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DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS

IRON STATUS AMONG KIDNEY TRANSPLANT RECIPIENTS AT KENYATTA NATIONAL HOSPITAL

BY

DR. MWANGO ANSON KIEMA

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DECLARATION

I hereby certify that this dissertation is my original work and it has not been presented to the best of my knowledge for award of a degree in any other university.

Signature: _____ **Date:** 08/11/2023.

Dr Mwango Anson Kiema

MBChB (University of Nairobi.)

H58/**34296/2019**

Principal Investigator

SUPERVISORS

This dissertation has been submitted with the approval of my supervisors:

1. **Prof. S.O. McLigeyo,**
   Professor of Medicine
   Consultant Physician and Nephrologist
   Department of Clinical Medicine and Therapeutics
   University of Nairobi.
   Signed..... Date 8/11/23

2. **Dr P.O. Oyiro,**
   Lecturer
   Consultant Physician and Haemato-Oncologist
   Department of Clinical Medicine and Therapeutics
   University of Nairobi.
   Signed..... Date 10/11/23

CHAIRMAN OF THE DEPARTMENT

Prof. E.O. Amayo,

Professor of Medicine

Consultant Physician and Neurologist

Department of Clinical Medicine and Therapeutics

University of Nairobi.

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
DEPARTMENT OF CLINICAL MEDICINE & THERAPEUTICS
P.O. Box 19676-00202 NAIROBI

Signed..... Date..14/11/2023.....

DEDICATION

This work is dedicated to my parents Eng. Fred Mwango and Martha Mwango for their continued support and encouragement.

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I thank the Almighty God for health, strength and blessing in undertaking this project

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TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ABBREVIATIONS AND ACRONYMS

ACEIs -	Angiotensin Converting Enzyme Inhibitors
AST -	American Society of Transplantation
BMI -	Body Mass Index
CKD -	Chronic Kidney Disease
DBP -	Diastolic Blood Pressure
DMT1 -	Divalent Metal Transporter 1
ECLIA -	Electrochemiluminiscence immunoassay
EPO -	Erythropoietin
ESKD -	End Stage Kidney Disease
FGF 23-	Fibroblast Growth Factor 23
GFR -	Glomerular Filtration Rate
IRE -	Iron Responsive Element
IRP -	Iron Regulatory Protein
KDIGO -	Kidney Disease Improving Global Outcomes
KNH -	Kenyatta National Hospital
KTRs -	Kidney Transplant Recipients
QoL -	Quality of Life
SBP -	Systolic Blood Pressure
TSAT -	Transferrin Saturation
UTR -	Untranslated Region
WHO -	World Health Organization

ABSTRACT

Background: Abnormalities of iron homeostasis have been described in kidney transplant recipients (KTRs) with iron deficiency being more prevalent. These abnormalities have a significant impact on morbidity and mortality among KTRs. However, the iron status among post-kidney transplant recipients in Kenya is unknown. This study aimed to determine the iron status in this population of KTRs.

Methods: This was a cross-sectional descriptive study that evaluated KTRs attending the kidney transplant clinic at Kenyatta National Hospital who were 13 years and above with informed consent/assent and were at least six (6) months post-transplantation. The study period was between 1st November 2022 and 18th January 2023. Selected demographic, clinical and laboratory data were obtained from the patients and patients' files by using a data extraction proforma. Subsequently, serum samples for determination of serum ferritin and transferrin saturation levels were collected. Serum transferrin was measured using immunoturbidimetric assay while serum ferritin was determined using electrochemiluminescence assay. The prevalence of iron abnormalities was presented as a proportion and reported as a percentage. The prevalence of anaemia in this population of KTRs was calculated as a proportion and reported as a percentage. Selected socio-demographic and clinical characteristics were used to describe KTRs with and without iron deficiency. The student's t-test and Mann Whitney U test was used to compare continuous variables while categorical variables were compared using Chi-square test of association. A p-value of ≤ 0.05 was considered to be significant at a 95% confidence.

Results: Ninety-one (91) KTRs were screened for eligibility out of which 77 were consecutively enrolled on the study The mean age was 47±15 years with a male: female ratio of 2.08:1. The median serum ferritin was 408.0 (104.0-1072.0) µg/L with a mean transferrin saturation (TSAT) at 24.8±4.8 µmol/L. Twenty-three (30%) of KTRs had iron deficiency, 41 (53%) were iron replete whereas 13(17%) were found have iron overload. We observed a higher platelet count in those with iron deficiency. The prevalence of anaemia was 30% and 11 (48%) were categorized as mild anaemia. In this study, 5(22%) of the KTRs with anaemia had iron deficiency.

Conclusion: This study demonstrated a 30% prevalence of iron deficiency and a 17% prevalence of iron overload among KTRs at KNH. These abnormalities may negatively impact graft function and survival.

CHAPTER ONE: INTRODUCTION

Kidney transplantation is the preferred modality of kidney replacement therapy due to its significant reduction in morbidity and improved quality of life (QoL)[1]. Iron metabolism imbalance (deficiency or overload) are common in patients with chronic kidney disease (CKD) and are associated with adverse outcomes[2]. These states may persist in the kidney transplant recipient (KTR). Iron status of the KTR has been shown to be key in transplantation medicine[3].

Iron deficiency is prevalent among the KTR population and represents a significant cause of post-transplantation anaemia. Studies have shown that iron deficiency in this population is associated with a greater mortality risk[4,5]. This risk was considered significant even independent of anaemia. Nevertheless, a small proportion of these patients have features of iron overload. Accumulation of iron in the hepatocytes and high ferritin levels are noted in patients with end-stage kidney disease (ESKD). In this population, these factors are associated with reduced survival. It has been noted that the negative effects of hyperferritinemia(>1100µg/l) remain even following transplantation. Iron deficiency remains the commoner of the two states in the kidney transplant population[3,6,7].

Therefore, identification of the various abnormalities of iron levels offers a potentially modifiable risk factor that could result in improved allograft and patient outcomes in kidney transplantation. Moreover, the evaluation of iron status helps stem or minimize the development of anaemia, a significant cardiovascular risk factor in the KTR. This study aims to determine the iron status among the kidney transplant population and more so, help determine the extent of iron deficiency and potential associated factors for this modifiable state.

CHAPTER TWO: LITERATURE REVIEW

2.1 Epidemiology

Iron deficiency is the most common cause of anaemia globally. More than 1.1 billion people have iron deficiency anaemia with its associated effects. Dietary iron deficiency was responsible for 30 million Years Lived with Disability (YLD) in the year 2017. In keeping with global trends, the incidence, prevalence and YLD of iron deficiency anaemia (IDA) in Sub-Saharan Africa has improved albeit slightly[8]. However, the global estimates of iron deficiency without anaemia are largely unknown. It is estimated that the prevalence of iron deficiency is two times that of iron deficiency anaemia[9].

In CKD, the prevalence of iron deficiency is relatively high. Iron deficiency anaemia is a known complication of CKD. Fishbane and his colleagues in an analysis of a dataset from the USA comprising non-dialytic CKD demonstrated an iron deficiency prevalence of 70% with higher percentages seen in women[10]. Awan et al however showed a prevalence of absolute iron deficiency of 30% in a non-dialysis-dependent population in the USA. Their study also showed a prevalence of 19% for functional iron deficiency[11]. The prevalence of iron overload in the non-dialytic CKD is much lower[12].

In the haemodialysis-treated population, several studies have also demonstrated higher prevalence of iron deficiency[13–15].Unpublished data on a Kenyan population of 165 haemodialysis-treated ESKD patients showed that iron deficiency had a prevalence of 61.3% with 2.4% having iron overload. The higher proportion of these patients had absolute iron deficiency. The prevalence of anaemia was 98.2% while that of iron deficiency anaemia was 34.5%[16].

Among KTRs, the clinical picture is postulated to be similar. In a study by Moore et al, up to 60% of KTRs without iron deficiency at transplantation became iron deficient at six months

post-transplantation. Several associated causes were noted to be inflammation, the effects of some medications and an increased need for iron post-transplant[17].

A study done in the Netherlands by Eisenga et al showed a prevalence of iron deficiency of 30% and iron deficiency anaemia of 13% among KTRs at one-year post-transplantation. In this study, the overall prevalence of anaemia was 34%[5]. In an evaluation of KTRs at Rabin Medical Centre by Schechter et al, it was noted that nutritional deficiencies accounted for 61% of KTRs with anaemia. Of note, 34.7% were attributable to iron deficiency[18].

In a study by Lorenz et al, it was noted that iron deficiency in KTRs was 20.1% and that associations were especially noted with male gender, creatinine clearance, transferrin saturation (TSAT), polycystic kidney disease and age[19]. Higher values of iron deficiency without anaemia were recorded by Jimeno et al among long-term KTRs and investigated an association with angiotensin converting enzyme inhibitors (ACEIs) use[20]. Research findings from other cohort studies show a prevalence of 6-47%. The median time post-kidney transplantation in these studies was 4 years[21–23].

A study done by Ayerdem et al noted a prevalence of iron deficiency without anaemia at 25% and 17% in two cohorts of KTRs. The presence of iron deficiency without anaemia was especially noted at higher GFRs and contrast was noted with CKD patients and the general population. As kidney dysfunction worsened, anaemia became more prevalent and iron deficiency without anaemia declined[24].

On the other hand, iron overload has not been extensively studied in the KTR population. In a study by Lorenz et al of a cohort of KTRs, it was noted that the prevalence of iron overload was 9.4% with a decrease noted over time. Among these KTR with iron overload, 36.3% of these had mutations in the *HFE* gene and these mutations influenced liver function[25].

A study done by Bilar et al demonstrated a prevalence of iron overload of 15% among KTRs. In this study, iron overload was associated with male sex, higher haemoglobin levels and a higher amount of parenteral iron utilised prior to transplantation. Higher hepcidin levels were noted in the group with iron overload reflecting the positive feedback exerted by the elevated ferritin levels[26].

Despite the above, iron deficiency as well as overload among the KTRs is largely overlooked and is an under-recognized problem especially here in Africa. In Kenya, unpublished data from a tertiary facility documented a prevalence of 21.3% of anaemia among KTRs[27]. Nonetheless, the associated causes for anaemia in that population were not elucidated. In our setup, little is known concerning these iron status abnormalities among KTRs. This, therefore, forms an important area of research.

2.2 Iron metabolism

Iron represents a key element in the metabolism of all living organisms contributing to numerous biologic processes. [28]. In as much as iron has immense benefits, it potentially has toxic effects both in excess as well as in deficiency states. Thus, the body developed proteins and homeostatic mechanisms to ensure just adequate amounts are availed for use.

The average adult human contains 4-5g of iron majority of which is in erythrocyte haemoglobin (65%) and is recycled by reticuloendothelial macrophages. The rest is distributed in storage forms, myoglobin, tissue compartments as well as in transferrin and a labile pool in varying concentrations (Figure 1)[29].

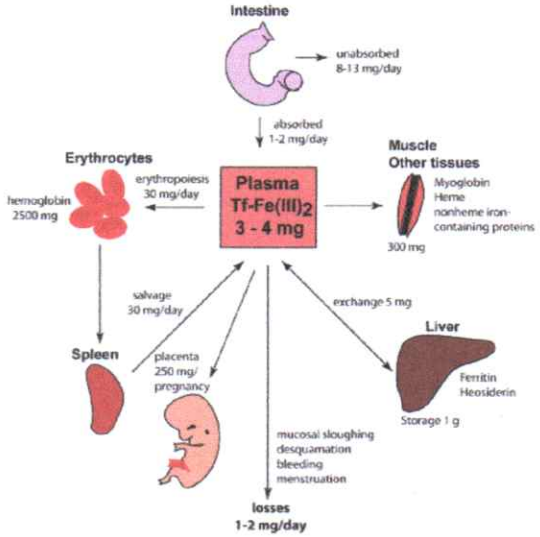

Figure 1 Metabolism of iron

Source: Pantopoulos K, Porwal SK, Tartakoff A et al Mechanisms of mammalian iron homeostasis. Biochemistry. 2012 Jul 24;51(29):5705-24. doi: 10.1021/bi300752r. Epub 2012 Jul 9. PMID: 22703180; PMCID: PMC3572738.

Our bodies have no efficient mechanism for iron excretion. The key areas are in controlling dietary iron uptake and release of iron[30]. Hepcidin regulates this balance. It is synthesized by the liver and exerts its effects on the enterocytes, macrophages and hepatocytes. This is achieved through binding to ferroportin and inducing its degradation. The key regulators of this hormone are iron, erythropoiesis and inflammation. Enhancing the activity of this hormone reduces the availability of iron whereas reducing the activity of hepcidin increases the availability of iron. The processes including the proteins involved are depicted in Figure 2.

