PREVALENCE AND CORRELATES OF ANAEMIA OF CHRONIC KIDNEY DISEASE AT KENYATTA NATIONAL HOSPITAL

Carol Kemmy Maina, B Pharm

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November 2015

DECLARATION

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Signature.................................... Date.......................................

Dr. Peter Karimi, MPharm, Msc, MBA

Department of Pharmaceutics and Pharmacy Practice

University of Nairobi

Signature...................................... Date.......................................

Dr. Sylvia Opanga, MPharm

Department of Pharmaceutics and Pharmacy Practice

University of Nairobi

DEDICATION

To my loving husband Kizito Mariita, my son Karoli and my parents Mr and Mrs. Maina.

ACKNOWLEDGEMENT

ABBREVIATION AND ACRONYMS

ACEIs	Angiotensin Converting Enzyme Inhibitors
AIDS	Acquired Immunodeficiency Syndrome
ARBs	Angiotensin II Receptor Blockers
ARV	Anti Retroviral drugs
BP	Blood Pressure
BPH	Benign Prostatic Hyperplasia
BUN	Blood Urea Nitrogen
CKD	Chronic Kidney Disease
CCB	Calcium Channel Blockers
CCM	Chronic Care Model
CREATE	Cardiovascular Risk Reduction by Early Anaemia Treatment with Erythropoetin beta trial
DM	Diabetes Mellitus
DMARDS	Disease Modifying Anti Rheumatic Drugs
EDTA	Ethylenediaminetetraacetic Acid
ESA	Erythropoietin Stimulating Agents
ESRD	End Stage Renal Disease
GCP	Good Clinical Practices
eGFR	Estimated Glomerular Filtration Rate
ERC	Ethics and Research Committee
GFR	Glomerular Filtration Rate
HAART	Highly Active Antiretroviral Therapy
Hb	Haemoglobin
HCTZ	Hydrochlorothiazide
HD	Hemodialysis

HIV	Human Immunodeficiency Virus
HIVAN	Human Immunodeficiency Virus Associated Nephropathy
HLA	Human Leukocyte Antigen
HTN	Hypertension
ICH	International Conference on Harmonisation
K/DOQI	Kidney Disease Outcome Quality Initiative
K/DIGO	Kidney Disease Improving Global Outcomes
KNH	Kenyatta National Hospital
L-Amp	Liposomal Amphotericin
MDRD	Modified Diet in Renal Disease
MCV	Mean Corpuscular Volume
MCH	Mean Corpuscular Hemoglobin
MCHC	Mean Corpuscular Hemoglobin Concentration
NHANES	National Health and Nutritional Health Survey
NICE	National Institutes for Health and Clinical Excellence.
NKDEP	National Kidney Disease Education Program
NKF	National Kidney foundation
PD	Peritoneal Dialysis
PKD	Polycystic Kidney Disease
PRESAM	Pre dialysis Survey on Anaemia Management
RBC	Red Blood Cell
RF	Renal Failure
SDF	Socio Demographic Factors
SOPs	Standard Operating Procedures
SPSS	Statistical Package for the Social Science

TRESAM	Transplant European Survey on Anaemia Management
UK	United Kingdom
UoN	University of Nairobi
USA	United States of America

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DEFINITION OF TERMS

Anaemia: A condition in which the number of red blood cells per mm^3, the amount of hemoglobin in 100 ml of blood, and/or the volume of packed red blood cells per 100 ml of blood are less than normal. Anaemia is frequently manifested by pallor of the skin and mucous membranes, shortness of breath, palpitations of the heart, soft systolic murmurs, lethargy, and fatigability.

Chronic kidney disease: A progressive loss of function over several months to years, characterized by gradual replacement of normal kidney architecture with interstitial fibrosis.

Correlates: The mutual or reciprocal relation of two or more items or parts.

Hemoglobin: The red respiratory protein of erythrocytes, consisting of approximately 3.8% heme and 96.2% globin, with a molecular weight of 64,450, which as oxyhemoglobin (HbO$_2$) transports oxygen from the lungs to the tissues where the oxygen is readily released and HbO$_2$ becomes Hb.

Incidence: Occurrence of new cases of diseases that develop in at risk population over a specified time period.

Prevalence: The number of cases of a disease existing in a given population at a specific period of time (period prevalence) or at a particular moment in time (point prevalence).

ABSTRACT

Background: Anaemia is a common complication of chronic kidney disease and is strongly predictive of complications and death from cardiovascular causes. It has also been shown to have an impact on the quality of life. There is paucity of local and regional data regarding anaemia in patients with chronic kidney disease in Kenya, its severity and associated co-morbidities, and its control.

Objective:

The broad objective of this study was to determine the prevalence of anaemia and its correlates in chronic kidney disease at Kenyatta National Hospital.

Methodology

A cross sectional study was carried out at the renal clinic of Kenyatta National Hospital over a period of three months from March 2015 to June 2015. The study targeted 212 chronic kidney disease patients who met the inclusion criteria. Consecutive sampling was employed in the selection of study participants attending the renal clinic. Following informed consent a questionnaire was used to interview patients who had been enrolled in the study. Clinical and laboratory information that the patient was unable to provide was extracted from their files. These included co-morbidities, duration of kidney disease, patient's medication, and serum haemoglobin and creatinine values. A full hemogram test and a serum creatinine test were conducted for individuals who did not have a recent haemoglobin and serum creatinine values. Data was analysed using the statistical software, statistical package for the social sciences version 20.

Results

There was male predominance, 120(56.6%) in this study. Hypertension was the most prevalent risk factor and was associated with lower glomerular filtration rate. Majority of Chronic Kidney disease patients were in stage 3-5. Most of the chronic kidney disease patients had had the renal failure for less than four years, 148(69.8%). There was a high prevalence of anaemia, 140(67%). A strong correlation was noted between deteriorating renal functions and anaemia, ($p<0.0001$). There was strong correlation between diabetes and anaemia. There was no correlation between social demographic factors and anaemia. Only a small proportion, 58(41%) of anaemic patients were

being managed for anaemia. A considerable proportion of patients either had a contraindicated or inappropriate in drug prescribed.

Conclusion

There was a high prevalence of anaemia of chronic kidney disease. The proportion of the anaemic patients prescribed for hematinics was low. Contraindication or inappropriateness in drug prescription was noted in some patients. Early screening and optimal management of anaemia of chronic kidney disease may contribute greatly in reducing morbidity and mortality from cardiovascular events. Proper knowledge, practice and attitudes towards the care of chronic kidney disease patients should always be emphasized.

Recommendation:

Regular screening for all patients with chronic kidney disease and proper management for anaemia should be emphasized. Treatment guidelines for management of chronic kidney disease in each stage should be formulated. Further studies on economic evaluation of therapeutic strategies which include maintaining of haemoglobin levels versus correction from low levels at different stages of chronic kidney disease should be conducted.

CHAPTER ONE: INTRODUCTION

1.1 Background

The kidneys play vital roles in the body including regulation of water and electrolytes, excretion of wastes, and production of hormones. In chronic kidney disease irreversible damage results in inability of the kidneys to perform their functions. CKD affects between 5-15% of the adult population in the developed world [1]. In Africa, CKD is estimated to affect about 10.4% of some populations making it a significant public health issue [2-3].

1.2 Stages of CKD

Chronic kidney disease is termed as abnormality of function or structure for a period of more than three months with health implication and is usually classified based on cause, category and albuminuria [4].

CKD is categorised by the level of kidney function as indicated in the table below:

Table 1: Stages of Chronic Kidney Disease

Stage	Description	Glomerular Filtration Rate $(ml/min/1.73m^2)$
1	Kidney damage with normal or increase GFR	>90
2	Kidney damage with mild or decreased GFR	60-89
3	Moderate decrease in GFR	30-59
4	Severe decrease in GFR	15-29
5	Kidney failure	<15 (includes patients on dialysis)

Stages 1 and 2 have not been directly associated with symptoms due to reduced GFR, but if present have been associated with underlying renal disease. However stages 3 and 4 have been associated with complications due to reduced GFR. Such complications include anaemia, renal osteodystrophy, metabolic acidosis and electrolyte imbalance. Uremic symptoms in addition to other complications are predominant in stage five [5].

1.3 Anaemia of Chronic Kidney Disease

Anaemia of CKD, which is primarily caused by a deficiency in the production of endogenous erythropoietin by the kidney, is a common complication and contributes to cardiovascular disease [6]. It is strongly predictive of complications and death from cardiovascular causes in patients with chronic kidney disease. It has been independently associated with the development of left ventricular hypertrophy [6].

Almost every organ of the body is affected by anaemia as a result of reduced oxygen delivery and utilization in the tissues. CKD patients suffering from anaemia have an impaired quality of life, exercise capacity, and cognitive function [7]. They also have increased blood transfusion requirements and erythropoietin treatment decreases the number of transfusions [7].

Anaemia should be investigated and treated as recommended by the guidelines on the management of anaemia in CKD. Guidelines state that anaemia should be diagnosed in adults and children >15 years with CKD when the Hb concentration is <13.0 g/dl (<13.0 g/dl) in males and <12.0 g/dl (<120 g/l) in females [4].

Management of anaemia includes administration of erythropoietin-stimulating agents (ESAs) and regular iron supplementation (oral or intravenous administration) to achieve target haemoglobin of at least 11 g/dl.

1.4 Problem Statement

Chronic kidney disease is often undetected and under treated because of its insidious onset and length of time to overt kidney failure. Anaemia due to renal disease commonly develops before the need for dialysis but is often clinically undetected and poorly controlled. This is because in the early stages of CKD, anaemia is asymptomatic. Patients tend to adapt to moderately low haemoglobin levels and may not necessarily present with the classic signs and symptoms of anaemia. Therefore, many patients start anaemia treatment too late [8].

Anaemia induces adaptive cardiovascular mechanisms to maintain tissue oxygen supply. This leads to left ventricular hypertrophy, left ventricular dilation and myocardial ischemia which increase the risk factors for cardiovascular disease and death. A relationship has also been described between anaemia and mortality in CKD patients [6].

In the Pre dialysis Survey on Anaemia Management [9] that evaluated anaemia treatment in CKD patients, most CKD patients were anaemic prior to dialysis (mean Hb concentration 9.5 +/- 1.7 g/dl). Only 27% of patients had started ESA treatment before dialysis therapy.

Anaemia in CKD has been associated with cardiovascular complications. A retrospective cohort study done by Kazmi et al revealed that onset of anaemia in CKD is diagnosed at later stages of CKD [10]. Diabetes as cause of CKD and single nephrology visit had greater odds of presence of anaemia. Management for anaemia has been found to be sub optimal even in cases at where nephrologists were involved in the management [10]. Better understanding on anaemia of CKD is really needed in order to optimise management.

1.5 Study Objectives

1.5.1 Broad Objectives

1. To determine the prevalence and correlates of anaemia of Chronic Kidney Disease.

1.5.2 Specific Objectives

The specific objectives were:

1. To determine the prevalence and severity of anaemia of CKD at KNH.
2. To find out the risk factors associated with anaemia of CKD at KNH.
3. To correlate stages of CKD with anaemia of CKD at KNH
4. To find out the proportion of anemic patients with CKD that is being managed for anaemia.

1.6 Research Questions

The research sought to answer the following questions:

1. What is the prevalence and severity of anaemia of CKD at KNH?
2. What are the risk factors associated with anaemia of CKD at KNH?
3. What is the correlation between stages of CKD and anaemia of CKD at KNH?
4. What is the proportion of anemic patients with CKD at KNH that's being managed?

