Health related quality of life |
| KDQOL | Kidney Disease-Quality of Life |
| KTQ-25 | Kidney transplant questionnaire-25 |
| KNH | Kenyatta National Hospital |
| KNH UON-ERC | Kenyatta National Hospital -University of Nairobi, Ethics Research Commission |
| IS | Immunosuppressant |
| MPA | Mycophenolic Acid |
| NHP | Nottingham Health Profile |
| SF-36 | 36-Item Short Form Health Survey |
| RT | Renal transplantation |
| RTR | Renal transplant recipients |
| PGWB | Psychological General Well-Being Index |

## DEFINITION OF TERMS

**Graft rejection:** This is a process in which a recipient's immune system attacks the donated organ and begins destroying it.

**Health related quality of life:** This is a measure of health outcome which looks at the impact of an illness or treatment modality from a patient's point of view. HRQoL is a multidimensional concept consisting of three domains: psychological, physical and social components usually affected by an individual's disease and/or treatment intervention.

**Immunosuppressant:** This is a drug that inhibits or prevents the activity of the body immune system.

**Renal transplantation:** A surgical procedure that involves replacing a failing kidney(s) with a working one in a patient with end stage renal disease.

**Psychological factors:** A domain of HRQoL that refers to issues ranging from severe mental distress, anxiety and depression to a positive sense of well-being.

**Physical factors:** A domain of HRQoL that refers to the ability to perform a range of activities of daily living and symptoms resulting from the one's disease or from treatment intervention.

**Social factors**: Refers to aspects of engagement and participation in societal activities and interactions of renal transplant recipients with others in the society.

**TABLE OF CONTENTS**

**LIST OF TABLES**

**LIST OF FIGURES**

**ABSTRACT**

**Background:** The prevalence of renal transplantation has recently been shown to increase globally. To prevent graft rejection and loss, renal transplant recipients are required to take immunosuppressive drugs for a prolonged period of time. Limited studies exist on the impact of immunosuppressive agents and transplantation on health related quality of life outcomes among renal transplant recipients in resource constrained settings.

**Study objective:** To determine the impact of immunosuppressive agents and transplantation on health related quality of life outcomes in renal transplant recipients at Kenyatta National Hospital (KNH).

**Study area and setting:** The study was conducted at the renal transplant clinic, within renal unit of KNH.

**Methodology:** A cross-sectional descriptive study involving 80 patients who were consecutively sampled was carried out between 1st July 2021 and 30th September 2021. Patients' socio-demographics, the type of immunosuppressive medication regimen, side effects, and adherence data were collected using a predesigned data collection tool. Assessment of health related quality of life was done using the kidney transplant questionnaire-25 (KTQ-25), a validated tool that has been used worldwide. Data analysis was carried out using Stata version 13 statistical software at $P \leq 0.05$. Categorical variables such as side effects of drugs were summarized as frequencies while continuous variables like participants' age were expressed using measures of central tendencies. Associations between immunosuppressant regimen type, side effects, adherence and sociodemographic variables with HRQoL score were determined using ANOVA. Linear regression analysis was conducted to determine independent predictors of low HRQoL scores.

**Results:** The mean (SD) age of the participants was 45.4(14.7) with a male predominance (70%). Hypertension was the most prevalent comorbidity among study participants (60%) followed by both diabetes and hypertension (25%). The most prevalent immunosuppressant regimen was prednisolone, tacrolimus, and mycophenolate (75%) and the adherence rate was 78.8%. Weight gain (33.8 %) was the commonest side effect experienced, followed by fatigue (27.5%) and diarrhea (23. 8%). The mean(SD) HRQoL

was 5.19(0.78), denoting good health related quality of life among the study participants. The highest score of the KTQ was in the appearance dimension 6.62(0.60) while the lowest was on uncertainty/fear domain 4.28(1.12). Variables that were significantly associated with low HRQoL were comorbidity (p=0.017) and immunosuppressant side effects of changes in appearance (p=0.002) and physical symptoms (p=0.011) domains. Immunosuppressant regimen and adherence to antirejection medication were not significantly associated with HRQoL. Having diabetes decreased the score of HRQoL by 11.67 units {95% CI (-21.283, -2.064)}.

**Conclusions:** Generally**,** HRQoL of kidney transplant patients was good. However, uncertainty and fear was the least scored domain in quality of life assessment reflecting fear and stress among kidney transplant patients. Side effects from immunosuppressant medication had an influence on the appearance and physical symptoms dimensions of health related quality of life. Immunosuppressant medication non-adherence rate was 21.2% which was attributed to unaffordability of immunosuppressant medication**.**

**Recommendations:** Blood sugar levels should routinely be monitored among renal transplant recipients to continue improving on the management. Future studies should correlate mean scores of quality of life domains before and after transplantation to ascertain the impact of transplantation on HRQoL to improve the management of renal transplant recipients.

# CHAPTER ONE: INTRODUCTION

## 1.1 Background

End stage kidney disease, also known as kidney failure, is a public health concern globally[1,2]. Kidney failure is characterized by permanent disruption of kidney function leading to a need for regular dialysis or kidney transplantation to maintain life [3]. The aim of kidney transplantation is to restore the patient's kidney function and consequently improve life.

According to Global Observatory on Donation and Transplantation(GODT), 95,479 renal transplants were conducted worldwide in 2018, with 36.2% representing donation from living donors [4]. In the USA, about 17,500 kidney transplants are performed annually[5]. A study done by Garcia *et al* reported that in 2010, approximately 30 per million kidney transplants were done in Western Europe, the USA, and Australia[6].The same study established that transplantation rates were low in developing countries due to insufficiently trained workforce and poor infrastructure. However, Kenya, Nigeria and South Africa conduct more renal transplantations than other countries in sub-Saharan Africa [6].

Renal transplantation has resulted in a pool of a transplanted community with unique psychological, clinical and social features [7]. Furthermore, transplant recipients may have to deal with strict regimens of immunosuppressive drugs, as well as the side effects associated with the drugs, for example, hypertension, hyperlipidemia excessive hair growth and gingival hyperplasia [8]. Psychologically, transplanted patients may suffer from depression or anxiety concerning the treatment or graft rejection [9]. Despite these observations, renal transplantation is considered the best treatment modality for end stage renal as it is cost effective, prolongs life, and improves health related quality of life (HRQoL) [10].

HRQoL is a significant measure of health outcomes that looks at the effect of an illness and its treatment from a patient's perspective[11]. HRQoL following kidney transplantation is gaining great significance as an outcome measure of treatment efficacy, patients' general health state, and graft survival [12]. There are generic and disease-specific instruments

available for evaluation of HRQoL. For instance, SF-36 and Kidney Transplant Questionnaire are validated tools for assessing the HRQoL among patients[13].

Studies have found an improvement in HRQoL among patients after transplantation[14]. A study comparing different immunosuppressive regimens reported improved HRQoL in renal transplant recipients(RTR) on tacrolimus treatment[15]. Evidence from studies in other countries document positive and negative aspects of transplantation and IS on HRQoL in kidney transplant recipients[16]. In Kenya, no study has been done to evaluate HRQoL outcomes among renal transplant recipients. In addition, the impact of immunosuppressants on HRQoL outcomes has not been studied in resource constrained settings. This study aims at assessing the impact of immunosuppressive drugs and transplantation on HRQoL among renal transplant recipients in Kenya.

### 1.2 Problem Statement

Kidney transplantation is the best treatment modality in end stage renal disease. It is associated with better survival as well as satisfactory health related quality of life at a reduced cost, compared to dialysis [12]. Although HRQoL improves post kidney transplant, studies have shown that renal transplant recipients may experience challenges that impact negatively on HRQoL outcomes. One systematic review reported a decrease in QoL among RTRs during the post-transplant period, where anxiety about graft loss was the main cause[17]. Rosenbergera *et a1* also documented side effects and complications due to immunosuppressive therapy as determinants of decreased QoL post transplantation[18]. A complex immunosuppressive regimen may also diminish compliance which in turn may cause non-adherence to immunosuppressive drugs resulting in graft rejection and low quality of life[19]. Furthermore, the type of immunosuppressant regimen may influence the quality of life in kidney transplant recipients, because some antirejection medications may cause more side effects than others[12].

Limited studies and data exist on the impact of immunosuppressive drugs and transplantation on HRQoL among RTRs in resource limited settings. HRQoL is an important indicator of therapeutic intervention outcomes and yet minimal evaluation of patient's QoL following renal transplantation is done by clinicians. Furthermore, lack of

HRQoL data hinders detection and management of problems that the patient may be experiencing resulting in poor disease management.

### 1.3 Research questions

i. What is the health related quality of life among patients following renal transplantation at Kenyatta National Hospital (KNH)?

ii. What is the impact of immunosuppressive drugs on health related quality of life of renal transplant recipients at KNH?

### 1.4 Objectives

#### 1.4.1 Main objective

To determine the impact of immunosuppressive drugs and transplantation on HRQoL in renal transplant recipients at Kenyatta National Hospital.

#### 1.4.2 Specific objectives

i. To determine health related quality of life (HRQoL) among renal transplant recipients at Kenyatta Nation Hospital.

ii. To find out the impact of immunosuppressive drugs regimens on HRQoL among renal transplant recipients at KNH.

iii. To determine the impact of side effects of immunosuppressants on HRQoL among renal transplant recipients at KNH

iv. To assess the impact of adherence on immunosuppressant agents on HRQoL among renal transplant recipients at KNH.

### 1.5 Study justification

The prevalence of renal transplantation has recently been shown to increase globally. Advancement in transplantation procedures and immunosuppressive therapy has contributed to prolonged patient and graft survival. To prevent rejection and loss of the transplanted kidney, renal transplant recipients are required to take immunosuppressive drugs for a prolonged period of time. These drugs, however, are associated with side effects and new pathologies that may have a negative impact on HRQoL. Additionally, transplant recipients may have to deal with complex and strict regimens of immunosuppressive drugs

that can diminish adherence, culminating in poor HRQoL and ultimately graft loss. This study may help identify domains of HRQoL mostly affected by the use of immunosuppressive drugs and transplantation thereby informing the healthcare workers on the overall functioning and well-being of the patient. The study may also identify potential areas that can maximize HRQoL in renal transplant recipients. Moreover, the findings may also guide incorporation of HRQoL assessment as a monitoring tool to measure patient general health and treatment outcomes in clinical practice.

### 1.6 Conceptual Framework

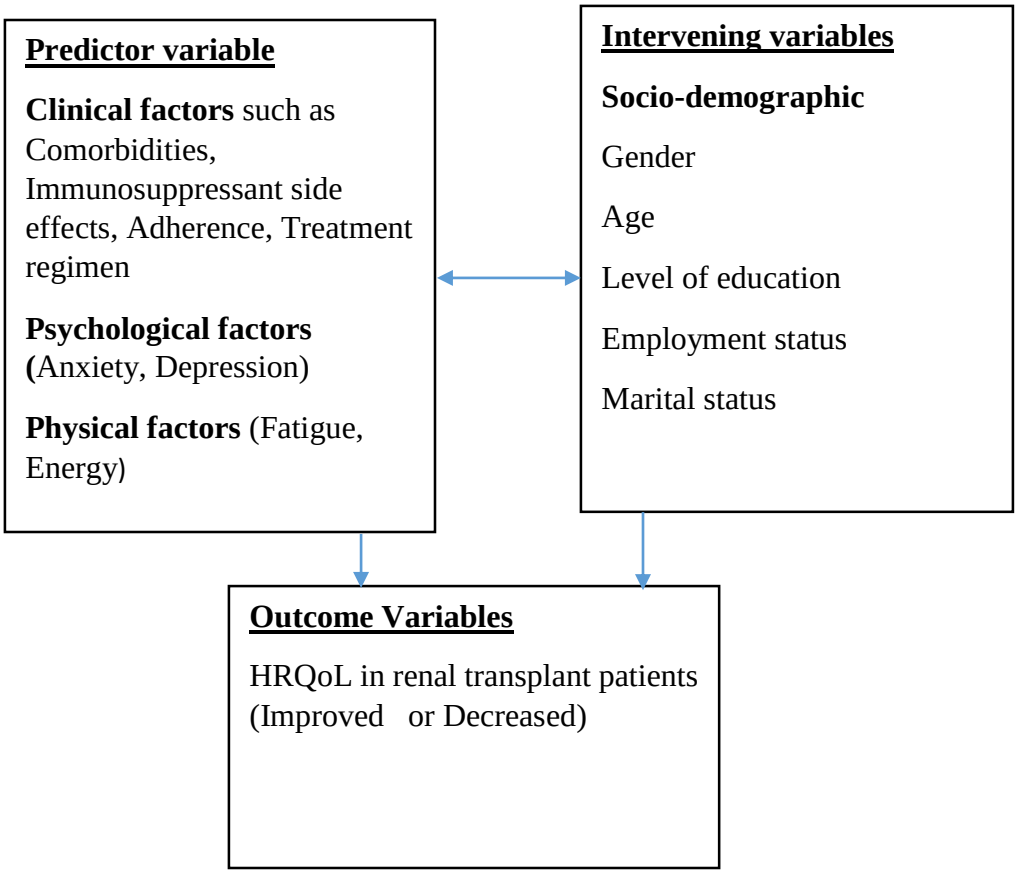


**Figure 1:** Conceptual framework of factors impacting health related quality life outcomes in renal transplant recipients.

#### 1.6.1: Predictor variable

**Clinical factors:** Clinical factors include comorbidities and immunosuppressant medication side effects, adherence, and the regimen type. Renal transplant recipients with

other comorbidities such as diabetes or hypertension may have poor HRQoL due to complications of the disease and increased pill burden associated with management [20]. Furthermore, side effects and multiple medications to prevent graft rejection may be a difficult experience for the patients thus decreasing HRQoL[21]. Additionally, non-compliance to immunosuppressants results in reduced graft survival and quality of life.

**Psychological factors:** Kidney transplantation results in freedom from restrictions associated with dialysis, among other benefits such as prolongation of life and cost effectiveness. These advantages are associated with improved HRQoL. However, fear of graft rejection, weight gain, and change in physical appearance may cause the patient to develop emotional distress, anxiety, and depression which can compromise HRQoL[22].

**Physical factors:** Return of kidney function to normal following transplantation has been associated with improved general health and physical functions thus improving HRQoL[23].

### 1.6.2: Intervening variable

A patient's socio-demographic characteristics have an impact on their HRQoL. Educated and employed patients are likely to adhere to instructions regarding management and treatment. Being married may result in improved HRQoL due to the social support system for the patient from the spouse. However, younger age may be associated with unsatisfactory HRQoL due to worry regarding the life span of their graft[10].

### 1.6.3: Outcome variable

HRQoL is a function of several factors. The predictor and intervening factors may positively or negatively influence HRQoL outcomes. Evaluation of these factors by clinicians is key in developing interventions that maximize the HRQoL outcomes in renal transplant recipients [23].

## 1.7 Delimitation

The study was limited to renal transplant recipients aged 18 years. For a renal transplant recipient to be included in the study, the procedure must have been carried out at least 3 months before the study. This is because a patient is considered stable and may not be

experiencing acute phase transplant reactions which may have resulted in overly low health related quality of life reporting. The study was conducted only in KNH. KNH is the only public facility in the country with a renal transplant program and offering care to post transplant patients. The set out study objectives were limited to HRQoL, immunosuppressive therapies, and transplantation among the kidney transplant recipients.

# CHAPTER TWO: LITERATURE REVIEW

## 2.1 Introduction

This chapter highlights a review of available literature that is relevant to the study. The review is divided into five sections. The first section presents literature on the epidemiology of renal transplantation. The second section reviews the literature and studies on health-related quality of life in renal transplant recipients, and the third section reviews the health-related quality of life measurements and tools. The fourth part presents a review of the importance of HRQoL evaluation, the fifth part present studies on the factors influencing HRQoL on renal transplant patients, and the last part provides gaps found in the existing literature.

## 2.2 Epidemiology of Renal Transplantation

Chronic kidney disease (CKD) is a significant public health concern globally, with an estimated prevalence of between 10-13% [24]. Patients with CKD are at the highest risk of advancement to end-stage renal disease (ESRD). Patients with CKD and ESRD need renal replacement therapy to maintain life. Renal transplantation (RT) is the best treatment modality for patients with CKD and ESRD because it prolongs life and improves health outcomes at a favorably minimal cost [25].

According to Global Observatory on Donation and Transplantation(GODT) 2018, an estimated 95,479 renal transplants were performed worldwide, with 36.2% representing donation from living donors [4]. In the USA, about 17,500 kidney transplants are done annually [5]. In 2016, about 119,521 patients were put on the waiting list for RT [26]. There has been a rise in the number of people awaiting RT globally, from 58,000 in 2004 to 119,521 in 2016 [26]. This indicates the level of the global burden of CKD. A study by Garcia *et al* reported that in 2010, approximately 30 per million population kidney transplants were done in Western Europe, the USA, and Australia [6]. The same study also established that developing countries had poor transplant rates because of insufficiently trained workforce and poor infrastructure[6]. Consequently, renal transplantation is not well developed in most African countries. By 2008, only 10 countries had the capability to perform RT, and only 5 (South Africa, Egypt, Tunisia, Sudan, and Algeria) had sustainable programs to perform more than 50 RT per year [27]. Additionally, in sub-Saharan Africa,

only Kenya, Nigeria and South Africa conducted more renal transplantations than any other country in the region[28]. In Kenya, KNH is the only public facility performing renal transplantation. The hospital has performed about 200 renal transplants since the inception of the program [29].

**2.3 Health-Related Quality of Life in Renal Transplant Recipients.**

Health related quality of life is an important measure of health outcomes that looks at the impact of an illness and its management from a patient's perspective [8]. HRQoL, therefore, denotes the perception of the patient concerning their symptoms, health, and treatment. When assessed using reliable measures, HRQoL is a good indicator for monitoring clinical RT practices and helps in informing healthcare policies and decision-making[23].

The advantages of RT on HRQoL are well established in the literature. Compared to patients on dialysis (peritoneal dialysis or hemodialysis), RT patients showed improved functioning in mental, physical, and social domains. A study by Jofre *et al.* evaluating HRQoL before and after RT found an overall improvement in quality-of-life indices[30]. However, the positive effects of RT were diminished by older age and prior comorbidity. In a cross-sectional study assessing HRQoL among 76 patients who had undergone RT compared to 65 ESRD patients waiting for RT, Overbeck *et al.* found significant improvement in HRQoL domains, including physical functioning and psychological, compared to those who were yet to undergo RT [31] . Fujisawa *et al.*, in a study comparing the effects of RT and hemodialysis on patients, found that the score for RT patients was significantly higher in bodily pain, physical functioning, social functioning, and general health scales compared to hemodialysis patients [32].

Improved post-RT HRQoL has been demonstrated to be significant in graft survival in RT patients. For instance, Prihadova *et al*, in a study involving 151 renal transplant patients, found that patients indicating improved HRQoL at 3 months after RT had significantly higher survival rates in the long-term (10 years follow-up period)[33] . In a study assessing HRQoL in 879 RT patients, Molnar-Varga *et al*. showed that participants reporting improved general health and physical functioning perceptions were linked to lower mortality risks [34]. Participants in Fisher and colleagues' qualitative study described improved functioning in their social, physical (including pain, fatigue, insomnia, and sexual dysfunction) and, psychological parameters six months after their surgery [35].

Another study assessing HRQoL in 220 RT patients, using KTQ, obtained maximum scores in appearance and minimum score in fear dimensions [36]. Similarly, Yujian *et al* reported the highest score in the appearance (5.77), while the lowest score was in the uncertainty/fear (4.18) dimensions [37].