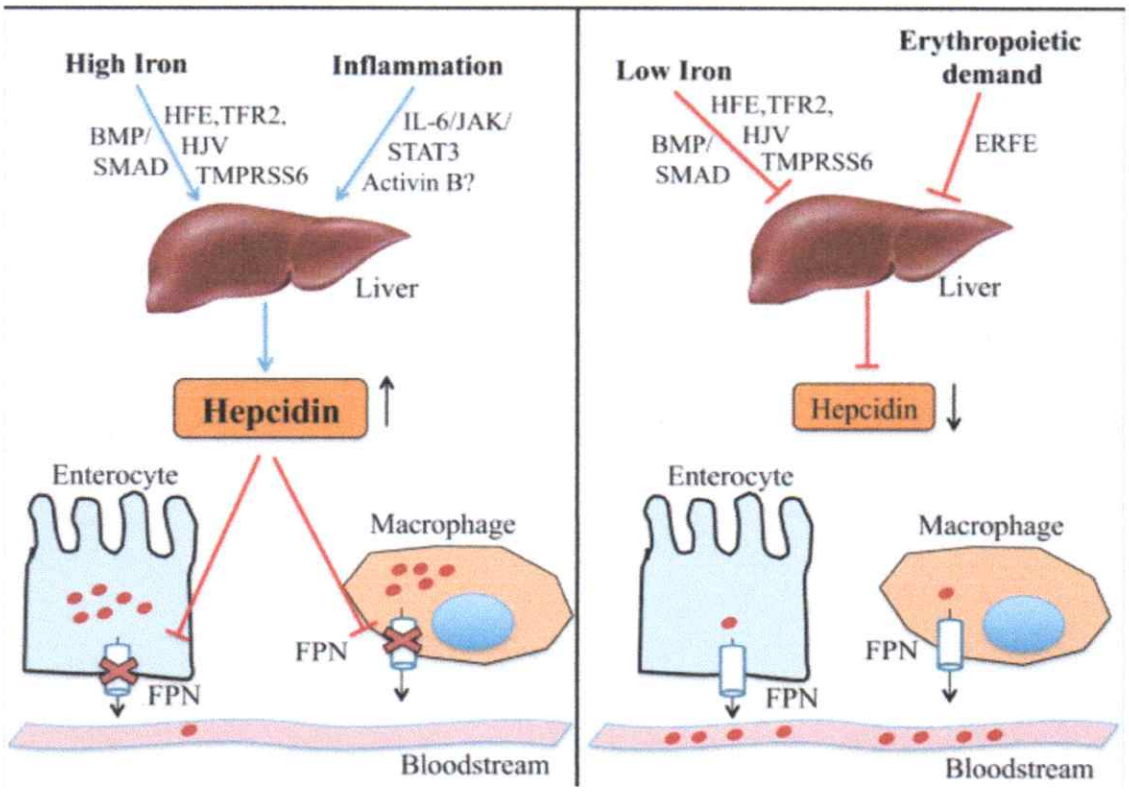

Figure 2 Systemic regulation of iron balance

Source: Dev S, Babitt JL. Overview of iron metabolism in health and disease. Hemodial Int. 2017 Jun;21 Suppl 1(Suppl 1): S6-S20. doi: 10.1111/hdi.12542. Epub 2017 Mar 15. PMID: 28296010; PMCID: PMC5977983.

Abbreviations: BMP, Bone morphogenetic protein; ERFE, Erythroferrone; FPN, Ferroportin; HFE, Hereditary hemochromatosis protein; HJV, Hemojuvelin; IL-6, Interleukin 6; JAK, Janus kinase; SMAD, Suppressor of Mothers Against Decapentaplegic; STAT 3, Signal transducer and activators of transcription 3; TMPRSS6, Transmembrane serine protease 6; TRF2, Transferrin receptor.

2.3 Classification of iron deficiency

It can be classified into two main forms:

Absolute iron deficiency: This refers to a state where the iron stores in the body are decreased. It is a serum ferritin of less than 100 ng/ml.

Functional/relative iron deficiency: This refers to a state that reflects altered iron distribution. It is a situation either where iron recruitment from the stores is inefficient or where there is increased erythropoiesis mediated endogenously or exogenously. The total body iron in this case is not reduced[31]. It is equivalent to serum ferritin of between 100-300ng/ml and TSAT of $\leq$ 20%.

If left unchecked, iron deficiency progresses to iron deficiency anaemia.

2.4 Pathophysiology of iron deficiency

Iron deficiency greatly affects iron homeostasis. It triggers adaptive mechanisms on the hepcidin-ferroportin axis, the iron regulatory protein (IRP)/iron-responsive element (IRE) component among others[9]. These mechanisms are intended to optimize iron use for erythropoiesis and counteract the physiological inhibition of iron absorption. The mechanisms of adaptation are:

a) *Systemic regulation*

Through liver hepcidin it binds to its receptor ferroportin thus blocking the export of iron and as well inducing the degradation of ferroportin[32,33]. Therefore, to enhance iron uptake, this hormone has to be suppressed. (Figure 3)

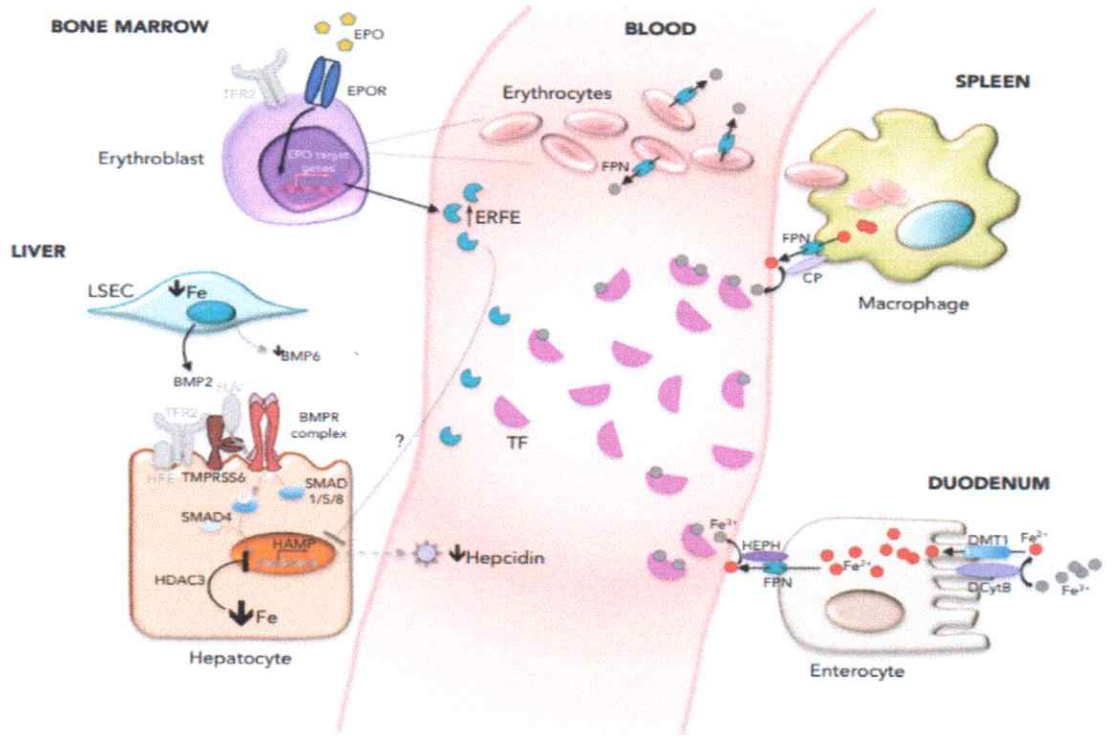

Figure 3 Role of hepcidin in iron deficiency

Source: Camaschella C. Iron deficiency. Blood. 2019 Jan 3;133(1):30-39. doi: 10.1182/blood-2018-05-815944. Epub 2018 Nov 6. PMID: 30401704.

Abbreviations: BMP2, Bone morphogenetic protein 2; BMPR, Bone morphogenetic protein receptor; DMT1, Divalent metal transporter 1; DCytB, Duodenal Cytochrome B; EPO, Erythropoietin; EPOR, Erythropoietin receptor; ERFE, Erythroferrone; HAMP, Hepcidin; HDAC3, Histone deacetylase 3; HEPH, Hephaestin; HFE, Hereditary hemochromatosis protein; LSEC, Liver sinusoidal endothelial cell; SMAD, Suppressor of Mothers Against Decapentaplegic; TMPRSS6, Transmembrane serine protease 6; TF, Transferrin; TRF2, Transferrin receptor 2.

Erythroferrone plays a greater role in cases where the haemoglobin count is low as opposed to the state of iron deficiency without anaemia[34,35].

At the level of the intestine, expression of HIF2α increases expression of both DMT1 and DCYTB on the apical side as well as increasing iron exporter ferroportin at the basolateral membrane[36].

Reuse of iron from phagocytosis of old erythrocytes by the reticuloendothelial system provides another source of iron. However, levels of iron recycled from hypochromic red blood cells reduces in parallel with the severity of iron deficiency since the haemoglobin content per cell is

reduced. One mechanism related to red blood cell ferroportin, which is increased in iron deficiency, contributes to maintaining plasma iron levels[9,37].

b) *Cellular regulation*

Control of cellular iron content is IRP-dependent. IRPs bind to the IREs in untranslated regions (UTRs) of iron genes to post-transcriptionally coordinate proteins of iron absorption, export, use and storage[38]. Still, there are IRP-independent mechanisms such as mTOR inhibition and ferritinophagy where cells recover their own stored iron for use[39,40].

c) *Iron Restricted Erythropoiesis*

Iron deficiency reduces early erythropoiesis and enhances iron utilization for terminal erythropoiesis. In vitro studies showed that the deficiency state blunts the EPO responsiveness of early progenitors through the inactivation of iron-dependent aconitase whereas terminal red blood cell production is altered with decreased apoptosis and an increased number of late erythroblasts[41]. With the onset of anaemia and hypoxia, EPO increases and other several factors inhibit hepcidin to improve iron supply. In this case, when there is an increase in the number of erythroblasts with a limited supply of iron, both haem and globin translation are reduced. This coordination between haem and globin produces microcytic-hypochromic erythrocytes. The optimization of erythropoiesis may preserve iron for vital functions[9].

2.5 Aetiology of iron deficiency in KTRs

The aetiology of iron deficiency in KTRs is multifactorial. In the early post-transplant phase, inadequate stores at the time of transplantation, blood loss and repeat phlebotomy may contribute to this occurrence. As effective erythropoiesis is enhanced following successful transplantation, the increasing demand arising from increased EPO production by the grafted kidney could account for this.

Other factors that are considered include gastrointestinal malignancies. Such include colonic cancer and intestinal post-transplant lymphoproliferative disorders. Erythrocyturia in KTRs with urinary tract malignancies can contribute to the iron deficiency state. Further in this population,

medications have been shown to contribute. These medications that have shown some association include immunosuppressive medications and proton pump inhibitors among others. Nonetheless, it has been noted that the use of EPO stimulant products before kidney transplantation is associated with reduced ferritin decline post-transplantation[42,43] Figure 4 gives an illustration of these potential aetiological factors.

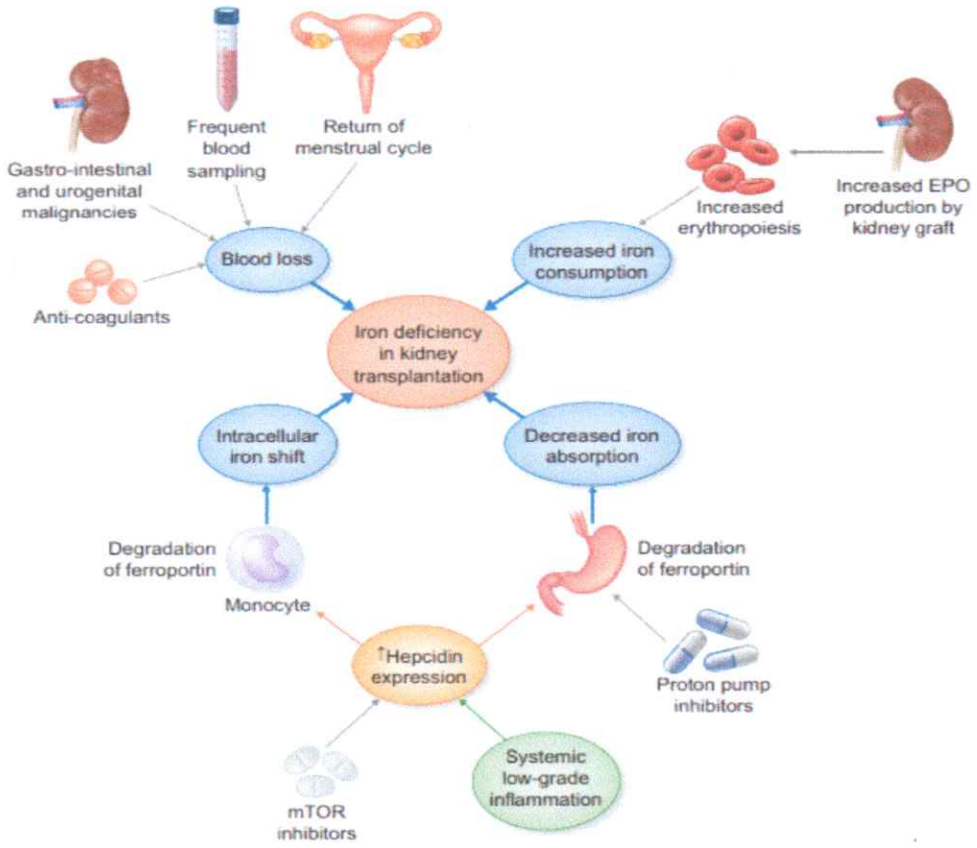

Figure 4 Aetiology of Iron Deficiency in KTRs

Source: Vinke JSJ, Francke MI, Eisenga MF, et al. Iron deficiency after kidney transplantation. Nephrol Dial Transplant. 2020;1–10

Abbreviations: EPO, Erythropoietin; mTOR, Mammalian target of rapamycin.

2.6 Consequences of iron deficiency in KTRs.

Iron deficiency is linked with a greater mortality risk in two studies of KTRs with good graft function (eGFR 52±20 ml/min/1.73m^2; eGFR 53±9 ml/min/1.73m^2, respectively)[4,5]. A few

studies have demonstrated that iron deficiency influences graft outcomes and kidney damage[4,44].

The underlying reasons for these adverse outcomes have not yet been clearly spelt out. However, it is imperative to note that iron deficiency is associated with increased cardiovascular risk. This could be attributed to the endogenous EPO resistance that is noted in iron deficiency[45]. Further, the association of a deficient state and heart failure and impaired cardiac myocyte function may contribute to poor outcomes[46].

Additionally, these poor outcomes of KTRs with iron deficiency could be attributed to increased myocardial workload, negative left ventricular remodelling and left ventricular hypertrophy as well as to the CKD, reduced nutritional state in cardiac cachexia and low albumin[47].

Some studies demonstrated the link between iron deficiency and increased mortality could also in part be mediated by FGF23 as an intermediary[48].

Iron deficiency and kidney allograft outcomes

There is paucity of data concerning iron deficiency and kidney allograft outcomes. Nonetheless, some studies have demonstrated that iron-replete KTRs are associated with higher allograft function and allograft survival[4,44]. Additionally, Gvili and colleagues demonstrated reduced iron levels as a factor contributing to a poor allograft outcome [49]. Iron deficiency is known to contribute to post-transplantation anaemia. Anaemia in the post-kidney transplant recipient is associated with kidney allograft loss[50–52].