1.7 Justification

Anaemia is a common complication that contributes to the burden of disease associated with chronic kidney disease [11]. Anaemia of chronic kidney disease is a strong predictor of cardiovascular events and has therefore been largely associated with a high morbidity and mortality [12]. Untreated anaemia negatively affects cardiac health, cognitive function, exercise capacity and quality of life among patients with chronic kidney disease [13]. Despite this adverse effects the identification and management of anaemia among patients with chronic kidney disease has been reported to be suboptimal [14-16]. Little is known about the prevalence and management of anaemia among patients with chronic kidney disease under the care of a physician. Therefore the purpose of this study is to describe prevalence and correlates of anaemia of chronic kidney disease since anaemia is the greatest cause of morbidity and mortality in chronic kidney disease patients.

1.8 CONCEPTUAL FRAMEWORK

Conceptual model showing the association of stages of CKD with anaemia and its complications
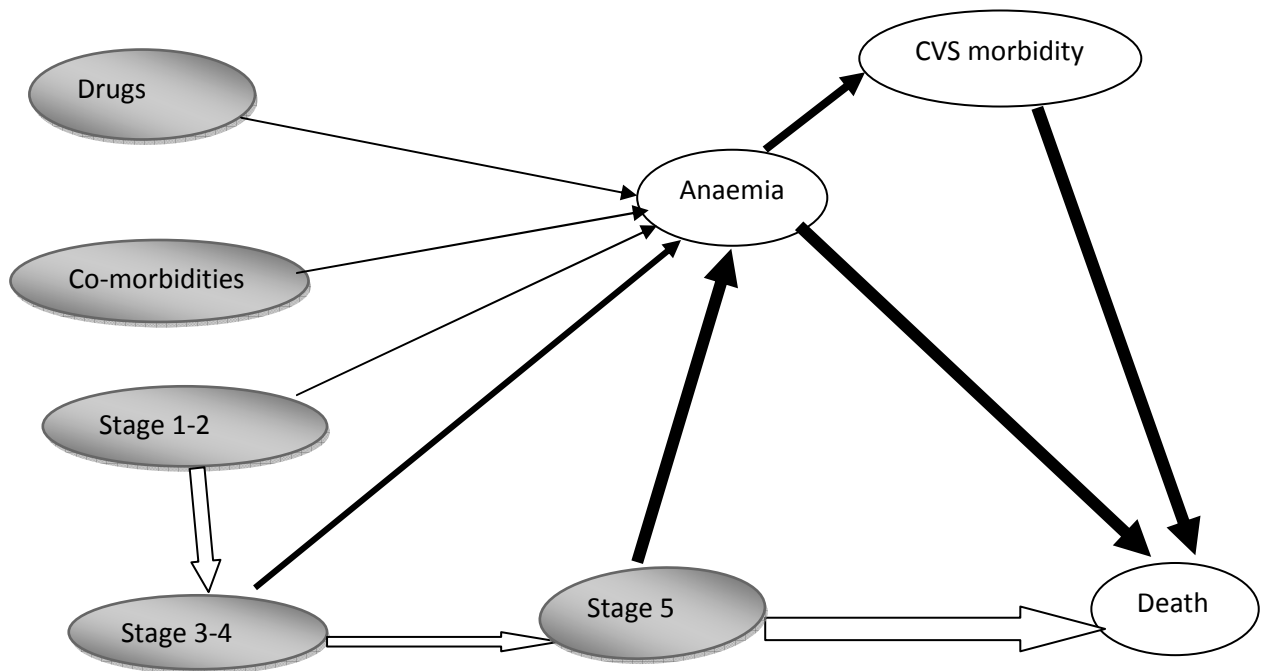
Figure 1: Conceptual Framework

The dependent variable is anaemia. The independent variables are co-morbidities, Stages of CKD, drugs and socio demographic factors. Shaded ellipses represent stages of CKD and other risk factors for development of anaemia in CKD patients. Un-shaded ellipses represent anaemia and its consequences in CKD. Increasing thickness of arrows connecting later stages to complications represents the increased risk of complications as kidney disease progresses. 'Co-morbidities' include the causes of CKD such as diabetes, hypertension and glomerulonephritis. Drugs which are nephrotoxic can worsen the renal functions and hence lead to anaemia. Block arrows indicate progression of chronic kidney disease.

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

This chapter covers the prevalence of chronic kidney disease and associated anaemia, co-morbidities, drugs that have nephrotoxic effect and management of anaemia of CKD.

2.2 Prevalence and Aetiology of Chronic Kidney Disease

The Centre for Disease Control and prevention found out that in the US an estimate of 16.8% of adults aged 20 years and older had CKD in the period between 1999 to 2004 [17]. In the UK estimates show that 8.8% have CKD [18]. In Africa, CKD is estimated to affect about 10.4% of some populations [2, 3].

A study done in the US revealed that an estimate of 8.3 million people had CKD stages 3 to 5 and 11.3 million Americans are at risk of developing or have mild decrease in kidney function [19]. It also revealed that the prevalence of these stages of CKD in the US population is as below: 1.8% for stage 1, 3.2% for stage 2, 7.7% for stage 3 and 0.35% for stages 4 and 5. Patients with stage 3 or 4 disease progress to end stage renal disease or stage 5 at a rate of 1.5% per year [19].

A study done in Ghana gave the following prevalence on aetiology of CKD. Chronic glomerulonephritis (33%), hypertension (21.2%) and diabetes mellitus (22.2%) were found to be the leading causes of CKD [20]. Studies done at KNH revealed that the main causes of CKD are chronic glomerulonephritis, diabetes mellitus and hypertension [21-23]. In one of the studies obstructive uropathy was also found to be a major cause [21]. Herget-Rosenthal et al revealed that currently diabetes is one of the leading cause of CKD worldwide [24].

2.3 Prevalence of Anaemia of Chronic Kidney Disease

Anaemia of CKD is due to decreased erythropoietin production from the kidneys, which stimulates RBC synthesis in the bone marrow and it worsens as GFR declines. There is a higher prevalence of anaemia when GFR is less than $60ml/minute/1.73m^2$. A significant consequence of anaemia is cardiovascular complications causing increased mortality in CKD patients. The documented causes of anaemia in CKD

patients include blood loss, shortened life span, erythropoietin deficiency and uremic milleu [25].

Blood loss is usually due to platelet dysfunction [26], while shortened red cell life span is prominent in haemodialysis where it is reduced by a third [27]. Erythropoietin deficiency is a functional response due to reduced GFR [28] and uremic milieu may explain why level and prevalence of anaemia may correlate with severity of CKD [29].

A study done in United States revealed that anaemia was twice prevalent in people with Chronic Kidney Disease as compared to the general population. This showed that CKD patients were more at risk of developing anaemia. The same study also revealed that a total of 22.8% of CKD patients with anaemia reported being on treatment within the previous three months. This showed that relatively few CKD patients were being treated for anaemia and therefore screening of anaemia in CKD patients is vital [8].

Findings from a study conducted in Saudi Arabia revealed that the prevalence of anaemia in CKD patients was slightly lower compared to other studies [30]. This is probably due to differences in population and geographic factors. Like other studies the prevalence of anaemia increased as the Kidney function worsened. The number of people who required treatment with erythropoietin was equally high.

Study done in a tertiary hospital in Nigeria found out that all the study participants had anaemia with their Hb ranging between 5.6g/dl to 9.0g/dl [31]. These results are consistent with the results of other investigators in the same country [32-34]. Study done in Ghana revealed that anaemia was the most common complication in CKD. Other complications include pulmonary oedema, high blood pressure and infections [20]. Sterner *et al* [35] in a systematic literature review observed that anaemia is the most common complication of CKD managed by clinical pharmacists and its management leads to improved disease oriented outcome. However there is paucity of local data regarding anaemia of CKD.

2.4 Co-morbidities associated with Anaemia of Chronic Kidney Disease

Anaemia is a documented complication in pre dialysis CKD patients. The prevalence of anaemia has been shown to increase as the GFR declines particularly among

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diabetic CKD patients. The prevalence of anaemia has been shown to vary depending on the associated co-morbidity. Evidence from literature suggests that there is a high prevalence of anaemia in each stage in African American and diabetic patients with CKD [25]. This has been corroborated by a study done to determine the prevalence and severity of anaemia. This study revealed that anaemia was more prevalent in diabetic CKD patients followed by vascular diseases and hypertension. Anaemia was also evident in CKD caused by multiple myeloma and chronic glomerulonephritis [36].

2.5 Correlates of Anaemia of Chronic Kidney Disease

A study done in the United States revealed a strong correlation between anaemia and female sex. Female are 2.2 times as likely as males to have values of less than 12g/dl. There was no strong association between severity of anaemia and age. The difference in prevalence of anaemia in different races was evident. Anaemia was observed to be highest in native Americans as compared to Caucasians, African Americans, Hispanics and Asians. The GFR measurements indicated a strong association between prevalence of anaemia and severity of CKD [36]. However there is paucity of local data showing correlation of anaemia with the several factors.

As kidney functions deteriorates the severity of anaemia increases [8]. This has been revealed from a study done in the United States where the prevalence increased gradually in the study population from 8.4% in stage one to 53.4% in stage 5.This has also been corroborated by another study done in Saudi Arabia where there was increase in prevalence of anaemia from 21% in stage one to 72% in stage five [30].

2.6 Nephrotoxic Drugs and Anaemia

Development of drug induced kidney disease is usually associated with various therapeutic agents. Nephrotoxicity is often reversible on discontinuation of offending agent, but in some cases may still be an acute kidney injury or even progress to stage 5 CKD. A retrospective study conducted at Taiwan University hospital revealed that 7.1% of patients taking anti-tuberculosis drugs had acute kidney injury. Reports have shown that renal function impairment is a common complication in anti-TB treatment in an aging population [37].

Evidence from a study to assess retrospectively the frequency of L-Amp induced anaemia, thrombocytopenia, nephrotoxicity, hepatotoxicity and hypokalemia reveal that anaemia and low RBC count is evident in about half of adult patients respectively [38]. Evidence from literature reveals that nephrotoxicity from aminoglycosides occurs in 10 to 20% of patients and is usually mild or moderate in terms of severity. Gentamycin has been shown to cause nephrotoxicity more frequently as compared to Tobramycin. Increase in nephrotoxicity has been observed when cephalothin is used with either Gentamycin or Tobramycin. Recommendation in patients with severe infections and use of aminoglycosides depends on relative toxicity of the drugs [39].

Report from a three year period single centre study set in Poland show that there is a strong association between complete blood count and renal function in ARV treated HIV patients who fulfil the criteria for anaemia. In the population that was anaemic the eGFR was positively correlated with red blood cells and platelet count, and negatively correlated with mean corpuscular volume (MCV) and mean corpuscular haemoglobin concentration (MCHC) and . The correlations were statistically significant and independent of gender and therefore eGFR in anaemic population with HIV and on treatment with nephrotoxic drugs should be frequently monitored [40].

2.7 Management of Anaemia of Chronic Kidney Disease

Anaemia should be managed as per clinical guidelines in CKD patients in order to achieve increase in cognitive and sexual function, exercise capacity and reduce transmission requirements [41]. A survey done in the United States to determine the prevalence of anaemia in CKD patients showed that only 22.8% of CKD patients were being anaemia in the previous three months [8].