Compared to the patients in the hemodialysis and peritoneal dialysis group, patients in the RT group in Czyżewski and colleagues' s study revealed significant improvement in bodily pain and appetite [38]. Similar findings were reported in a cross-sectional study by Jansz *et al* [39].

Similarly, compared to patients receiving dialysis, those who have undergone successful RT demonstrate less emotional distress, such as improved depressive symptoms and anxiety as well as cognition [23]. However, Szeifert *et al.* showed evidence that mood disorders may improve but cannot be completely eliminated after RT[40]. Improved psychological well-being in RT patients is closely linked to the improvement in their uremic state, consequently enhancing their sleep and energy. Furthermore, patients who have undergone RT are liberated from the stressful conditions of daily dialysis [23]. However, according to Shetty *et al*, RT patients often do not maintain a long-term psychological state in HRQoL domains, unlike physical elements [23]. This variation is attributed to factors such as the effects of immunosuppressive drugs as well as the high prevalence of infections and comorbidity, including hypertension and diabetes. In addition, RT patients, compared to those on dialysis, show better engagement in social activities and are more independent [32]. This is linked to a better physical state, which allows them to integrate well into society, most of RT patients are able to resume work and prove very engaged in their careers.

### 2.4 Tools used to measure HRQL after kidney transplantation

Various tools have been developed for the measurement of HRQoL after RT. For example, tools used in HRQoL measurement can be divided into generic and disease specific [23]. Generic measures are useful in quantifying overall functional and health status and may be utilized to assess populations with diverse diseases and health states. Though they are good at comparing outcomes across diseases ad interventions, they are limited to capturing details that may be specific to HRQoL that are essential to an individual patient [12]. Generic assessment tools include Short Form-36 (SF-36). SF-36 has extensively been used and

tested in various conditions and settings [12]. SF-36 is one of the most used HRQoL assessment instruments with more than 2000 publications. It is a self-administered questionnaire comprising 36 items that may take 5-10 minutes to complete[12].

Disease measurement instruments are narrower compared to generic, hence providing a more focused assessment. They include End-Stage Renal Disease Symptoms Checklist—Transplantation Module (ESRD-SCL) [41], Kidney Disease-Quality of Life (KDQOL) [42], and the Kidney Transplant Questionnaire (KTQ) [43]. KTQ developed by Laupacis is a widely used HRQoL assessment instrument with 25 items categorized into five dimensions: fatigue (5 items), physical symptoms (6 items), emotional (6 items), appearance (4 items), and uncertainty/fear (4 items). The scores in all dimensions are rated [44]on a 7-point Likert scale (from 1 worst state to 7 best state of health). Scores in individual dimensions are added and divided by the number of items for analysis, the highest quality of life is represented by the highest score. The Psychometric Properties of KTQ has been found to be effective in assessing HRQoL in RT patients, hence recommended for clinical practice [44].

The effectiveness of these measurement instruments in assessing HRQoL in renal transplant recipients has been widely studied. Krantz *et al*, carried out an observational empirical comparative study of commonly used HRQoL assessment instruments, including the Psychological General Well-Being Index (PGWB), Nottingham Health Profile (NHP), and SF-36 [45]. The authors analyzed scores for their internal consistency, psychometric properties, discriminative ability, and construct validity. The authors found similarities in effectiveness among the assessment instruments used. All the instruments were able to determine the existence of self-rated ill-health. There was a strong correlation between the quick and simple self-rated health and the assessment tools. Krantz *et al*. research supports the strong correlation between the HRQoL and self-rated health scale (including physical, psychological, and social well-being) [45]. Fujisawa *et al.* found SF-36 survey scores to be a comprehensive assessment tool for evaluating the HRQoL of patients [32]. The authors found SF-36 to be effective in proving the hypothesis of improved HRQoL among RT patients. They found improved general health perception ($p < 0.01$), physical functioning ($p < 0.01$), social functioning ($p < 0.01$), and physical summary value ($p < 0.01$). In

essence, there are various HRQoL measurement tools available for researchers who are interested in analyzing the concepts. However, their effectiveness differed.

### 2.5 Importance of HRQoL evaluation

There are many problems associated with RT, including physical and psychological well-being. Kidney transplant recipients are often affected by the totality of the process as well as external support factors, including family and peers. It is essential to understand these factors affecting the body and mind in order to develop proper interventions that maximize HRQoL in RT patients.

In their study of physical performance and HRQoL in RT patients, Esposito *et al*. concluded that RT systematic functional evaluation is important in determining the needs of the patients and those who require intensive and personalized rehabilitation [46]. Accordingly, evaluation of HRQoL among RT patients is important in informing decision-making and evidence-based intervention. Similarly, assessing HRQoL is important in determining the level of effectiveness of RT therapeutic intervention compared to other available interventions[23]. Similarly, according to Jansz *et al*., analyzing HRQoL in RT patients and comparing data with other modalities of renal replacement is essential when advising and counseling patients on the best therapy and intervention [39].

### 2.6 Immunosuppressant related factors influencing HRQoL in Kidney transplant recipients.

#### 2.6.1 Immunosuppressant regimen

The type of immunosuppressant regimen may affect HRQoL. Appearance and physical functioning are elements of HRQoL that may be influenced by the type of immunosuppressant regimen [12]. Several studies have assessed the effect of different immunosuppressant regimens on HRQoL after renal transplantation. A randomized open-label trial by Oberbauer and colleagues assessed the side effects of ciclosporin versus sirolimus based regimen. During the trial, cyclosporine was eliminated from the combination regimen with sirolimus[47]. The study found that sirolimus based regimen had minimal appearance related problems such as hirsutism and gingival hyperplasia, compared to the cyclosporine regimen. In another randomized controlled trial conducted by Reimer *et al*, 63 patients on cyclosporine and another 63 on tacrolimus were each

compared for effect of immunosuppressant regimen on HRQoL. Patients on tacrolimus regimen demonstrated statistically better scores on physical functioning and general health compared to patients on cyclosporine [48]. Another multicenter study investigated HRQoL among adult patients on tacrolimus based regimen. The study reported low scores of HRQoL compared to the general population. In the same study, RTRs on regimens that contained tacrolimus and steroids exhibited low scores in the mental domain. Additionally, comparison of steroid containing regimen to steroid free regimen among patients on tacrolimus based regimen reported poor quality of life [49].

### 2.6.2 Immunosuppressant drugs in kidney transplantation.

After kidney transplantation, the host immune system may trigger an immune reaction, and destruction of the grafted kidney may occur. To prevent graft rejection and loss, it is compulsory that RTRs take immunosuppressant drugs to suppress the host immunity. An ideal immunosuppressant should have minimal toxicity and at the same time be able to promote patient and graft survival[50]. Immunosuppression with antirejection drugs constitutes an induction phase, followed by a maintenance phase that involves the use of three immunosuppressant drugs [51]. The induction phase involves administration of antirejection drugs at the time of transplantation. The most common drugs used are interleukin-2 receptor antibodies (IL2-RA) such as basiliximab or antithymocyte globulin (ATG). IL-2-RA is considered first line in induction therapy[52]. Maintenance phase immunosuppressants are classified into: calcineurin inhibitors which include tacrolimus and cyclosporine as well as corticosteroids for example prednisolone and methylprednisone[51]. Others agents include antimetabolites like mycophenolate mophetil and azathioprine and mTor inhibitors such as sirolimus and everolimus[53]. Usually, a combination of three immunosuppressants consisting of calcineurin inhibitors (CNI), an antimetabolite or m-TOR inhibitor and a corticosteroid is recommended [53]. Combination of drugs optimizes immunosuppression, allowing small doses of each drug to be used to while minimizing the dose-related side effects [54,55]. The choice of what combination to use depends on patient characteristics, training, and expertise of healthcare workers in a particular transplantation clinic.

### 2.6.3 Immunosuppressants drugs side effects.

Successful renal transplantation requires effective and long-term maintenance immunosuppression to prevent graft rejection [52]. Despite immunosuppressants' role in preventing graft rejection and loss, immunosuppressive drugs have side effects that may negatively impact patient's HRQoL[21]. These side effects need to be identified, controlled and treated [56] to improve patient health and wellbeing.

**Corticosteroids.**

Corticosteroids are an essential part of immunosuppressant therapy in renal transplantation immunosuppression [57]. Corticosteroids are predominantly used because they are affordable, are easy to administer and are effective in reducing acute rejection [58]. Prolonged steroid use, however, is associated with side effects as hypertension, cataracts, diabetes mellitus, osteoporosis, peptic ulcer disease, weight gain, acne, hyperlipidemia, and increased susceptibility to infections [59]. Due to these side effects, RTR prefers removal of steroids from their immunosuppressive drugs regimen and replacing it with other immunosuppressants [58]. A meta-analysis demonstrated that hypertension, hypercholesterolemia, and new onset diabetes mellitus risk were significantly reduced in steroid avoidance or withdrawal or minimization [60].

**Calcineurin inhibitors (Tacrolimus and Cyclosporine)**

Calcineurin inhibitors remain a critical component of immunosuppressive therapy in renal transplantation. Calcineurin inhibitors have a narrow therapeutic index and as such therapeutic drug monitoring is recommended to ensure effective plasma concentration while limiting adverse effects [61]. The most frequent side-effects of CNIs are nephrotoxicity, new onset diabetes, dyslipidemias, neurotoxicity, and malignancy. Others are hypertension, gingival hypertrophy and hirsutism[61]. Adverse effects of CNIs that are dose dependent are hypertension, nephrotoxicity, gingival hyperplasia, and hirsutism. Alopecia, new onset diabetes, and neurotoxicity are commonly seen in tacrolimus treatment whereas hypertension, hyperlipidemia, hirsutism and gingival hypertrophy, are predominant in cyclosporine based therapy [51,55].

**Mycophenolate mofetil**

Mycophenolate (MMF) is a very effective agent for the prevention of acute rejection, in combination with other immunosuppressant agents, such as cyclosporine and tacrolimus following renal transplantation [62]. Despite of its proven efficacy ,MMF adverse events such as leukopenia, cytomegalovirus infection, and gastrointestinal side effects namely diarrhea, gastritis, mycophenolate related gastritis are a cause of MMF dose reduction or discontinuation [63] in immunosuppression therapy.

**Mammalian target of rapamycin (mTOR) inhibitors**

Mammalian target of rapamycin (mTOR) inhibitors such as sirolimus and everolimus are considered calcineurin sparing alternatives with less nephrotoxicity, lower neoplastic and minimal hypertension potential [64]. The adverse effects associated with sirolimus include anemia, delayed wound healing, thrombocytopenia, hypercholesterolemia and hypertriglyceridemia. Hypercholesterolemia and hypertriglyceridemia [65] which occur in 50% of patients on sirolimus based regimen are a cause of cardiovascular disease and mortality in renal transplant patients. Studies indicate that sirolimus may potentiate cyclosporine nephrotoxicity and as such should not be used concurrently, and should they be used concurrently then dose reduction is recommended [66]. By contrast, everolimus and cyclosporin can be combined to achieve immunosuppression. Everolimus side effects include proteinuria, delayed wound healing, dyslipidemia and, anaemia [67].

**Induction agents**

Induction agents, which are antithymocyte globulins and basiliximab, have side effects which include thrombocytopenia, leukopenia and cytokine release syndrome, mainly seen in antithymocyte globulin , whereas hypersensitivity reactions adverse effects which occur in basiliximab use[53,51].

### 2.6.4 Comorbidities

Renal transplant recipients may have two or more other conditions such as diabetes, heart failure, hyperlipidemia and hypertension[68]. These conditions may require the patient to take drugs for their management, adding to the already high pill burden. The associated

complexity in treatment and management, as well as complications from these comorbidities, may result in unsatisfactory health related quality of life (HRQoL) [69]. Comorbidities that result from immunosuppressant medication also are the main cause of dosage adjustment or termination which may have a negative impact on graft survival and HRQoL[70]. A study in Pennsylvania found that comorbidity was the main cause of mortality before and after kidney transplantation at (hazard ratio 3.20; P = 0.01) and (hazard ratio 2.63 P < 0.001 respectively)[20]

### 2.6.5 Adherence

Graft survival and satisfactory HRQoL heavily depend on the patient's adherence to immunosuppressive medication. Non-adherence therefore may result in poor graft outcomes as well as decreased HRQoL [71]. Several factors such as younger age, increased time since the transplant, medicine dosage, complex schedules as well as medication cost have been cited as barriers to adherence [72]. Additionally, depression and anxiety among renal transplant patients have been associated with non-compliance to antirejection medication too, thus decreasing graft survival and impaired HRQoL[73,74]. Identification and mitigation of factors that cause non adherence in renal transplant patients are key in enhancing adherence and ultimately HRQoL[19].

In a descriptive cross-sectional study in Mashhad, Iran, a total of 244 kidney transplant patients were included in the study. A total of 111 patients representing 45.5% of participants were adherent to anti-rejection medication. The study also demonstrated that female patients were more adherent to medication than their male counterparts (OR=0.48, p<0.01). Moreover, high scores of HRQoL were observed in adherent patients (OR=1.078, p<0.05) [75].

## 2.7 Gaps in Literature

The main limitation in the existing literature is that there is limited research on HRQoL in RT patients in Africa, though such studies are highly dominant in other countries. In Kenya, there is only one research, Kamau *et al*.[76], which assessed HRQoL in patients on maintenance hemodialysis at KNH. Consequently, there is no research pertaining to HRQoL and associated factors in RTR in Kenya. This study seeks to fill that gap.

# CHAPTER THREE: METHODOLOGY

## 3.1 Perspective of Research Methodology

This chapter highlights the conceptual framework, research design, the study area and site, the study population, including the inclusion and exclusion criteria. In addition, sampling technique, sample size, research instruments, study piloting, data collection method, data management, and analysis, as well as the ethical considerations. Aspects of quality assurance, validity and reliability of the collected data together with internal and external validity will also be discussed.

## 3.2 Study Design

The study was a cross-sectional descriptive study. This type of study design involved determining exposure and outcome simultaneously. Also, no investigator intervention and follow up were required. The study design was applied because the investigator needed to determine exposure and outcome at a given time and there were time constraints.

This study design was appropriate in this research because of time constraints.

## 3.3 Study Area and Site

The study was conducted at the renal transplant clinic, within the renal unit of Kenyatta National Hospital (KNH). This specialized clinic offers renal transplantation and post-transplant care to recipients on follow-up. KNH is a tertiary and referral teaching hospital situated in Nairobi, Kenya. It is the largest hospital in East and Central Africa with a bed capacity of 2000. The hospital is located near central business district of Nairobi, the capital city of Kenya. Its catchment areas include the whole of Kenya and neighboring countries in part of East and central Africa. The health services offered by the institution include preventive, curative, surgical and clinical diagnostic health services. It is also a training and research institution for different cadres of healthcare professionals such as medical doctors, pharmacists, nurses, and dentists, among others. Kenyatta National Hospital is the only public facility with a specialized renal transplant program in the country. Kidney transplant recipients' clinic days are held on a weekly basis every Tuesday and about 15 to 20 patients are reviewed per day. A total of 200 patients have undergone transplantation since the program's inception [29].

### 3.4 Study Population

The target population was all adult renal transplant recipients in Kenya. Study population constituted adult patients who previously underwent renal transplant and are followed up at KNH.

### 3.5 Inclusion criteria

i. Patients with currently functioning graft.
ii. Adult patient 18 years or older having kidney transplant from either living or deceased donor.
iii. Patient who underwent a kidney transplant at least 3 months prior to recruitment .This is because, after 3 months of transplantation , the patient is considered stable and may not be experiencing acute phase transplant reactions[77], which may result in overly low health related quality of life reporting.
iv. Patient on follow up at renal transplant clinic KNH, even those who had their transplant in other centres.
v. Must have been on immunosuppressive anti-transplant rejection treatment.
vi. Patient willing to participate in the study by written, informed consent.

### 3.6 Exclusion criteria

i. Hospitalized patients who were too weak to participate. This is because they may not have been in a capacity to give voluntary and informed consent. Also, they may have reported bias information in favor of very low HRQoL scores
ii. Patients with cognitive impairment. This is because patient may not have been in a capacity to give voluntary informed consent due to impaired judgement.
iii. Patients with other organ failure because they would have acted as a possible confounder.

### 3.7 Sample Size Estimation

The following formula was used to calculate the sample size.

$$n = \frac{t^2\ SD^2}{d^2}$$

Where

n- sample size

t-1.96(95% confidence interval)

SD-standard deviation of the overall mean score of HRQoL of a study in Ethiopia 0.79[78].

d-desired level of precision of the variance = 0.1

Substitution of the estimates into the equation gave a sample size of 239.

Since the sample size was drawn from a small population, a finite population correction was applied, as shown below.

$$n = \frac{no}{1 + \frac{no}{N}}$$

Where:

N- number of patients on follow up at KNH (130)

*no* – calculated sample size (239)

n- adjusted sample size (84)

N was obtained from the hospital records where,130 renal transplant patients were on follow up at the renal unit, Kenyatta National Hospital.

Therefore, a total of 92 renal transplant patients were screened for eligibility, but, 80 were eligible hence included in the study. Six were excluded because of repeat hospital visits,3 were hospitalized and were too weak to participate in the study while the other 3 patients declined consent.

### 3.8 Sampling Method

Consecutive sampling was used in selection of study participants. Files of patients on follow up were scrutinized for eligibility criteria by the principal investigator. Files of patients who met eligibility criteria were tagged and the file number was recorded on a list. This was to help with tracking and retrieval of the files of eligible patients for the study. Different tags were used to mark files of patients to be seen on different months. This was to prevent repeated sampling. This procedure was repeated until the required sample size

was achieved. Patients identified during the sampling process were recruited on their scheduled clinic days.

### 3.9 Participants Recruitment and Consenting Process

Eligible patients presenting for follow up at the renal transplant outpatient clinic were recruited by the principal investigator before seeing their physician. The principal investigator introduced herself and stated the purpose of the study. Those willing to participate in the study were screened for eligibility criteria using the eligibility form (Appendix 1). The patients eligible were taken through informed consent process. Adequate oral and written information about the purpose, nature and possible risks and benefit of the study were provided. Additionally, they were notified about the right to withdraw from the study without dire consequences. Furthermore, they were given an opportunity to ask questions and time to understand the information provided. A patient was considered recruited upon signing the English or Kiswahili version of the consent form provided and the questionnaire will be administered. The Recruitment and consenting process were done every Tuesday until the required sample size was achieved.

### 3.10 Research Instruments and Data Collection

Kidney transplant questionnaire-25 (KTQ-25), socio-demographic form and a data collection form designed based on the research objectives, were used to obtain information on HRQoL, immunosuppressant protocol, adherence and side effects of immunosuppressants in the renal transplant recipient. Information on comorbidity, serum creatinine levels and socio-demographics was also collected.

The KTQ-25 is a disease specific HRQoL assessment tool specific for kidney transplant patients[79]. The questionnaire was designed by Pus *et al*[80]. It is a validated tool for the assessment of HRQoL in transplant patients and it is self-administered. It contains 25 questions with each question scored from 1 to 7. The 25 questions are further summarized and classified into five domains namely: physical symptoms which are based on six items, fatigue based on five items, fear/uncertainty based on six items, appearance based on four items and emotion based on six items.

For scoring of the tool, the score of an item in each domain are added up and are divided by the number of item in each domain to get a mean final score. The scores are normally reported in ranges of 1 to 7 for each of the five domains, with 7 representing satisfactory well-being while 1 indicates low quality of life.