Iron and the immune system.

Iron is key for T cell homeostasis[3,42]. Figure 5 shows that a deficient state negatively impacts cellular immunity.

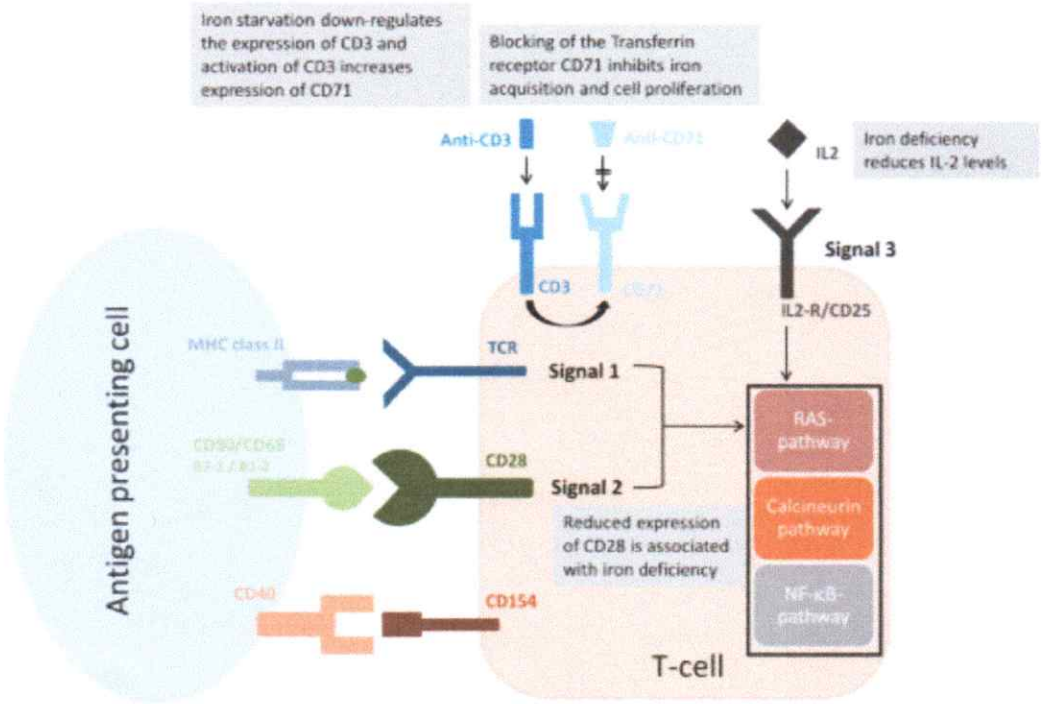

Figure 5 Iron deficiency and the cellular immunity

Source: Schaefer B, Effenberger M, Zoller H. Iron metabolism in transplantation. Transpl Int. 2014;27(11):1109–17.

Abbreviations: CD, Cluster of differentiation; IL-2, Interleukin 2; MHC, Major histocompatibility complex; NF-kB, Nuclear factor kappa-light-chain-enhancer of activated B cells; RAS, Rat sarcoma; TCR, T cell receptor.

Emerging evidence has demonstrated that this deficient state hampers antibody responses independent of its T-cell effects[53].

In as much as macrophages have a part in iron storage and recycling of iron, iron on the other hand plays a role in macrophage proliferation, differentiation and function. Alteration in iron utilization affects all these components[54].

2.7 Iron overload

Little is known about iron overload and its underlying mechanisms in KTRs. However, it is known that most of the cases of systemic iron overload are related to primary hereditary haemochromatosis, ineffective erythropoiesis or are transfusion-related. In primary hereditary haemochromatosis, the gene mutations therein result in an inability of the liver to detect rising iron levels hence leading to lower levels of hepcidin, unregulated ferroportin activity, inability to inhibit iron absorption or release from macrophages and thus iron accumulation in tissues, Ineffective erythropoiesis is seen in iron loading anaemias such as thalassemia. In these forms, the hepcidin levels are suppressed with consequent increased dietary absorption of iron and secondary iron overload. In the dialytic period, the higher number of blood transfusions and the use of iron supplementation could result in a secondary iron overload state that could persist post-transplantation. Other factors that could contribute to similar biochemical features of an overload state include the underlying kidney disease, malignancies, liver disease as well as infections[30,55].

In these overload states, highly reactive non-transferrin bound iron predominates and accumulates in organs such as the liver, heart and endocrine glands leading to complications such as cirrhosis, cardiomyopathies, diabetes and other endocrinopathies[30]. This potentially puts the KTRs at risk for adverse outcomes. In addition, a positive iron balance is associated with a depressed immune response increasing the risk for infection in this population as well as complicating their care. In the population of KTRs, higher serum ferritin have been shown to be associated with an increased risk of mortality[7,56].

2.8 Diagnostic evaluation of iron status

Bone marrow studies are considered the gold standard for the investigation and diagnosis of iron deficiency. This technique usually highlights the lack of stainable iron in the smears. However, this method is invasive and the differentiation of iron within macrophages from artefacts requires skill and experience. Due to their increasing availability, serum markers of iron deficiency are more utilized[31,57].

One such marker is ferritin. Reduced concentrations are a hallmark of iron deficiency and usually reflect depleted stores. Nonetheless, in the context of multiple comorbidities, the ferritin threshold for diagnosis is even higher. These cut-offs assist with therapeutic decisions as well. The World Health Organization (WHO) recommends its use in populations for the assessment of iron deficiency with varying cut-offs for various conditions[58]. In a population of healthy individuals, some studies that were screening for iron deficiency showed a sensitivity of 63-100% and specificity of 92-98%. On the flip side, in patients undergoing medical care, a pooled sensitivity of 79% and specificity of 98% was noted[59,60].

A variety of methods are utilised to assess and determine all possible iron statuses. These include non-radiometric assays [enzyme-linked immunoassays (ELISA) and electrochemiluminescence immunoassay (ECLIA)], radiometric assays (radioimmunoassay and immunoradiometric) and agglutination-based assays (turbidimetric and nephelometric). These methods are all recommended by WHO and are comparable[58,61]. However, it has been shown that ECLIA methods provide better precision and accuracy. This method has also been shown to retain the ability to measure over wide ranges of concentrations especially so at low or high ferritin levels. Further it carries a low risk of radioactive contamination compared to radiometric assays[62].

Another marker is transferrin saturation (TSAT). This test provides a measure of total iron availability in the body and the equilibrium between the release of iron from stores and use for erythropoiesis. It is equivalent to the ratio of serum iron and total iron binding capacity. A low TSAT (<20 %) implies iron deficiency regardless of the underlying mechanism. This is especially useful in patients with chronic inflammatory states. Additionally, it has utility in prognosis[63,64]. When used in association with serum ferritin, there is an increase in the diagnostic performance of both markers[65,66].

The iron levels can be determined using various analytical methods such as spectrophotometry, chromatography, voltammetry, titration among others. Spectrophotometric methods are simple, widely used and accurately assess iron levels. Among these spectrophotometric methods are the ferrozine reaction method which has been shown to be adequate in serum iron determination and at a relatively lower cost as compared to newer methods[67,68].

Determination of the liver iron content through biopsy or imaging represents the gold standard for diagnosis of iron overload states. These methods are invasive, expensive and largely unavailable. Other methods such as the labile plasma iron estimation have not yet established clinical utility. Serum ferritin and TSAT are available and effective methods. Ferritin levels have shown some correlation with the liver and iron cardiac content in the body and the use together with TSAT enhances this. Indeed, a normal serum ferritin with a TSAT < 45% excludes iron overload with a 97% negative predictive value[55,69].

2.9 Study justification

Kidney transplantation is an effective therapy for ESKD. Iron status is an important determinant of outcomes among transplant recipients. Iron deficiency is a prevalent condition among KTRs. Studies done in KTRs have shown that iron deficiency is linked to poor graft outcomes and contributes to the development of post-transplantation anaemia with its resultant adverse consequences. When present in transplant recipients, iron deficiency is associated with significant morbidity and premature mortality.

Anecdotal observations indicate that the monitoring iron deficiency is suboptimal at KNH. Previous studies have revealed that iron status is investigated and appropriate therapy instituted in only 25% of KTRs[70,71]. Other studies have shown that in KTRs with anaemia only 26-46% had their iron status checked[19,21,72,73]. The authors concluded that determination of iron status among KTRs may provide information that aids in the management of these patients.

Among the KTR patients on treatment and follow-up at KNH, there is no data on the extent of this deficiency, its management and any associated factors. The KTR population at the KNH renal unit continues to grow with complications such as iron deficiency posing a significant impact on health-related quality of life. Thus, the information generated will help bring to the fore the unrecognized burden of this deficient state. Further, it will contribute to the body of knowledge in the field of transplantation in general as well as provide useful reference material.

This study aims to determine the iron status and consequently, the prevalence of the deficient state in KTRs at KNH as well as any associated factors. The results are expected to provide information to aid in the care of these recipients and sensitize healthcare workers on this commonly missed or ignored complication of kidney transplant. Moreover, it helps raise hypotheses for future studies such as the evaluation of the efficacy and outcomes of iron supplementation in this population as well as inform policy regarding the care of KTRs both pre- and post-operatively.

2.9 Research question

What is the iron status among kidney transplant recipients seen at the Kenyatta National Hospital?

2.10 Study objectives

Broad objective

To determine the iron status among KTRs attending the kidney transplant clinic at the KNH

Specific objectives

i. To determine the iron status among KTRs attending the KNH kidney transplant clinic.

ii. To describe the clinical and socio-demographic characteristics of KTRs with and without iron deficiency.

iii. To determine the prevalence of anaemia among KTRs attending the KNH kidney transplant clinic.

CHAPTER THREE: METHODOLOGY

3.1 Study design

This was a cross-sectional descriptive study.

3.2 Study area

This study was carried out at the KNH kidney transplant clinic. Kenyatta National Hospital is a national teaching referral hospital situated in Nairobi. It is the biggest facility in Eastern and Central Africa. The hospital has a bed capacity of 1800 beds. It serves the population from across Kenya, as well as the East and Central African region. It also serves as the teaching hospital for the University of Nairobi, Faculty of Health Sciences for both the undergraduate and postgraduate programs. It runs general and specialized clinics and in-patient services in medical, surgical, obstetrics and gynaecology, paediatrics, ophthalmology and dental care.

The kidney transplant clinic is carried out every Tuesday at the transplant block located in the renal unit. It is attended by kidney transplant recipients and donors, those who have been transplanted and prospective donors. The clinic also attends to patients who had been transplanted in other health facilities both within and outside Kenya. About 100 patients are enrolled in this clinic and are on follow-up in the clinic. Each week about 14-16 KTRs attend the clinic.

3.3 Study population

The study population were kidney transplant recipients attending the kidney transplant clinic at KNH.

3.3.1 Population characteristics

Post KTRs aged 13 years and above with consent/assent and who are at least six (6) months post-transplant.

3.3.2 Outcome variables

Iron status definition:

Normal iron status : Serum ferritin levels of 100-500µg/L and transferrin saturation of 20-40%

Absolute Iron deficiency : Serum ferritin levels of < 100µg/L

Functional iron deficiency : Serum ferritin levels of 100-299µg/L and transferrin saturation of < 20%

Iron overload : Serum ferritin levels of >1000µg/L and transferrin saturation >45%

Anaemia:

Anaemia was defined according to the WHO and American Society of Transplantation (AST) criteria whereby haemoglobin levels of less than 13g/dl in males and 12g/dl in females was adopted. In males aged between 13-14, the cut-off used was 12g/dl in line with the above guidelines. The severity of anaemia was further classified according to the WHO criteria:

Table 1 Severity of anaemia

Population	**Mild anaemia**	**Moderate anaemia**	**Severe anaemia**
Children 12-14 years of age	11.0- 11.9 g/dL	8.0-10.9 g/dL	Less than 8.0g/dL
Non-pregnant women (15 years and above)	11.0- 11.9 g/dL	8.0- 10.9 g/dL	Less than 8.0 g/dL
Men (15 years of age and above)	11.0-12.9 g/dL	8.0-10.9 g/dL	Less than 8.0 g/dL

3.3.3 Inclusion criteria

i. KTRs who were at least 6 months post-transplant and were on follow-up at the kidney transplant clinic in KNH

ii. Consenting adults above 18 years of age and assenting persons over 13 years of age with consent from parents or guardians.

3.3.4 Exclusion criteria

i. Patients who declined to participate in the study.

3.4 Sample size determination

About 100 KTRs were on regular clinic attendance at KNH. On the basis of this number, the accessible population is described as finite (less than 10,000) therefore the relevant formula used to calculate sample size was:

$$n = \frac{Nz^2P(1-P)}{d^2(N-1)+Z^2P(1-P)}$$ [74]

where:

n= required sample size

N= the expected number of accessible population- total KTRs in KNH- 100

z= confidence level at 95% (standard value of 1.96)

p= estimated prevalence of iron deficiency (30%)[5]

d= margin of error (5%)

A minimum of 77 KTRs were required to be recruited into the study. For determination of iron overload a sample size of 67 KTRs was required using an estimated prevalence of 15%[26]. The

sample size needed to determine prevalence of anaemia was 75 KTRs using an estimated prevalence of 26%[24]. Thus, a minimum sample size of 77 KTRs was recruited.

3.5 Sampling procedure

All eligible patients were consecutively sampled till the desired sample size was achieved.

3.6 Recruitment and consenting procedure

All patients who had satisfied the inclusion criteria and signed the informed consent were recruited into the study. The study's principal investigator administered the consent forms to the study participants.

3.7 Screening and Recruitment

All who satisfied the inclusion criteria and subsequently signed an informed study consent were enrolled on the study and issued a unique study number.