Retrospective and prospective studies have observed suboptimal management of anaemia among pre dialysis patients with CKD. This inadequate treatment has been seen to negatively impact on cognitive function, cardiac function, and quality of life. Early intervention in the correction of anaemia has been associated with the reduction of morbidity and mortality [36].

A study conducted by PRESAM on evaluation management of anaemia in CKD study revealed that only 27% of the patients were on ESAs therapy before dialysis. This shows that there is mismanagement regarding anaemia of CKD [9]. This observation

has been corroborated by report from TRESAM that showed only 10.8% of anaemic transplant patients were on ESAs [42].

A prevalence study based on routine health care of diabetic CKD patients in North West England demonstrates improvement of quality of life with management of anaemia. The study show a higher prevalence of anaemia in diabetic CKD which worsened as eGFR declined. The recommendations were that proper screening for anaemia in diabetic CKD and proper management should be extended to routine diabetic care [43]. This is in consistent with another study done in nursing homes that showed that only few people with anaemia that are being treated although not managed properly [44].

2.8 Treatment Guidelines and Recommendations

The prevalence and incidence of anaemia increases as the kidney functions deteriorates. Frequent monitoring of haemoglobin levels is required in order to determine the most appropriate management. The severity of anaemia and state of CKD usually determines the choice of intervention from iron administration, ESA therapy or blood transfusion.

According to KDIGO clinical practice guidelines for anaemia several recommendations are to be considered when implementing blood transfusion as a haematinic [45]. Red blood cell transfusion is recommended in urgent treatment of anaemia, especially where rapid correction of anaemia is required to stabilise condition and where rapid pre operative correction of haemoglobin is required [45].

Red cell transfusion is also recommended where the benefits outweigh the risks in patients with CKD patients where ESAs therapy risks outweigh benefits and in cases where ESAs therapy is ineffective due to resistance or bone marrow failure. Red cell transfusion may be avoided in order to reduce the risk of allosensitization or to generally reduce risks associated with their use [45]. In hemodynamically stable patients blood transfusion should be considered in very low haemoglobin levels of less than 7g/dl or levels of less than 8g/dl in post operative surgical patients, ESA resistance, clear symptoms related to anaemia and cardiovascular diseases [46].

Iron therapy is recommended when there is benefit of avoiding or minimizing ESA therapy, red cell transfusion or anaemia related symptoms. Intravenous iron therapy is

recommended for adult CKD patients not on iron or ESA therapy. A one to three month oral iron therapy can be an alternative to non dialysis CKD patients. Intravenous iron therapy is recommended for adult CKD patients on ESA therapy who are currently not taking iron supplements or oral iron therapy for a period of one to three months for pre dialysis patients. The route for pre dialysis patients is based on severity of iron deficiency, availability, side effects with prior oral or intravenous iron, cost and patient compliance.

In initiating ESAs therapy the potential benefits associated with reduction of red cell transfusion, anaemia related symptoms should be considered. ESAs therapy should not be initiated in individuals with Hb concentration of more than 10g/dl in pre dialysis patients. In individuals whose Hb is less than 10g/dl in pre dialysis patients, ESAs initiation should be individual based on ESAs risks related therapy, prior iron therapy response and severity of anaemia. ESAs therapy is recommended in stage 5 CKD patients to avoid level going below 9g/d [45].

ESAs are regarded as effective agents in correcting and maintaining stable haemoglobin levels. The newer erythropoietin derivatives have longer administration interval due to their longer half life and lower binding affinity to receptor. Complete correction of anaemia has shown no benefit and has been associated with various adverse effects hence a target haemoglobin level of 11-12g/dl has been suggested [6].

Study done on normalization of haemoglobin levels in patients with CKD and anaemia revealed that complete correction of anaemia has no added advantage, This is in consistent with the CREATE study that adds evidence to confirm the current guidelines which recommend partial correction of anaemia [47].

Stage 5 CKD patients have been shown to require higher ESAs doses than pre-dialysis patients. Haemoglobin levels should increase slowly during the correction phase. Target haemoglobin level rise should not exceed 1g/dl in a two week interval. Higher incremental rates have been associated with cardiovascular and thromboembolic events [6].

ESAs should be given cautiously in CKD patients with anaemia while targeting a haemoglobin level of between 11-12g/dl. Erythropoietin alfa, an ESA has been associated with side effects such as worsening of hypertension and injection site reactions. Recommendation on use of iron supplementation during therapy with ESAs

has been encouraged as pharmacologically induced erythropoiesis is limited by iron supply [25].

2.9 Role of Community Health Care Workers

The management of CKD has been largely left for nephrologists. The primary care providers have tended to defer treatment hence missing opportunities for early management which can greatly slow down the process to ESRD. This slowing down also reduces rate of onset of complications including anaemia of CKD. The NKDEP has played a major role in encouraging both non physician and physician health profession in taking an active role in CKD screening, education and management prior to referral. The program further encourages patients to better understand and manage their CKD and its related conditions. The NKDEP uses the CCM as an approach towards improving care of chronic illness. This care summarises the basic elements for improved health care in community organization practices and patient levels and offers a systematic way of identifying needs and setting priorities within this elements [48].

CHAPTER THREE: METHODOLOGY

3.1 Introduction

This chapter describes the research design, study site, study population, study period, sampling technique and study participants. The sample size calculation is illustrated and how these subjects were recruited. Data collections and analysis is also outlined.

3.2 Study Design

A cross sectional study was employed targeting patients with an established diagnosis of CKD who were on follow up at the renal clinic of KNH. An interviewer administered questionnaire was used to collect information from the patients who met the inclusion criteria. Any clinical information that the patient was unable to provide was obtained from their patient file. Those who did not have recent haemoglobin level had to undergo a full hemogram test done according to Appendix 6, while those who did not have a recent serum creatinine levels had to undergo a serum creatinine test done according to appendix.5.

3.3 Study Area

The study was conducted at the renal clinic of Kenyatta National Hospital. The hospital is the largest in Kenya located at its capital city. It serves individuals from different parts of the country. The renal clinic serves patient who have CKD that are on follow. The clinic runs once a week, every Friday morning except public holidays. Approximately eighty patients are seen every week and of these 75% have CKD translating to about 50 patients a week.

3.4 Study Period

The study was carried out over a three month period between March 2015 to June 2015. This period was sufficient for enough sample size to be collected and also allowed for sufficient time needed for data analysis and presenting the findings

3.5 Study Population

The study population involved adult patients who had been diagnosed with CKD and were on follow up at the renal clinic of KNH between March 2015 to June 2015.

3.5.1 Inclusion Criteria

The study included patients who had an established diagnosis of CKD, aged above 18 years and agreed to consent.

3.5.2 Exclusion Criteria

Patients who had a known cause of anaemia other than renal disease, renal transplant patients, pregnant women and those who did not consent to participate in the study.

3.6 Sample Size Determination

The sample size was estimated based on the prevalence of anaemia in chronic kidney disease patients in the renal clinic of a Ghanaian tertiary hospital. In this study, 86.7% of patients with CKD were found to be anaemic with haemoglobin values less than 11.0g/dl [20].

Using Fisher's formula [49].

$$N = \frac{Z^2_{\alpha/2} \, P \, (1-P)}{\delta^2}$$

Where

N = Minimal sample size required.

p = Estimated prevalence of anaemia in chronic kidney disease = 86.7% [11].

$Z_{\alpha/2}$ = Standard normal deviate at 95% confidence interval corresponding to 1.96

δ = Absolute error between the estimated and true population prevalence of CKD of 5%.

The calculated sample size

$$N = \frac{1.96^2_{\alpha/2} \, 0.876(1-0.876)}{0.05^2}$$

=177 patients.

Adjusted for 20% incomplete data, the sample size was 212.

3.7 Sampling Method

Consecutive sampling was used until the sample size was achieved.

3.8 Research Instruments

A screening eligibility form: This was used to guide selection of patients who met the inclusion criteria.

Informed consent form: This was used to obtain consent from those who met the eligibility criteria. Those unable to understand the English version were given the Kiswahili version of the same

Data Collection Form: A well structured questionnaire was used to collect information file after the patient signed the consent form. It had three sections. The first section had socio demographics details. The second section had medical history which was to collect relevant clinical and laboratory information, and the third section had the medication history which involved collecting information on the currently prescribed drugs.

3.9 Case Definition

Anaemia was defined as haemoglobin of <13g/dl in males and < 12g/dl in females according to KDIGO 2012 Guidelines.

The stage of kidney disease was categorized using eGFR calculated based on the serum creatinine levels using the MDRD formula [5]. This is illustrated below:

eGFR (ml/min/1.73m2) = $175 * (\text{serum creatinine})^{-1.154} * \text{Age}^{-0.203} * (0.742 \text{ if female}) * (1.212 \text{ if black})$

Stage	Description	eGFR(ml/min/1.73m^2)
Stage 1	Kidney damage with normal or increased eGFR	≥90
Stage 2	Kidney damage with mild decrease in eGFR	60-89
Stage 3	Kidney damage with moderate decrease in eGFR	30-59
Stage 4	Kidney damage with severe decrease in eGFR	15-29
Stage 5	Kidney failure	<15

3.10 Recruitment and Consenting Procedure

On the clinic day the study was fully explained to the patients after they had been seen by the doctor. This was done by the researcher who used the screening and eligibility form (Appendix 1) to recruit eligible patients. An explanation on the procedure, harm, benefits and confidentiality of the study was given to those eligible before administering a consent explanation form (Appendix 2). Those who were willing to consent were required to sign a consent declaration form (Appendix 3).

3.11 Data Collection Procedure

A structured questionnaire was used to interview patients who signed a consent form. To maintain consistency in questions asked all questionnaires were administered by the principal investigator in the same manner. The questionnaire had three main sections (Appendix 4).

The first section was used to obtain social demographic information such as age, sex, marital status, level of education, occupation, level of income and patient status on alcohol intake and cigarette smoking. The second section was used to obtain medical history. Duration of the renal failure and laboratory information were obtained from this section. If the laboratory tests had not been done within 30 days for either serum creatinine or full hemogram test then the respective laboratory procedures were done.

The laboratory tests were done at the renal laboratory of the renal unit at KNH by a qualified laboratory technician based at the renal unit. The tests done included a

serum creatinine test or full hemogram test. A serum creatinine test was carried out according to determine the level which will then be used to calculate the eGFR using the MDRD formula which will later be used for the staging of CKD (appendix 5).

If the haemoglobin levels had not been done for the past 30 days then a full hemogram test was carried out to determine the haemoglobin level. Anaemia was defined as haemoglobin levels of less than 13.0g/dl in adult male and less than 12g/dl in adult female according to KDIGO 2012 guidelines (Appendix 6).

The third section consisted of the medication history which was used to obtain information on the type of medication the patient was currently taking.

3.12 Study Variables

3.12.1 Dependent Variables

Anaemia: Patients was considered to have anaemia if the Hb level is less than 13g/dl in males and less than 12g/dl in females. WHO classification for anaemia was used:

Normal: ≥12g/dl for female; male≥13g/dl

Mild Anaemia: Female Hb (9.5-11.9) g/dl: Male Hb (9.5-12.9)

Moderate anaemia: Hb 8g/dl-9.4g/dl

Severe anaemia: Hb 6.5g/dl- 7.9g/dl

Life threatening: < Hb 6.5g/dl

3.12.2 Independent Variables

 These included:

Socio- demographic factors like: Age, Sex, Marital status, Level of education and Occupation.