To collect information on clinical variables, the data collection tool designed by the researcher was used. Variables to be collected included duration of ESRD disease, comorbidity type and duration of dialysis as well as type of donor. Additionally, medication information such as the side effects, adherence and immunosuppressant medication regimen was collected.

Socio-demographic data which included gender, age marital status, employment status and educational level were collected using the socio-demographic tool.

### 3.11 Medical Record and Medication Chart Review

The principal investigator extracted information from medical records in accordance with the data collection instrument. The medical record review exercise helped in obtaining information not readily available when administering the questionnaire directly to the patient. Information obtained from medical records included comorbidities and immunosuppressant medication regimens. Additionally, laboratory test namely creatinine levels, a renal function test, was reviewed.

### 3.12 Piloting of the Study

Ten questionnaires and data collections forms representing 10% of the sample size was pretested to ensure their validity and reliability.

### 3.13 Quality Assurance, Validity and Reliability of the Collected Data

To ensure quality assurance of collected data, the principal investigator complied to laid down standard operating procedures on quality assurance. The principal investigator recruited only participants who met eligibility criteria into the study. Additionally, data collection forms were completely and accurately filled. Routine data cross checks and cleaning through a systematic review of collected data was also done to guarantee quality of collected data.

To ensure validity and reliability of collected data, the data collection tools were pretested to ensure that information collected was reproducible.

### 3.14 Internal and External Validity

To ensure internal validity, clear methodological structures were put in place, to yield credible findings. The correct sampling method was used in the selection of participants. A well designed data collection tool was used in data collection and a correct statistical test was applied during analysis.

To guarantee external validity, the target population was exhaustively described in terms of place, person and time. Careful consideration was given to inclusion criteria as very restricted inclusion criteria would minimize generalizability.

### 3.15 Study Variables

The predictor variables were: Immunosuppressant regimen, immunosuppressant side effects, and adherence while the intervening variables were age, gender, marital status, employment and education level. Continuous variables in this study included age, duration of treatment and HRQoL summary score. On the other hand, categorical variables were comorbidity, education level and immunosuppressant side effects.

The outcome variable was health related quality of life (HRQoL) score.

### 3.16 Data Management

Patient files were perused and the required information was extracted into the questionnaire. The files were then returned to the records officer for safe keeping. The questionnaires were checked for errors after which data was entered into a database template resembling the hardcopy questionnaire. Each participant's questionnaire had a unique serial number. Data entry was done on a daily basis as well as checked frequently for accuracy and completeness. Moreover, any discrepancy identified was corrected immediately. This process continued until all the questionnaires were put into the database after which data was cleaned and exported to Stata version 13 for analysis. The principal investigator ensured that the electronic database was backed up daily in an external drive and confidentiality maintained through computer password and locking the cabinets.

### 3.16.1 Data Processing

Data was analyzed using STATA Version 13.0. The results were presented in form of tables, charts and graphs. Normally distributed continuous variables were summarized as means and standard deviations of the means. Abnormally distributed variables were summarized as median and interquartile range. Categorical variables were summarized as percentages and frequencies.

### 3.16.2 Statistical Methods

To determine the impact of selected demographic and immunosuppressant regimen as well as the impact immunosuppressant side effects and adherence on HRQoL, univariate and multivariate analyses were performed. An association between immunosuppressant regimen, immunosuppressant side effects and adherence to HRQoL score was determined by performing bivariate analysis. Linear regression was conducted to determine predictors of quality of life in kidney transplant recipients. The level of significance was set at $P < 0.05$.

## 3.17 Ethical Considerations

The proposal was submitted to KNH/UoN Ethics and Research Committee(ERC)for review and approval vide reference number P70/02/2021 (Appendix 4) was granted before commencement of the study. Written and oral informed consent was sought from eligible patients and only consenting participants were included in the study. To ensure confidentiality, patient information was safeguarded using unique identifier codes. All questionnaires and forms used in data collection were under lock and key in a cabinet. Moreover, the electronic database was password protected. Also, patients were treated with respect and were free to withdraw from the study without victimization. Furthermore, the study findings were disseminated to renal unit, Kenyatta National Hospital.

### 3.17.1 Informed Consent

Informed consent was sought from eligible participants. Patients were required to sign an informed consent for participation. Adequate oral and written information about the purpose, nature and possible risks and benefits of the study was provided. Additionally, they were notified about the right to withdraw from the study without victimization.

Furthermore, they were given an opportunity to ask questions and time to understand the information provided. The patient's rights in research was observed all through, participation was voluntary and they were free to withdraw from the study at any point.

### 3.17.2 Confidentiality

Before consenting, eligible patients were assured of confidentiality and anonymity. Several strategies were put in place to ensure confidentiality. Firstly, all data collection forms did not have patient hospital number or name. Instead, a unique identifiers code was used. Secondly, patients were interviewed confidentially to ensure that all the information shared was done in privacy. Thirdly, all data collection materials were stored in a cabinet under lock and key with access limited to only the principal investigator. Finally, all electronic database was password protected and only accessible to the principal investigator.

### 3.17.3 Benefits from the Study

Participants in this study obtained immediate benefits from the research. For instance, if non-adherence was identified, patients were advised on the importance of compliance to medication.

### 3.17.4 Risks from the Study

The participants were not being subjected to any invasive procedures thus this was a minimal risk study.

# CHAPTER FOUR: RESULTS

## 4.1 Introduction

This chapter presents the results obtained from analysis of data collected from a sample of 80 renal transplant recipients at the renal clinic, Kenyatta National Hospital, in the period of July 2021 to September 2021. The results are presented in form of frequency tables and bar graphs. Additionally, associations between variables are presented.

## 4.2 Characteristics of study participants.

A total of 80 study participants were recruited into the study. Table 1 summarizes their sociodemographic characteristics.

**Table 1: Participant sociodemographic characteristics.**

| Variable | Characteristic | Frequency (n) | Percentage(%) |
|---|---|---|---|
| **Sex** | | | |
| | Male | **56** | **70.0** |
| | Female | 24 | 30.0 |
| **Marital status*)*** | | | |
| | Married | 64 | 80.0 |
| | Single | 16 | 20.0 |
| **Highest education** | | | |
| | Primary | 6 | 7.5 |
| | Secondary | **40** | **50.0** |
| | Tertiary | 34 | 42.5 |
| **Employment** | | | |
| | Employed | 36 | **45.0** |
| | Self-employed | 22 | 27.5 |
| | Unemployed | 10 | 12.5 |
| | Retired | 12 | 15.0 |
| **Denomination** | | | |
| | Christian | 76 | 95.0 |
| | Muslim | 4 | 5.0 |
| **Comorbidity** | | | |
| | Diabetes | 4 | 5.0 |
| | Diabetes and Hypertension | 20 | 25.0 |
| | Hypertension | **48** | **60.0** |
| | Hypertension and Thrombosis | 1 | 1.3 |
| **History of smoking** | | | |
| Smoker | | 9 | 11.3 |
| Non-smoker | | **71** | **88.8** |
| **History of alcohol use** | | | |
| | Consumers | 15 | 18.8 |
| | Non-consumers | **65** | **81.3** |
| **Kidney source** | | | |
| | Living donor – relative | 80 | 100.0 |
| **Dialysis type** | | | |
| | Haemodialysis | 80 | 100.0 |
| **Dialysis duration in months *(median, IQR)*** | | 12.0 | 12.0 – 26.5 |
| **Creatinine in umol/L*(median, IQR)*** | | **105.0** | **98.0 – 120.0** |
| **Duration after transplant in months*(median, IQR)*** | | **51.5** | **30.0 – 84.0** |
| **Age (mean, SD)** | | 45.4 | 14.7 |
| **(median, IQR)** | | 47.5 | 33.0-58.0 |

The population under study was largely constituted of males (n=56, 70%). The mean (SD) age of participants was 45.4 (14.7) years, where the youngest participant was 18.0 years, while the oldest was 72.0 years. Most of the patients were married (n=64,80%). Majority of patients (40, 50.0%) had secondary education level while (n= 36 ,45.9%) were employed. Close to half the study participants (n=48,60%) had hypertension while a quarter (20,25%) had both diabetes and hypertension. The vast majority of patients (n=71,88%) were nonsmokers but (n=15,18%). had a history of alcohol The median creatinine level of study participants was 105 (IQR 98,120) umol/L. All the study participants received their kidney from living donor relative and the median duration post kidney transplantation was 51.5 (IQR 30,84) months (Table 1).

### 4.3 Causes of end stage renal disease among the study patients

Table 2 displays the possible causes of ESRD. Hypertension was the leading cause of ESRD in most of the participants attributing to (45,56.3 %) followed by both diabetes and hypertension at (13,16. 3%) and focal segmental glomerulosclerosis contributing (8,10.1%). Reflux nephropathy, and polycystic kidney disease were represented in equal proportions at 2.6%. Furthermore, (4, 10.1%) of patients in our sample attributed ESRD to unknown causes, while (1,1.3%) to autoimmune disease (Table 2).

**Table 2: Causes of end stage renal disease among study participants**

| | Frequency | Percent(%) |
|---|---|---|
| Hypertension | 45 | 56.3 |
| Diabetes and Hypertension | 13 | 16.3 |
| Focal segmental glomerulosclerosis | 8 | 10.1 |
| Diabetes | 3 | 3.8 |
| Reflux nephropathy | 2 | 2.6 |
| Nephrotoxic drugs | 2 | 2.6 |
| Polycystic kidney disease (congenital) | 2 | 2.6 |
| Autoimmune disease | 1 | 1.3 |
| Unknown | 4 | 5.0 |

### 4.4 Immunosuppressant medications among the study participants

Immunosuppressant regimen used by the study participants is summarized in Table 3 below. Most patients were on three types of immunosuppressant drugs.

**Table 3: Proportion of patients on different immunosuppressant regimen**

| Regimen | Frequency | Percentage |
|---|---|---|
| Prednisolone, Tacrolimus, Mycophenolate | **60** | 75.0% |
| Prednisolone, Mycophenolate, Cyclosporin | 9 | 11.25% |
| Prednisolone, Tacrolimus, Azathioprine | 6 | 7.50% |
| Prednisolone, Tacrolimus | 2 | 2.50% |
| Prednisolone, Azathioprine | 1 | 1.25% |
| Prednisolone, Cyclosporin, Azathioprine | 4 | 5% |
| Prednisolone, Mycophenolate | 1 | 1.25% |
| Prednisolone, Mycophenolate, Everolimus | 1 | 1.25% |

The most common immunosuppressant regimen among the study participants was prednisolone, tacrolimus and mycophenolate (n=60, 75%).The least used immunosuppressant medication combination was prednisolone, mycophenolate and everolimus (n=1,1.25%).

### 4.5 Prevalence of immunosuppressant side effects

The bar graph below gives information about immunosuppressant medication side effects among kidney transplant recipients (Figure 2).

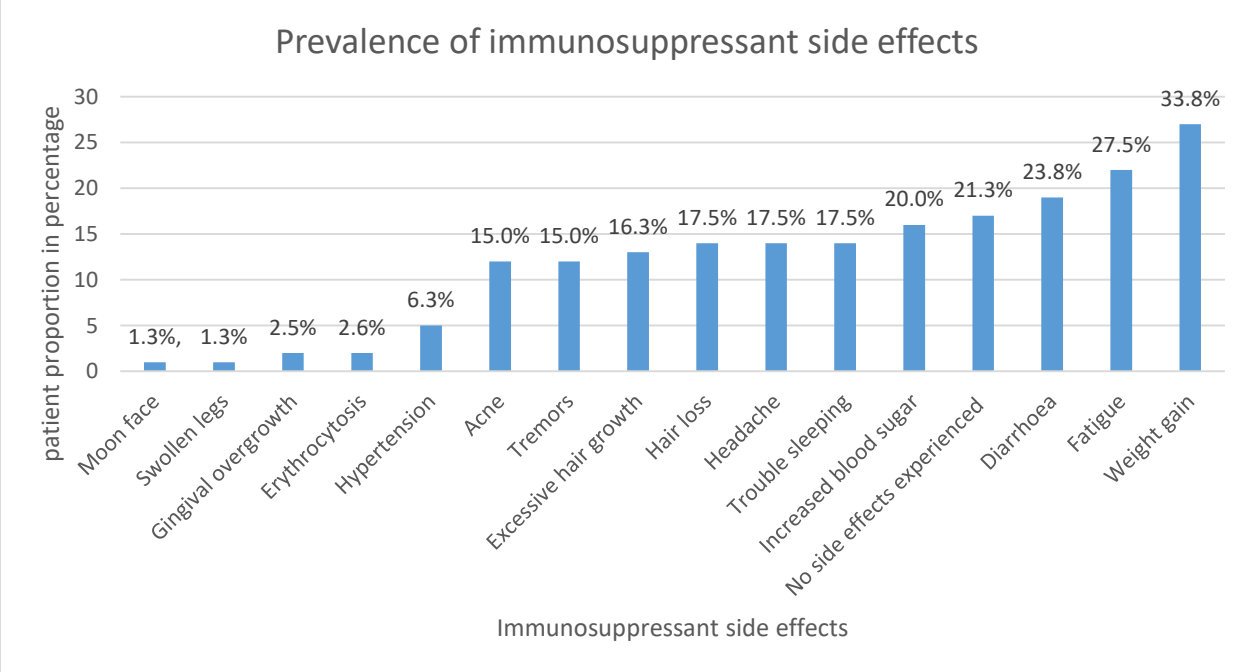


**Figure 2: Prevalence of immunosuppressant side effects among study participants.**

Majority of participants (33.8%), reported weight gain as the commonest side effect experienced, followed by fatigue (27.5%) and diarrhea (23.8%). The least common side

effect was moon face (1.3%) and swollen legs (1.3%). Almost a fifth (21.3%) of the participants indicated that they did not experience any side effects due to antirejection medication use (Figure 2).

### 4.6 Adherence to immunosuppressant medication.

Details of study participants' adherence to immunosuppressant medication are given in Table 4 below.

**Table 4: Adherence to immunosuppressant medication among study participants**

| Variable characteristic | Frequency | Percent |
|---|---|---|
| **Missed taking a dose of immunosuppressant medication** | | |
| Once | 9 | 11.3 |
| 2-3 times | 6 | 7.5 |
| None | 65 | 81.3 |
| **Missed taking 2 or more doses of immunosuppressant medication** | | |
| 2 times | 2 | 2.5 |
| >4 times | 3 | 3.8 |
| None | 75 | 93.8 |
| **Taking drug 2 hrs before or after the scheduled time** | | |
| Yes | 7 | 8.8 |
| No | 73 | 91.3 |
| **Reduced or increased dose of immunosuppressant medication** | | |
| Yes | 2 | 2.5 |
| No | 78 | 97.5 |
| **Stopped taking medication** | | |
| Yes | 2 | 2.5 |
| No | 78 | 97.5 |
| **Overall adherence** | | |
| Non-adherence | 17 | 21.3 |
| Adherence | **63** | **78.8** |
| **Reasons for non-adherence** | | |
| Financial constraints | 10 | 12.5 |
| Forgetfulness | 6 | 7.5 |
| Admission due to Covid-19 | 1 | 1.3 |

Overall, (63,78.8%) of recipients reported total adherence to immunosuppressant medication while (17,21.3%) did not adhere to one or more of the 5 dimensions evaluated within the last four weeks. Among the non-adherent patient, the majority (10,12.5%) reported financial constraints as a reason for not adhering to medication, (6,7.5%)

mentioned forgetfulness as a cause while one patient reported missing a dose following admission due to Covid-19.

### 4.7 Health related quality of life scores as assessed by the kidney transplant questionnaire.

#### 4.7.1 Physical symptoms experienced by participants based on kidney transplant questionnaire

Table 5 below depicts patient specific physical symptoms identified as most bothersome during the previous four weeks of the study.

**Table 5: Distribution of physical symptoms experienced among study participants.**

| | Frequency | Percent of patients |
|---|---|---|
| Forgetfulness | 28 | 35.0% |
| Aching, tired legs | 26 | 32.5% |
| Urinary tract infection | 23 | 28.7% |
| Decreased sexual ability | 20 | 25.0% |
| Headaches | 17 | 21.3% |
| Side-effects from medications | 16 | 20.0% |
| Trouble getting to sleep | 16 | 20.0% |
| Light-headedness or dizziness during daily activities | 16 | 20.0% |
| Aching bones | 15 | 18.8% |
| Constipation or diarrhoea | 15 | 18.8% |
| Very little strength | 14 | 17.5% |
| Increased appetite | 14 | 17.5% |
| Loss of weight and muscle | 13 | 16.3% |
| Itchy/dry skin | 12 | 15.0% |
| Coughing during day or night | 12 | 15.0% |
| Loss of appetite | 12 | 15.0% |
| Trouble getting a good night's sleep | 11 | 13.8% |
| Waking up during the night | 10 | 12.5% |
| Excessive weight gain | 10 | 12.5% |
| Nausea or upset stomach | 9 | 11.3% |
| Need to rest frequently because of shortness of breath | 7 | 8.8% |
| Difficulty in concentrating | 6 | 7.5% |
| Acne | 6 | 7.5% |
| Muscle pain | 6 | 7.5% |
| Vomiting | 4 | 5.0% |
| Shortness of breath in daily activities | 4 | 5.0% |
| Confusion | 3 | 3.8% |
| Decreased mental ability | 2 | 2.5% |
| Embarrassment caused by appearance or access site | 2 | 2.5% |
| Regulating bowel movements | 2 | 2.5% |
| Difficulty focusing attention | 2 | 2.5% |
| Shivering | 1 | 1.3% |
| Palpitations | 1 | 1.3% |
| No patient specific physical symptom | 5 | 6.3% |

Generally, the most common and reported bothersome symptom experienced was forgetfulness (n=28,35%) followed by aching, tired legs (n=26,32.5%), urinary tract infections (n=23,28.7%), decreased sexual ability (n=20,25.0%) and headaches (n=17,21. 3%).The least common physical symptom was shivering (n=1,6.3%) and palpitation (n=1,6. 3%).Five study participants (6.3%) did not experience bothersome physical symptom during the study (Table 5).

### 4.7.2 Appearance domain scores

Figure 3 below gives information about appearance domain score. Majority of the patients had a score of 7 at 73.8%, demonstrating that most patients had no worries about their appearance.

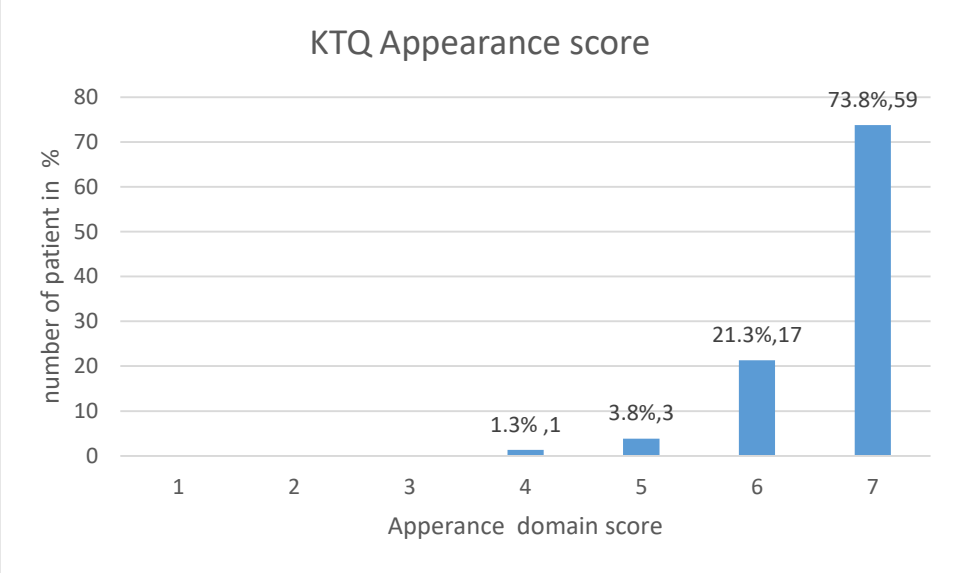


**Figure 3: KTQ Appearance score**

### 4.7.3 Fatigue domain scores

Figure 4 below presents information about fatigue domain. Majority of the study participants experienced moderate fatigue (30%) at a score of 5, while only 1.3% of the study participants scored 1 denoting severe fatigue.