3.8 Clinical methods

The patient's medical history was taken and documented in a data extraction proforma (see Appendix VI below). Sociodemographic data, duration post-transplantation, immunosuppressive medications, duration of ESKD, and donor age were documented. The KTRs' files were then perused to corroborate these aspects of history and also obtain additional data on the aetiology of ESKD. Blood pressure measurement (mmHg) was measured using a standard mercury sphygmomanometer. Height was measured in centimetres to the nearest 0.5cm barefooted, back and scalp against the wall using a stadiometer. This was then converted to meters. Weight was measured in kilograms to the nearest 0.5kg using a standard weighing scale and the Body Mass Index (BMI) was then calculated.

Selected details from the full blood count and kidney function test (urea, electrolytes and creatinine) done on the date of clinic review were recorded in the abstraction form. Estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease (MDRD) formula. Staging severity of CKD with kidney transplant was done using the guideline

by the Kidney Disease Improving Global Outcomes 2009 Clinical Care Practice Guideline for the Care of Kidney Transplant Recipients[75].

3.9 Laboratory methods

About 5mls of blood was drawn aseptically and placed in a labelled sterile plain vacutainer for measurement of ferritin, iron, transferrin and total iron binding capacity. The blood samples were immediately transferred to a cooler box at 4-8°C. The samples collected at the end of clinic day were transported for analysis. The analysis of the markers of iron status was carried out at the Pathologists Lancet Kenya laboratories.

Serum ferritin was assayed by electrochemiluminescence immunoassay (ECLIA) using COBAS® E 411 immunoassay analyser (see Appendix VII below). Serum iron and total iron binding capacity (TIBC) were assayed using COBAS INTEGRA® 400/800 based on the Ferro Zinc method without deproteinization (see Appendix VIII below). Transferrin saturation (TSAT) was then calculated from the serum iron and TIBC. Transferrin saturation is serum iron divided by TIBC and expressed as a percentage.

The samples were refrigerated at -20 degrees Celsius until the study was completed and the results presented and validated. After which they were discarded as per standard bio-safety procedures.

The kidney function tests were determined using automated clinical chemistry analyser Mindray Clinical Chemistry Analyser while the full blood count was determined using the automated CELL-DYN 3200. Both of these assays were carried out at the KNH renal unit laboratory.

3.10 Quality assurance

The standard operating procedures in all aspects of this study were adhered to at all times. The recommended procedure for specimen collection was adhered to at all times. This included phlebotomy site cleaning and the use of appropriate vacutainers. Careful labelling and proper storage of the specimens was done to minimize pre-analytical sources of errors. Standard operating procedures for laboratory analyses were followed.

The laboratory analyses for the iron status were outsourced from the Pathologists Lancet Kenya Laboratories since one (TSAT) is not routinely available in the KNH. This is located on 5th Ngong Avenue and is about 500 metres from KNH. This is a subsidiary of Cerba Lancet Africa and is an internationally accredited laboratory offering routine, specialized and esoteric tests. To minimize inter-assay variability, both tests of iron status were done in this laboratory.

The Pathologist Lancet Kenya Laboratories runs external and internal quality controls regularly.

The laboratory analyses for the full blood count and the kidney function tests were done at the KNH renal unit laboratory. This laboratory runs external and internal quality checks regularly.

3.11 Ethical consideration

Before starting this study, authority was sought from the University of Nairobi Department of Clinical Medicine and Therapeutics, as well as the KNH/UoN Ethics and Research Committee. The study was then registered with the KNH Research and Programs Department and KNH Renal Department. No patient was coerced into participating. No participant was discriminated against for refusing to join. Confidentiality was maintained by storing the study proformas in a lockable cabinet accessible only by the PI. Patient-identifiable data was not included in the data collection proforma. Patients were issued with a unique study number to conceal their identity. The information which was deemed crucial to the care of the patient was shared with the primary clinician.

3.12 Data analysis

Each study proforma was assigned a study-specific number to avoid duplication. All data collected was entered into a password-protected computer spreadsheet in Microsoft Excel 2016. Upon completion of entry, the hard copy forms were then stored safely in a lockable cabinet. The electronic file was backed up in three flash drives and stored offsite. Statistical analyses were done using Statistical Package for the Social Sciences (SPSS) version 21 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.).

Categorical variables were presented in tables as frequencies and percentages. Continuous variables had means and standard deviations (SD), medians and interquartile ranges (IQR) and calculated as appropriate.

The prevalence of iron deficiency is presented as a proportion and reported as a percentage. This was calculated as the total number of KTRs with iron deficiency divided by the total number of KTRs sampled. Selected characteristics of patients with and without iron deficiency were described in tabular form. The prevalence of anaemia in this population of KTRs was calculated as a proportion and reported as a percentage. This was calculated as the total number of KTRs with anaemia divided by the total number of KTRs sampled.

Between group comparisons were done using Student's t -test and Mann-Whitney U test for continuous variables and using Chi-square test of association for categorical variables. A p-value of ≤ 0.05 was considered to be significant at a 95% confidence.

CHAPTER FOUR: RESULTS

4.1 Participant recruitment

This study was conducted between 1st November 2022 and 18th January 2023. Ninety-one (91) patients were screened for eligibility from the list of KTRs attending the clinic out of which seventy-seven (77) were subsequently enrolled on the study. Figure 6 highlights the recruitment flow chart.

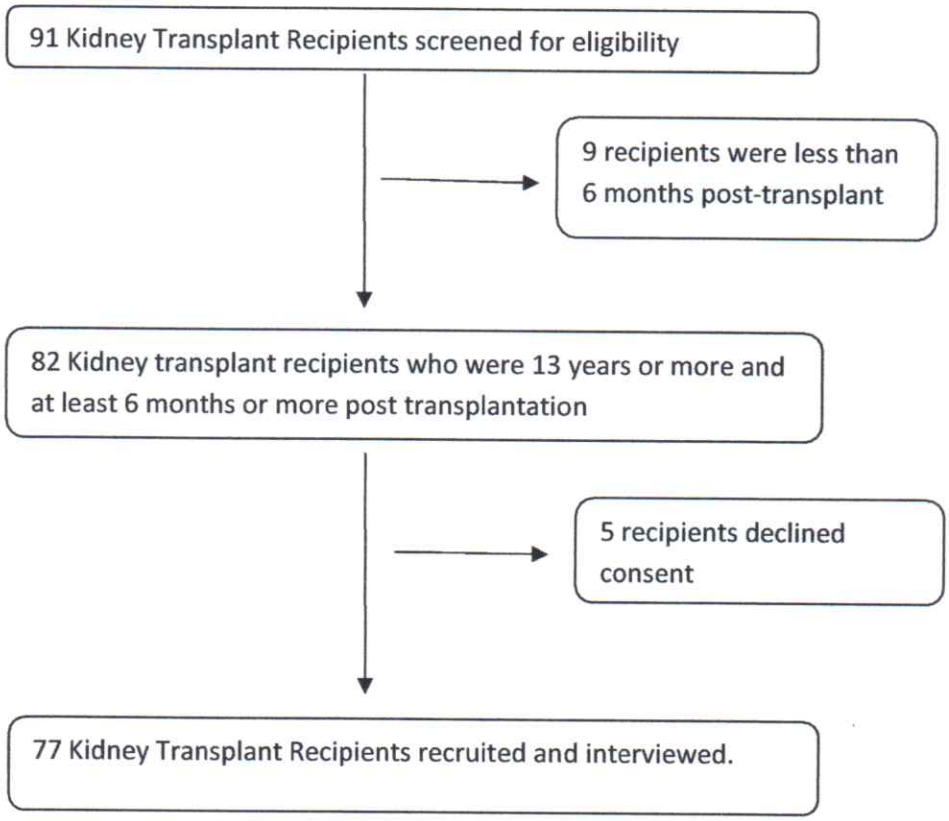

Figure 6 Recruitment flow chart

4.2 Sociodemographic Characteristics of kidney transplant recipients

The baseline sociodemographic characteristics of the study sample are shown in Table 2. The mean age was 47±15 years and included 52 (68%) males, a male: female ratio of 2.08:1. Thirty-four (44%) study participants were above the age of 50 years.

Among our KTR sample, 56 (73%) were married and 36 (47%) had attained a tertiary level of education. Forty-eight (62%) participants were engaged in employment either as self-employed or in formal employment. Additionally, 61 (79%) KTRs had no prior history of smoking.

Table 2 Socio-demographic characteristics of study participants

Characteristic	Overall *(n=77)*	Male *(n=52)*	Female *(n=25)*
Age in years, *Mean ± SD*	47 ± 15	48 ± 15	45 ± 16
Marital status, *n (%)*			
Single	18 (23)	11 (21)	7 (28)
Married	56 (73)	40 (77)	16 (64)
Widowed	3	1	2
Occupation, *n (%)*			
Unemployed	18 (24)	11 (21)	7 (28)
Employed	24 (31)	16 (30)	8 (32)
Self-employed	24 (31)	18 (35)	6 (24)
Retired	11 (14)	7 (14)	4 (16)
Education, *n (%)*			
None	1	1	0
Primary	5 (6)	5 (10)	0
Secondary	35 (46)	21 (40)	14 (56)
College	36 (47)	25 (48)	11 (44)
Smoking history, *n (%)*			
Never	61 (79)	36 (69)	25 (100)
Past	16 (21)	16 (31)	0

Abbreviations: n, number; SD, standard deviation

4.2 Clinical Characteristics of kidney transplant recipients

The baseline clinical characteristics of the sample are shown in Table 3. Glomerulonephritis was the most prevalent underlying kidney disease at 51%. Twenty (26%) of the study subjects had diabetes, 11 (14%) had hypertensive nephropathy and 2 (3%) had autosomal dominant polycystic kidney disease as the aetiologies for kidney disease. The median duration since transplantation

was 4.5 (2.7-8.3) years with a dialysis vintage of 18 (9.0-18.0) months. Among these patients, 75 (96%) were taking calcineurin inhibitors (cyclosporin A or tacrolimus) and 70 (91%) were on antimetabolites (mycophenolic acid analogues or azathioprine). The mean systolic blood pressure was 130±17 mmHg and the mean diastolic blood pressure was 81±12 mmHg. The average BMI was 24.7±4.8 kg/m^2. Sixty-one (79%) study participants had a previous history of blood transfusion. Twelve (16%) patients were on renin-angiotensin-aldosterone system (RAAS) blockade.

The median serum creatinine was 108.6 (87.7-141.0) µmol/l. Mean eGFR was 66.7±28.2 ml/min/1.73m^2 as calculated using the MDRD formula. Thirty-one (40%) participants were in Stage 2T CKD. Stages of CKD were distributed as shown in figure 7.

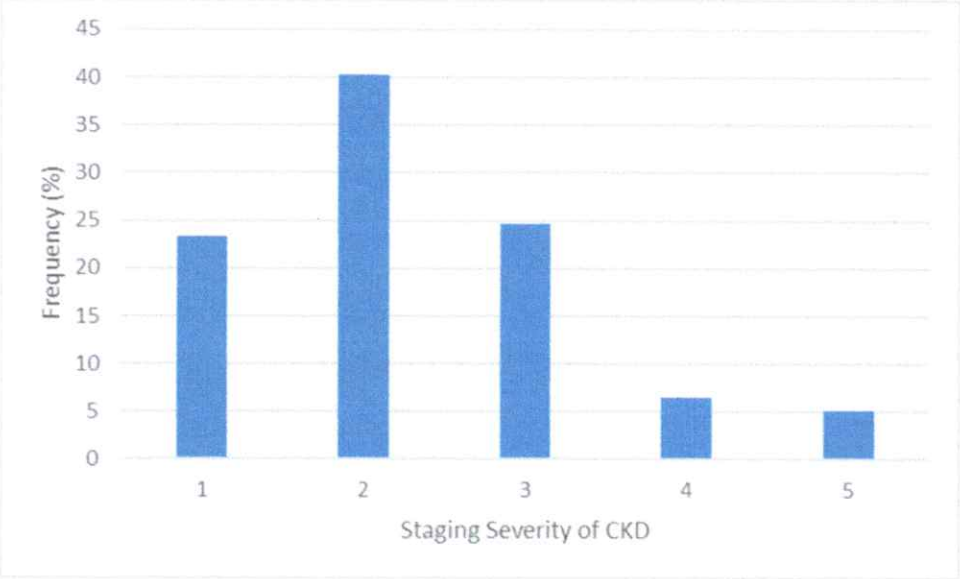

Figure 7 Staging severity of KTRs at KNH

Abbreviations: CKD, chronic kidney disease; KTRs, kidney transplant recipients; KNH, Kenyatta National Hospital

Table 3 Clinical characteristics of KTRs at KNH

	Overall *(n=77)*	Male *(n=52)*	Female *(n=25)*
Aetiology of Kidney disease, *n (%)*			
Glomerulonephritis	39 (51)	22 (42)	17 (68)
Polycystic kidney disease	2	2	0
Diabetic kidney disease	20 (26)	17 (33)	3 (12)
Hypertension	11 (14)	7 (13)	4 (16)
Others	5	4	1
Dialysis vintage (months), *Median (IQR)*	18.0 (9.0 – 36.0)	18 (9.5 – 36.0)	18.0 (8.0 – 28.0)
Duration post-transplantation (years), *Median (IQR)*	4.5 (2.7 – 8.3)	4.3 (2.4 – 8.8)	6.6 (2.9 – 7.7)
SBP, *Mean ± SD*	130 ± 17	129 ± 17	131 ± 17
DBP, *Mean ± SD*	81 ± 12	81 ± 11	82 ± 13
BMI, *Mean ± SD*	24.7 ± 4.8	24.1 ± 4.3	25.8 ± 5.6
Transfusions, *n (%)*			
Yes	61 (79)	37 (71)	24 (96)
No	16 (21)	15 (29)	1
Laboratory, *Mean±SD*			
Urea (mmol/l)	7.3 ± 4.9	7.0 ± 3.8	7.9 ± 6.8
eGFR (ml/min/1.73m^2)	66.7 ± 28.2	69.8 ± 25.4	60.1 ± 32.8
RBC ($\times 10^{12}$/L)	4.6 ± 0.9	4.8 ± 0.9	4.0 ± 0.9
Haemoglobin (g/dl)	13.7 ± 2.5	14.5 ± 2.1	12.1 ± 2.3
MCV (fL)	90.8 ± 5.9	90.0 ± 6.0	92.5 ± 5.6
Platelets ($\times 10^9$/L)	237.5 ± 83.1	223.4 ± 64.7	222.4 ± 107.9
Laboratory, *Median (IQR)*			
Creatinine (µmol/l)	108.6 (87.7 – 141.0)	110.9 (92.1 – 140.6)	99.4 (75.8 – 167.6)

Abbreviation: ANC, absolute neutrophil count; BMI, body mass index; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; IQR, interquartile range; MCV, mean corpuscular volume; n, number; RBC, red blood cell; SBP, systolic blood pressure; SD, standard deviation; WBC, white blood cell

4.3 Iron status assessment

The median serum ferritin level was 408.0 (104.0-1072.0) µg/L. The mean serum iron was 16.2±6.9 µmol/L with a serum transferrin of 24.8±4.8 µmol/L. The mean TSAT level was 34.9±19.4%. Overall, we defined 23 recipients with iron deficiency which corresponds to 30% (95%CI 21-41) of the total sample. Thirteen (17%) of the recipients had iron overload. The higher proportion of women with iron deficiency did not reach statistical significance. Table 4 highlights these categories of iron status.