Stage of CKD: It was assessed by use of the serum creatinine level to calculate the eGFR using the MDRD formula. Then graded as per the case definition above (Table 1)

Aetiology of Chronic Kidney Disease like: Diabetes mellitus, Hypertension, Chronic Glomerulonephritis etc

Anaemia treatment modality: This was defined as the current pharmaco-therapeutic modalities employed by the patient to achieve anaemia control.

3.13 Quality Assurance Procedure

A pilot study was done before initiating the questionnaire and the findings were used to improve the data collection instrument. Adjustment was done to improve the clarity, interpretation and quality of data collected. There was strict adherence to case definition.

Laboratory Investigations: Aseptic technique for handling and storage were followed to prevent pre analytical, analytical and post analytical errors.

3.14 Pilot Study

The investigator- administered questionnaires were used to collect information from twelve randomly selected patients with their files from the renal clinic who met the inclusion criteria. This was to test whether the tool could capture all necessary details regarding the patient condition and laboratory details. Necessary modification was made after the pilot study.

Validity

External validity of the study was enhanced by choosing an appropriate sample size and internal validity was confirmed by the accuracy of the tool through further modification of the tool after the pilot study

Reliability

The tool during the pilot study was tested for reproducibility of data and ambiguity was corrected before the main study. Reproducible result confirmed the tool effectiveness

3.15 Data Management

Data was collected using structured standardized tool and entered into a password protected Microsoft Access Database (Appendix 4). To ensure confidentiality collected data was locked up and accessed only by the principle investigator preserved to avoid loss and breach of confidentiality.

All collected data was coded, cleaned, processed and stored at the end of each day by the principal investigator. Data entry was done on the day of collection and backed up every three days. This was done in a CD which was stored at a separate site. Any data that had patient identification information was kept separate from the main data base. Hard copies were locked up and accessed only by the principal investigator.

The standards outlined in the GCP and ICH guidelines were adhered to. The laboratory personnel involved in this study were screened to determine whether they had appropriate qualifications and were briefed on the specific objectives and relevant procedures. They received supportive supervision to ensure maintenance of quality. The blood indices were measured at the KNH haematology laboratory. The equipments were regularly validated for accuracy.

3.16 Statistical Analysis

Once data entry was complete, Data was analysed using SPSS version 20. Descriptive data analysis was carried out to describe study population and identify extreme values and outliers. Categorical data such as sex, stage of CKD, anaemia treatment modality and status of anaemia control were presented as proportions.

Bivariate analysis was done to determine factors associated with anaemia. These variables included patient demographics, stage of CKD, primary aetiology of CKD and the anaemia treatment modalities being employed. To do this, correlation of anaemia with other variables was done using Chi square for independence. In each case, p values of less than 0.05 were considered statistically significant.

Multivariate stepwise backward logistic regression procedures were used to determine independent factors associated with anaemia. Odds ratios were computed and 95% confidence intervals and p values less than 0.05 was considered significant (appendix 6).

3.17 Ethical Considerations

Ethical approval was obtained from the KNH/UoN Ethics and Research Committee before commencement of the study. Consent was obtained in writing from the patient after a thorough explanation of what the study entailed. The patient was adequately informed that he/she was at liberty to withdraw from the study at any particular time without any penalty or consequence. The risks, benefits and confidentiality issues were conveyed before consenting to participate in the study. All data obtained were kept under lock and key or in password protected computer files to restrict access to only the principle researcher and her supervisors. The data collection instrument did not bear patient name, hospital registration number and the patients were only identified by study numbers.

CHAPTER FOUR: RESULTS

4.1 Introduction

This chapter depicts the findings of the research. The results have been summarised into tables of frequency, pie charts, bar graphs and percentages. The P values and Odds ratio and corresponding confidence intervals have been calculated. The results were based on the social demographic characteristics of study participants, co morbidity of CKD, duration and staging of CKD, Prevalence and severity of anaemia in renal failure, correlating duration of risk factors of CKD with staging in renal failure, correlating risk factors of CKD with anaemia and the their medication history.

4.2 Socio Demographic Characteristics of the Study Participants

There were more males, 120(56.6%) than females as shown in table 2. The median age was 55 years and the range was 19-91 years. Most of the patients, 125(59%) were aged between 35-65 years. Majority, 163(77.3%) of the patients were married with the divorced and separated having the least percentage. A relatively high proportion, 84(40.5%) of patients had obtained primary education followed by secondary level of education. Most, 148(71.8%) of the patients were low income earners with a similarly large proportion being non alcoholic and non smokers (Table 2).

Table 2: Socio Demographic Characteristics of the Study Participants

Variable	Frequency (%)
Sex	
Male	120(56.6)
Female	92(43.4)
Age group (years)	
18-35	31(14.6)
36-65	125(59)
> 65	56(26.4)
Marital status	
Single	23(10.8)
Married	163(76.8)
Separated	6(2.8)
Divorced	6(2.8)
Widowed	14(6.6)
Level of education	
Informal level	22(10.3)
Primary	84(39.6)
Secondary	75(35.3)
Tertiary	31(14.6)
Average Monthly Income (shillings)	
<10,000	150(70.7)
10,000-30,000	46(21.7)
>30,000	16(7.5)
Takes alcohol	
Never	147(69.3)
Occasionally	44(20.7)
Regularly	21(9.9)
Smokes cigarettes	
No	173(81.6)
Yes	39(18.4)

4.3 Clinical Characteristics of the Study Participants

4.3.1 Aetiology of Chronic Kidney Disease

Majority of the patients, 93(43.9%) had both diabetes and hypertension (Table 3). Hypertension was seen to be a greater risk whether present alone or in combination with other co morbidities. Polycystic kidney disease recorded the least prevalence even when present with other co morbidities. There were few patients, 6(2.8%) with a combination of HTN, DM and HIV.

Table 3: Aetiology of Chronic Kidney Disease

N=212 Study Participants

Aetiology	n (%)	Aetiology	n (%)
Diabetes only	4(1.9)	DM and UTO	10(4.7)
Hypertension only	35(16.5)	DM and other illness	22(10.4)
CGN only	17(8)	HTN and HIV	12(5.7)
HIV only	8(3.8)	HTN and PKD	3(1.4)
DM and HTN	93(43.9)	HTN and UTO	18(8.5)
DM and HIV	9(4.2)	HTN and other illness	43(20.3)
DM and PKD	0(0.0)	DM and HTN and HIV	6(2.8)

* CGN-Chronic Glomerulonephritis; DM- diabetes, HIV- Human Immunodeficiency Virus; PKD-Polycystic Kidney Disease, UTO-Urinary Tract Obstruction.

4.3.2 Duration and Staging in Renal Failure

A great proportion, 148(69.8%) of the patients had had renal failure for less than four years (Figure 2). There were much fewer patients who had had renal failure for more than ten years. Most of the patients were in stage five followed by four and three respectively (Figure 3). There were fewer patients in the early stages of CKD.
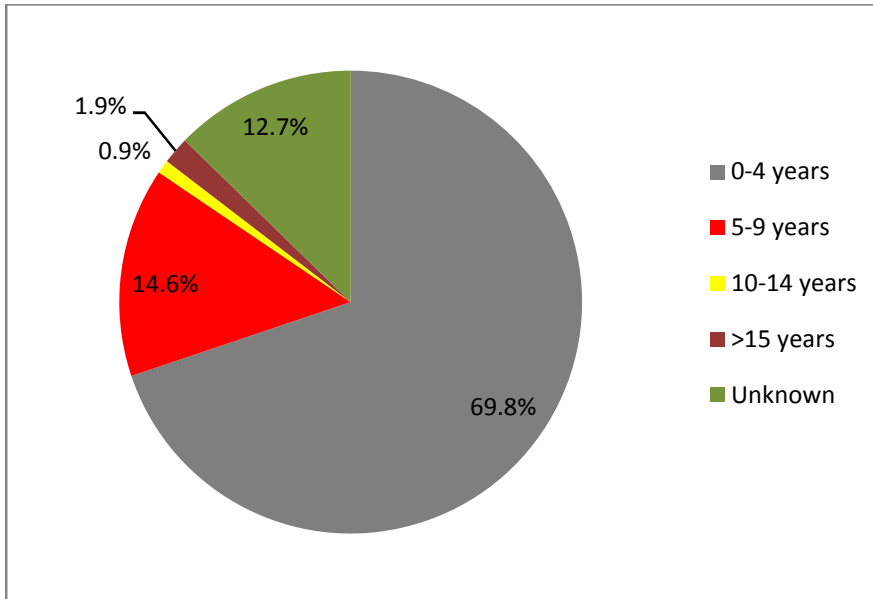
Figure 2: Duration of Renal Failure
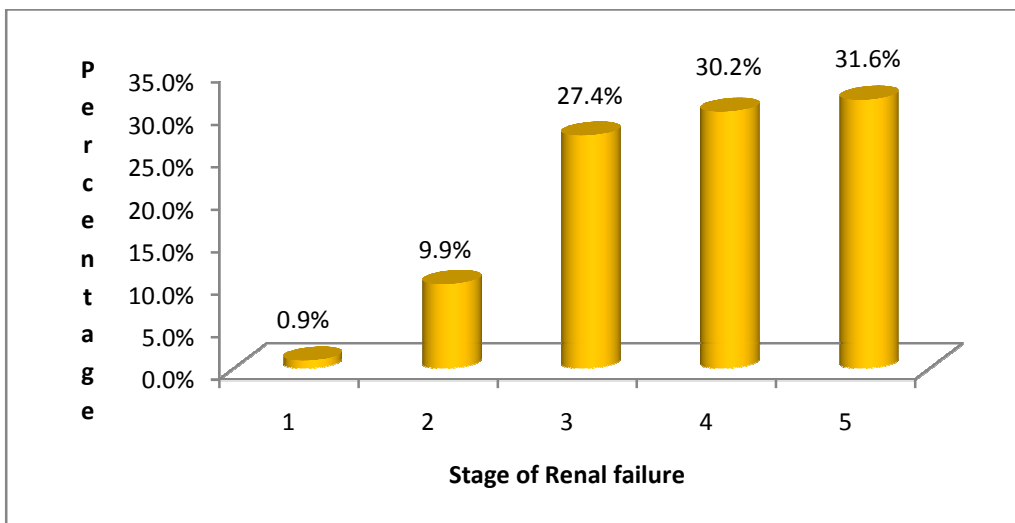
Figure 3: Proportion of Patients in different Stages of Renal Failure

4.3.3 Correlation of Socio Demographic Factors with Severity of Renal Failure

The only socio demographic factor that was significantly associated with stage of CKD was age (Table 4). Patients aged 18-35 years were more likely to have severe renal dysfunction compared to the other age groups (p=0.04). A bigger proportion of those who did not smoke had stage 5 CKD compared to those who smoked. However this difference was not statistically significant.