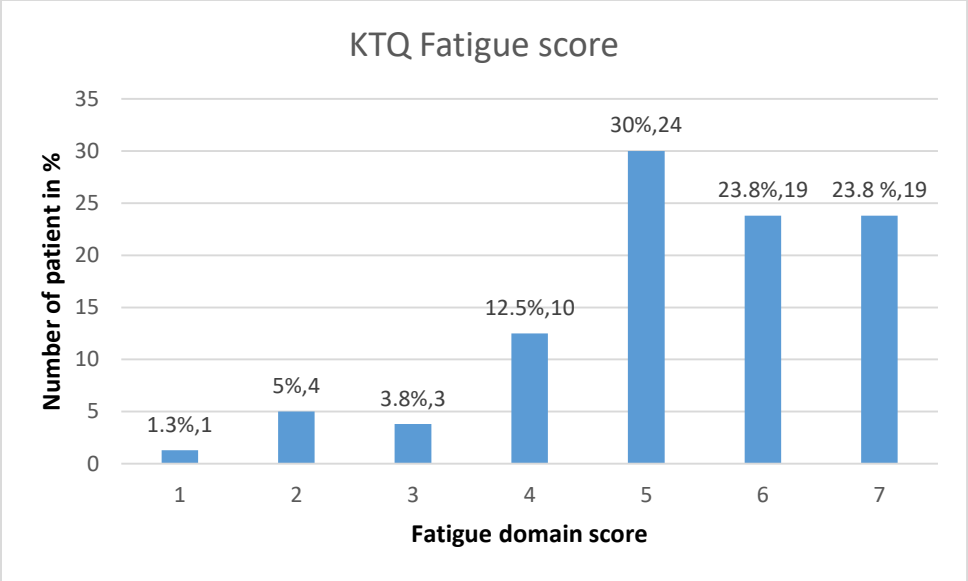


**Figure 4: Fatigue domain score among study participants**

### 4.7.4 Uncertainty/Fear domain scores

Figure 5 below provides information on uncertainty/fear domain. Majority of the study participants experienced symptoms related to uncertainty /fear (33.5%) at a score of 5. Also, a fairly large number had a score of 3 and 4 at 16.3% and 27.5 % respectively indicating presence of fear /uncertainty. Only, 17.6% of study participants hand a score ranging from 6 to 7 denoting no uncertainty and fear.

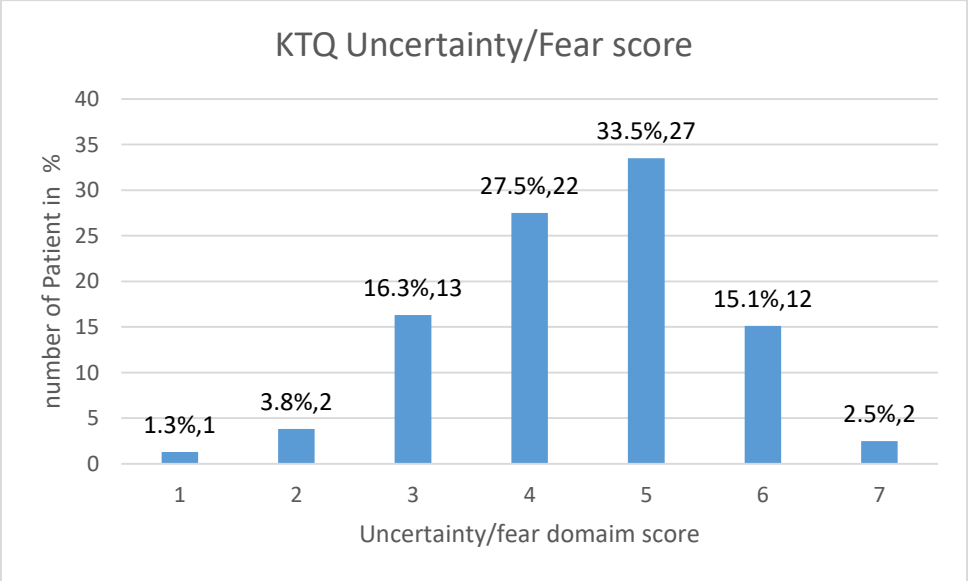


**Figure 5: Uncertainty/Fear score among study participants**

### 4.7.6 Emotions domain scores

Approximately, half 51.3% of the study participants had no trouble with emotional symptoms at a score of 6 and 7. However,48.7% of patients had severe to moderate trouble in emotions domain with scores ranging from 3 to 5 (Figure 6).

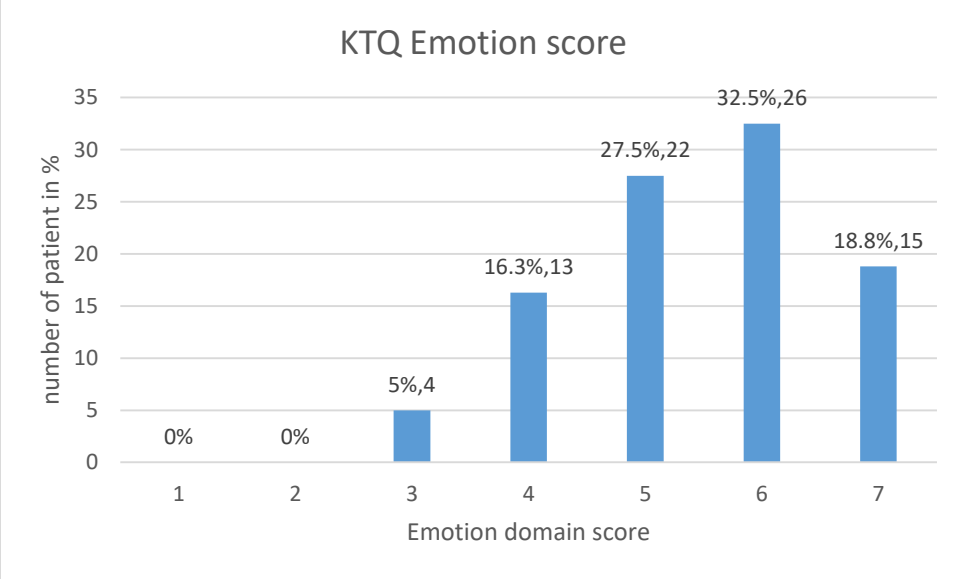


**Figure 6: Emotions domain score among study participants**

### 4.7.7 Health related quality of life summary score based on KTQ-25.

The table below illustrates the distribution of health related quality of life summary scores as assessed by the kidney transplant questionnaire (Table 6). The overall mean health related quality of life score was 5.19(0.78). The highest score was obtained in appearance domain 6.62(0.60), followed by emotions 5.37(1.12), and fatigue 5.33(1.38). Physical symptoms and fear/uncertainty dimensions had the least score of 4.64(1.34) and 4.28(1.12), respectively.

**Table 6: Health related quality of life summary score among study participants**

| Scale | Mean score (SD) |
|---|---|
| Appearance | **6.62(0.60)** |
| Emotions | 5.37(1.12) |
| Fatigue | 5.33(1.38) |
| Physical symptoms | 4.64 (1.34) |
| Fear/Uncertainty | **4.28 (1.12)** |
| KTQ-25 Total | **5.19 (0.78)** |

**Bivariate analysis**

### 4.8 Association between demographic characteristics and health related quality of life subscale score.

As shown in Table 7, none of the sociodemographic variables had a significant effect on health related quality of life subscale domains.

**Table 7: Association between demographic characteristics and mean HRQoL subscale score**

| | | Mean scores | | | | |
|---|---|---|---|---|---|---|
| | **N** | **Physical symptoms** | **Fatigue** | **Fear/ Uncertainty** | **Appearance** | **Emotions** |
| **Age** | | | | | | |
| ≤25 | 6 | 4.11 (1.52) | 5.37 (1.04) | 4.29 (1.64) | 6.50 (0.79) | 5.67 (0.80) |
| 26-40 | 29 | 4.80 (1.26) | 5.31 (1.49) | 4.02 (1.30) | 6.71 (0.43) | 5.19 (1.29) |
| 41-65 | 39 | 4.59 (1.38) | 5.39 (1.35) | 4.46 (0.83) | 6.58 (0.68) | 5.49 (1.07) |
| >65 | 6 | 4.67(1.80) | 4.97(1.55) | 4.42(1.22) | 6.63(0.63) | 5.19(0.92) |
| P-value | | p= 0.716 | p=0.922 | p=0.439 | p=0.805 | p=0.630 |
| **Gender** | | | | | | |
| Male | 56 | 4.67 (1.27) | 5.26 (1.23) | 4.25 (1.15) | 6.70 (0.44) | 5.26 (1.14) |
| Female | 24 | 4.55(1.60) | 5.48(1.69) | 4.38(1.05) | 6.43(0.84) | 5.63(1.08) |
| P-value | | p=0.712 | p=0.512 | p=0.636 | p=0.051 | p=0.191 |
| **Education** | | | | | | |
| Primary | 6 | 3.97 (1.19) | 4.60 (1.99) | 4.29 (1.05) | 6.25 (0.95) | 4.94 (0.59) |
| Secondary | 40 | 4.74 (1.32) | 5.37 (1.34) | 4.43 (1.04) | 6.73 (0.46) | 5.57 (1.00) |
| Tertiary | 34 | 4.63(1.45) | 5.41(1.31) | 4.11(1.20) | 6.63(0.65) | 5.22(1.29) |
| P-value | | p=0.445 | p=0.406 | p=0.471 | p=0.151 | p=0.252 |
| **Marital status** | | | | | | |
| Married | 64 | 4.55 (1.40) | 5.29 (1.46) | 4.31 (1.10) | 6.61 (0.60) | 5.39 (1.18) |
| Single | 16 | 4.96(1.22) | 5.47(1.03) | 4.17(1.20) | 6.66(0.60) | 5.31(0.91) |
| P= value | | p=0.293 | p=0.635 | p=0.654 | p=0.816 | p=0.812 |
| **Employment** | | | | | | |
| Employed | 36 | 4.73 (1.30) | 5.66 (1.28) | 4.41 (1.10) | 6.63 (0.57) | 5.38 (1.20) |
| Self-employed | 22 | 4.78 (1.30) | 5.34 (1.15) | 4.19 (0.97) | 6.58 (0.78) | 5.34 (1.11) |
| Unemployed | 10 | 4.07 (1.85) | 4.76 (1.98) | 3.78 (1.69) | 6.80 (0.31) | 5.33 (1.20) |
| Retired | 12 | 4.57 (1.27) | 4.80 (1.34) | 4.50 (0.78) | 6.56 (0.49) | 5.46 (0.98) |
| P-value | | p=0.544 | p=0.138 | p=0.374 | p=0.777 | p=0.992 |

### 4.9 Association between socio-demographic characteristics and health related quality of life summary score.

As shown in Table 8, none of the sociodemographic variables such as age, gender, education, marital status and employment had a statistically significant association with HRQoL summary score. However, there was statistically significant association between

comorbidity and health related quality of life (p = 0.017), with lower HRQoL score among study participants with diabetes and hypertensive comorbidity at 4.79 (0.82) (Table 8).

**Table 8: Association between socio demographic and clinical characteristics with HRQoL score**

| | HRQoL Mean (SD) Score | p-value |
|---|---|---|
| **Age** | | |
| ≤25 | 5.15 (0.99) | 0.988 |
| 26-40 | 5.18 (0.87) | |
| 41-65 | 5.22 (0.65) | |
| >65 | 5.13 (1.07) | |
| **Gender** | | |
| Male | 5.16 (0.68) | 0.586 |
| Female | 5.27 (0.99) | |
| **Education** | | |
| Primary | 4.75 (0.64) | 0.165 |
| Secondary | 5.33 (0.79) | |
| Tertiary | 5.11 (0.78) | |
| **Marital status** | | |
| Married | 5.17 (0.81) | 0.574 |
| Single | 5.29 (0.67) | |
| **Employment** | | |
| Employed | 5.28 (0.74) | 0.597 |
| Self-employed | 5.22 (0.71) | |
| Unemployed | 4.90 (1.21) | |
| Retired | 5.14 (0.62) | |
| **Comorbidity** | | |
| Diabetes | 5.50(0.80) | **0.017** |
| Hypertension | 5.24(0.69) | |
| Diabetes and Hypertension | **4.79(0.82)** | |
| Hypertension and Thrombosis | 5.28(-) | |

### 4.10 Association between immunosuppressant regimen and HRQoL scores

Table 9 describes the association between the type of immunosuppressive regimen and HRQoL scores. No statistical significance was obtained among immunosuppressant use with respect to HRQoL mean score.

**Table 9: Association between immunosuppressant regimen and HRQoL**

| | N | HRQoL |
|---|---|---|
| **Immunosuppressant regimen** | | |
| Pred. Tac. Mycop | 60 | 5.20 (0.85) |
| Pred. Mycop. Cyclo | 9 | 5.22 (0.64) |
| Pred. Tac. Azath. | 6 | 5.10 (0.63) |
| Pred. Cyclo. Azath. | 4 | 5.57 (0.66) |
| Pred. Mycop. Ever. | 1 | 4.88 (-) |
| P-value | | p=0.899 |

Further analysis of KTQ domains and various immunosuppressive regimens revealed no statistically significant differences among the type of immunosuppressive medications with respect to KTQ-25 domains (Table 10). Patients on prednisolone, tacrolimus and azathioprine combination showed the lowest score for the fear/uncertainty domain.

**Table 10: Association between immunosuppressant regimen and HRQoL sub score among study participants**

| | n | Physical symptoms | Fatigue | Fear/ Uncertainty | Appearance | Emotions | HQRoL |
|---|---|---|---|---|---|---|---|
| **Immunosuppressant regimen** | | | | | | | |
| Pred. Tac. Mycop | 60 | 4.62 (1.48) | 5.27 (1.36) | 4.31 (1.08) | 6.61 (0.61) | 5.40 (1.12) | 5.20 (0.85) |
| Pred. Mycop. Cyclo | 9 | 4.52 (1.13) | 5.64 (1.06) | 4.19 (1.57) | 6.75 (0.66) | 5.22 (1.34) | 5.22 (0.64) |
| Pred. Tac. Azath. | 6 | 4.56 (0.89) | 5.50 (1.38) | 3.71 (0.94) | 6.38 (0.52) | 5.39 (0.94) | 5.10 (0.63) |
| Pred. Cyclo. Azath. | 4 | 5.42 (0.48) | 4.85 (2.46) | 5.06 (0.55) | 7.00 (0.00) | 5.71 (1.09) | 5.57 (0.66) |
| Pred. Mycop. Ever. | 1 | 4.00 (-) | 6.80 (-) | 4.00 (-) | 6.25 (-) | 3.83 (-) | 4.88 (-) |
| P-value | | p=0.813 | p=0.692 | p=0.453 | p=0.490 | p=0.668 | p=0.899 |

### 4.11 Association between immunosuppressant side effects and HRQoL scores

Association between KTQ-25 domains and the number of side effects experienced per patient, revealed statistically significant differences in physical symptoms and appearance

domain, p-0.011 and 0.002, respectively. Participants with less than one side effect showed a better HRQoL score for physical symptom and appearance domain **(**Table 11**).**

**Table 11: Association between immunosuppressants side effects and HRQoL sub score among study participants.**

| | n | Physical symptoms | Fatigue | Fear/ Uncertainty | Appearance | Emotions |
|---|---|---|---|---|---|---|
| **Number of side effects** | | | | | | |
| 0 | 17 | 5.08 (1.57) | 5.29 (1.35) | 4.46 (0.96) | 6.81 (0.33) | 5.69 (1.17) |
| 1 | 19 | 5.29 (1.00) | 5.68 (1.24) | 4.39 (0.90) | 6.82 (0.35) | 5.53 (1.03) |
| 2 | 15 | 4.63 (1.40) | 5.79 (0.94) | 4.50 (0.98) | 6.42 (0.75) | 5.51 (1.08) |
| 3 | 10 | 4.17 (0.84) | 4.90 (1.63) | 3.80 (1.41) | 6.65 (0.49) | 4.87 (0.84) |
| 4 | 7 | 4.55 (1.15) | 5.26 (2.05) | 3.93 (1.10) | 6.79 (0.37) | 5.45 (1.39) |
| 5 | 6 | 3.31 (1.46) | 4.90 (1.63) | 3.67 (1.42) | 5.71 (1.02) | 4.75 (1.52) |
| 6 | 5 | 3.47 (1.13) | 4.76 (1.65) | 4.50 (1.55) | 6.70 (0.41) | 4.80 (0.94) |
| 7 | 1 | 3.83 (-) | 2.40 (-) | 6.00 (-) | 6.75 (-) | 6.17 (-) |
| P-Value | | **p=0.011** | p=0.193 | p=0.320 | **p=0.002** | p=0.374 |

Patients were clustered into, ones with side effects and no side effects. Influence of side effects Vs no side effect on health related quality of life was investigated. No statistical difference was obtained for all KTQ domains (Table 11).

**Table 12: Effect of immunosuppressant side effect on HRQoL domains**

| KTQ domains | No side effects (0) | Side effects (≥1) | p-value |
|---|---|---|---|
| Physical symptoms | 5.08 (1.57) | 4.52 (1.29) | 0.132 |
| Fatigue | 5.29 (1.35) | 5.34 (1.40) | 0.911 |
| Fear/ Uncertainty | 4.46 (0.96) | 4.24 (1.15) | 0.477 |
| Appearance | 6.81 (0.33) | 6.58 (0.64) | 0.152 |
| Emotions | 5.69 (1.17) | 5.29 (1.11) | 0.197 |
| HRQoL | 5.44 (0.77) | 5.15 (0.80) | 0.177 |

Further analysis comparing the influence of immunosuppressant side effects Vs no side effects on HRQoL mean score also showed no statistical significance. However, patients with more than one side effect had a low HRQoL mean score compared to those with no side effects.

### 4.12 Association of adherence and HRQoL scores

Table 13 provides detailed information on the association between adherence and health related quality of life sub score. No difference was detectable among adherent and non-adherent patients for all the KTQ-25 dimensions, although non-adherent patients had the lowest score for the fear/ uncertainty dimension.

**Table 13: Association between adherence and HRQoL sub score among study participants**

| HRQoL domains | Non-adherence | Adherence | p-value |
|---|---|---|---|
| Physical symptoms | 4.68 (1.03) | 4.62 (1.45) | 0.890 |
| Fatigue | 5.18 (1.13) | 5.37 (1.45) | 0.614 |
| Fear/ Uncertainty | 3.84 (1.07) | 4.40 (1.10) | 0.065 |
| Appearance | 6.75 (0.29) | 6.59 (0.65) | 0.148 |
| Emotions | 5.28 (1.03) | 5.40 (1.16) | 0.716 |
| HRQoL | 5.12 (0.54) | 5.24 (0.85) | 0.592 |

Further analysis to explore association between adherence and HRQoL mean score revealed no statistical significance among the two groups (Table 13).