Among these KTRs, 17 KTRs (22%) were defined with absolute iron deficiency and 6 KTRs (8%) with functional iron deficiency.

Among those with iron overload (n=13), 10 (77%) had a previous history of blood transfusion. The median ferritin levels and mean TSAT levels for both those with and without a history of transfusion are highlighted in Table 5.

Table 4 Iron status among study participants

	Overall *(n=77)*	Male *(n=52)*	Female *(n=25)*	*P* value
Overload (Serum ferritin l>1000µg/L and TSAT >45%) *n (%)*	13 (17) (95%CI 9-27)	11 (21)	2 (8)	0.149
Normal (Serum ferritin (100-500µg/L and TSAT 20-40%), *n (%)*	41 (53)	28 (54)	13 (52)	0.879
Deficient (Serum ferritin levels of < 100µg/L and serum ferritin levels 100-299µg/L and TSAT <20%), *n (%)*	**23 (30) (95%CI 21-41)**	13 (25)	10 (40)	0.178

Abbreviations: n, number; TSAT, transferrin saturation

Table 5 Transfusion status among study participants with iron overload

		Transfusions	
	Overall *(n=13)*	Yes *(n=10)*	No *(n=3)*
Overload	13 (100)	10 (77)	3 (23)
Ferritin, *Median (IQR)*	2337 (1568 - 2818)	1836 (1560 - 2818)	2460 (2399 - 2815)
TSAT, *Mean ± SD*	67.3 ± 16.1	67.5 ± 17.1	66.8 ± 15.6
Iron, *Mean ± SD*	25.5 ± 5.0	26.5 ± 5.3	22.4 ± 1.8

Abbreviation: IQR, interquartile range; n, number; SD, standard deviation; TSAT, Transferrin Saturation.

The further analysis of the transfusion status was curtailed by the small numbers noted and as such relative risk/risk ratios could not be done.

4.4 Comparison of KTRs with and without iron deficiency.

Following bivariate analysis, there was no difference in age and sex between those with and without iron deficiency (Table 6). The difference in the median dialysis vintage between the two groups was 7.0 months was statistically significant (p 0.044). The longer median post-transplant duration of 2.6 months was not statistically significant (p 0.136). The difference in eGFR between the two groups was 2.9ml/min/1.73m^2 (95% CI 1.9-3.9) was not statistically significant (p 0.673). The difference in haemoglobin between the two groups of 0.2g/dl (95%CI 0.1-0.5) was not statistically significant (p 0.794). The higher platelet count of 52.6 (95% CI 17.3-87.9) was statistically significant (p 0.032).

Table 6 Selected characteristics of KTRs with and without iron deficiency

	Deficient, *(n=23)*	Normal, *(n=41)*	OR (95% CI)	p-value
Age in years, *Mean ± SD*	48.4 ± 15.8	46.9 ± 15.7		0.725
Sex, *n (%)*				
Male	13 (57)	28 (68)	0.6 (0.2 – 1.7)	0.348
Female	10 (43)	13 (32)	Reference	
Smoking status, *n (%)*				
Never	18 (78)	32 (78)	Reference	
Past	5 (22)	9 (22)	1.0 (0.3 – 3.4)	0.984
Clinical characteristics				
BMI (kg/m^2)	24.1 ± 4.8	25.6 ± 5.1		0.242
Dialysis vintage (months)	19.0 (12.0 – 33.0)	12.0 (6.0 – 24.0)		**0.044**
Duration post-transplantation (years)	7.3 (4.0 – 9.4)	4.7 (2.7 – 8.3)		0.136
Creatinine (mmol/l)	100.2 (86.5 – 123.4)	109.6 (92.1 – 154.1)		0.434
eGFR ($ml/min/1.73m^2$)	66.7 ± 27.6	63.8 ± 26.6		0.673
RBC ($\times 10^{12}/L$)	4.6 ± 1.0	4.6 ± 1.0		0.952
Haemoglobin (g/dL)	13.7 ± 2.3	13.9 ± 2.6		0.794
MCV (fL)	89.5 ± 5.8	90.9 ± 6.5		0.397
Platelets ($\times 10^9/L$)	279.7 ± 105.8	227.1 ± 70.5		**0.032**
Positive previous transfusion				
Yes	17 (74)	34 (83)	0.6 (0.2 – 2.0)	0.390
No	6 (26)	7 (17)	Reference	

Abbreviations: BMI, Body Mass Index; eGFR, estimated glomerular filtration rate; MCV, mean corpuscular volume; n, number; RBC, red blood cell; SD, standard deviation; WBC, white blood cell.

4.5 Prevalence of anaemia

The mean haemoglobin concentration was 13.8±2.4 g/dl. Overall, 23 (30%) patients were defined as anaemic as shown in Table 7. Among them, 11(14%) patients had mild; 10 (13%) moderate; and 2 (3%) severe anaemia. Figure 8 summarises the above severity of anaemia.

In this study, 5 (7%) of the KTRs were defined to have iron deficiency anaemia. Among the KTRs with anaemia, 22% had iron deficiency as a contributor to development of anaemia.

Table 7 Prevalence of anaemia

	Frequency *(n=77)*	Per cent	95% CI
Anaemia	23	30	21 – 41
No anaemia	54	70	

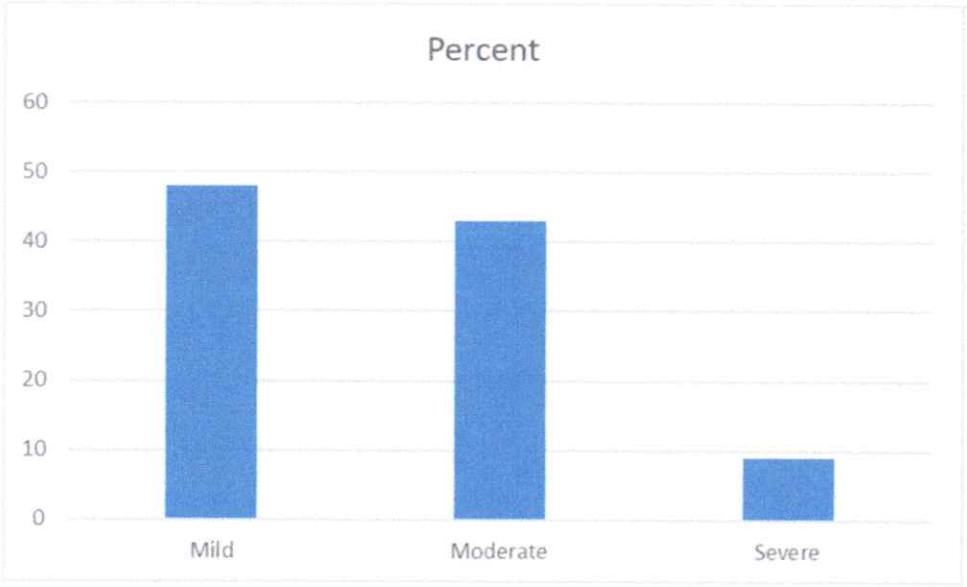

Figure 8 Severity of anaemia

CHAPTER FIVE: DISCUSSION

Iron status is an important contributor to graft function and mortality among KTRs especially with regard to iron deficiency. A significant burden of iron deficiency among KTRs at the KNH kidney transplant clinic was seen. We demonstrated a prevalence of iron deficiency of 30%. Absolute iron deficiency was more prevalent in our population than functional iron deficiency. Contributors to iron deficiency in this group could be a nutritional deficiency, an iron-deficient state at transplantation as well as a systemic low-grade inflammatory response that increases the expression of hepcidin.

In a study by Eisenga et al in 2016 investigating iron deficiency, anaemia and mortality in KTRs sampled and using similar assay methods and definitions of iron deficiency, the prevalence of iron deficiency in that sample was 30%, similar to our detected prevalence. Moreover, a study by Ayerdem et al in 2021 using similar methods demonstrated a similar prevalence of iron deficiency. The global prevalence of iron deficiency in KTRs ranged from 6-47% with the variation due to differences in methods and cut-offs used to determine the prevalence of iron deficiency. To the best of our knowledge, there is no documented data on the prevalence of iron deficiency in KTRs in SSA[5,24]. We also found that 17% of the KTRs were at risk for iron overload and for these evaluation for comorbidities that could account for the elevation in iron status parameters is warranted.

In this study, the median serum ferritin was 408.0 µg/L. We observed that the ferritin levels were higher than in other studies done in populations of KTRs in Europe and Asia[5,19,76]. This finding could potentially be attributed to ethnic differences in the population under study with our study having a higher proportion of black participants. Additionally, factors such as the effects of inflammation, alcohol use, systemic infections as well as underlying malignancy could contribute to this difference[77–79].

We demonstrated a prevalence of iron overload of 17% among KTRs. This prevalence was similar to what was noted in other studies[25,26]. Certainly, the overload state is less prevalent than the deficient state, a finding highlighted in our study. The transfusion history was associated

with higher TSAT levels and serum iron levels. The overloaded state could be attributed to this positive history of transfusion. This study however did not evaluate the details of the transfusion history including the number of transfusions as well as extent of parenteral iron administration.

In this study, the clinical characteristics between those with iron deficiency and those with normal iron status were largely similar except for the platelet counts. The mean platelet count among those with iron deficiency was 279.7 whereas that of those without iron deficiency was 227.1. We observed that the mean increase in platelet count of 52.6 in KTRs with iron deficiency was statistically significant. Increased platelet count was negatively associated with the iron indices. It has been shown previously that iron deficiency usually results in normal or elevated platelet counts; in comparison to persons with normal iron levels, higher platelet counts are seen in iron deficient persons, a finding consistent with our study findings. This phenomenon is not very well understood and could be attributed to an enhanced production (reactive process) where there is an augmentation of megakaryopoiesis. Other potential reasons could be increased release from the spleen, prolonged survival of platelets or platelet division in circulation[80–82].

The longer median dialysis vintage among those with iron deficiency was significant. The positive association could be attributed to a dialysis diet deficient in iron, gastrointestinal bleeding and losses, blood loss seen during the dialysis process and other external factors that contribute to external blood loss in dialysis[13].

Anaemia is highly prevalent in the population of KTRs. In our study, the prevalence of anaemia was 30%. This finding is comparable to earlier unpublished data from a study carried out in KTRs at the renal department. In that study, the prevalence was found to be 21%[27]. Anaemia in the post-transplant period could be due to graft dysfunction, iron deficiency, medications, the inflammatory response and other nutritional deficiencies among other potential reasons. In this study population, iron deficiency anaemia was found in 7% of the total KTRs, making iron deficiency an important contributor towards the development of anaemia. The other contributors towards post-transplantation anaemia were not the focus of this study. In terms of severity, most of the KTRs with anaemia had mild anaemia.

These findings are comparable to studies done elsewhere. In the study by Eisenga et al, the prevalence of anaemia was 34%. However, in that study population, the prevalence of iron deficiency anaemia was higher at 13%. Ayerdem et al in an analysis of two cohorts of KTRs found a prevalence of anaemia of 26% and 32% respectively. Similar findings are noted in earlier studies with a prevalence of between 36-42%[18,19,22,49,83]. Further in keeping with the trend found in our study, the degree of anaemia in these centres is of mild severity[22,83]. These findings are in contrast to our haemodialysis-treated population which had a higher prevalence[16]. This could be attributed to a declining eGFR with declining levels of EPO, dialytic losses as well as dietary restrictions faced by this group. A majority of our KTRs were stage 2T.

Our study showed a predominantly male recipient population at 68%. Despite the higher prevalence of CKD among women in SSA, there are more men noted with ESKD and at transplantation. Thus, more men than women would be noted at transplantation. The possible reasons behind this phenomenon could be biological with potentially more rapid progression to ESKD in men than women or other social factors such as earning and educational disparities in women and less access to screening and prevention for men[84,85]. The above findings in our sample are also similar to other local and international studies[5,16,22,86]

The mean age of our study participants was 47 years, a somewhat younger population. This is probably a reflection of the younger population noted at ESKD and on maintenance haemodialysis at our facility[16]. Similar findings were described in other studies on KTRs done locally. This is in contrast to studies in the west whose mean age of their transplant population is higher at 53 years[5,86]. The median duration post-transplantation was similar when compared to previous studies carried out which is a reflection of the progression of the local kidney transplantation program with associated better outcomes for these KTRs[19,24].

The prevalence of iron deficiency in KTRs is high. Despite the differences between high- and low-income nations, the data is consistent with the extent of iron deficiency in this population. Certainly, this is the first study to determine the iron profiles among KTRs at the Kenyatta National Hospital and represents a significant addition to our understanding of iron deficiency in

KTRs in our sub-Saharan population. Iron deficiency remains an important contributor to anaemia. Nonetheless, there is a growing body of evidence in the transplant population of the increasing prevalence of iron deficiency independent of anaemia. These indeed provide an avenue for targeted screening and intervention to improve iron status. In turn, this will have a consequent improvement in morbidity and reduction in mortality among this population. Therefore, tests of iron status should be considered in KTRs routinely. Early detection and treatment of iron deficiency in kidney transplant recipients is important with resultant improvement in outcomes.