Table 4: Correlation between Socio Demographic Factors with Severity of renal failure

Variable	Stage of Renal failure					P value
	1	**2**	**3**	**4**	**5**	
	n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**	
Age(Years)						
18-35	1(3.2)	3(9.7)	7(22.6)	3(9.7)	17(54.8)	**0.040**
36-65	1(0.8)	14(11.2)	36(28.8)	38(30.4)	26(28.8)	
>65	0(0)	4(7.1)	15(26.8)	23(41.1)	14(25)	
Sex						
Male	1(0.8)	15(12.5	35(29.2)	31(25.8)	38(31.7)	0.408
Female	1(1.1)	6(6.5)	23(25)	33(35.9)	29(31.5)	
Takes alcohol						
Never	2(1.4)	13(8.8)	41(27.9)	48(32.7)	43(29.3)	0.314
Occasionally	0(0)	5(11.9)	11(26.2)	9(21.4)	7(40.5)	
Regularly	0(0)	3(14.3)	5(23.8)	7(33.3)	6(28.6)	
Smoke Cigarettes						
No	2(1.2)	16(9.3)	46(26.7)	53(30.8)	55(32.0)	0.916
Yes	0(0)	5(12.8)	11(28.2)	11(28.2)	12(30.8)	

4.3.4 Correlation between Duration of Aetiology of CKD with Severity of Renal Failure

The duration of hypertension and that of HIV disease were significantly associated with the stages of renal dysfunction (Table 5). Most of the patients that had hypertension as a risk factor were in stages 3, 4, and 5 of CKD while those that had

had hypertension for the longest duration, were in stages 2, 3, and 4 of CKD (p=0.003). Similarly, patients who had lived with HIV infection for over 10 years were in stage 3 of CKD (p=0.007). The duration of the other risk factors such as diabetes and glomerulonephritis was not significantly associated with the severity of renal function.

Table 5: **Correlation between duration of aetiology of CKD with severity of renal failure**

Variable	Stage of Renal failure			
Risk factor	Stage of CKD	No of Patients	Mean duration (Years)	P value
Diabetes				
	1	1	17	0.920
	2	10	13.60	
	3	23	12.26	
	4	43	13.21	
	5	18	12.00	
Hypertension				
	1	2	8	**0.003**
	2	16	10.69	
	3	43	11.05	
	4	54	9.35	
	5	52	5.21	
Glomerulonephritis				
	1	0	0	
	2	0	0	0.858
	3	3	2	
	4	1	3	
	5	11	3.82	
HIV				
	1	0	0	**0.007**
	2	3	6	
	3	6	11.17	
	4	3	4.67	
	5	6	2.83	

4.3.5 Regression Analysis of Various Factors against Renal Failure

The analysis revealed that male were more likely to develop renal dysfunction [0.488(95%CI 0.257-0.927), P=0.03]. Lower HB grouping was associated with worsening renal function, [0.388(95%CI 0.253-0.594), P<0.0001]. Diabetes, hypertension, age group and HIV showed no statistical significance when regressed against renal failure (Table 6).

Table 6: Regression Analysis of Various Factors against Renal Failure

Risk factor	Coefficient	S.E of coefficient	P value	OR	95%CI for OR	
					Lower	Upper
Diabetes	.384	.325	.238	.681	.360	1.288
Age group	.343	.256	.180	.710	.430	1.172
HIV	.617	.513	.229	1.854	.678	5.067
Hypertension	.022	.484	.964	1.022	.396	2.637
Sex	-.718	.327	**.028**	.488	.257	.927
HB group	-.948	.218	**.000**	.388	.253	.594

4.4 Anaemia of Chronic Kidney Disease

This section incorporates the prevalence, severity of anemia and its correlation with the independent variables.

4.4.1: Prevalence and Severity of Anaemia of Chronic Kidney Disease

Anaemia was prevalent in 142(67%) of patients. Patients with mild anaemia were the majority, 71(34%) while a lower percentage had moderate, severe and life threatening. The prevalence of anaemia decreased with increasing severity (Figure 4).
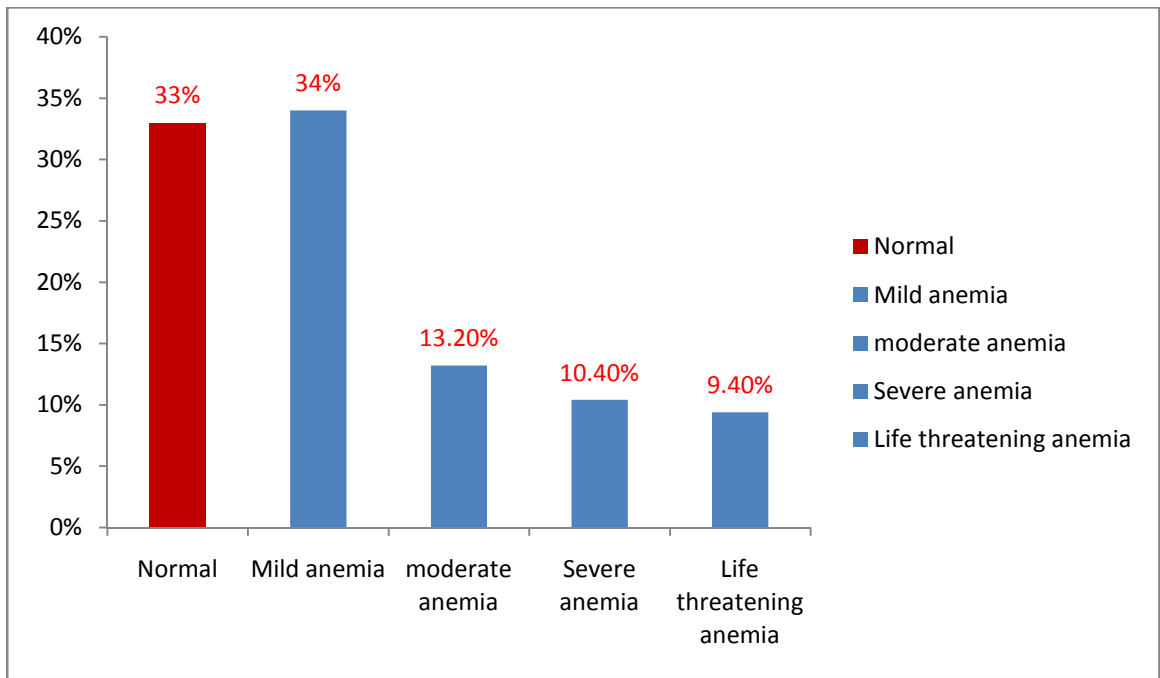
Figure 4: Prevalence and Severity of Anaemia of Chronic Kidney Disease

4.4.2: Prevalence and Severity of Anaemia in the different Stages of CKD

The chance of being anaemic increased with worsening kidney function and the association was statistically significant (Table 7). Majority of the patients with mild anaemia were in stages three and stage four. Severe and life threatening anaemia was most prevalent among patients in stage five of renal failure.

Table 7: Prevalence and Severity of Anaemia in the different stages of CKD

Variable	Severity of Anaemia					P value
	Normal	**Mild**	**Moderate**	**Severe**	**Life threatening**	
	n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**	
Stage of Renal failure						
1	2(0.9)	0(0)	0(0)	0(0)	0(0)	<0.0001
2	15(7.07)	3(1.4)	1(0.5)	2(0.9)	0(0)	
3	30(14.2)	20(9.4)	6(2.8)	0(0)	3(1.4)	
4	17(8.01)	31(14.6)	9(4.2)	4(1.9)	4(1.9)	
5	6(2.83)	17(8)	12(5.7)	16(7.5)	14(6.6)	
Total	**70(33)**	**71(33.4)**	**28(13.2)**	**22(10.4)**	**21(9.9)**	**212(100)**

4.4.3 Correlation between Socio demographics with Anaemia of CKD

Our study demonstrated no correlation between the socio demographics with Anaemia CKD as all the p values> 0.05 as shown in Table 8.

Table 8: Correlation between Socio Demographics with Anaemia of CKD

Variable		Severity of Anemia					
		Normal n (%)	Mild n(%)	Moderate n(%)	Severe n(%)	Life threatening n(%)	P value
Age group (years)	18 - 35	9(30.0)	9(30.0)	4(13.3)	3(10.0)	5(16.7)	0.239
	36 – 65	37(30.1)	40(32.5)	19(15.4)	13(10.6)	14(11.4)	
	>65	24(42.9)	22(39.3)	4(7.1)	5(8.9)	1(1.8)	
Sex	Male	39(33.3)	39(33.3)	16(13.7)	11(9.4)	12(10.3)	0.983
	Female	31(33.7)	32(34.8)	11(12.0)	10(10.9)	8(8.7)	
Marital status	Single	8(38.1)	7(33.3)	2(9.5)	0(0.0)	4(19.0)	0.652
	Separated	1(16.7)	4(66.7)	0(0.0)	1(16.7)	0(0.0)	
	Married	54(33.5)	51(31.7)	24(14.9)	17(10.6)	15(9.3)	
	Divorced	3(50.0)	3(50.0)	0(0.0)	0(0.0)	0(0.0)	
	Widowed	4(28.6)	6(42.9)	1(7.1)	2(14.3)	1(7.1)	
Education level	Informal	8(38.1)	4(19.0)	2(9.5)	4(19.0)	3(14.3)	0.752
	Primary	27(32.5)	27(32.5)	12(14.5)	9(10.8)	8(9.6)	
	Secondary	25(34.2)	26(35.6)	11(15.1)	6(8.2)	5(6.8)	
	Tertiary	10(34.5)	12(41.4)	2(6.9)	1(3.4)	4(13.8)	
Occupation	Unemployed	16(26.2)	19(31.1)	11(18.0)	6(9.8)	9(14.8)	0.334
	Self-employed	23(31.9)	24(33.3)	10(13.9)	7(9.7)	8(11.1)	
	Employed	12(37.5)	11(34.4)	5(15.6)	2(6.2)	2(6.2)	
	Retired	19(44.2)	17(39.5)	1(2.3)	5(11.6)	1(2.3)	
Income	<10000	47(32.2)	49(33.6)	19(13.0)	14(9.6)	17(11.6)	0.606
	10000-30000	16(36.4)	15(34.1)	7(15.9)	4(9.1)	2(4.5)	
	>30000	6(46.2)	6(46.2)	0(0.0)	0(0.0)	1(7.7)	
Takes alcohol	Never	51(35.2)	49(33.8)	19(13.1)	14(9.7)	12(8.3)	0.991
	Occasionally	14(34.1)	14(34.1)	5(12.2)	4(9.8)	4(9.8)	
	Regularly	5(23.8)	8(38.1)	3(14.3)	2(9.5)	3(14.3)	
Smokes cigarettes	No	57(33.7)	56(33.1)	24(14.2)	19(11.2)	13(7.7)	0.340
	Yes	13(33.3)	15(38.5)	3(7.7)	2(5.1)	6(15.4)	

4.4.4 Correlation between Aetiology of CKD with Anaemia

Association was observed between diabetes (p=0.010), glomerulonephritis (p=0.021) and Systemic lupus erythematosus (P=0.007) with anaemia (Table 9).

Table 9: Correlation between Aetiology of CKD with Anaemia

Aetiology	Category of Anaemia					P value
	Normal n(%)	**Mild** n(%)	**Moderate** n(%)	**Severe** n(%)	**Life threatening** n(%)	
Diabetes						
No	28(25.7)	34(31.2)	19(17.4)	13(11.9)	15(13.8)	**0.010**
Yes	42(42)	37(37)	8(8)	8(8)	5(5)	
Hypertension						
No	10(30.3)	9(27.3)	5(15.2)	2(6.1)	7(21.2)	0.138
Yes	60(34.1)	62(35.2)	22(12.5)	19(10.8)	13(7.4)	
Glomerulonephritis						
No	68(35.2)	66(34.2)	24(12.4)	20(10.4)	15(7.8)	**0.021**
Yes	2(12.5)	5(31.2)	22(18.8)	1(6.2)	5(312.)	
Systemic lupus erythematosus						
No	70(33.7)	71(34.3)	27(13)	19(9.2)	20(9.7)	**0.001**
Yes	0(0)	0(0)	0(0)	2(100)	0(0)	

4.5: Utilization of Drugs

This section outlines the drugs currently prescribed to the study participants.