**Impact of transplantation duration on health related quality of life.**

Table 14 below describes impact of transplantation duration on health related quality of life. No statistical significant difference was observed between the time elapsed from transplantation and HRQoL scores. The highest quality of life score was observed in the group that had 3-6 months passed since their transplant, while the lowest quality of life in participants that had more than 60 months elapsed since transplantation.

**Table 14: Impact of transplantation duration on HRQoL score**

| Duration of transplantation | n | HRQoL | P-Value |
|---|---|---|---|
| 3-6 months | 6 | 5.46(0.77) | |
| 7-36 months | 25 | 5.26(0.88) | |
| 37-60 months | 22 | 5.24(0.87) | p=0.748 |
| >60 months | 27 | 5.10(0.68) | |
| | | | |
| ≤ 1year | 9 | 5.42(0.62) | p=0.405 |
| >1 year | 71 | 5.19(0.82) | |

Patients were also stratified into, ones with kidney a transplants for less than a year and more than a year. The influence of duration of transplantation on health related quality of

life was investigated. No statistical difference was observed between the two groups. However, patients with a kidney transplants for less than a year showed a high mean HRQoL score compared to those with more than a year of transplantation.

Further analysis by HRQoL domains (Table 15) revealed no statistical significance, but low a score in the fear/uncertainty domain, in patients with transplant for more than 60months 3.93(1.08).

**Table 15: Impact of transplantation duration on HRQoL subscore.**

| | n | Physical symptoms | Fatigue | Fear/ Uncertainty | Appearance | Emotions |
|---|---|---|---|---|---|---|
| **Duration in months** | | | | | | |
| 3-6 | 6 | 4.50 (1.88) | 5.17 (1.54) | 4.88 (0.86) | 6.50 (0.79) | 6.36 (0.57) |
| 7-36 | 25 | 4.59 (1.43) | 5.46 (1.35) | 4.43 (1.12) | 6.67 (0.52) | 5.35 (1.18) |
| 37-60 | 22 | 4.61 (1.53) | 5.45 (1.32) | 4.40 (1.14) | 6.59 (0.66) | 5.36 (1.16) |
| >60 | 27 | 4.73 (1.09) | 5.13 (1.47) | 3.93 (1.08) | 6.64 (0.59) | 5.19 (1.07) |
| P-Value | | p=0.976 | p=0.796 | p=0.065 | P=0.923 | p=0.716 |

### 4.13 Multiple linear regression analysis for independent correlates of HRQoL

Multiple linear regression analysis was conducted to determine the independent predictors of HRQoL in the population under study (Table 16). Being male gender showed a reduction in the overall HRQoL by 0.248 points. The same was observed in patients with diabetes where having diabetes reduced the overall HRQoL score by 11.673 points. Side effects also had a negative effect on HRQoL reducing the quality of life by 7.004 units. Increasing level of creatinine by a unit had a minimal reduction to the points of 0.048, while a unit increase on duration of transplant increased by a negligible amount to the HQRoL of about 0.006. Overall, the only statistically significant factor within the model was diabetes.

**Table 16: Independent predictors of HRQoL among study participants**

| | | | | 95% CI for B | |
|---|---|---|---|---|---|
| | **B** | **T** | **p-value** | **Lower** | **Upper** |
| **(Constant)** | 145.159 | 20.3 | 0.000 | 130.920 | 159.399 |
| Gender(Male) | -0.248 | -0.051 | 0.960 | -10.005 | 9.509 |
| Diabetes(Yes) | -11.673 | -2.421 | **0.018** | -21.283 | -2.064 |
| Side effect(Yes) | -7.004 | -1.307 | 0.195 | -17.684 | 3.675 |
| Creatinine levels | -0.048 | -1.684 | 0.096 | -0.105 | 0.009 |

| | | | | | |
|---|---|---|---|---|---|
| Duration of transplantation | 0.006 | 0.125 | 0.901 | -0.092 | 0.104 |

## CHAPTER FIVE: DISCUSSION, CONCLUSION AND RECOMMENDATIONS

### 5.1 Introduction

This chapter discusses the findings of the research in the context of study objectives. Concurrences and differences of study with other related studies have been discussed. Conclusions and recommendations for policy, practice and further research is included.

### 5.2 Discussion

Study findings revealed that majority of the participants were male (70%). This finding tallies with what was reported by studies in Iran and Palestine that showed male predominance [81,82] at 58.7% and 79.8%, respectively. The consistency may reflect higher prevalence and incidence rates of end stage renal disease in men than in women[83]. The findings may also reflect what related studies have found with regards to gender bias ,lack of social support systems and lower income among women pertaining to access to transplantation services[84]. The mean age(SD) of the participants was 45.4(±14.7) years, which is comparable with a closely related study done in the same setting[85] that reported a mean (SD) of 43.5(13.4) .The congruity in mean age is explained by the fact that ESRD tends to affect the young and the middle aged individuals in sub-Saharan Africa. Conversely, a study in Germany showed the mean age to be greater than 55 years where the inclusion criteria involved adult participants with functioning kidney graft for more than 15 years [86] and perhaps the higher mean age. Majority of the participants were married (80%), which tallies with other studies done in the same setting which revealed a proportion of 67.1%[87].

Hypertension (60%) was the most reported comorbidity, followed by both diabetes and hypertension (25%). This finding is contrary to findings of a study conducted in Canada among 6324 renal transplant recipients which established that cardiac disease (27.5%) and diabetes (4.0%) were the most common comorbidities [88] . The reasons for this discrepancy is that our study was much smaller and possibly could not identify many patients. However, the present study identified hypertension as the chief cause of ESRD among the participants, followed by both diabetes and hypertension. In line with current

findings, a study conducted in Egypt [89]showed hypertension (28%) as the leading cause of end stage renal disease. End stage renal disease is among the commonest complications of poorly managed diabetes and hypertension.

Regarding the type of donor, all the study participants received their kidneys from living donor relatives. This finding concurs with a study conducted in Palestine that showed living donor relatives as main graft contributors [82].In contrast, the study in Iran had the majority of participants receiving graft from non-relatives and cadavers [81]. This contrast may be due to difference in policies, laws and advocacy regarding organ donation across countries.

This study showed prednisolone, tacrolimus and mycophenolate combination as the principal (75%) immunosuppressant protocol among the participants. Similarly, studies conducted in the same setting by Rupal *et al* and Wambugu *et al* revealed that, indeed, this was the most prevalent immunosuppressant regimen at 40 % and 49 %, respectively[87,85]. This finding is in agreement with studies that recommended use of prednisolone, tacrolimus and mycophenolate as the standard immunosuppressant therapy[90]. Furthermore, studies have suggested that maintenance of renal transplant patients on tacrolimus and mycophenolate with or without corticosteroids is associated with lower rates of acute kidney rejection, renal dysfunction and non-adherence [91] compared with other regimens. Perhaps the renal transplant clinicians in KNH were aware of these suggestions. The least utilized immunosuppressant combination was prednisolone, mycophenolate and everolimus at 1.25% and factors such as patient characteristics, medication cost as well as health care workers' training and experience may have influenced the prescription of this regimen.

This study identified weight gain as the most common side effect followed by fatigue and diarrhea. This is in contrast to a study in America and Iran, that identified unusual hair growth as the most common side effect following antirejection medication use[92,56]. The inconsistency may be explained by the difference in immunosuppressant protocol between our study and the two studies. In this study, most patients were on prednisolone, tacrolimus and mycophenolate while in the Iran study, the majority were on prednisolone, mycophenolate and cyclosporin protocol. It should be noted that, weight gain, fatigue, moon face, and swollen legs are side effects associated with corticosteroids [93]. Diarrhea

on the other hand may be due to mycophenolate [94,87] while hypertrichosis may be due to ciclosporin [65].

Graft survival heavily depends on adherence to immunosuppressant medication. Our study revealed that 78.8% of the study participants adhered to medication while 21.2% were non-adherent. A recent systematic review of fifteen cross-sectional studies reported that, a median of 22.3% of kidney transplant recipients were non-adherent [95]. A comparable results was yielded in a study conducted in Singapore, where the non-adherence rate was 19.7% [96]

Conversely, a study conducted in Iran reported a non-adherence rate of 54.5 % among their study participants[97]. The difference in non-adherence prevalence between our study and Iran may be attributed to recall bias, where the measurement of adherence relied on patient self-reporting thus resulting in discrepancy. In our study, financial constraint was the main reason for non-adherence, followed by forgetfulness and missing medication due to Covid 19. On the other hand, confusion in medication taking, forgetfulness, and knowledge gap on immunosuppressant usefulness were the main barriers to adherence in the Iran study[97].

Participants in this study reported a number of physical symptoms that may be attributed to the side effects of immunosuppressant medication and transplantation. Forgetfulness (35%) was the most common symptom experienced by participants. Although the cause of forgetfulness is complex, some studies have suggested tacrolimus might be among the possible culprits[98]. A study by Rostami *et al*, however, reported aching tired legs as the most reported physical problem[99]. This is in contrast to our study and the reasons for the difference were not clear. However, forgetfulness may result in poor compliance to antirejection medication leading to graft loss. This finding underscores the need for patients counselling and education on possible side effects such as forgetfulness, and the need to have reminders as an intervention of enhancing compliance to antirejection medication.

Majority of the patients (73.8%) had a score of 7, demonstrating that they had no worries about their appearance. It seems that appearance related issues post-transplantation was not as distressing among our study participants. This however contradicts a study by Antje *et al* that revealed that change in appearance was a distressing symptom in women [100]. Studies have also indicated that distressing symptoms are subjective and are determined by

individual and socio-cultural factors[100]. Comparable studies using the kidney transplant questionnaire have yielded similar results where the appearance domain had the highest score. For instance, Siyoum *et al* reported a mean(SD) score of 6.50 (0.98) while our study had a mean score of 6.62(0.60) in the appearance domain[78].

This study established that the majority of the patients (30%) had moderate fatigue, with nearly half (47.6%) of the remaining participants experiencing no fatigue at all. Only 22% of patients had severe fatigue. A systematic review and meta-analysis reported the prevalence of fatigue to be 40-50% among kidney transplant recipients[101]. Despite our study not differentiating between disease related fatigue from drug associated symptoms, we attribute fatigue findings to immunosuppressant medication, though the study did not further investigate the specific causative immunosuppressant. However, studies on immunosuppressant regimen have suggested that patients on tacrolimus based regimen have less fatigue[102] compared to those on cyclosporin based regimens. Perhaps this may explain why there was a small proportion (22%) of the participants with fatigue in the present study because most of them were on tacrolimus-based immunosuppressants.

We found that majority of the study participants (82.4%) experienced symptoms related to uncertainty /fear, while only, 17.6% of study participants experienced no uncertainty/fear. Uncertainty/fear domain scored the lowest, among the domains assessed by the kidney transplant questionnaire at a score of 4.28(1.12). These findings agree with studies conducted using the KTQ-25 in Iran and Ethiopia where uncertainty /fear scored the lowest at 4.53(1.82) and 4.18(1.80) respectively [103,78]. Kholoud *et al* also found low score in the fear /uncertainty dimension [82] at mean (SD) 3.36(1.23). This finding may be reflective of fear regarding graft rejection and returning to dialysis. Uncertainty and fear of graft rejection may cause emotional distress and anxiety among kidney transplant patients, resulting in non-compliance to immunosuppressant medication.

Renal transplantation is considered the best treatment modality for end stage renal as it is cost effective, prolongs life, and improves HRQoL. Despite these benefits, literature shows that transplanted patients may suffer emotionally through depression and anxiety [104] due to fear of failing graft, the anxiety of regular medical checkup, strict immunosuppressive therapy as well as their side effects [105,22].In our study, approximately half of the study participants (48.7%) had severe to moderate trouble with emotions. In contrast, a qualitative study in the UK reported that 25% of kidney transplant patients had emotional

distress[104].The findings disagrees with our findings because of the difference in study methodology. In the UK study, inclusion criteria required a patient to be categorized as mild to moderate using a distress thermometer. This may have introduced some sort of bias. Nevertheless, psychological and emotional distress appears to be a problem in kidney transplant patients that should be addressed. This finding underscores the need for routine psychological support before and after kidney transplantation.

The overall mean (SD) HRQoL score of our study participants was 5.19(0.78), which shows that our patients had a good quality of life. Comparable studies in Iran, Ethiopia, and Spain [81,78,106] using the same questionnaire reported means of 4.9(1.27), 6.06(0.79) and 5.9(1.18), respectively.

The highest score in our study was obtained in appearance domain 6.62(0.60), which is consistent with the Iran, Ethiopia and Palestine [81,78,82] which reported mean scores of 5.75(1.53), 6.50(0.98) and 5.40(1.23), respectively. The lowest score in this study was related to fear /uncertainty domain ,which, concurs with findings from studies done in Iran and Palestine [81,82] , reporting mean (SD) scores of 4.53(1.82) and 3.36(1.23), respectively. Our study demonstrates that fear and uncertainty about the future were the main concerns among the study participants. Consequently, there is a need for patient education on graft rejection and coping mechanisms post transplantation.

The study found a statistically significant association between comorbidity and health related quality of life ($p = 0.017$), with a low HRQoL score among study participants comorbid with diabetes and hypertensive at mean score of 4.79 (0.82). A possible reason would be that comorbidity requires patients to take drugs for management of a specific comorbid condition, causing a pill burden to the already burdened regimen. Moreover, complications of medical conditions such as diabetes and hypertension may affect the kidneys leading to graft loss. Studies that have investigated comorbid conditions in renal transplant patients found that comorbidity has a negative effect on the quality of life. This finding is supported by Rosenberger *et al* who demonstrated that comorbidity correlated with poor quality of life[107]. Given this finding on comorbidity and the possibility of the complexity of medication regimen due to comorbidity, it is important that medication

reconciliation and counselling is conducted by health care providers to enhance efficacy while preventing side effects.

In this study, there was a statistical significance between the number of side effects experienced by each patient and HRQoL in the physical symptoms and appearance domain, p=0.011 and p= 0.002, respectively. Participants with less than one side effect showed a better HRQoL score for physical symptoms and appearance domain compared to those who had more than one adverse effect. This suggests that our study participants who experienced side effects from antirejection medication were most bothered by side effects that affected their appearance in addition to physical adverse effects. Literature suggests that side effects from immunosuppressants are a cause of poor HRQoL [56] Furthermore, side effects related to changes in appearance, energy and mood are often bothersome compared to the metabolic side effects such as hyperlipidemia[108].Given these findings, health care workers should be keen to identify adverse effect symptoms and manage them effectively. Additionally, they should educate patients on possible side effects due to antirejection medication and the need to report the side effects for prompt management.

In order to see the impact of transplantation on HRQoL. We investigated the association between time since transplantation and HRQoL. No statistical significance was obtained on the duration of transplantation and mean HRQoL score or the HRQoL domains. However, patients with long duration since transplantation (over 60 months) showed low HRQoL scores on the fear/uncertainty domain. Although not statistically significant, this finding suggests that years after transplantation, patients develop concerns about fear of graft rejection which may affect their quality of life. As time goes by, kidney transplant patients of more than five years, should have their fear of graft rejection diminish. Differently from our study, Rebollo *et al* demonstrated increasing HRQoL score [12] as time goes by after transplantation. Similarly, Michael *et al* in a study that included transplant patients with graft for more than 15 years yielded improved HRQoL in all domains over time[109].

Linear regression analysis demonstrated that having diabetes decreased HRQoL score by 11.67 units. This depicts that renal transplant patients with diabetes are likely to have low health related quality of life. Studies focusing on health related quality of life in kidney transplant patients with diabetes have confirmed low scores in functional performance as

well as the quality of life in these patients[110]. Literature indicates that microvascular and macrovascular complications of diabetes are a cause of morbidity and low quality of life[111].

### 5.3 Study strengths, weaknesses and limitations

Our study is the first study to assess HRQoL among kidney transplant patients, this data will serve as research literature for future quality of life evaluation. We have also established that presence of comorbidities is likely to decrease the HRQoL among renal transplant recipients.

Recall bias may have affected the participant's capacity to report side effects.

Measurement of immunosuppressant adherence relied on self-report questionnaire which was susceptible to reporting bias.

The interpretation of results in our study is limited by the relatively small number of patients and lack of randomization.

Factors causing distress such as Covid -19 pandemic may have influenced patient's perception of life resulting in low reporting.

### 5.4 Conclusions

HRQoL of kidney transplant patients was good, having a mean summary score of 5.19 (0.98).

Uncertainty and fear was the least scored domain in quality of life assessment reflecting fear and stress among kidney transplant patients.

Side effects from immunosuppressant medication had an influence on the appearance and physical symptoms dimensions of quality of life

Immunosuppressant medication non-adherence rate was 21.2% which was attributed to unaffordability of immunosuppressant medication.

### 5.5 Recommendations for policy and practice.

Diabetes and hypertension were the main cause of ESRD. Therefore, early renal function screening, tight glycemic control, and high blood pressure treatment should be emphasized amongst patients to avert complications such as renal failure.

Interventions that promote adherence among kidney transplant recipients such as patient education on importance of adherence are recommended.

Fear and uncertainty regarding graft survival were noted among the participants. We recommend strategies such as counselling and psychological care before and after transplantation to help kidney transplant patients cope with life post transplantation.

### 5.6 Recommendation for further research

An interventional study comparing the mean score of quality of life domains before and after renal transplantation to ascertain the impact of transplantation on HRQoL scores should be carried out to improve the practice of management of renal transplant recipients.

**REFERENCES**


1. Thurlow JS, Joshi M, Yan G, Norris KC, Agodoa LY, Yuan CM, et al. Global epidemiology of end-stage kidney disease and disparities in kidney replacement therapy. Am J Nephrol 2021;52(2):98–107.

2. Lv JC, Zhang LX. Prevalence and Disease Burden of Chronic Kidney Disease [Internet]. Springer Singapore; 2019. Available from: http://dx.doi.org/10.1007/978-981-13-8871-2_1

3. Neild GH. Chronic renal failure [Internet]. In: The Scientific Basis of Urology, Second Edition. CRC Press; 2004 [cited 2021 Jan 11]. page 257–64.Available from: https://www.ncbi.nlm.nih.gov/books/NBK535404/

4. Home - GODT [Internet]. [cited 2021 Jan 27];Available from: http://www.transplant-observatory.org/

5. Held PJ, McCormick F, Chertow GM, Peters TG, Roberts JP. Would government compensation of living kidney donors exploit the poor? An empirical analysis. PLoS One [Internet] 2018 [cited 2021 Jan 27];13(11):e0205655. Available from: https://dx.plos.org/10.1371/journal.pone.0205655

6. Garcia Garcia G, Harden P, Chapman J. The Global role of kidney transplantation. J Nephropathol [Internet] 2012 [cited 2021 Nov 15];1(2):69. Available from: /pmc/articles/PMC3886138/

7. Bona PB and M De. Quality of life following organ transplantation. Eur Soc Organ Transplant 2007;20:397–409.

8. Gentile S, Beauger D, Speyer E, Jouve E, Dussol B, Jacquelinet C, et al. Factors associated with health-related quality of life in renal transplant recipients: results of a national survey in France [Internet]. 2013. Available from: http://www.hqlo.com/content/11/1/88

9. Sampaio De Brito DC, Leandro E, Ii M, Afonso I, Iii R, Pires De Freitas L, et al. Depression and anxiety among patients undergoing dialysis and kidney transplantation: a cross-sectional study. Sao Paulo Med J 2019;137(2):137–84.