5.1 Study limitations

i. This study was carried out at a single site. Therefore, care should be taken when generalizing to the entire kidney transplant recipient population.

CHAPTER SIX: CONCLUSION

6.1 Conclusion

From this study, we can conclude that:

1. Among KTRs, a significant burden of iron deficiency was seen which was at 30%. Also, 17% of the KTRs were found to have iron overload.
2. The prevalence of anaemia in the KTRs is high at 30% and 22% of the KTRs with anaemia had iron deficiency.
3. There was a trend towards a higher platelet count in KTRs with iron deficiency.

6.2 Recommendations

Based on these study findings, the following are the recommendations:

1. Routine monitoring of the iron status is warranted among KTRs on follow-up at the kidney transplant clinic which includes the measurement of ferritin and TSAT.
2. Follow-up studies are carried out to evaluate the iron status over a longer period and the potential impact on graft function as well as the impact of interventions done to stem iron deficiency.

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APPENDICES

Appendix IA: Study explanation form

Study Title: "*Iron Status among Kidney Transplant Recipients at Kenyatta National Hospital Renal Unit*"

Principal Investigator\and institutional affiliation: Dr Mwango Anson Kiema,

University of Nairobi, School of Medicine.

Co-Investigators and institutional affiliation:

Prof. S.O. McLigeyo

University of Nairobi

Dr P.O. Oyiro

University of Nairobi

Introduction:

I would like to tell you about a study being conducted by the above listed researchers. The purpose of this consent form is to give you the information needed to help you decide whether or not to be a participant in the study. Feel free to ask any questions about the purpose of the research, what happens if you participate in the study, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions to your satisfaction, you may decide to be in the study or not. This process is called 'informed consent'. Once you understand and agree to be in the study, I will request you to sign your name on this form. You should understand the general

principles which apply to all participants in medical research: i) Your decision to participate is entirely voluntary ii) You may withdraw from the study at any time without necessarily giving a reason for your withdrawal iii) Refusal to participate in the research will not affect the services you are entitled to in this health facility or other facilities. We will give you a copy of this form for your records.

May I continue? YES / NO

This study has approval by The Kenyatta National Hospital-University of Nairobi Ethics and Research Committee will No. _____

What is This Study About?

The researchers listed above are interviewing kidney transplant recipients who are on follow up at the kidney transplant clinic at Kenyatta National Hospital, Renal Unit. The purpose of the interview is to determine the iron status of kidney transplant recipients and any associated factors therein. The study is also part of the curriculum requirements for successful completion of the Masters in Internal Medicine (MMed) program.

The study will involve obtaining information regarding your medical history and conducting laboratory investigations.

Are There Any Risks, Harms, Discomforts Associated with This Study?

Medical research has the potential to introduce psychological, social, emotional and physical risks. Effort should always be put in place to minimize the risks. One potential risk of being in the study is loss of privacy. We will keep everything you tell us as confidential as possible. We will use a code number to identify you in a password-protected computer database and will keep all of our paper records in a locked file cabinet. However, no system of protecting your confidentiality can be absolutely secure, so it is still possible that someone could find out you

were in this study and could find out information about you. Also, answering questions in the interview may be uncomfortable for you. If there are any questions you do not want to answer, you can skip them. You have the right to refuse the interview or any questions asked during the interview. You may feel some discomfort from the needle prick at the region of blood sample removal. Rarely, bleeding and swelling may occur from the puncture site but we will make sure bleeding has stopped before we depart.

Are there any benefits being in this study?

You may benefit by receiving free lab testing for iron status. The results will form part of your usual care. Copies of the recorded in your file. Also, the information you provide will help us better understand iron status of kidney transplant recipients in your clinic. This information is a contribution to science and will inform the health policy in our country with the aim of reducing morbidity and improving outcomes among kidney transplant recipients

Will Being in This Study Cost You Anything?

You will not be charged for any laboratory tests (Iron studies) included in the study.

What Are Your Other Choices?

Your decision to participate in research is voluntary. You are free to decline participation in the study and you can withdraw from the study at any time without injustice or loss of any benefits.

What If You Have Questions in Future?

If you have any further questions or concerns about participating in this study, please feel free to contact the following:

1. DR. MWANGO ANSON KIEMA, UNIVERSITY OF NAIROBI, DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS, Mobile: 0728 036688 ***OR***
2. PROF. S.O. MCLIGEYO, UNIVERSITY OF NAIROBI, DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS, Mobile: 0722 525722
3. SECRETARY/CHAIRPERSON, KENYATTA NATIONAL HOSPITAL-UNIVERSITY OF NAIROBI ETHICS AND RESEARCH COMMITTEE TELEPHONE NO. 2726300 EXT. 44102. P.O. BOX 20723, NAIROBI. Email uonknh_erc@uonbi.ac.ke.

Appendix IB: Fomu ya maelezo ya utafiti

Study Title: "*Iron Status among Kidney Transplant Recipients at Kenyatta National Hospital Renal Unit*"

Mtafiti mkuu: Dr Mwango Anson Kiema,

Chuo Kikuu cha Nairobi.

Wachunguzi-wenza:

Prof. S.O. McLigeyo

Chuo Kikuu cha Nairobi

Dr P.O. Oyiro

Chuo Kikuu cha Nairobi

Utangulizi:

Ningependa kukuambia kuhusu utafiti unaofanywa na watafiti walioorodheshwa hapo juu. Madhumuni ya fomu hii ya idhini ni kukupa taarifa inayohitajika ili kukusaidia kuamua kama au kutokuwa mshiriki katika utafiti huu. Jisikie huru kuuliza maswali yoyote kuhusu madhumuni ya utafiti, nini kitatokea ikiwa utashiriki katika utafiti, hatari na manufaa yanayoweza kutokea, yako haki kama mtu wa kujitolea, na kitu kingine chochote kuhusu utafiti au fomu hii ambacho hakiko wazi. Wakati tumejibu maswali yako yote kwa kuridhika kwako, unaweza kuamua kuwa katika utafiti au sivyo. Utaratibu huu unaitwa 'ridhaa ya taarifa'. Mara baada ya kuelewa na kukubali kuwa katika soma, nitakuomba utie sahihi jina lako kwenye fomu hii. Unapaswa kuelewa kanuni zinazotumika kwa washiriki wote katika utafiti wa matibabu: i) Uamuzi wako wa kushiriki ni kwa hiari kabisa ii) Unaweza kujiondoa kwenye utafiti wakati wowote bila ya lazima kutoa sababu ya kujitoa iii) Kukataa kushiriki katika utafiti hakutaathiri huduma unazostahili kupata katika kituo hiki cha afya au vituo vingine. Tutakupa a

nakala ya fomu hii kwa kumbukumbu zako.

Naweza kuendelea? NDIO / LA

Utafiti huu umeidhinishwa na Hospitali ya Kitaifa ya Kenyatta-Chuo Kikuu cha Maadili cha Nairobi na

Itifaki ya Kamati ya Utafiti Nambari. _____

Utafiti Huu Unahusu Nini?

Watafiti walioorodheshwa hapo juu wanawahoji waliopandikizwa figo ambao wanafuatilia katika kliniki ya upandikizaji figo katika Hospitali ya Kitaifa ya Kenyatta, Kitengo cha Figo. Madhumuni ya mahojiano ni kubainisha hadhi ya chuma ya wapokeaji wa upandikizaji wa figo na mambo yoyote yanayohusiana nayo. Utafiti huo pia ni sehemu ya mahitaji ya mtaala ya kukamilisha kwa mafanikio mpango wa Masters in Internal Medicine (MMed)

Utafiti utahusisha kupata taarifa kuhusu historia yako ya matibabu na kufanya uchunguzi wa kimaabara.

Je, Kuna Hatari, Madhara, Masumbuko Yoyote Yanayohusishwa na Utafiti Huu?

Utafiti wa kimatibabu una uwezo wa kuanzisha hatari za kisaikolojia, kijamii, kihisia na kimwili. Jitihada zitawekwa kila wakati ili kupunguza hatari. Hatari moja inayoweza kutokea ya kuwa katika utafiti ni kupoteza faragha. Tutaweka kila kitu unachotuambia kama siri iwezekanavyo. Tutatumia nambari ya msimbo kukutambua katika hifadhi ya kompyuta iliyolindwa na nenosiri na tutaweka rekodi zetu zote za karatasi kwenye kabati ya faili iliyofungwa. Hata hivyo, hakuna mfumo wa kulinda usiri wako unaoweza kuwa salama kabisa, kwa hivyo bado kuna uwezekano kwamba mtu anaweza kujua ulikuwa kwenye utafiti huu na kupata taarifa kukuhusu. Pia, kujibu maswali katika mahojiano kunaweza kuwa na wasiwasi kwako. Ikiwa kuna maswali yoyote ambayo hutaki kujibu, unaweza kuyaruka. Una haki ya kukataa mahojiano au maswali yoyote yaliyoulizwa wakati wa mahojiano. Unaweza kuhisi usumbufu kutokana na kuchomwa sindano katika eneo la uondoaji wa sampuli ya damu. Mara chache, kutokwa na damu na uvimbe kunaweza kutokea kwenye tovuti ya kuchomwa lakini tutahakikisha kutokwa na damu kumekoma kabla hatujaondoka.

Je, kuna manufaa yoyote katika utafiti huu?

Unaweza kufaidika kwa kupokea majaribio ya bure ya maabara kwa hadhi ya chuma. Matokeo yatakuwa sehemu ya utunzaji wako wa kawaida. Nakala za kumbukumbu katika faili yako. Pia, maelezo utakayotoa yatatusaidia kuelewa vyema hali ya chuma ya wapokeaji wa upandikizaji wa figo katika kliniki yako. Taarifa hizi ni mchango wa sayansi na zitafahamisha sera ya afya katika nchi yetu kwa lengo la kupunguza maradhi na kuboresha matokeo miongoni mwa wanaopandikizwa figo.

Je, Kuwa Katika Utafiti Huu Kutakugharimu Chochote?

Hutatozwa kwa majaribio yoyote ya kimaabara (Iron studies) yaliyojumuishwa katika utafiti.

Umechagua Nini Nyingine?

Uamuzi wako wa kushiriki katika utafiti ni wa hiari. Uko huru kukataa kushiriki katika utafiti na unaweza kujiondoa kwenye utafiti wakati wowote bila dhuluma au hasara ya manufaa yoyote.

Nini Ikiwa Una Maswali Katika Wakati Ujao?

Ikiwa una maswali zaidi au wasiwasi wowote kuhusu kushiriki katika utafiti huu, tafadhali jisikie huru kuwasiliana na wafuatao:

1. DR. MWANGO ANSON KIEMA, UNIVERSITY OF NAIROBI, DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS, Mobile: 0728 036688 ***OR***
2. PROF. S.O. MCLIGEYO, UNIVERSITY OF NAIROBI, DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS, Mobile: 0722 525722
3. SECRETARY/CHAIRPERSON, KENYATTA NATIONAL HOSPITAL-UNIVERSITY OF NAIROBI ETHICS AND RESEARCH COMMITTEE TELEPHONE NO. 2726300 EXT. 44102. P.O. BOX 20723, NAIROBI. Email uonknh_erc@uonbi.ac.ke.

Appendix IIA: Screening consent form

STUDY TITLE: IRON STATUS AMONG KIDNEY TRANSPLANT RECIPIENTS AT THE KENYATTA NATIONAL HOSPITAL RENAL UNIT

Statement of Consent

I have read the above information concerning the study on iron status among kidney transplant recipients. This study has been given ethical approval for a period of one (1) year. I have asked any questions I had regarding the study and they have been answered to my satisfaction. I consent to undergo screening to determine whether I shall be eligible to participate in the study.

Name of Participant:

Signature of Participant: Date:

INVESTIGATOR'S STATEMENT:

I, the Principal Investigator, have fully educated the research participant on the purpose and implication of this study, and that he/she must first undergo screening to determine their eligibility to participate in the study.

Signed: Date:

CONTACT INFORMATION

If you have any further questions or concerns about participating in this study, please feel free to contact the following:

1. DR. MWANGO ANSON KIEMA, UNIVERSITY OF NAIROBI, DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS, Mobile: 0728 036688 ***OR***
2. PROF. S.O. MCLIGEYO, UNIVERSITY OF NAIROBI, DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS, Mobile: 0722 525722
3. SECRETARY/CHAIRPERSON, KENYATTA NATIONAL HOSPITAL-UNIVERSITY OF NAIROBI ETHICS AND RESEARCH COMMITTEE TELEPHONE NO. 2726300 EXT. 44102. P.O. BOX 20723, NAIROBI. Email uonknh_erc@uonbi.ac.ke.

Appendix IIB: Fomu ya ridhaa ya kuchunguza

STUDY TITLE: IRON STATUS AMONG KIDNEY TRANSPLANT RECIPIENTS AT THE KENYATTA NATIONAL HOSPITAL RENAL UNIT

Taarifa ya Idhini

Nimesoma maelezo hapo juu kuhusu utafiti kuhusu hali ya chuma kati ya wapokeaji wa upandikizaji wa figo. Utafiti huu umepewa kibali cha kimaadili kwa muda wa mwaka mmoja (1). Nimeuliza maswali yoyote niliyokuwa nayo kuhusu utafiti na yamejibiwa kwa kuridhika kwangu. Ninakubali kuchunguzwa ili kubaini kama nitastahiki kushiriki katika utafiti.

Jina la Mshiriki:

Sahihi ya Mshiriki: Tarehe:

TAARIFA YA MTAFITI:

Mimi, Mtafiti Mkuu, nimemweleza mshiriki wa utafiti kikamilifu kuhusu madhumuni na maana ya utafiti huu, na kwamba lazima kwanza achunguzwe ili kubaini kustahiki kwao kushiriki katika utafiti.