4.5.1: Classes of Prescribed Drugs to the Study Participants

The types of drugs used by the patients are summarised in Table 10. The most commonly prescribed drugs were diuretics where furosemide and HCTZ were the most preferred. Calcium channel blockers were also highly recommended. Among the Beta Blockers 91(43%), carvedilol was the drug of choice. The ARBs were preferred twice as much as the ACEIs. In the management of diabetes Insulin was the most prescribed at 71(33.49%). The oral hypoglycaemic agents frequently prescribed were the biguanides and metformin the most prescribed. NSAIDs were the analgesics of choice. Antilipidemics were prescribed more often with more preference to atorvastatin as opposed to rosuvastatin. The alpha 1 antagonist were prescribed to patients with BPH. Hematinics were prescribed to a small proportion of CKD patients. The most commonly prescribed hematinics included the oral and injectable

iron supplementation and erythropoietin derivatives. Red blood cell transfusion was an option to individuals who had severe anaemia.

Table 10: Classes of Prescribed Drugs to the Study Participants

N=212 Respondents

Drug	n(%)	Drug	n(%)
Diuretics	165(77.89)	Hematinics	58(27.3)
Calcium channel blockers	130(61.3)	Antiretroviral	17(8.0)
Beta blockers	91(43)	Antidiabetics	107(55.2)
ARBs	68(32)	Antilipidemics	72(34)
ACEIs	36(17)	Anticoagulants	4(1.9)
Direct arteriole vasodilators	21(9.9)	Asthma medication	8(3.8)
Alpha 1 antagonists	5(2.3)	Drugs acting in the GI	39(18.4)
Alpha 2 agonists	8(3)	Analgesics	7(3.3)
Antiplatelets	45(22.5)	Drugs for neuropathy	10(4.8)
Antibiotics	20(9.9)	Others	33(15.6)

*ARBs: Angiotensin II receptor blockers * ACEIs: Angiotensin converting enzyme inhibitors.

4.5.2: Contraindications in prescribed medicines.

Majority, 168(79.2%) of patients had no contraindicated drug prescribed. Thirty five (16.5%) had one drug contraindicated (Figure 5). The most common contraindicated drugs prescribed being metformin and NSAIDs for end stage renal disease patients.

Frequency of Drugs Contraindicated

3.80%   0.50%

16.50%

79.20%

- None
- 1 drug
- 2 drugs
- 3 drugs
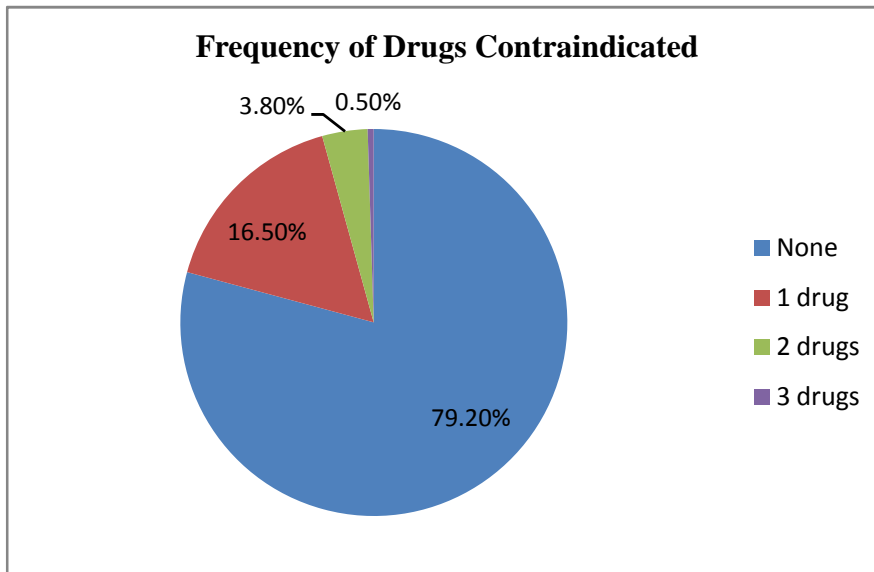
Figure 5: Contraindications in drugs prescribed

4.5.3: Inappropriate Dosing of Drugs to CKD Patients.

A great of fraction of CKD patients 174(82.1%) had appropriated dosages of drugs prescribed. Despite the fact that the remaining proportion of patients had the correct drug prescribed there was inappropriate dosing with no consideration to renal adjustments (Figure 6). Most patients of who were not given appropriate dose were on one drug. In some cases there were as high as more than five drugs inappropriately dosed.
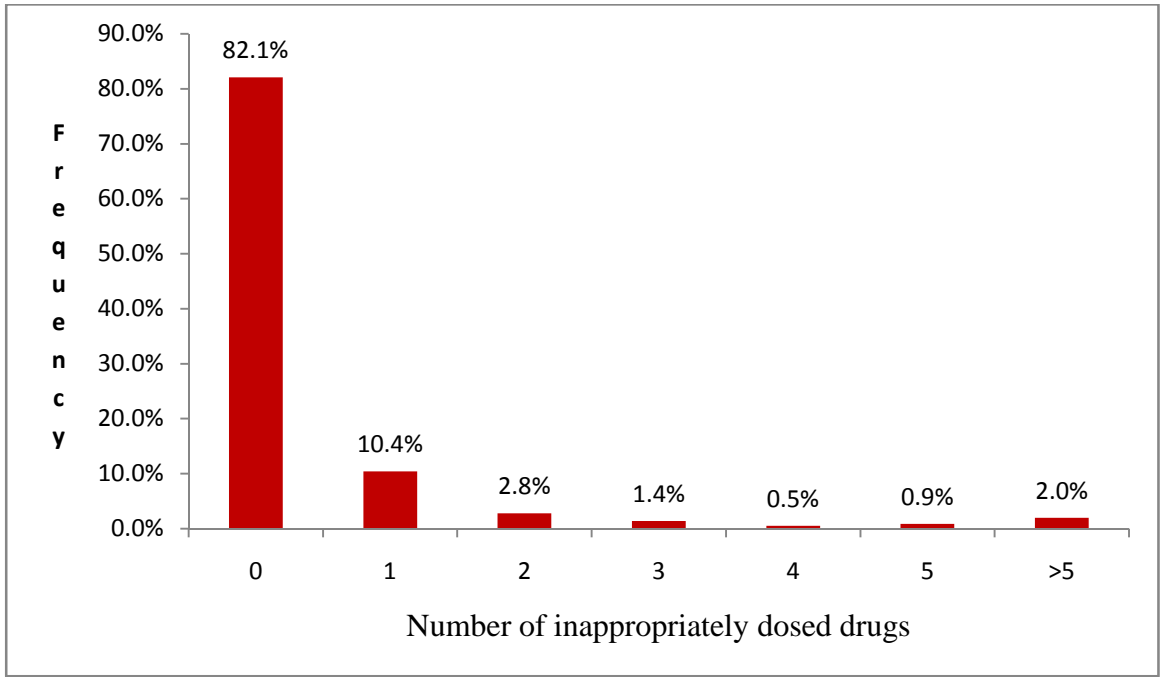
Figure 6: Number of Drugs Inappropriately Dosed

CHAPTER FIVE: DISCUSSION, CONCLUSION AND RECOMMENDATION

5.1: Introduction

This chapter discusses the result findings within the perspective of previous research literature. Conclusions and recommendations have been drawn based on the research findings.

5.2: Discussion

This study showed male predominance which is consistent with findings of a study done in Ghana [20]. Studies done in Spain, USA and Nigeria also had higher male to female ratio [50-52]. Male predominance could be a reflection of the fact that CKD and its risk factors such as hypertension, smoking and alcoholism are common in males than females. Majority of the study participants had formal education. The median age was 55 years with a range of 19-91 years. Most patients were less than 60 years which is the economically active age group. These findings are consistent with findings from a study done in Ghana [20]. Majority of the study participants were low income earners which could partially explain why the high prevalence of CKD in a middle age group probably due to lack of finances to seek medical care in controlling the risk factors. The only social demographic factor that was significantly associated with stage of CKD was age. Patients aged 18-35 years were more likely to have severe renal dysfunction compared to the other age groups. Age associated loss of kidney functions has been recognized for decades. In contrast with our findings one would expect the severity to renal failure to be more in a higher age group.

The results of the aetiology of CKD was based on a combination of risk factors that the study participant had in contrast to most previous study where they only addressed the individual risk factors. Patients who had both DM and HTN recorded the highest prevalence at 93 (43.9%). Hypertension or diabetes with other illness equally had a high prevalence respectively. The above results are consistent with studies done in our local setting that revealed CGN, diabetes and hypertension as being the major risk factors for CKD [21-23]. The above findings are consistent with a study done in Ghana [20]. Hypertension had the highest prevalence as a single risk factor as opposed to diabetes and HIV. This is in consistent with most studies although other studies have reported diabetes to be the most prevalent [5]. It has also been documented that diabetes is the leading cause of CKD in the United States [53]. A

strong correlation was seen with duration of hypertension and severity of renal failure. Those who had hypertension as a risk factor with a long duration were in the later stages of CKD. This is probably due to the fact that hypertension has a high prevalence worldwide and causes increase in morbidity and mortality of cardiovascular diseases and chronic kidney disease [54].Since the advent of HIV/AIDs epidemic there has been a rapid development of irreversible chronic kidney disease. The results revealed a considerable proportion of HIVAN (3.8%). This is in consistent with studies that revealed a high prevalence of HIVAN in the developing world [55]. The research findings demonstrated a strong correlation between HIV and renal dysfunction. The longer the period the patients had HIV then the more the probability of developing severe renal dysfunction. The advancement of HAART has been shown to slow down the progression to HIVAN [56].

Most patients had the renal dysfunction for a period of less than four years. This could probably be explained by the high mortality associated with CKD. It has been demonstrated that CKD is currently the twelve highest cause of death and seventeenth highest cause of disability [57]. This high mortality could be explained by a study done in our local setting to determine the factors associated with late presentation of CKD patients to nephrologists. The study demonstrated high prevalence of late presentation in stage four and five [58]. A considerable proportion had renal failure for a period of 5-9 years while quite a reasonable proportion could not recall the duration. The most prevalent stages of CKD were stage 3stage 4 and stage 5. This is consistent with a study done in multi centre done in Saudi Arabia [30]. Findings from another study done in our local setting demonstrated the same higher prevalence of the later stages of CKD [58].

Anaemia is a common complication in CKD patients. Our study recorded a high prevalence of anaemia. That is consistent with findings from other African studies [32, 33]. Similarly data from NHANES [8] revealed that anaemia was as twice as prevalent in people with CKD as in the general population. A prospective cross sectional study [20] conducted in a tertiary hospital in Ghana equally reported a high prevalence of anaemia. The social demographic factors showed no correlation with anaemia of CKD. All parameters had a P value of>0.05. This is in contrast with a cross sectional US multi survey study [36], that demonstrated a strong relationship

between female sex and anaemia. The study demonstrated that females were 2.2 times as likely as males to have values of <12g/dl.