10. El Rasheed AH, Khedr E, Naguib R, Eid M, Elkholy H, Rabie S. Quality of life in a sample of Egyptian renal transplant recipients. Middle East Curr Psychiatry 2020;27(1).

11. Luk WSC. The HRQoL of renal transplant patients. J Clin Nurs 2004;13(2):201–9.

12. Fiebiger W, Mitterbauer C, Oberbauer R. Health and Quality of Life Outcomes Health-related quality of life outcomes after kidney transplantation [Internet]. 2004. Available from: http://www.hqlo.com/content/2/1/2

13. Tayyebi A, Raiesifar A, Mehri SN, Ebadi A, Einolahi B, Pashandi S. Measuring Health Related Quality of Life (Hrqol) in Renal Transplant Patients: Psychometric Properties and Cross-Cultural Adaptation of Kidney Transplant Questionnaire (Ktq-25) in Persian Implication for health policy/practice/research/medical education. 2012;4(4):617–38. Available from: www.NUmonthly.com

14. Maglakelidze N, Pantsulaia T, Tchokhonelidze I, Managadze L, Chkhotua A. Assessment of Health-Related Quality of Life in Renal Transplant Recipients and Dialysis Patients. TPS [Internet] 2011;43(1):376–9. Available from: http://dx.doi.org/10.1016/j.transproceed.2010.12.015

15. Oppenheimer F, Rebollo P, Grinyo JM, Ortega F, Sanchez-Plumed J, Gonzalez-Molina M, et al. Health-related quality of life of patients receiving low-toxicity immunosuppressive regimens: A substudy of the symphony study. Transplantation 2009;87(8):1210–3.

16. Hwangid Y, Kimid M, Min K. Factors associated with health-related quality of life in kidney transplant recipients in Korea. 2021;Available from: https://doi.org/10.1371/journal.pone.0247934

17. Pasquale C De, Veroux M, Indelicato L, Sinagra N, Giaquinta A, Fornaro M, et al. Psychopathological aspects of kidney transplantation: Efficacy of a multidisciplinary team. World J Transplant [Internet] 2014 [cited 2021 Oct 24];4(4):267. Available from: /pmc/articles/PMC4274596/

18. Rosenbergera J, Geckovab AM, Jitse P van Dijkc RR, And WJ van den H,

Groothoff JW. Factors modifying stress from adverse effects of immunosuppressive medication in kidney transplant recipients. Clin Transplant 2004;19:70–6.

19. Tong A, Howell M, Wong G, Webster AC, Howard K, Craig JC. The perspectives of kidney transplant recipients on medicine taking: A systematic review of qualitative studies. Nephrol Dial Transplant 2011;26(1):344–54.

20. Wu C, Evans I, Joseph R, Shapiro R, Tan H, Basu A, et al. Comorbid Conditions in Kidney Transplantation: Association with Graft and Patient Survival. J Am Soc Nephrol [Internet] 2005 [cited 2021 Jan 28];16:3437–44. Available from: www.jasn.org.

21. Akbarzadeh Pasha A, Alijanpour S, Khafri S, Basim H, Afshang M. Side Effects of Transplant Immunosuppressive Therapy in Post Renal Transplant Recipients, Mazandaran, Northern Iran. Zahedan J Res Med Sci [Internet] 2017 [cited 2021 Jan 28];19(4). Available from: https://sites.kowsarpub.com/zjrms/articles/6560.html

22. Habwe VQ. Posttransplantation quality of life: More than graft function. Am J Kidney Dis 2006;47(4 SUPPL. 2):98–110.

23. Shetty AA, Wertheim JA, Butt Z. Health-Related Quality of Life Outcomes After Kidney Transplantation [Internet]. In: Kidney Transplantation, Bioengineering, and Regeneration: Kidney Transplantation in the Regenerative Medicine Era. Elsevier Inc.; 2017 [cited 2021 Jan 28]. page 699–708.Available from: https://www.scholars.northwestern.edu/en/publications/health-related-quality-of-life-outcomes-after-kidney-transplantat

24. Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, Lasserson DS, et al. Global prevalence of chronic kidney disease - A systematic review and meta-analysis. PLoS One2016;11(7).

25. El Rasheed AH, Khedr E, Naguib R, Eid M, Elkholy H, Rabie S. Quality of life in a sample of Egyptian renal transplant recipients. Middle East Curr Psychiatry

[Internet] 2020 [cited 2021 Nov 15];27(1):1–10. Available from: https://mecp.springeropen.com/articles/10.1186/s43045-020-00041-0

26. Urological involvement in renal transplantation - Sackett - 2011 - International Journal of Urology - Wiley Online Library [Internet]. [cited 2021 Jan 29];Available from: https://onlinelibrary.wiley.com/doi/pdf/10.1111/j.1442-2042.2010.02707.x?src=getftr

27. Kobayashi S, Hidaka S. Can we still ignore renal replacement therapy in sub-Saharan Africa? All living beings are created equal [Internet]. Ren. Replace. Ther.2020 [cited 2021 Jan 28];6(1):5. Available from: https://rrtjournal.biomedcentral.com/articles/10.1186/s41100-019-0243-6

28. Pozo ME, Leow JJ, Groen RS, Kamara TB, Hardy MA, Kushner AL. An overview of renal replacement therapy and health care personnel deficiencies in sub-Saharan Africa. Transpl Int [Internet] 2012 [cited 2021 Nov 15];25(6):652–7. Available from: https://pubmed.ncbi.nlm.nih.gov/22458851/

29. Ministry of Health; 10 years and 200 transplants later! KNH celebrates a milestone –Internet]. [cited 2021 Jan 28];Available from: https://www.health.go.ke/10-years-and-200-transplants-later-knh-celebrates-a-milestone/

30. Rosa Jofre´, MD, Juan M. Lo´pez-Go´mez, MD, Fuensanta Moreno M, Damaso Sanz-Guajardo, MD, and Fernando Valderra´bano M. Changes in Quality of Life After Renal Transplantation. Natl kidney Found 1998;32(93–100).

31. Overbeck I, Bartels M, Decker O, Harms J, Hauss J, Fangmann J. Changes in quality of life after renal transplantation. In: Transplantation Proceedings. Elsevier; 2005. page 1618–21.

32. Fujisawa M, Ichikawa Y, Yoshiya K, Isotani S, Higuchi A, Nagano S, et al. Assessment of health-related quality of life in renal transplant and hemodialysis patients using the SF-36 health survey. Urology [Internet] 2000 [cited 2021 Jan 28];56(2):201–6. Available from: https://pubmed.ncbi.nlm.nih.gov/10925078/

33. Prihodova L., Nagyova I., Rosenberger J., Majernikova M., Roland R., Groothoff

J.W. et al. Adherence in patients in the first year after kidney transplantation and its impact on graft loss and mortality: a cross-sectional and prospective study. Journal of Advanced Nursing 70 (12), 2871–2883.

34. Molnar-Varga M, Molnar MZ, Szeifert L, Kovacs AZ, Kelemen A, Becze A, et al. Health-related quality of life and clinical outcomes in kidney transplant recipients. Am J Kidney Dis [Internet] 2011 [cited 2021 Jan 29];58(3):444–52. Available from: http://www.ajkd.org/article/S0272638611008328/fulltext

35. Fisher R, Gould D, Wainwright S, Fallon M. Quality of life after renal transplantation. J Clin Nurs [Internet] 1998 [cited 2021 Jan 29];7(6):553–63. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1046/j.1365-2702.1998.00189.x

36. Tayebi A, Raiesifar A, Ebadi A, Eynollahi B, Rafiyan Z KF. Investigation of renal transplantation patients' quality of life by kidney transplantation questionnaire (KTQ-25). Iran J Crit Care Nurs 2010;3(3).

37. Yujian Niu, Wenxin Zhang, Sha Mao, Yanhong Gao Jianli Wang1, Jun Li, Letian Wang1 ZG, Shen Z. Pilot feasibility research of Chinese version of kidney transplant questionnaire in recipients of living donor kidney transplantation. Int J Clin Exp Med 2015;8(12):22570–6.

38. Czyżewski Ł, Sańko-Resmer J, Wyzgał J, Kurowski A. Assessment of health-related quality of life of patients after kidney transplantation in comparison with hemodialysis and peritoneal dialysis. Ann Transplant [Internet] 2014 [cited 2021 Jan 29];19(1):576–85. Available from: https://pubmed.ncbi.nlm.nih.gov/25382249/

39. Jansz TT, Bonenkamp AA, Boereboom FTJ, Van Reekum FE, Verhaar MC, et al. Health-related quality of life compared between kidney transplantation and nocturnal hemodialysis. 2018;Available from: https://doi.org/10.1371/journal.pone.0204405

40. Szeifert L, Molnar MZ, Ambrus C, Koczy AB, Kovacs AZ, Vamos EP, et al.

Symptoms of Depression in Kidney Transplant Recipients: A Cross-sectional Study. Am J Kidney Dis [Internet] 2010 [cited 2021 Jan 29];55(1):132–40. Available from: https://pubmed.ncbi.nlm.nih.gov/19932540/

41. Gabriele H. F, Jens R, Mathias K, Peter L, Nicole M. Uwe H. Quality of Life in End-Stage Renal Disease Patients after Successful Kidney Transplantation: Development of the ESRD Symptom Checklist – Transplantation Module. Nephron, 83(1), 31–39 | 10.1159/000045470 [Internet]. [cited 2021 Jan 30];Available from: https://sci-hub.se/10.1159/000045470.

42. Hays R.D, Kallich J.D, Mapes D.L, Coons S.J, Carter W.B.Development of the Kidney Disease Quality of Life (KDQOL TM ) Instrument | SpringerLink [Internet]. [cited 2021 Jan 30];Available from: https://link.springer.com/article/10.1007%2FBF00451725

43. Andreas L ,Norman M,Paul K ,Cindy et al. A Disease-Specific Questionnaire for Assessing Quality of Life in Patients on Hemodialysis. Nephron, 60(3), 302–306 | 10.1159/000186769 [Internet]. [cited 2021 Jan 30];Available from: https://sci-hub.se/10.1159/000186769.

44. Tayyebi A, Raiesifar A, Mehri SN, Ebadi A, Einolahi B, Pashandi S. Measuring Health Related Quality of Life (Hrqol) in Renal Transplant Patients: Psychometric Properties and Cross-Cultural Adaptation of Kidney Transplant Questionnaire (Ktq-25) in Persian Implication for health policy/practice/research/medical education. 2012 [cited 2021 Jan 13];4(4):617–38. Available from: www.NUmonthly.com

45. Krantz E, Wide U, Trimpou P, Bryman I, Landin-Wilhelmsen K. Comparison between different instruments for measuring health-related quality of life in a population sample, the WHO Monica Project, Gothenburg, Sweden: An observational, cross-sectional study. BMJ Open [Internet] 2019 [cited 2021 Jan 29];9(4):e024454. Available from: http://bmjopen.bmj.com/

46. Esposito P, Furini F, Rampino T, Gregorini M, Petrucci L, Klersy C, et al. Assessment of physical performance and quality of life in kidney-transplanted

patients: A cross-sectional study. Clin Kidney J [Internet] 2017 [cited 2021 Jan 29];10(1):124–30. Available from: /pmc/articles/PMC5469555/?report=abstract

47. Oberbauer R, Hutchison B, Eris J, Arias M, Claesson K, Mota A, et al. Health-related quality-of-life outcomes of sirolimus-treated kidney transplant patients after elimination of cyclosporine A: results of a 2-year randomized clinical trial1. Transplantation [Internet] 2003 [cited 2021 Jan 26];75(8):1277–85. Available from: http://journals.lww.com/00007890-200304270-00045

48. Reimer J, Franke GH, Philipp T, Heemann U. Quality of life in kidney recipients: Comparison of tacrolimus and cyclosporine-microemulsion. Clin Transplant 2002;16(1):48–54.

49. Moons P, Vanrenterghem Y, Hooff JP van, Squifflet J-P, Margodt D, Mullens M, et al. Health-related quality of life and symptom experience in tacrolimus-based regimens after renal transplantation: a multicentre study. Transpl Int 2003;16:653–4.

50. Jones-Hughes T, Snowsill T, Haasova M, Coelho H, Crathorne L, Cooper C, et al. Health technology assessment Immunosuppressive therapy for kidney transplantation in adults: a systematic review and economic model. 2016;

51. Kalluri HV. Current state of renal transplant immunosuppression: Present and future. World J Transplant [Internet] 2012 [cited 2021 Jan 30];2(4):51. Available from: /pmc/articles/PMC3782235/?report=abstract

52. Neuwirt H, Rudnicki M, Schratzberger P, Pirklbauer M, Kronbichler A, Mayer G. Immunosuppression after renal transplantation [Internet]. Memo - Mag. Eur. Med. Oncol.2019 [cited 2021 Jan 30];12(3):216–21. Available from: https://doi.org/10.1007/s12254-019-0507-4

53. Muntean A, Lucan M. Immunosuppression in kidney transplantation. Clujul Med [Internet] 2013 [cited 2021 Nov 16];86(3):177. Available from: /pmc/articles/PMC4462507/

54. Moloney FJ, de Freitas D, Conlon PJ, Murphy GM. Renal transplantation,

immunosuppression and the skin: An update. Photodermatol Photoimmunol Photomed 2005;21(1):1–8.

55. Smith JM, Nemeth TL, McDonald RA. Current immunosuppressive agents: Efficacy, side effects, and utilization. Pediatr Clin North Am 2003;50(6):1283–300.

56. Akbarzadeh Pasha A, Alijanpour S, Khafri S, Basim H, Afshang M. Side Effects of Transplant Immunosuppressive Therapy in Post Renal Transplant Recipients, Mazandaran, Northern Iran. Zahedan J Res Med Sci [Internet] 2017 [cited 2021 Jan 27];19(4). Available from: https://sites.kowsarpub.com/zjrms/articles/6560.html

57. Veenstra DL, Best JH, Hornberger J, Sullivan SD, Hricik DE. Incidence and cost of steroid side effects after renal transplantation. Transplant Proc 1999;31(1–2):301–2.

58. Lerut J, Bonaccorsi-Riani E, Finet P, Gianello P. Minimization of steroids in liver transplantation. Transpl Int 2009;22(1):2–19.

59. Gupta G, Unruh ML, Nolin TD, Hasley PB. Primary care of the renal transplant patient [Internet]. J. Gen. Intern. Med.2010 [cited 2021 Jan 29];25(7):731–40. Available from: /pmc/articles/PMC2881977/?report=abstract

60. Knight SR, Morris PJ. Steroid avoidance or withdrawal after renal transplantation increases the risk of acute rejection but decreases cardiovascular risk. A Meta-analysis. Transplantation 2010;89(1):1–14.

61. Malvezzi P, Rostaing L. The safety of calcineurin inhibitors for kidney-transplant patients. Expert Opin Drug Saf 2015;14(10):1531–46.

62. Pelletier RP, Akin B, Henry ML, Bumgardner GL, Elkhammas EA, Rajab A, et al. The impact of mycophenolate mofetil dosing patterns on clinical outcome after renal transplantation. Clin Transplant 2003;17(3):200–5.

63. Hosohata K, Matsuoka E, Inada A, Oyama S, Niinomi I, Mori Y, et al. Differential profiles of adverse events associated with mycophenolate mofetil between adult

and pediatric renal transplant patients. J Int Med Res 2018;46(11):4617–23.

64. Morath C, Arns W, Schwenger V, Mehrabi A, Fonouni H, Schmidt J, et al. Sirolimus in renal transplantation. Available from: https://academic.oup.com/ndt/article/22/suppl_8/viii61/1841984

65. Kalluri HV, Hardinger KL, Giusti A. W J T. World J Transpl [Internet] 2012;2(4):51–68. Available from: http://www.wjgnet.com/2220-3230officeURL:http://www.wjg-net.com/2220-3230/full/v2/i4/51.htmDOI:http://dx.doi.org/10.5500/wjt.v2.i4.51

66. Haller MC, Kammer M, Kainz A, Baer HJ, Heinze G, Oberbauer R. Steroid withdrawal after renal transplantation: A retrospective cohort study. BMC Med [Internet] 2017;15(1):1–9. Available from: http://dx.doi.org/10.1186/s12916-016-0772-6

67. Pascual J. International Journal of Nephrology and Renovascular Disease The use of everolimus in renal-transplant patients [Internet]. 2009. Available from: www.dovepress.com

68. Malyszko J, Dryl-Rydzynska T, Marcinkowski W, Prystacki T, Malyszko JS. Comorbidities on kidney transplantation waiting list relative to the status of the potential recipient [Internet]. Arch. Med. Sci.2018 [cited 2021 Jan 30];14(4):941–4. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6040131/

69. Khan IH. Nephrology Dialysis Transplantation Comorbidity: the major challenge for survival and quality of life in end-stage renal disease. 1998.

70. Akbarzadeh Pasha A, Alijanpour S, Khafri S, Basim H, Afshang M. Side Effects of Transplant Immunosuppressive Therapy in Post Renal Transplant Recipients, Mazandaran, Northern Iran. Zahedan J Res Med Sci [Internet] 2017 [cited 2021 Jan 30];19(4). Available from: https://sites.kowsarpub.com/zjrms/articles/6560.html

71. Ganjali R, Ghorban Sabbagh M, Nazemiyan F, Mamdouhi F, Badiee Aval S, Taherzadeh Z, et al. <p>Factors Associated With Adherence To

Immunosuppressive Therapy And Barriers In Asian Kidney Transplant Recipients</p>. ImmunoTargets Ther [Internet] 2019 [cited 2021 Jan 29];Volume 8:53–62. Available from: /pmc/articles/PMC6844196/?report=abstract

72. Allison Tong, Martin Howell, Germaine Wong, Angela C. Webster KH, Craig and JC. The perspectives of kidney transplant recipients on medicine taking: a systematic review of qualitative studies. Nephrol Dial Transpl 2011;26(344–355).

73. Müller HH, Englbrecht M, Wiesener MS, Titze S, Heller K, Groemer TW, et al. Depression, Anxiety, Resilience and Coping Pre and Post Kidney Transplantation - Initial Findings from the Psychiatric Impairments in Kidney Transplantation (PI-KT)-Study. PLoS One [Internet] 2015 [cited 2021 Nov 16];10(11). Available from: https://pubmed.ncbi.nlm.nih.gov/26559531/

74. Scheel JF, Schieber K, Reber S, Stoessel L, Waldmann E, Jank S, et al. Psychosocial variables associated with immunosuppressive medication non-adherence after renal transplantation. Front Psychiatry 2018;9(FEB):23.

75. Ganjali R, Sabbagh MG, Nazemiyan F, Mamdouhi F, Aval SB, Taherzadeh Z, et al. Factors Associated With Adherence To Immunosuppressive Therapy And Barriers In Asian Kidney Transplant Recipients. 2019;Available from: http://doi.org/10.2147/ITT.S212760

76. Kamau E, Kayima J, Otieno CF. The determinants of health related quality of life of patients on maintenance Haemodialysis at Kenyatta national hospital, Kenya. East Afr Med J 2014;91(10):368–74.

77. Burra P, Bona and M De. Kidney, Investigation of renal transplantation patients' quality of life by (KTQ-25), transplantation questionnaire. Iran J Crit Care Nurs 2010;3(3):125–8.