Imetiwa saini: Tarehe:

TAARIFA ZA MAWASILIANO

Ikiwa una maswali zaidi au wasiwasi wowote kuhusu kushiriki katika utafiti huu, tafadhali jisikie huru kuwasiliana na wafuatao:

1. DR. MWANGO ANSON KIEMA, UNIVERSITY OF NAIROBI, DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS, Mobile: 0728 036688 ***OR***
2. PROF. S.O. MCLIGEYO, UNIVERSITY OF NAIROBI, DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS, Mobile: 0722 525722
3. SECRETARY/CHAIRPERSON, KENYATTA NATIONAL HOSPITAL-UNIVERSITY OF NAIROBI ETHICS AND RESEARCH COMMITTEE TELEPHONE NO. 2726300 EXT. 44102. P.O. BOX 20723, NAIROBI. Email uonknh_erc@uonbi.ac.ke.

Appendix III: Screening proforma

Name: Hospital Number:

Study Date:

1. CONSENT GIVEN

YES NO IF YES PROCEED TO 2

2. AGE OVER 12 YEARS

YES NO IF YES PROCEED TO 3

3. MORE THAN 6 MONTHS POST KIDNEY TRANSPLANT

YES NO IF NO, EXCLUDE.

FOR OFFICIAL USE ONLY

RECRUITED?

YES NO

Interviewer's Name:

Signature: Date:

Appendix IVA: Study consent form

STUDY TITLE: IRON STATUS AMONG KIDNEY TRANSPLANT RECIPIENTS AT THE KENYATTA NATIONAL HOSPITAL RENAL UNIT

Statement of Consent

I have read this consent form or had the information read to me. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my participation in this study is voluntary and that I may choose to withdraw any time. I freely agree to participate in this research study.

I understand that all efforts will be made to keep information regarding my personal identity confidential.

By signing this consent form, I have not given up any of the legal rights that I have as a participant in a research study.

Name of Participant:

Signature of Participant: Date:

INVESTIGATOR'S STATEMENT:

I, the Principal Investigator, have fully educated the research participant on the purpose and implication of this study.

Signed: Date:

CONTACT INFORMATION

If you have any further questions or concerns about participating in this study, please feel free to contact the following:

1. DR. MWANGO ANSON KIEMA, UNIVERSITY OF NAIROBI, DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS, Mobile: 0728 036688 ***OR***
2. PROF. S.O. MCLIGEYO, UNIVERSITY OF NAIROBI, DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS, Mobile: 0722 525722
3. SECRETARY/CHAIRPERSON, KENYATTA NATIONAL HOSPITAL-UNIVERSITY OF NAIROBI ETHICS AND RESEARCH COMMITTEE TELEPHONE NO. 2726300 EXT. 44102. P.O. BOX 20723, NAIROBI. Email uonknh_erc@uonbi.ac.ke.

Appendix IVB: Fomu ya ridhaa ya masomo

STUDY TITLE: IRON STATUS AMONG KIDNEY TRANSPLANT RECIPIENTS AT THE KENYATTA NATIONAL HOSPITAL RENAL UNIT

Taarifa ya Idhini

Nimesoma fomu hii ya idhini au nimesomewa maelezo. Nimejibiwa maswali yangu kwa lugha ninayoielewa. Hatari na faida zimeelezewa kwangu. Ninaelewa kuwa ushiriki wangu katika utafiti huu ni wa hiari na kwamba ninaweza kuchagua kujiondoa wakati wowote. Ninakubali kwa uhuru kushiriki katika utafiti huu.

Ninaelewa kuwa juhudi zote zitafanywa ili kuweka taarifa kuhusu utambulisho wangu wa kibinafsi kuwa siri.

Kwa kutia saini fomu hii ya idhini, sijaacha haki zozote za kisheria nilizo nazo kama mshiriki katika utafiti wa utafiti.

Jina la Mshiriki:

Sahihi ya Mshiriki: Tarehe:

TAARIFA YA MTAFITI:

Mimi, Mtafiti Mkuu, nimemweleza mshiriki wa utafiti kikamilifu kuhusu madhumuni na maana ya utafiti huu.

Imetiwa saini: Tarehe:

TAARIFA ZA MAWASILIANO

Ikiwa una maswali zaidi au wasiwasi wowote kuhusu kushiriki katika utafiti huu, tafadhali jisikie huru kuwasiliana na wafuatao:

1. DR. MWANGO ANSON KIEMA, UNIVERSITY OF NAIROBI, DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS, Mobile: 0728 036688 ***OR***
2. PROF. S.O. MCLIGEYO, UNIVERSITY OF NAIROBI, DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS, Mobile: 0722 525722
3. SECRETARY/CHAIRPERSON, KENYATTA NATIONAL HOSPITAL-UNIVERSITY OF NAIROBI ETHICS AND RESEARCH COMMITTEE TELEPHONE NO. 2726300 EXT. 44102. P.O. BOX 20723, NAIROBI. Email uonknh_erc@uonbi.ac.ke.

Appendix VA: Parental consent form and assent form

Study Title: "*Iron Status among Kidney Transplant Recipients at Kenyatta National Hospital Renal Unit*"

Principal Investigator\and institutional affiliation: Dr Mwango Anson Kiema,

University of Nairobi, School of Medicine.

Co-Investigators and institutional affiliation:

Prof. S.O. McLigeyo

University of Nairobi

Dr P.O. Oyiro

University of Nairobi

Introduction:

I would like to tell you about a study being conducted by the above listed researchers. The purpose of this consent form is to give you the information needed to help you decide whether or not your child should participate in the study. Feel free to ask any questions about the purpose of the research, what happens if your child participates in the study, the possible risks and benefits, the rights of your child as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions to your satisfaction, you may decide if you want your child to be in the study or not. This process is called 'informed consent'. Once you understand and agree for your child to be in the

study, I will request you to sign your name on this form. You should understand the general principles which apply to all participants in medical research: i) Your child decision to participate

is entirely voluntary ii) Your child may withdraw from the study at any time without necessarily giving a reason for his/her withdrawal iii) Refusal to participate in the research will not affect the services your child is entitled to in this health facility or other facilities.

May I continue? YES / NO

For children below 18 years of age we give information about the study to parents or guardians. We will go over this information with you and you need to give permission in order for your child to participate in this study. We will give you a copy of this form for your records.

Once fully informed, your child will be required to agree to participate in this study.

What is This Study About?

The researchers listed above are interviewing kidney transplant recipients who are on follow up at the kidney transplant clinic at Kenyatta National Hospital, Renal Unit. The purpose of the interview is to determine the iron status of kidney transplant recipients and any associated factors therein. The study is also part of the curriculum requirements for successful completion of the Masters in Internal Medicine (MMed) program.

The study will involve obtaining information regarding your medical history and conducting laboratory investigations specifically tests of iron status. There will be 77 participants in this study chosen. We are asking for your consent to consider your child to participate in this study.

Are There Any Risks, Harms, Discomforts Associated with This Study?

Medical research has the potential to introduce psychological, social, emotional and physical risks. Effort should always be put in place to minimize the risks. One potential risk of being in the study is loss of privacy. We will keep everything you tell us as confidential as possible. We

will use a code number to identify your child in a password-protected computer database and will keep all of our paper records in a locked file cabinet. However, no system of protecting your confidentiality can be absolutely secure, so it is still possible that someone could find out your child was in this study and could find out information about your child. Also, answering questions in the interview may be uncomfortable for you. If there are any questions you do not want to answer, you can skip them. You have the right to refuse the interview or any questions asked during the interview. Your child may feel some discomfort from the needle prick at the region of blood sample removal. Rarely, bleeding and swelling may occur from the puncture site but we will make sure bleeding has stopped before we depart.

Are there any benefits being in this study?

Your child may benefit by receiving free lab testing. The results will form part of his/her usual care. Copies of the recorded in your file. Also, the information you provide will help us better understand iron status of kidney transplant recipients in your clinic. This information is a contribution to science and will inform the health policy in our country with the aim of reducing morbidity and improving outcomes among kidney transplant recipients

Will Being in This Study Cost You Anything?

You will not be charged for any laboratory tests (Iron studies) included in the study.

What Are Your Other Choices?

Your decision to have your child participate in this research is voluntary. You are free to decline or withdraw participation of your child in the study at any time without injustice or loss of any benefits.

What If You Have Questions in Future?

If you have any further questions or concerns about participating in this study, please feel free to contact the following:

1. DR. MWANGO ANSON KIEMA, UNIVERSITY OF NAIROBI, DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS, Mobile: 0728 036688 ***OR***

2. PROF. S.O. MCLIGEYO, UNIVERSITY OF NAIROBI, DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS, Mobile: 0722 525722
3. SECRETARY/CHAIRPERSON, KENYATTA NATIONAL HOSPITAL-UNIVERSITY OF NAIROBI ETHICS AND RESEARCH COMMITTEE TELEPHONE NO. 2726300 EXT. 44102. P.O. BOX 20723, NAIROBI. Email uonknh_erc@uonbi.ac.ke.

STUDY TITLE: IRON STATUS AMONG KIDNEY TRANSPLANT RECIPIENTS AT THE KENYATTA NATIONAL HOSPITAL RENAL UNIT

Statement of Consent

I have read the above information concerning the study on iron status among kidney transplant recipients. This study has been given ethical approval for a period of one (1) year. I have asked any questions I had regarding the study and they have been answered to my satisfaction. I consent for my child to undergo screening to determine whether he/she shall be eligible to participate in the study.

Parent/Guardian name:

Parent/Guardian signature: Date:

INVESTIGATOR'S STATEMENT:

I, the Principal Investigator, have fully educated the research participant on the purpose and implication of this study, and that he/she must first undergo screening to determine their eligibility to participate in the study.

Signed: Date:

STUDY TITLE: IRON STATUS AMONG KIDNEY TRANSPLANT RECIPIENTS AT THE KENYATTA NATIONAL HOSPITAL RENAL UNIT

The person being considered for this study is unable to consent for him/herself because he or she is a minor (a person less than 18 years of age). You are being asked to give your permission to include your child in this study.

Parent/guardian statement

I have read this consent form or had the information read to me. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my participation and that of my child in this study is voluntary and that I may choose to withdraw any time.

I understand that all efforts will be made to keep information regarding me and my child's personal identity confidential.

By signing this consent form, I have not given up any of the legal rights that I have as a participant in a research study.

Parent/Guardian name:

Parent/Guardian signature: Date:

INVESTIGATOR'S STATEMENT:

I, the Principal Investigator, have fully educated the research participant on the purpose and implication of this study.

Signed: Date:

STUDY TITLE: IRON STATUS AMONG KIDNEY TRANSPLANT RECIPIENTS AT THE KENYATTA NATIONAL HOSPITAL RENAL UNIT

We are doing a research study about the iron status in kidney transplant recipients. Permission has been granted to undertake this study by the Kenyatta National Hospital-University of Nairobi Ethics and Research Committee (KNH-UoN ERC Protocol No. _____) This research study is a way to learn more about people who have received a kidney transplant. If you decide that you want to be part of this study, you will be asked some information about your medical history and a blood sample drawn. There are some things about this study you should know. These are that you may feel some discomfort from the needle prick at the region of blood sample collection and that at times bleeding and swelling may occur. We will make sure bleeding has stopped before we leave. Not everyone who takes part in this study will benefit. A benefit means that something good happens to you. We think these benefits include free lab testing for iron status. When we are finished with this study, we will write a report about what was learned. This report will not include your name or that you were in the study. You do not have to be in this study if you do not want to be. If you decide to stop after we begin, that's okay too. Your parents know about the study too. If you decide you want to be in this study, please sign your name. I, _____, want to be in this research study

Appendix VB: Fomu ya idhini ya mzazi na fomu ya kuidhinisha

Study Title: "*Iron Status among Kidney Transplant Recipients at Kenyatta National Hospital Renal Unit*"

Mtafiti mkuu: Dr Mwango Anson Kiema,

Chuo Kikuu cha Nairobi.

Wachunguzi-wenza:

Prof. S.O. McLigeyo

Chuo Kikuu cha Nairobi

Dr P.O. Oyiro

Chuo Kikuu cha Nairobi

Utangulizi:

Ningependa kukuambia kuhusu utafiti unaofanywa na watafiti walioorodheshwa hapo juu. The madhumuni ya fomu hii ya idhini ni kukupa taarifa inayohitajika ili kukusaidia kuamua kama au mtoto wako asishiriki katika utafiti. Jisikie huru kuuliza maswali yoyote kuhusu madhumuni ya utafiti, nini kinatokea ikiwa mtoto wako atashiriki katika utafiti, hatari na faida zinazowezekana, na haki za mtoto wako kama mtu wa kujitolea, na kitu kingine chochote kuhusu utafiti au fomu hii ambacho hakiko wazi. Lini tumejibu maswali yako yote kwa kuridhika kwako, unaweza kuamua kama ungependa mtoto wako awe kwenye utafiti au sivyo. Utaratibu huu unaitwa 'ridhaa iliyoarifiwa'. Mara tu unapoelewa na kukubali mtoto wako kuwa ndani soma, nitakuomba utie sahihi jina lako kwenye fomu hii. Unapaswa kuelewa mkuu

kanuni zinazotumika kwa washiriki wote katika utafiti wa matibabu: i) Uamuzi wa mtoto wako kushiriki

ni kwa hiari kabisa ii) Mtoto wako anaweza kujiondoa kwenye utafiti wakati wowote bila lazima

kutoa sababu ya kujiondoa iii) Kukataa kushiriki katika utafiti hakutaathiri

huduma ambazo mtoto wako anastahili kupata katika kituo hiki cha afya au vituo vingine.

Naweza kuendelea? NDIO LA

Kwa watoto walio chini ya umri wa miaka 18 tunatoa taarifa kuhusu utafiti kwa wazazi au walezi. Tutapitia maelezo haya nawe na unahitaji kutoa ruhusa ili mtoto wako ashiriki katika utafiti huu. Tutakupa nakala ya fomu hii kwa rekodi zako.

Baada ya kufahamishwa kikamilifu, mtoto wako atahitajika kukubali kushiriki katika utafiti huu.

Utafiti Huu Unahusu Nini?

Watafiti walioorodheshwa hapo juu wanawahoji waliopandikizwa figo ambao wanafuatilia katika kliniki ya upandikizaji figo katika Hospitali ya Kitaifa ya Kenyatta, Kitengo cha Figo. Madhumuni ya mahojiano ni kubainisha hali ya chuma ya wapokeaji wa upandikizaji wa figo na mambo yoyote yanayohusiana nayo. Utafiti huo pia ni sehemu ya mahitaji ya mtaala ya kukamilisha kwa mafanikio mpango wa Uzamili katika Tiba ya Ndani (MMed).