Prevalence of anaemia has strongly been associated with declining glomerular filtration rate. This is comparable with findings from different studies. Our research findings demonstrated an increase in prevalence with declining GFR. These findings are consistent with a large scale cross sectional US multicenter survey [36]. A report by NHANES equally revealed that prevalence of anaemia increased from 8.4% in stage 1 to 53.4% in stage five [8]. Another study done in Saudi Arabia gave consistent findings [30]. Kazmi *et al* [10] demonstrated that prevalence of anaemia increased progressively from stage 1 to stage 5. The second group with hemoglobin less than 11g/dl equally recorded a similar trend of anaemia prevalence of 24% in stage 1 to 74% in stage five. The severity of anaemia was noted to worsen with deteriorating renal functions. Our research findings observed a prevalence of mild to moderate anaemia in the earlier stages of CKD while later stages of CKD had a greater prevalence of severe and life threatening anaemia.

A strong correlation was evident between diabetes, chronic glomerulonephritis and SLE with anaemia of CKD. This is consistent with a large scale cross sectional US multi survey which revealed a strong correlation between diabetes and anaemia [36]. Clinical practice guidelines for diabetes and CKD have shown that a combination of diabetes and CKD to be the most potent predictor of adverse cardiovascular events and deaths [59].

Patients with CKD are more likely to die of cardiovascular events than require dialysis. Optimal management of cardiovascular risk factors have been shown to reduce morbidity and mortality [53]. Various antihypertensive agents were prescribed to the study participants. The reviewed literature explains the important role of antihypertensive therapy in slowing down the rate of CKD in both diabetic and non diabetic patients [60. 61]. Diuretics were the most prescribed with furosemide being the most preferred. This could be explained by the fact that loop diuretics have more profound effects in later stages of CKD. Thiazide diuretics only have significant effect in early stages of CKD while potassium sparing diuretics may increase the risk of hyperkalemia. Calcium channel blockers have been considered for prevention of kidney disease due to their effect on renal hemodynamic, cytoprotective and

antiproliferative properties which prevent mesangial expansion and renal scarring. CCBs were the second most prescribed antihypertensive agents. Preference was given to the dihydropyridines (nifedine and amlodipine). This is in contrast with literature that explains the non dihydropyridines has being more effect in reducing proteinuria [62]. The NKF-KDOQI guidelines suggest that dihydropyridines should be used in combination with ACEIs. Beta blockers were similarly prescribed with more preference to carvedilol. They have been shown to offer beneficial effects in the management of diabetic nephropathy [63]. ACEIs and ARB therapy have been shown to reduce chronic increase in glomerular pressure mediated by angiotensin II which causes progressive kidney failure. Our research findings demonstrated high prescription of ACEIs and ARBs. ARBs were preferred twice as much as the ACEIs. This is contrast to findings of a study conducted in our local setting which revealed the ACEIs to be superior to ARBs [64].

Lipid metabolism is altered early in the course of kidney disease and becomes pronounced with more advanced disease making hyperlipidemia common in patients with chronic kidney disease. Despite uncertainty to delay progression, treatment of dyslipidemia should be considered because abnormal lipid metabolism predisposed patients to cardiovascular disease. This is in consistent with recent NKF-K/DOQI guidelines which classify CKD patients in the highest risk of cardiovascular disease and choice of lipid lowering agent should be based on individual lipid profile.

The research results demonstrated that a great proportion of diabetic CKD patients used insulin as opposed to the oral hypoglycaemic agents. This could have been attributed to its safety in later stages of CKD. Metformin was the oral hypoglycaemic agent mostly prescribed, however its use is limited due to the associated metabolic acidosis. Strict glycemic control has been associated with reduced proteinuria and slowing the rate of decline of eGFR [59].

Anaemia is strongly predictive of complications and death from cardiovascular causes in patients with CKD. Findings involving several countries revealed that as haemoglobin concentration decreases there was a corresponding rates of hospitalization and mortality [65]. Early and adequate treatment of anaemia has a positive impact on morbidity and mortality in these patients. Our results findings revealed a large prevalence of anaemia in the study participants but only a small proportion was being managed for anaemia. This is consistent with findings from

NHANES analysis [8]. Similarly a cross sectional multi centre survey done in the United States revealed a high percentage of anaemia in CKD patients who were not being managed [36]. Another study conducted in Saudi Arabia revealed a high prevalence of anaemia of CKD and relatively a large burden of patients who required treatment with erythropoietin [30]. A survey on anaemia management by PRESAM showed that although 57% of patients had been under the care of nephrologists for 12 months only 27% had started ESA prior to dialysis [9]. This is further evident in another survey done by TRESAM which revealed that only a minority of anaemic transplant recipients received ESA treatment for their anaemia [42]. The suboptimal management of anaemia among predialysis CKD patients has been reported in both retrospective and prospective cohort studies conducted within nephrology practices [14-16]. The study results confirmed that erythropoietin and iron were the preferred hematinics. This is consistent with a review article on current treatment of anaemia in patients with CKD which confirmed use of ESAs in the last two decade and their effectiveness in correcting and maintaining stable Hb levels [6]. Oral or intravenous iron supplementation has been shown to reduce severity of anaemia in patients with CKD. KDIGO guidelines on anaemia management recommend correction of iron deficiency since untreated iron deficiency is an important cause of hypo responsiveness to ESA treatment.

Majority of the patients were also being prescribed for calcium supplements. Calcium binders have been used to correct hyperphosphatemia and hypocalcaemia. However recent data has indicated the high prevalence of calcium supplementation may lead to vascular calcification. On the basis of existing data it may be safer to have the upper limit of calcium intake up to 1gram [66].

The high prevalence of renal insufficiency in hospitals and the fact that quite a number of drugs and their active metabolites are eliminated via the kidney makes these patients vulnerable to adverse drug reactions. The research results indicated quite a considerable proportion of CKD patients who had either a contraindicated drug prescribed or inappropriate dosages recommended. This is in consistent with a retrospective study conducted in a major tertiary hospital in the Kingdom of Saudi Arabia [67], Fourteen percent of these drugs were contraindicated and resulted in a system alert. The contraindicated drugs administered were gliclazide, acetyl salicylic acid, nitrofurantoin and spironolactone. ASA accounted for approximately 60%. It is

recommended that physicians need to consider renal dosing of medicines in order to avoid toxicity or further worsening of renal functions.

5.3: Study Limitations:

Like all other cross sectional studies it was prone to selection bias as some patients declined to consent to the study

Some patients especially those over 70 years found it difficult to recall all aspects regarding their illness hence this could have lead to distortion of information

There was likelihood that some patients did not give truthful information on aspects like adherence to medication, smoking, and income. This was however minimized by explaining in details the importance of the study and getting consent from only those who accepted to participate in the study.

The study did not factor in dietary issues which would have somehow affected the severity of anaemia.

5.4: Conclusion

Chronic kidney disease was more prevalent in males than females. Late referral of CKD patients to nephrologists was noted due to high prevalence of stage four and five and the highest proportion of patients with the shortest duration of renal failure. Hypertension recorded the highest prevalence and was associated with lower eGFR. There was a high prevalence of anaemia of chronic kidney disease. Anaemia was more prevalent in patients with diabetes. There was increase in prevalence and severity of anaemia with worsening kidney functions. Antihypertensives were prescribed with diuretics having the greatest proportion. ARBs were more preferred compared to the ACEIs. Insulin was preferred for management of diabetes as opposed to the oral hypoglycaemic agents. There was sub-optimal management of anaemia patients with CKD. The preferred hematinics were the erythropoietin derivatives and injectable iron. Quite a considerable proportion of CKD patients either had contraindicated drug prescribed or inappropriate dosing of drugs.

5.5 Recommendations

5.5.1 Recommendation for Policy and Practice

1. Due to the high prevalence of anaemia of chronic kidney disease regular screening of all patients with chronic kidney disease and proper management should be instituted.

2. Treatment guidelines for managing chronic kidney disease in each stage should be formulated to ensure rational use of medication.

5.5.2 Recommendation for Research

1. Economic evaluation of therapeutic strategies which include maintenance of hemoglobin and correction from low levels at different stages of CKD should be done to improve quality of care.

2. Further studies should be carried out to evaluate the relationship between erythropoietin levels, hemoglobin levels and iron status in patients with chronic kidney disease at each stage of the disease in order to institute the best treatment modality.

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APPENDIX 1: SCREENING AND ELIGIBILITY FORM.

Screening No.................................   Date of screening......................

Section A: Inclusion criteria; Items 1-3 need to be answered yes for the participant to be eligible.

1. Is the patient diagnosed with CKD?   Yes ☐   No ☐

2. Is the patient aged 18 years and over?   Yes ☐   No ☐

3. Has the patient consented to participate? Yes ☐   No ☐

Section B: Exclusion criteria; Items 3-5 need to be answered NO for the participant to be eligible.

3. Is the participant a post renal transplant patient? Yes ☐   No ☐

4. Is the participant pregnant   Yes ☐   No ☐

5. Does the patient have any bleeding disorder, haemolysis or malignancy?   Yes ☐

    No ☐

6. Based on the criteria above is the participant eligible   Yes ☐   No ☐

7. If not eligible what is/are reason(s) for exclusion...

    ....

8. Comments (enrolled/not enrolled)..

APPENDIX 2: CONSENT EXPLANATION FORM

STUDY TITLE: PREVALENCE AND CORRELATES ANAEMIA OF CHRONIC KIDNEY DISEASE AT KENYATTA NATIONAL HOSPITAL

To be read in the language the patient understands best.

Introduction

My name is Dr Carol Maina. I am a postgraduate student in the Department of Pharmaceutics and Pharmacy practice; I am pursuing a degree of Master of Pharmacy in Clinical Pharmacy. I am conducting a study on **prevalence and correlates of anaemia of chronic kidney disease at KNH.** Results of this study are to form a background for better planning and management of anaemia of chronic kidney disease.

I would like to seek your permission to participate in the study. Kindly read the consent form below.

Purpose of the Study

This study aims to find out the prevalence and correlates of anaemia of chronic kidney disease at KNH. The study will last approximately three months and will involve a review of the patients' records to get pertinent clinical and laboratory data. Where recent laboratory indices will not be available, the patient will be requested to have these conducted.

Procedure:

If you agree to participate in the study you will be required to spare 20 minutes of your time at stipulated setting during your normal clinic day, where you will have a one to one interview with the principal investigator. This interview will be guided by a structured questionnaire. You may also be required to have some laboratory tests done to determine your haemoglobin levels and your kidney function state.

Benefits:

You may not benefit from this study immediately, but on completion of this study when the results have been collected and analyzed, they will be used to form a background for better planning and management of anaemia of chronic kidney disease at KNH.

Risks:

Good clinical and laboratory guidelines will be practiced during the collecting and handling of blood from you to minimize the risks of infections, excessive blood loss and physical injury.

Confidentiality:

Information collected from you will be stored safely at the institution under lock and key, by the principal investigator who is the only one who can access it. Your name will not be linked with findings from you and no single response will be reported on its own, but as a summation of all the responses. Your personal information will never be made public to other researchers or anyone else.

Compensation:

There will be no form of direct compensation in this study.