78. Siyoum M, Muleta M, Gebretsadik T, Gelan E, Ketema T, Teshome T, et al. Quality of life and associated factors of kidney transplant patients in Ethiopia Surgery , Saint Paul Hospital Millennium Medical College , Addis Ababa , Ethiopia ; 2 Public Health , Saint Paul Hospital Millennium Medical College ,

Addis Ababa , Ethiopia . 2020;104(September):2019–20.

79. Fiebiger W, Mitterbauer C, Oberbauer R. Health-related quality of life outcomes after kidney transplantation [Internet]. Health Qual. Life Outcomes2004 [cited 2021 Jan 20];2:2. Available from: /pmc/articles/PMC317371/?report=abstract

80. Chisholm-Burns MA, Erickson SR, Spivey CA, Gruessner RW, Kaplan B. Patient Preference and Adherence Concurrent validity of kidney transplant questionnaire in US renal transplant recipients. 2011;Available from: http://dx.doi.org/10.2147/PPA.S24261

81. Tayebi A RA, , Ebadi A, Eynollahi B, Rafiyan Z KF. Investigation of renal transplantation patients' quality of life by kidney transplantation questionnaire (KTQ-25). Iran J Crit Care Nurs 2010;3(3):125–8.

82. Charfeddine K, Kharrat M, Yaich S, Jarraya F, Mkawar K, Hachicha J. of Kidney Diseases and Transplantation Renal Data from the Arab World Infection in Kidney Transplant Recipients in Tunisia. 2002;13(2):195–8.

83. Muehrer RJ. Sexuality , an important component of the quality of life of the kidney transplant recipient . Transplant Rev [Internet] 2009;23(4):214–23. Available from: http://dx.doi.org/10.1016/j.trre.2009.06.001

84. Jindal R.M, Ryan J.J, Sajjad I, Murthy M.H, Baines L.S. Kidney Transplantation and Gender Disparity - Abstract - American Journal of Nephrology 2005, Vol. 25, No. 5 - Karger Publishers [Internet]. [cited 2021 Oct 25];Available from: https://www.karger.com/Article/Abstract/87920

85. Esbon NW. Prevalence and Determinants of Dyslipidemias Among Renal. MPharm Dissertation, 2018;

86. Neipp M, Karavul B, Jackobs S, zu Vilsendorf AM, Richter N, Becker T, et al. Quality of Life in Adult Transplant Recipients More than 15 Years after Kidney Transplantation. Transplantation [Internet] 2006 [cited 2021 Jan 12];81(12):1640–4. Available from: http://journals.lww.com/00007890-200606270-00006

87. Maru R. M. Gastrointestinal Symptoms and Gastrointestinal Quality of Life in

Renal Transplant Patients : a Descriptive Cross Sectional Study for the Award of the Degree of Master of Medicine ( Internal. 2016;

88. Jassal S V., Schaubel DE, Fenton SSA. Baseline comorbidity in kidney transplant recipients: A comparison of comorbidity indices. Am J Kidney Dis 2005;46(1):136–42.

89. Afifi A, Karim MA. Renal replacement therapy in Egypt: First annual report of the Egyptian Society of Nephrology, 1996. East. Mediterr. Heal. J.1999;5(5):1023–9.

90. Journal A. Special Issue: KDIGO Clinical Practice Guideline for the Care of Kidney Transplant Recipients. Am J Transplant 2009;9:S1–155.

91. Guerra G, Ciancio G, Gaynor JJ, Zarak A, Brown R, Hanson L, et al. Randomized trial of immunosuppressive regimens in renal transplantation. J Am Soc Nephrol 2011;22(9):1758–68.

92. Hilbrands LB, Hoitsma AJ, Koene RAP. The effect of immunosuppressive drugs on quality of life after renal transplantation. Transplantation 1995;59(9):1263–70.

93. Gallon LG, Winoto J, Leventhal JR, Parker MA, Kaufman DB. Effect of prednisone versus no prednisone as part of maintenance immunosuppression on long-term renal transplant function. Clin J Am Soc Nephrol 2006;1(5):1029–38.

94. Davies NM, Grinyo´2 JG, Heading R, Maes B, Meier-Kriesche H-U, Oellerich M. Gastrointestinal side effects of mycophenolic acid in renal transplant patients: a reappraisal. Available from: https://academic.oup.com/ndt/article/22/9/2440/1842291

95. Butler JA, Roderick P, Mullee M, Mason JC, Peveler RC. Frequency and impact of nonadherence to immunosuppressants after renal transplantation: a systematic review. Transplantation [Internet] 2004 [cited 2021 Apr 15];77(5):769–76. Available from: http://journals.lww.com/00007890-200403150-00025

96. Griva K, Neo HLM, Vathsala A. Unintentional and intentional non-adherence to immunosuppressive medications in renal transplant recipients. Int J Clin Pharm [Internet] 2018;40(5):1234–41. Available from: https://doi.org/10.1007/s11096-

018-0652-6

97. Shih MH, Tsai CH. Factors associated with adherence to immunosuppressive therapy among transplant recipients. J Nurs 2014;61(4):21–5.

98. Pflugrad H, Nösel P, Ding X, Schmitz B, Lanfermann H, Barg-Hock H, et al. Brain function and metabolism in patients with long-term tacrolimus therapy after kidney transplantation in comparison to patients after liver transplantation. PLoS One [Internet] 2020 [cited 2021 Oct 23];15(3):e0229759. Available from: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0229759

99. Rostami Z, Tavallaii S-A, Jahani Y, Einollahi B. Assessment of Quality of Life in a Single-Center Transplantation Population Using the Kidney Transplant Questionnaire-25 Questionnaire. TPS 2011;43:590–1.

100. Koller A, Denhaerynck K, Moons P, Steiger J, Bock A, De Geest S. Distress associated with adverse effects of immunosuppressive medication in kidney transplant recipients. Prog Transplant 2010;20(1):40–6.

101. Bossola M, Arena M, Urciuolo F, Antocicco M, Pepe G, Calabrò GE, et al. Fatigue in Kidney Transplantation: A Systematic Review and Meta-Analysis. Diagnostics [Internet] 2021 [cited 2021 Oct 28];11(5). Available from: /pmc/articles/PMC8147914/

102. Fiebiger W, Mitterbauer C, Oberbauer R. Health-related quality of life outcomes after kidney transplantation [Internet]. Health Qual. Life Outcomes2004 [cited 2021 Jan 12];2(1):2. Available from: http://hqlo.biomedcentral.com/articles/10.1186/1477-7525-2-2

103. Hamedan MS, Aliha JM, Aliha JM. Relationship between Immunosuppressive Medications Adherence and Quality of Life and Some Patient Factors in Renal Transplant Patients in Iran. Glob J Health Sci 2014;6(4).

104. Jones J, Damery S, Allen K, Nicholas J, Baharani J, Combes G. Open access "You have got a foreign body in there": renal transplantation, unexpected mild-to-moderate distress and patients' support needs: a qualitative study. BMJ Open

[Internet] 2020;10:35627. Available from: http://bmjopen.bmj.com/

105. Fardeazar FE, Solhi M, Soola AH, Amani F. Depressive symptoms and associated factors among kidney transplant recipients. Electron J Gen Med 2018;15(6).

106. Rebollo P, Ortega F, Ortega T, Valdés C. Health and Quality of Life Outcomes Spanish validation of the "Kidney Transplant Questionnaire": a useful instrument for assessing health related quality of life in kidney transplant patients Mónica García-Mendoza †1 and Ernesto Gómez †3 [Internet]. 2003. Available from: http://www.hqlo.com/content/1/1/56

107. Rosenberger J, Van Dijk JP, Nagyova I, Zezula I, Geckova AM, Roland R, et al. Predictors of perceived health status in patients after kidney transplantation. Transplantation 2006;81(9):1306–10.

108. Rosenberger J, Geckova AM, van Dijk JP, Roland R, van den Heuvel WJA, Groothoff JW. Factors modifying stress from adverse effects of immunosuppressive medication in kidney transplant recipients. Clin Transplant [Internet] 2005 [cited 2021 Jan 28];19(1):70–6. Available from: https://pubmed.ncbi.nlm.nih.gov/15659137/

109. Neipp M, Karavul B, Jackobs S, Zu Vilsendorf AM, Richter N, Becker T, et al. Quality of life in adult transplant recipients more than 15 years after kidney transplantation. Transplantation 2006;81(12):1640–4.

110. Dukes JL, Seelam S, Lentine KL, Schnitzler MA, Neri L. Health-related quality of life in kidney transplant patients with diabetes. Clin Transplant 2013;27(5):6–10.

111. Gebremedhin T, Workicho A, Angaw DA. Health-related quality of life and its associated factors among adult patients with type II diabetes attending Mizan Tepi University Teaching Hospital, Southwest Ethiopia. BMJ Open Diabetes Res Care 2019;7(1):1–8.

## APPENDICES

Appendix 1: Eligibility screening form

Appendix 2: Participant Information and Consent Form (English Version)

| Renal Transplant Out Patient Clinic<br>Unique identifier_____ | | |
|---|---|---|
| **Criteria** | **Remark** | |
| Adult aged ≥ 18 years | YES ☐ | NO ☐ |
| Received transplant ≥ 3months | YES ☐ | NO ☐ |
| On follow up at KNH, renal transplant clinic | YES ☐ | NO ☐ |
| Not mentally challenged | YES ☐ | NO ☐ |
| Patient not too weak | YES ☐ | NO ☐ |
| No symptoms of organ failure | YES ☐ | NO ☐ |
| Given consent | YES ☐ | NO ☐ |
| If all **yes**, the participant to fill the questionnaire | | |

**ADULT PARTICIPANT INFORMATION AND CONSENT FORM FOR ENROLLMENT IN THE STUDY**

**Title of Study**: Impact of immunosuppressant therapies and transplantation on health related quality of life among renal transplant recipients at Kenyatta national hospital.

**Principal Investigator\and institutional affiliation:**

**Dr. Phaustine Adhiambo**, Master of Pharmacy in Clinical Pharmacy student, Department of Pharmaceutics and Pharmacy Practice, School of Pharmacy, University of Nairobi

**Supervisors/Co-Investigators and institutional affiliation:**

**Dr. G.D. Nyamu**, Senior Lecturer, Department of Pharmaceutics, and Pharmacy Practice, School of Pharmacy, University of Nairobi.
**Dr. S. Opanga**, Senior Lecturer, Department of Pharmaceutics, and pharmacy, School of Pharmacy, University of Nairobi

**Introduction:**

I would like to bring to your attention a research being conducted by the above named researchers.
The purpose of this consent form is to give you detailed information about the study so that you make an informed decision on whether to participate or not. You are free to ask questions regarding, what will happen to you as a participant, the potential risks, or benefits, the rights you have as a participant or any other information. When your concerns are addressed and you feel satisfied with the study, you are free to enroll into the study by giving consent and signing your name on this form.
You should understand the principles in medical research which apply to participants namely:

i. Participation in this study is totally voluntary.

ii. You are free to withdraw from the study at any point without necessarily giving reason for your withdrawal.

iii. Refusal to participate in the study will not affect the normal services you are entitled to in this health facility or others. A copy of this form will be provided to you for your records.

May I continue? **YES** ☐ **NO** ☐

This study has the approval of Kenyatta National Hospital-University of Nairobi Ethics and Research Committee via protocol No._____

**What is this study about?**

The purpose of this study is to assess the well-being of patients who have a kidney transplant as well as look at issues that impacting on their general health from the patient's perspective. The findings of this study will help your doctor better manage you given that some factors may be corrected to improve your health.

**What will happen if you decide to be in this research study?**

If you consent to participate in this study, you will be interviewed privately, answering questions relevant to this study. You will be asked questions about your general health including emotional as well as medication problems you have experienced since the transplant This interview will take approximately 20 minutes of your time. Additionally, the interviewer will look at your medical file for medication history. Your telephone number or address may be requested in case further clarification is needed for this study. Your number will not be shared with any other person for other purposes except the study.

**Are there any risks or harms discomforts associated with this study?**

In this study you will not be exposed to any invasive procedures. However, you could suffer a loss of privacy. To minimize this risk, every measure will be put in place to prevent breach of confidentiality. You will be interviewed in a private setting. Moreover, a code number will be used to refer to you in computer database that is password-protected, and all paper records will be kept in a well-secured cabinet.

**Are there any benefits to being in this study?**

There will be no direct benefits to you. However, the results of this study will be useful for improving the quality of care received by you and future patients.

**Will being in this study cost you anything?**

This study will require you to spare about 20 minutes to answer questions relevant to this study. However, participating in this study will not cost you any money.

**Will you get a refund for any money spent as part of this study?**

There will be no reimbursement for participating in this study as no expenses will be incurred by you as a participant.

**What if you have questions in the future?**

In case you have any additional concerns about being part of this study, please send a text message, or call the investigator on the following number:

Dr. Phaustine Adhiambo (0710214767). You may also contact my supervisor, Dr. G.D. Nyamu (0722403671). If you need additional information about your rights as a research participant, please contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee through the telephone number 2726300 Ext. 44102 or the email address: uonknh_erc@uonbi.ac.ke.

The researchers in this study should compensate you for the charges you incur if you call these numbers for study-related queries.

**What are your other choices?**

Participating in this research is voluntary. You are free to decline to participate or to withdraw from this study at any point without dire consequence.

**Researcher's statement**

Having explained all the relevant details of this study to the above participant, I trust that he/she has understood and voluntarily given his/her consent to participate.

**Researcher's Name**: _____

**Date**: _____

**Signature: _____**

**CONSENT FORM**

**Participant's statement**

This is to confirm that I have read and been explained information on this consent form. I have fully understood what the study entails. My questions and concerns have been addressed. Additionally, the risks and benefits have been explained. I understand that my participation is voluntary and I can withdraw from the study at any time without injustice or loss of any benefit. I also know that all efforts will be made to keep information regarding my personal identity confidential.

**Name of participant _____**

**Date _____**

**Signature of participant _____**

For more information, please contact the investigator, Phaustine Adhiambo at cell phone number 0710214767, from 8 am to 5 pm during week days.

Appendix 2: Participant information and consent form (Kiswahili Version)

**HABARI YA MSHIRIKI WA WAKUU NA FOMU YA RIDHARA YA UANDIKISHAJI KATIKA MASOMO**

**Kichwa cha Utafiti:** Athari ya dawa zinazozuia kukataliwa kwa figo na ubora wenye uhusiano wa kiafya miongoni mwa wagonjwa waliopandikizwa figo katika hospitali ya kitaifa ya kenyatta

**Mtafiti Mkuu**

**Dk. Phaustine Adhiambo**.

**Watafiti Wengine pia wasimamizi:**

1. **Dk. GD Nyamu**, Mhadhiri Mwandamizi, Idara yaPharmaceutics and Pharmacy Practice Shule ya Famasia, Chuo Kikuu cha Nairobi.

2. **Dk. Opanga**, Mhadhiri Mwandamizi, Idara ya Pharmaceutics and Pharmacy Practice, Shule ya Famasia, Chuo Kikuu cha Nairobi

**Utangulizi:**

Ningependa kukuletea utafiti unaofanywa na watafiti waliotajwa hapo juu.
Kusudi la fomu hii ya idhini ni kukupa maelezo ya kina juu ya utafiti ili uweze kufanya uamuzi sahihi ikiwa utashiriki au la. Uko huru kuuliza maswali kuhusu, nini kitatokea kwako kama mshiriki, hatari zinazoweza kutokea, au faida, haki ulizonazo kama mshiriki au habari nyingine yoyote. Unapojiskia kurithika na utafiti, uko huru kujiandikisha kwenye somo kwa kutoa idhini na kujiandikisha kwenye fomu hii.
Unapaswa kuelewa kanuni katika utafiti wa matibabu ambayo inatumika kwa washiriki ambayo ni:
i) Kushiriki katika utafiti huu ni hiari kabisa.
ii) Uko huru kutoa utafiti katika hatua yoyote bila kutoa sababu ya kujitoa yako.
iii) Kukataa kushiriki katika utafiti hakutaathiri huduma za kawaida unazostahili katika

kituo hiki cha afya au nyingine.

Utapokea nakala ya fomu hii kwa rekodi zako.

Naweza kuendelea? **NDIYO** ☐ **HAPANA** ☐

Kamati ya Kitaifa ya Hospitali ya Maadili na Utafiti ya Kenya ya Kenyatta na Chuo Kikuu cha Nairobi imeidhinisha utafiti huu kupitia itifaki nambari

**Je! Utafiti huu unahusu nini?**

Kusudi la utafiti huu ni kutathmini ustawi wa wagonjwa ambao wana upandikizaji wa figo na pia kuangalia maswala ambayo yanaathiri afya yao kwa jumla kutoka kwa mtazamo wa mgonjwa. Matokeo ya utafiti huu yatasaidia daktari wako kukusimamia vizuri ikizingatiwa kuwa sababu zingine zinaweza kusahihishwa ili kuboresha afya yako.

**Je! Ni nini kitatokea ikiwa utaamua kuwa katika utafiti huu?**

Ikiwa unakubali kushiriki katika utafiti huu, utahojiwa kwa faragha, ukijibu maswali yanayofaa kwa utafiti huu. Utaulizwa maswali kuhusu afya yako kwa ujumla ikiwa ni pamoja na hisia pamoja na matatizo ya dawa una uzoefu tangu kupandikiza mahojiano haya itachukua dakika 20 ya muda wako. Zaidi ya hayo, mhoji itaangalia faili yako kwa ajili ya historia ya dawa. Mtafiti anaweza kuuliza nambari yako ya simu au anwani ili ladba kesi ikitaka kufafanuliwa zaidi baadaye. Nambari yako haitashirikiwa na mtu mwingine yeyote kwa madhumuni mengine isipokuwa utafiti.

**Je! Kuna hatari yoyote au hudhuru usumbufu unaohusishwa na utafiti huu?**

Katika utafiti huu hautakuwa wazi kwa taratibu zozote za uvamizi. Walakini, unaweza kupoteza faragha. Ili kupunguza hatari hii, kila hatua itawekwa ili kuzuia ukiukaji wa usiri. Utahojiwa katika mazingira ya kibinafsi. Kwa kuongezea, nambari ya nambari itatumiwa kukurejelea kwenye hifadhidata ya kompyuta ambayo inalindwa na nenosiri, na rekodi zote za karatasi zitahifadhiwa kwenye baraza la mawaziri lenye usalama.

**Je! Kuna faida yoyote kuwa katika utafiti huu?**

Hakutakuwa na faida ya moja kwa moja kwako. Walakini, matokeo ya utafiti huu yatakuwa muhimu kwa kuboresha ubora wa huduma unayopokea na wewe na wagonjwa wa baadaye.

**Je! Kuwa katika utafiti huu kutagharimu chochote?**

Utafiti huu utakuhitaji uepushe kama dakika 20 kujibu maswali yanayohusiana na utafiti huu. Walakini, kushiriki katika utafiti huu hakutakugharimu pesa yoyote.

**Je! Utapata marejesho ya pesa yoyote uliyotumia kama sehemu ya utafiti huu?**

Hakutakuwa na marejesho ya kushiriki katika utafiti huu kwani hakuna gharama itakayotokana na wewe kama mshiriki.