Utafiti utahusisha kupata taarifa kuhusu historia yako ya matibabu na kufanya uchunguzi wa kimaabara hasa vipimo vya hali ya chuma. Kutakuwa na washiriki 77 katika utafiti huu waliochaguliwa. Tunaomba idhini yako ya kuzingatia mtoto wako kushiriki katika utafiti huu.

Je, Kuna Hatari, Madhara, Masumbuko Yoyote Yanayohusishwa na Utafiti Huu?

Utafiti wa kimatibabu una uwezo wa kuanzisha hatari za kisaikolojia, kijamii, kihisia na kimwili. Jitihada zinapaswa kuwekwa kila wakati ili kupunguza hatari. Hatari moja inayoweza kutokea ya kuwa katika utafiti ni kupoteza faragha. Tutaweka kila kitu unachotuambia kama siri iwezekanavyo. Tutatumia nambari ya msimbo kumtambua mtoto wako katika hifadhidata ya kompyuta iliyolindwa na nenosiri na tutaweka rekodi zetu zote za karatasi kwenye kabati ya faili iliyofungwa. Hata hivyo, hakuna mfumo wa kulinda usiri wako unaoweza kuwa salama kabisa, kwa hivyo bado kuna uwezekano kwamba mtu anaweza kujua mtoto wako alikuwa katika utafiti huu na kupata taarifa kuhusu mtoto wako. Pia, kujibu maswali katika mahojiano kunaweza kuwa na wasiwasi kwako. Ikiwa kuna maswali yoyote ambayo hutaki kujibu, unaweza kuyaruka. Una haki ya kukataa mahojiano au maswali yoyote yaliyoulizwa wakati wa mahojiano. Mtoto wako anaweza kujisikia usumbufu kutokana na kuchomwa sindano katika eneo la utoaji wa sampuli ya

damu. Mara chache, kutokwa na damu na uvimbe kunaweza kutokea kutoka kwa tovuti ya kuchomwa lakini tutahakikisha kutokwa na damu kumekoma kabla ya kuondoka.

Je, kuna manufaa yoyote katika utafiti huu?

Mtoto wako anaweza kufaidika kwa kupokea majaribio ya maabara bila malipo. Matokeo yatakuwa sehemu ya utunzaji wake wa kawaida. Nakala za kumbukumbu katika faili yako. Pia, maelezo utakayotoa yatatusaidia kuelewa vyema hali ya chuma ya wapokeaji wa upandikizaji wa figo katika kliniki yako. Taarifa hizi ni mchango wa sayansi na zitafahamisha sera ya afya katika nchi yetu kwa lengo la kupunguza maradhi na kuboresha matokeo miongoni mwa wanaopandikizwa figo.

Je, Kuwa Katika Utafiti Huu Kutakugharimu Chochote?

Hutatozwa kwa majaribio yoyote ya kimaabara (Iron studies) yaliyojumuishwa katika utafiti.

Je Umechagua Nini Nyingine?

Uamuzi wako wa kumfanya mtoto wako ashiriki katika utafiti huu ni wa hiari. Uko huru kukataa au kuondoa ushiriki wa mtoto wako katika utafiti wakati wowote bila dhuluma au hasara ya manufaa yoyote.

Nini Ikiwa Una Maswali Katika Wakati Ujao?

Ikiwa una maswali zaidi au wasiwasi wowote kuhusu kushiriki katika utafiti huu, tafadhali jisikie huru kuwasiliana na wafuatao:

1. DR. MWANGO ANSON KIEMA, UNIVERSITY OF NAIROBI, DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS, Mobile: 0728 036688 ***OR***
2. PROF. S.O. MCLIGEYO, UNIVERSITY OF NAIROBI, DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS, Mobile: 0722 525722
3. SECRETARY/CHAIRPERSON, KENYATTA NATIONAL HOSPITAL-UNIVERSITY OF NAIROBI ETHICS AND RESEARCH COMMITTEE TELEPHONE NO. 2726300 EXT. 44102. P.O. BOX 20723, NAIROBI. Email uonknh_erc@uonbi.ac.ke.

STUDY TITLE: IRON STATUS AMONG KIDNEY TRANSPLANT RECIPIENTS AT THE KENYATTA NATIONAL HOSPITAL RENAL UNIT

Taarifa ya Idhini

Nimesoma maelezo hapo juu kuhusu utafiti kuhusu hali ya chuma kati ya wapokeaji wa upandikizaji wa figo. Utafiti huu umepewa kibali cha kimaadili kwa muda wa mwaka mmoja (1). Nimeuliza maswali yoyote niliyokuwa nayo kuhusu utafiti na yamejibiwa kwa kuridhika kwangu. Ninakubali mtoto wangu achunguzwe ili kubaini kama atastahiki kushiriki katika utafiti.

Jina la Mzazi/Mlezi:

Sahihi ya Mzazi/Mlezi: Tarehe:

TAARIFA YA MTAFITI:

Mimi, Mtafiti Mkuu, nimemweleza mshiriki wa utafiti kikamilifu kuhusu madhumuni na maana ya utafiti huu, na kwamba lazima kwanza achunguzwe ili kubaini kustahiki kwao kushiriki katika utafiti.

Imetiwa saini: Tarehe:

STUDY TITLE: IRON STATUS AMONG KIDNEY TRANSPLANT RECIPIENTS AT THE KENYATTA NATIONAL HOSPITAL RENAL UNIT

Mtu anayezingatiwa kwa utafiti huu hana uwezo wa kujikubali kwa sababu yeye ni mtoto mdogo (mtu aliye chini ya miaka 18). Unaombwa kutoa idhini yako ya kujumuisha mtoto wako katika utafiti huu.

Taarifa ya mzazi/mlezi

Nimesoma fomu hii ya idhini au nimesomewa maelezo. Nimejibiwa maswali yangu kwa lugha ninayoielewa. Hatari na faida zimeelezewa kwangu. Ninaelewa kuwa ushiriki wangu na wa mtoto wangu katika utafiti huu ni wa hiari na kwamba ninaweza kuchagua kujiondoa wakati wowote.

Ninaelewa kuwa jitihada zote zitafanywa ili kuweka maelezo kunihusu na ya mtoto wangu kuwa siri.

Kwa kutia saini fomu hii ya idhini, sijaacha haki zozote za kisheria nilizo nazo kama mshiriki katika utafiti wa utafiti.

Jina la Mzazi/Mlezi:

Sahihi ya Mzazi/Mlezi: Tarehe:

TAARIFA YA MTAFITI:

Mimi, Mtafiti Mkuu, nimemweleza mshiriki wa utafiti kikamilifu kuhusu madhumuni na maana ya utafiti huu.

Iliyosainiwa: Tarehe:

STUDY TITLE: IRON STATUS AMONG KIDNEY TRANSPLANT RECIPIENTS AT THE KENYATTA NATIONAL HOSPITAL RENAL UNIT

Tunafanya utafiti kuhusu hali ya chuma katika wapokeaji wa upandikizaji wa figo. Ruhusa imetolewa kufanya utafiti huu na Hospitali ya Kitaifa ya Kenyatta-Kamati ya Maadili na Utafiti ya Chuo Kikuu cha Nairobi (KNH-UoN ERC Protocol No. _____) Utafiti huu ni njia ya kujifunza zaidi kuhusu watu ambao wamepandikizwa figo. Ukiamua kuwa ungependa kuwa sehemu ya utafiti huu, utaulizwa baadhi ya taarifa kuhusu historia yako ya matibabu na sampuli ya damu iliyochukuliwa. Kuna baadhi ya mambo kuhusu utafiti huu unapaswa kujua. Haya ni kwamba unaweza kuhisi usumbufu kutokana na kuchomwa sindano katika eneo la ukusanyaji wa sampuli ya damu na kwamba wakati fulani kutokwa na damu na uvimbe kunaweza kutokea. Tutahakikisha kutokwa na damu kumekoma kabla ya kuondoka. Sio kila mtu atakayeshiriki katika utafiti huu atafaidika. Faida inamaanisha kuwa kitu kizuri kinatokea kwako. Tunadhani manufaa haya yanajumuisha majaribio ya bila malipo ya maabara ili kujua hali ya chuma. Tukimaliza na somo hili tutaandika ripoti kuhusu kile tulichojifunza. Ripoti hii haitajumuisha jina lako au kwamba ulikuwa kwenye utafiti. Si lazima uwe katika utafiti huu ikiwa hutaki kuwa. Ukiamua kuacha baada ya sisi kuanza, hiyo ni sawa pia. Wazazi wako wanajua kuhusu utafiti pia. Ukiamua ungependa kuwa katika utafiti huu, tafadhali saini jina lako. Mimi, _____, nataka kuwa katika utafiti huu

Appendix VI: Data collection tool

IRON STATUS AMONG KIDNEY TRANSPLANT RECIPIENTS AT KENYATTA NATIONAL HOSPITAL RENAL UNIT

Study number: ☐☐☐

Socio demographic characteristics

1. Age of patient (Years): ☐☐
2. Gender: Code, (Male=1, Female=2) ☐
3. Marital status:
    a. Single=1
    b. Married=2 ☐
    c. Divorced=3
    d. Widowed=4
    e. Missing=9
4. Occupation (Unemployed=1, Employed=2, Self-employed=3, Retired=4) ☐
5. Level of Education
    a. (None=1, Primary=2, Secondary=3, College=4, Adult education ☐
6. Smoking history: Code, (Never=1, Past=2, Current=3) ☐

Donor profile

6. Age of patient (Years): ☐☐
7. Gender: Code, (Male=1, Female=2) ☐
8. Aetiology of end stage kidney disease: ☐

    Glomerulonephritis=1
    Polycystic kidney disease=2
    Diabetes nephropathy=3
    Other=4

9. Dialysis vintage (months)……

10. Duration post transplantation (years)……..

11. Blood pressure systolic: ☐☐☐ /diastolic ☐☐☐

12. Weight: ☐☐ kg Height: ☐☐☐

13. BMI (kg/m^2) ……..

14. Current immunosuppression medication

Immunosuppressant	Yes	No
Tacrolimus		
Sirolimus		
Mycophenolate Mofetil		
Azathioprine		
Cyclosporine		

15. Previous blood transfusions……..

16. Current ACEI/ARB use (Yes=1, No=2)

Laboratory parameters

16. Serum creatinine (µmol/l)……

17. Estimated GFR (ml/min/1.73m^2):……

18. Haemoglobin (g/dl):……

19. MCV (fL):……

20. Ferritin (µg/L):……

21. Serum Iron (µmol/l):……..

22. TSAT (%):……

Appendix VII: Serum ferritin assay

Principle:

It combines a one-step enzyme immunoassay sandwich method with a final fluorescent detection (ELFA). The Solid Phase Receptacle (SPR) serves as the solid phase as well as the pipetting device for the assay. The reaction medium is cycled in and out of the SPR several times

Procedure:

1. Remove the reagents from the refrigerator and allow them to come to room temperature for at least 30 minutes.
2. Use one FER strip and one FER SPR for each sample, control or calibrator
3. Type or select FER on the instrument to enter the test code
4. Mix the three using a vortex type mixer
5. Pipette 100µl of calibrator, control or sample into the sample as well
6. Insert SPRs and the strips into the instrument and initiate the assay as directed.
7. Following completion of the assay, remove the SPRs and strips from the instrument.

Appendix VIII: Serum iron and TIBC assay

Principle:

Iron is quantitated by measuring the intensity of the violet complex formed in the reaction between ferrozine and iron in acetate buffer at 562 nm. Addition of thiourea helps to complex Copper which can bind ferrozine as well.

In TIBC, serum is mixed with 400µg/dl iron solution to saturate the iron binding sites of the serum transferrin molecules. Magnesium carbonate is used to remove excess iron. It is then centrifuged to precipitate magnesium carbonate and the supernatant is measured for iron content.

Procedure:

1. Filter 0.3ml of well mixed serum into 0.5ml serum cup and proceed with analysis for iron.
2. Next, using a plastic filtration column, remove fibrin and any other debris noted
3. Dilute 0.2ml well mixed serum with 0.4ml of 400 ug/dl iron saturating solution
4. Mix well by vortexing and allow to stand for 30 minutes
5. Add 0.1g of magnesium carbonate directly to each tube of diluted solution
6. Mix the content of the tubes and allow to stand for 45 minutes, mixing at 15-minute intervals.
7. Centrifuge the tubes to pack the magnesium carbonate.
8. Filter the supernatant into sample cups and proceed as with iron analysis.

Plagiarism report

IRON STATUS AMONG KIDNEY TRANSPLANT RECIPIENTS AT KENYATTA NATIONAL HOSPITAL RENAL UNIT

ORIGINALITY REPORT

13%	12%	9%	8%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Submitted to The University of Manchester Student Paper	1%
2	iapsmupuk.org Internet Source	1%
3	ouci.dntb.gov.ua Internet Source	1%
4	Submitted to Maryville University Student Paper	1%
5	Submitted to University College London Student Paper	1%
6	ir.mu.ac.ke:8080 Internet Source	1%
7	Submitted to University Of Tasmania Student Paper	1%
8	Amin S I Banaga. "Risk Factors of Post Renal Transplant Anaemia among Sudanese patients, a study in three renal transplant	1%

Lead supervisor and chairman of department

This dissertation has been submitted with the approval of my lead supervisor and chairman of the department of clinical medicine and therapeutics.

Lead supervisor:

Prof. S.O. McLigeyo,

Professor of Medicine

Consultant Physician and Nephrologist

Department of Clinical Medicine and Therapeutics

University of Nairobi

Signed..... Date. 8/11/23

Chairman of the Department:

Prof. E.O. Amayo,

Professor of Medicine

Consultant Physician and Neurologist

Department of Clinical Medicine and Therapeutics

University of Nairobi.

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
DEPARTMENT OF CLINICAL MEDICINE & THERAPEUTICS
P.O. BOX 19676-00202 NAIROBI

Signed..... Date. 14/11/2023