Conclusion

Your inclusion in this study is purely at your own voluntary will. You are free to decline participating in this study without any penalty. Should you understand the scope of your involvement in this study and wish to participate, you are still free to pull out of this study at any point for whatever reason without any consequence or loss of any benefit incurred.

Contacts: In case you have questions related to this study, you can contact the following:

Principal Investigator:

Dr. Carol Maina, Post graduate student (Clinical Pharmacy)

Department of Pharmaceutics and Pharmacy Practice, P.O. Box 30197-00400, School of Pharmacy, University of Nairobi, Mobile number 0728806849.

First Supervisor

Dr. Peter Karimi

Lecturer, Department of Pharmaceutics and Pharmacy Practice, P.O.Box 19676-00202 School of Pharmacy, University of Nairobi. Department's telcom No 2726300 Ext 4373

Second Supervisor

Dr. Sylvia Opanga

Lecturer, Department of Pharmaceutics and Pharmacy Practice, P.O. Box 19676-00202, School of Pharmacy University of Nairobi, Department telecom No: 272630 Ext 43673.

The Secretary, KNH/UoN-ERC

Kenyatta National Hospital, P.O Box 20723-00202, Nairobi Tel No. 2726300-9/ 2716450 Ext 44102, Fax 725272

Ethical Approval

Ethical approval will be granted by Kenyatta National Hospital/ University of Nairobi /Ethics and Research committee (KNH/UoN-ERC) to conduct this study at the renal clinic of Kenyatta National Hospital.

KIAMBATISHO 2B: MAELEZO YA IDHINI

KICHWA: PREVALENCE AND CORRELATES ANAEMIA OF CHRONIC KIDNEY DISEASE AT KENYATTA NATIONAL HOSPITAL

Isomwe kwa lugha anayoifahamu mshiriki

Utangulizi

Jina langu ni Dkt. Carol Maina. Mimi ni mwanafunzi wa shahada ya uzamifu katika kitengo cha Utabibu dawa, katika chuo kikuu cha Nairobi. Ninafanya utafiti wa upungufu wa damu mwilini kwa watu walio na ugonjwa wa figo na wanaohudhuria kliniki katika hospitali kuu ya Kenyatta

Nia ya Utafiti

Utafiti huu si wa kupeana tiba yoyote ila ni wa kuangalia idadi ya walio na upungufu damu mwilini kutokana na ugonjwa wa figo. Pia kuangalia jinsi wanavyotibiwa.

Utaratibu Utakaofuatwa

Ukikubali kushiriki katika zoezi hili basi utahitajika kuweka sahihi yako kwenye fomu ya hati ya makubaliano. Utaulizwa maswali kuhusu afya yako na familia yako. Maswala mengine yatatolewa katika faili yako ya hospitali. uenda ikawa kiwango chako cha damu na uwezo wa figo zako hazijajulikana kwa kipindi cha mwezi mmoja basi utatolewa damu ya mililita sita ili kiwango cha damu na uwezo wa figo zako kujulikana.

Hatari

Damu yako itatolewa kwa njia iliyo salama kulingana na masharti yaliyoko ili hathari zote zipungue kadri inavyowezekana. Hathari hizi zaweza kuwa ni viini wakati damu inapochukuliwa, uchungu, au kuvuja damu kuzidi kiwango kinachohitajika.

Usiri

Nakala yoyote inayotokana na huu uchunguzi itahifadhiwa kwa siri na itatumika tuu kwa utafiti huu.

Faida ya Kushiriki

Hakuna faida moja kwa moja kutokana na kushiriki kwako ila majibu ya utafiti huu yatatumiwa kuboresha jinsi wagonjwa wa jinsia yako wanavyotibiwa katika hospitali

kuu ya Kenyatta. Ingawa utapata nafasi ya kuuliza swali lolote kuhusiana na matibabu unayoyapata.

Hitimisho

Kushiriki kwako kwa utafiti huu ni kwa hiari yako, na huko huru kukubali au kukataa au kutoka wakati wowote wa utafiti huu. Kutoshiriki kwako kwa utafiti huu hakutahatarisha kwa vyovyote huduma unazozipata katika hospitali kuu ya Kenyatta.

 Kwa maswali yoyote kuhusu utafiti huu uku huru kuuliza:

Mtafiti Mkuu:

Dkt. Carol Maina, Mwanafunzi uzamili (Utabibu dawa)

Idara ya Pharmaceutics and Pharmacy Practice, S.L.P 30197-00400, Shule ya Pharmacy, Chuo kikuu cha Nairobi, Nambari ya simu 0728806849.

Msimamizi wa kwanza

Dkt. Peter Karimi

Mhadhiri, Idara ya Pharmaceutics and Pharmacy Practice, S.L.P 19676-00202, Shule ya Pharmacy, Chuo kikuu cha Nairobi. Simu ya idara 2726300 Ext 4373

Msimamizi wa pili

Dkt. Sylvia Opanga

Mhadhiri, Idara ya Pharmaceutics and Pharmacy Practice, S.L.P 19676-00202, Shule ya Pharmacy, Chuo kikuu cha Nairobi. Simu ya idara No: 272630 Ext 43673.

Katibu Mkuu, KNH/UoN-ERC

Hospitali kuu ya Kenyatta

S.L.P 20723-00202, Nairobi

Namba ya simu 2726300-9/ 2716450 Ext 44102, Fax 725272

Uthibitisho wa kimaadili

Utafiti huu utathibitishwa kimaadili na hospitali kuu ya Kenyatta/Chuo kikuu cha Nairobi/ Kamati ya maadili ya utafiti(KNH/Uon-ERC) ili ufanyike katika kliniki ya hospitali kuu ya Kenyatta.

APPENDIX 3: CONSENT DECLARATION FORM

Consent and Signature:

I confirm that I have read the information above and wish to participate in this research being conducted by Dr. Carol Maina. I understand that I am free to ask any questions or to withdraw from participation at any time without penalty. Having agreed on the above I voluntarily agree to participate in this study.

Name of the patient...................................... Signature.........................

Date...

KIAMBATISHO 3B: HATI YA MAKUBALIANO

Baada ya kusoma kwa makini na kuelezwa kwa kina na Dkt. Carol Maina juu ya utafiti huu na kufahamu ya kwamba kujihusisha kwa utafiti huu ni kwa hiari yangu na niko huru kujiondoa wakati wowote bila kudhuru kiwango cha matibabu yangu basi napea idhini yangu kwa kutia sahihi kwa fomu hii.

Jina ya mgonjwa:..................................   Sahihi................................

Tarehe........................

APPENDIX 4: QUESTIONNAIRE

Code Number of the participant: ....

Section 1: Baseline demographics.

1. Date of Birth: Day......................Month......................Year...................
2. Sex : Male ☐   Female ☐
3. Marital status: Single☐   Separated ☐   Married ☐   Divorced ☐
   Widowed☐
4. Highest level of education completed
   Informal level☐   Primary level☐   Secondary level☐   Tertiary level ☐
5. Occupation:
   Unemployed☐   Self employed ☐ Employed ☐   Retired ☐
6. Income per month (Ksh):
   < 10,000 ☐   10,000-30,000 ☐   > 30,000 ☐
7. Do you take alcohol?   Never ☐   Occasionally☐   Regularly☐
8. Do you smoke cigarettes?   Yes ☐   No ☐

SECTION 2: Medical history.

1. Is there any record or feature of patient having suffered the following

	Disease	YES	NO	If yes ,give duration in years
a	Diabetes mellitus			
b	Hypertension			
c	Glomerulonephritis			
d	HIV			
E	Polycystic kidney disease			
g	Urinary stones			
h	SLE			
I	Urinary tract obstruction			
j	Drug toxicity			
	Any other illness			

2. When was renal failure diagnosed? ....

3. Laboratory data within the last 30 days:

TEST	Value	Referance range
Hemoglobin (g/dl)		
Serum creatinine (mmol/L)		
Estimated GFR (ml/min)		
Stage of renal failure		

Section 3: Medication History

1.1 State the drug the patient currently taking:

	Name of the Drug	Current Dose		Contraindications	
		Appropriate	Not Appropriate	Yes	No
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					

4. Has the patient had a blood transfusion in the last 1 month? Yes ☐   No ☐

APPENDIX 5: PROCEDURE FOR SERUM CREATININE TEST

Objective: To demonstrate the ability of the kidney to eliminate waste products such as creatinine

Procedure

The following are required in order to perform the above test.

1. A 5cc syringe.
2. A needle: gauge 21
3. Plain vaccutainer
4. Mindray machine BS 400

The procedure below will be done by a qualified laboratory technician at the renal laboratory of the renal unit at KNH.

- Draw 3ml of blood from the patient forearm by use of 5cc syringe and a gauge 21 needle.
- Put the blood in a plain vaccutainer and leave it for 20 minutes to allow it to clot.
- Put it in a centrifuge machine and let it centrifuge at 2500 revolutions per minute in order to separate the clot from the serum.
- Pipette the serum in another container and put it in a mindray machine BS 400.
- Programme machine to run serum creatinine.
- Validate the results.

Quality control:

- Tests should be done at 37 degrees Celsius
- Grossly hemolysed samples should not be used.
- Blood samples should not stay longer than 2 hours at room temperature or more than 4 hours at 2-8 degrees Celsius before analysis is done.
- Participation in quality control checks regularly

APPENDIX 6: PROCEDURE FOR FULL HEMOGRAM TEST

Objective:

The following will be required to perform the above test:

- A 5cc syringe
- Vaccutainer with EDTA.
- Needle-gauge 21.
- Hemogram cell dyne 3700 machine.

Procedure:

The procedure below will be done by a qualified laboratory technician at the renal laboratory of the renal unit at KNH.

- Draw 3ml of blood from the patient forearm by use of 5cc syringe and a gauge 21 needle.
- Put it in a vaccutainer with EDTA.
- Roll gently four times for blood to mix with anticoagulant.
- Run the sample in a hemogram cell dyne 3700 machine.
- Validate the results.

Quality control:

- Tests should be done at 37 degrees Celsius
- Grossly hemolysed samples should not be used.
- Blood samples should not stay longer than 2 hours at room temperature or more than 4 hours at 2-8 degrees Celsius before analysis is done.
- Participation in quality control checks regularly

Appendix 7: Ethics Approval Letter

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

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

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

Ref: KNH-ERC/A/130

19th March, 2015

Carol Kemmy Maina
School of Pharmacy
University of Nairobi

Dear Carol

Research Proposal: Prevalence and correlates of anemia of chronic kidney disease at Kenyatta National Hospital   (P728/12/2014)

This is to inform you that the KNH/UoN-Ethics & Research Committee (KNH/UoN-ERC) has reviewed and **approved** your above proposal. The approval periods are 19th March 2015 to 18th March 2016.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH/UoN ERC before implementation.
c) Death and life threatening problems and severe adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH/UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH/UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
f) Clearance for export of biological specimens must be obtained from KNH/UoN-Ethics & Research Committee for each batch of shipment.
g) Submission of an *executive summary* report within 90 days upon completion of the study
This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

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

Yours sincerely

PROF. M. L. CHINDIA
SECRETARY,   KNH/UON-ERC

c.c.   The Principal, College of Health Sciences, UoN
         The Deputy Director CS, KNH
         The Chair, KNH/UoN-ERC
         The Dean, School of Pharmacy, UoN
         The Chairman: Dept. of Pharmaceutics and Pharmacy Practice, UoN
         Supervisor: Dr. Peter Karimi, Dr. Sylvia Opanga