**Je! Ikiwa una maswali katika siku zijazo?**

Ikiwa una wasiwasi wowote wa ziada juu ya kuwa sehemu ya utafiti huu, tafadhali tuma ujumbe mfupi, au piga simu kwa mpelelezi kwa nambari ifuatayo:

**Dr. Phaustine Adhiambo (0710214767**). Unaweza pia kuwasiliana na msimamizi wangu, **Dk. GD Nyamu (0 722403671).** Ikiwa unahitaji habari zaidi kuhusu haki yako kama mshiriki wa utafiti, tafadhali wasiliana na Katibu / Mwenyekiti, Hospitali ya Kitaifa ya Kenyatta-Kamati ya Maadili na Utafiti ya Chuo Kikuu cha Nairobi kupitia nambari ya simu 2726300 Ext. 44102 au anwani ya barua pepe: uonknh_erc@uonbi.ac.ke.

Watafiti wa utafiti huu wanapaswa kulipia fidia kwa mashtaka unayopata ikiwa utapiga nambari hizi kwa maswali yanayohusiana na utafiti.

**Je! Chaguzi zako zingine ni zipi?**

Kushiriki katika utafiti huu h ni hiari. Uko huru kukataa kushiriki au kujiondoa kwenye utafiti huu wakati wowote bila matokeo mabaya.

**Kauli ya mtafiti**

Baada ya kuelezea maelezo yote muhimu ya utafiti huu kwa mshiriki hapo juu, ninaamini kwamba ameelewa na kwa hiari yake ameruhusu kushiriki.

**Jina la Mtafiti: _____**

**Tarehe: _____**

**Saini: _ _____**

**FOMU YA RIDHARA**

**Taarifa ya mshiriki**

Hii ni kudhibitisha kuwa nimesoma na kuelezewa habari kwenye fomu hii ya idhini. Nimeelewa kikamilifu kile utafiti unamaanisha. Maswali na wasiwasi wangu umeshughulikiwa. Kwa kuongezea, hatari na faida zimeelezewa. Ninaelewa kwamba ushiriki wangu ni wa hiari na naweza kujitoa katika utafiti wakati wowote bila udhalimu au kupoteza faida yoyote. Ninajua pia kuwa juhudi zote zitafanywa kutunza habari kuhusu kitambulisho changu binafsi kuwa siri.

**Jina la mshiriki_____**

**Tarehe _____**

**Saini ya mshiriki _____**

Kwa habari zaidi, tafadhali wasiliana na mpelelezi, Phaustine Adhiambo kwa simu ya rununu 0710214767, kutoka saa mbili asubuhi hadi saa kumi na moja jioni wakati wa siku za wiki.

**Appendix 3: Data collection forms (English Version)**

**SECTION A**

**BIODATA**

Patient unique key……  Study number ……

Patient initials……..  Date of enrollment……...

**SOCIO-DEMOGRAPHICS**

1. What is your age(AGE)_____ (years)?
2. Patient's gender (0) Female (1) Male
3. What is your marital status?

   (0) Single (1) Married (2) Widowed (3) Divorced (4) Separated
4. Level of education (0) Primary (2) Secondary (3) College (4) University
5. Where do you live(Residence) (0) Rural (1) Urban?
6. What is your employment status (0) Employed (1) Retired (2) Unemployed?
7. Patient socio-economic status based on employment

   (0) Low socio-economic status (1) High socio-economic status
8. History of alcohol consumption (0) Uses alcohol (1) No alcohol use
9. History of smoking (0) Smoker (1) Non-Smoker
10. What is your denomination. (0) Christian (1) Traditional (2) Muslim (3) Other

**SECTION B**

**MEDICAL HISTORY/COMMORBIDITIES**

1. How long has the patient had the transplanted kidney? ____months
2. What was the cause of ESRD in this patient?

   (0) Diabetes mellitus (1) Hypertension (2) Diabetes mellitus and Hypertension

(3) Glomerular disease (4) Obstructive uropathy (5) HIV associated nephropathy (6) Cancer (7) Others specify_____

3. What was the source of the patient's kidney?

   (0) Living donor –relative (1) Living donor-non relative (2) Cadaver(deceased)

   (3) other, specify_____

4. What type of dialysis and duration, was the patient on before the transplantation?

   (0) Peritoneal dialysis (1) Hemodialysis

   Duration _____

5. What is the patient creatinine levels at the time of the clinic visit_____?

6. What comorbidities does the patient have, how long have they had the condition, what drugs and dose are they on for the condition/s

| **CONDITION** | **DURATION** | **DRUG USED** | **DOSAGE** |
|---|---|---|---|
| | | | |
| | | | |
| | | | |

6. What immunosuppressive drug is the patient on (Tick all the relevant)?

| **IMMUNOSUPPRESSIVE PROTOCOL** | **DOSAGE** | **Duration of therapy(Days)** |
|---|---|---|
| | | |

| | | |
|---|---|---|
| Corticosteroids,<br><br>Specify_____ | | |
| Tacrolimus | | |
| Mycophenolate | | |
| Everolimus | | |
| Cyclosporin | | |
| Sirolimus | | |
| Azathioprine | | |
| Anti-thymocyte globulins | | |
| Monoclonal antibodies<br><br>Specify e.g Basiliximab | | |
| Other, specify_____ | | |

**PATIENT COMPLIANCE/ADHERENCE TO MEDICATION**

1. How many days in the past 4 weeks have you missed taking a dose of your immunosuppressive medication?

   (0) None (1) Once (2) 2-3times

2. How many days in the past 4 weeks have you skipped two or more doses of your immunosuppressive medication in a row?

   (0) None (1) Once (2) 2 times (3) 3 times (4) 4 times (5) > 4 times

3. Have you in the past 4 weeks taken your immunosuppressive medication more than 2 h before or after the prescribed dosing time.

   (0) No (1) Yes

   If yes, how many times (1) Once (1) 2-3times (3) 4-5 times (4) every 2-3 days (5) every day

4. In the previous 4 weeks, have you reduced or increased the dose of your immunosuppressant drug without your doctor telling you to do so.

   (0) No (1) Yes

5. Have you in the past 4 weeks stopped taking your immunosuppressive medication without telling your doctor

   (0) No (1) Yes

6. What are the reasons for non –adherence

(0) Financial constrains (1) Fear of side effects (2) Too many medication (3) Forgetfulness

**SIDE EFFECTS OF IMMUNOSUPRESSANTS IN RENAL TRANSPLANT RECIPIENT**

Kindly tick all the relevant problems that the patient has experienced due to immunosuppressant medication in the table below.

| Complication | Response (Yes or No) |
|---|---|
| 1. Excessive hair growth | |
| 2. Weight gain | |
| 3. Fatigue | |
| 4. Headache | |
| 5. Acne | |
| 6. Diarrhea | |
| 7. Trouble sleeping | |
| 8. Hair loss | |
| 9. Gingival overgrowth | |
| 10. Increased blood sugar | |
| 11. Hypertension | |
| 12. Tremors | |

**SECTION C**

**KIDNEY TRANSPLANT QUESTINNAIRE (KTQ-25) FOR HEALTH RELATED QUALITY OF LIFE ASSESSMENT.**

**This questionnaire is designed to learn how you have been feeling during the last two weeks. You will be asked about how tired you have been feeling, how your mood has been, and what physical symptoms or problems you have experienced**.

Please **mark up to 6 problems or symptoms** from the list that follows that you have experienced frequently during the last two weeks. If you have experienced more than 6, please mark the 6 that were most troublesome.

1) Loss of weight and muscle
2) Decreased mental ability
3) Itchy/dry skin
4) Infections
5) Hypotension
6) Embarrassment caused by appearance or access site
7) Aching, tired legs
8) Coughing during day or night
9) Very little strength
10) Side-effects from medications
11) Forgetfulness
12) Confusion
13) Aching bones
14) Trouble getting to sleep
15) Regulating bowel movements
16) Constipation or diarrhea
17) Vomiting
18) Headaches
19) Nausea or upset stomach
20) Shivering
21) Waking up during the night
22) Loss of appetite
23) Lightheadedness or dizziness during daily activities
24) Shortness of breath in daily activities
25) Decreased sexual ability
26) Difficulty focusing attention
27) Difficulty concentrating
28) Need to rest frequently because of shortness of breath
29) Increased appetite
30) Excessive weight gain
31) Acne
32) Trouble getting a good night's sleep
33) Muscle pain

Other: _____

1. **Of the 6 items that you listed, please choose the problem that troubles you most and indicate how much trouble or distress you have had during the last two weeks by choosing one of the following options**:
    1) A very great deal of trouble or distress
    2) A great deal of trouble or distress
    3) A good deal of trouble or distress
    4) A moderate amount of trouble or distress
    5) Some trouble or distress
    6) Very little trouble or distress
    7) No trouble or distress

2. **Of the 6 items that you listed, please choose the problem that troubles you the second most and indicate how much trouble or distress you have had during the last two weeks by choosing one of the following options**:
    1) A very great deal of trouble or distress
    2) A great deal of trouble or distress
    3) A good deal of trouble or distress
    4) A moderate amount of trouble or distress
    5) Some trouble or distress
    6) Very little trouble or distress
    7) No trouble or distress
3. **Of the 6 items that you listed, please choose the problem that troubles you the third most and indicate how much trouble or distress you have had during the last two weeks by choosing one of the following options**:
    1) A very great deal of trouble or distress
    2) A great deal of trouble or distress
    3) A good deal of trouble or distress
    4) A moderate amount of trouble or distress
    5) Some trouble or distress
    6) Very little trouble or distress
    7) No trouble or distress
4. **Of the 6 items that you listed, please choose the problem that troubles you the fourth most and indicate how much trouble or distress you have had during the last two weeks by choosing one of the following options:**
    1) A very great deal of trouble or distress
    2) A great deal of trouble or distress
    3) A good deal of trouble or distress
    4) A moderate amount of trouble or distress
    5) Some trouble or distress

6) Very little trouble or distress
7) No trouble or distress

5. **Of the 6 items that you listed, please choose the problem that troubles you the fifth most and indicate how much trouble or distress you have had during the last two weeks by choosing one of the following options**:
   1) A very great deal of trouble or distress
   2) A great deal of trouble or distress
   3) A good deal of trouble or distress
   4) A moderate amount of trouble or distress
   5) Some trouble or distress
   6) Very little trouble or distress
   7) No trouble or distress
6. **Of the 6 items that you listed, please choose the problem that troubles you the sixth most and indicate how much trouble or distress you have had during the last two weeks by choosing one of the following options:**
   1) A very great deal of trouble or distress
   2) A great deal of trouble or distress
   3) A good deal of trouble or distress
   4) A moderate amount of trouble or distress
   5) Some trouble or distress
   6) Very little trouble or distress
   7) No trouble or distress
7. **In the last two weeks, how much trouble or distress have you had because of excessive appetite?**
   1) A very great deal of trouble or distress
   2) A great deal of trouble or distress
   3) A good deal of trouble or distress
   4) A moderate amount of trouble or distress
   5) Some trouble or distress
   6) Very little trouble or distress
   7) No trouble or distress

8. **In the last two weeks, how much trouble or distress have you had because of excessive hair growth?**
   1) A very great deal of trouble or distress
   2) A great deal of trouble or distress
   3) A good deal of trouble or distress
   4) A moderate amount of trouble or distress

5) Some trouble or distress
6) Very little trouble or distress
7) No trouble or distress

9. **In the last two weeks, how much trouble or distress have you had because of excessive weight?**
   1) A very great deal of trouble or distress
   2) A great deal of trouble or distress
   3) A good deal of trouble or distress
   4) A moderate amount of trouble or distress
   5) Some trouble or distress
   6) Very little trouble or distress
   7) No trouble or distress
10. **In the last two weeks, how much trouble or distress have you had because of acne?**
   1) A very great deal of trouble or distress
   2) A great deal of trouble or distress
   3) A good deal of trouble or distress
   4) A moderate amount of trouble or distress
   5) Some trouble or distress
   6) Very little trouble or distress
   7) No trouble or distress

11. **During the past two weeks, how often have you felt weak?**
   1) All of the time
   2) Most of the time
   3) A good bit of the time
   4) Some of the time
   5) A little of the time
   6) Hardly any of the time
   7) None of the time
12. **How often during the past two weeks have you felt sluggish?**
   1) All of the time
   2) Most of the time
   3) A good bit of the time
   4) Some of the time
   5) A little of the time

6) Hardly any of the time
7) None of the time

13. **During the past two weeks, how much trouble or difficulty have you had because of having very little strength?**
    1) A very great deal of trouble or difficulty
    2) A great deal of trouble or difficulty
    3) A good deal of trouble or difficulty
    4) A moderate amount of trouble or difficulty
    5) Some trouble or difficulty
    6) Very little trouble or difficulty
    7) No trouble or difficulty at all
14. **During the past two weeks, how much trouble or difficulty have you had because of increased tiredness?**
    1) A very great deal of trouble or difficulty
    2) A great deal of trouble or difficulty
    3) A good deal of trouble or difficulty
    4) A moderate amount of trouble or difficulty
    5) Some trouble or difficulty
    6) Very little trouble or difficulty
    7) No trouble or difficulty at all
15. **During the past two weeks, how often have you felt low in energy?**
    1) All of the time
    2) Most of the time
    3) A good bit of the time
    4) Some of the time
    5) A little of the time
    6) Hardly any of the time
    7) None of the time
16. **How often during the past two weeks have you felt fear or panic related to rejection of the kidney?**
    1) All of the time
    2) Most of the time
    3) A good bit of the time
    4) Some of the time
    5) A little of the time
    6) Hardly any of the time
    7) None of the time
17. **How often during the past two weeks have you felt uncertain about your future?**

1) All of the time
2) Most of the time
3) A good bit of the time
4) Some of the time
5) A little of the time
6) Hardly any of the time
7) None of the time

**18. How often during the past two weeks have you felt worried?**

1) All of the time
2) Most of the time
3) A good bit of the time
4) Some of the time
5) A little of the time
6) Hardly any of the time
7) None of the time

**19. How often during the past two weeks have you felt protective of your transplant?**

1) All of the time
2) Most of the time
3) A good bit of the time
4) Some of the time
5) A little of the time
6) Hardly any of the time
7) None of the time

**20. How often in the last two weeks have you felt depressed?**

1) All of the time
2) Most of the time
3) A good bit of the time
4) Some of the time
5) A little of the time
6) Hardly any of the time
7) None of the time

**21. How often during the past two weeks have you felt stubborn?**

1) All of the time
2) Most of the time
3) A good bit of the time
4) Some of the time
5) A little of the time
6) Hardly any of the time
7) None of the time

22. **How often in the last two weeks have you felt anxious?**
    1) All of the time
    2) Most of the time
    3) A good bit of the time
    4) Some of the time
    5) A little of the time
    6) Hardly any of the time
    7) None of the time
23. **How often during the past two weeks have you felt impatient?**
    1) All of the time
    2) Most of the time
    3) A good bit of the time
    4) Some of the time
    5) A little of the time
    6) Hardly any of the time
    7) None of the time
24. **How often in the last two weeks have you felt irritable or difficult to get along with?**
    1) All of the time
    2) Most of the time
    3) A good bit of the time
    4) Some of the time
    5) A little of the time
    6) Hardly any of the time
    7) None of the time

25. **How often in the last two weeks have you felt generally frustrated?**
    1) All of the time
    2) Most of the time
    3) A good bit of the time
    4) Some of the time
    5) A little of the time
    6) Hardly any of the time
    7) None of the time.

## Appendix 4: KNH/UON Ethics and Research Commiittee

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/201

11th June 2021

Phaustine Adhiambo Onyango
Reg. No. U56/34534/2019
Dept.of Pharmaceutics and Pharmacy Practice
School of Pharmacy
College of Health Sciences
University of Nairobi

APPROVED 1 JUN 2021 KNH/UoN-ERC

Dear Phaustine,

**RESEARCH PROPOSAL:** **IMPACT OF IMMUNOSUPPRESSANT THERAPIES AND TRANSPLANTATION ON HEALTH RELATED QUALITY OF LIFE AMONG RENAL TRANSPLANT RECIPIENTS AT KENYATTA NATIONAL HOSPITAL (P70/02/2021)**

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 11th June 2021 – 10th June 2022.

This approval is subject to compliance with the following requirements:

i. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
ii. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
iii. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
v. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (Attach a comprehensive progress report to support the renewal).
vii. Submission of an executive summary report within 90 days upon completion of the study.

This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

For more details consult the KNH- UoN ERC website **http://www.erc.uonbi.ac.ke**

Yours sincerely,

**PROF. M. L. CHINDIA**
**SECRETARY, KNH-UoN ERC**

C.C. The Principal, College of Health Sciences, UoN
The Senior Director, CS, KNH
The Chair, KNH- UoN ERC
The Dean, School of Pharmacy, UoN
The Chair, Dept. of Pharmaceutics and Pharmacy Practice, UoN
Supervisor: Dr. David G. Nyamu, Dept.of Pharmaceutics and Pharmacy Practice, UoN
Dr.Sylvia Opanga, Dept.of Pharmaceutics and Pharmacy Practice,UoN

Appendix 5: KNH Study Registration Certificate

KNH/R&P/FORM/01

KENYATTA NATIONAL HOSPITAL
P.O. Box 20723-00202 Nairob

Tel.: 2726300/2726450/2726565
Research & Programs: Ext. 44705
Fax: 2725272
Email:

## Study Registration Certificate

1. Name of the Principal Investigator/Researcher
PHAUSTINE ADHIAMBO ONYANGO
2. Email address: phaustheadhi@gmail.com Tel No. 0710214767
3. Contact person (if different from PI).....
4. Email address: ..... Tel No. .....
5. Study Title
IMPACT OF IMMUNOSUPPRESSANT THERAPIES AND TRANSPLANTATION ON HEALTH RELATED QUALITY OF LIFE AMONG RENAL TRANSPLANT RECIPIENTS AT KNH
6. Department where the study will be conducted RENAL TRANSPLANT CLINIC
*(Please attach copy of Abstract)*
7. Endorsed by KNH Head of Department where study will be conducted.
Name ..... Signature ..... Date 14.6.21
8. KNH Ethics Research Committee approved study number _____
*(Please attach copy of ERC approval)*
9. I PHAUSTINE ADHIAMBO ONYANGO commit to submit a report of my study findings to the Department where the study will be conducted and to the Department of Medical Research.
Signature ..... Date 15TH JUNE, 2021
10. Study Registration number (Dept/Number/Year) Dental/164/2021
(To be completed by Medical Research Department)
11. Research and Program Stamp 16 JUN 2021

All studies conducted at Kenyatta National Hospital must be registered with the Department of Medical Research and investigators must commit to share results with the hospital.

Version 2: August, 2014

**Appendix 6: Plagiarism Report**

IMPACT OF IMMUNOSUPPRESSANT THERAPIES AND TRANSPLANTATION ON HEALTH RELATED QUALITY OF LIFE AMONG RENAL TRANSPLANT RECIPIENTS AT KENYATTA NATIONAL HOSPITAL

ORIGINALITY REPORT

| 14% | 12% | 7% | 1% |
|---|---|---|---|
| SIMILARITY INDEX | INTERNET SOURCES | PUBLICATIONS | STUDENT PAPERS |

PRIMARY SOURCES

| | | |
|---|---|---|
| 1 | Handbook of Disease Burdens and Quality of Life Measures, 2010.<br>Publication | 1% |
| 2 | erepository.uonbi.ac.ke<br>Internet Source | 1% |
| 3 | www.dovepress.com<br>Internet Source | <1% |
| 4 | dspace.alquds.edu<br>Internet Source | <1% |
| 5 | link.springer.com<br>Internet Source | <1% |
| 6 | bmcnephrol.biomedcentral.com<br>Internet Source | <1% |
| 7 | onlinelibrary.wiley.com<br>Internet Source | <1% |
| 8 | www.ahrq.gov<br>Internet Source | <1% |