PREVALENCE AND ASSOCIATIONS OF ANAEMIA AMONG PATIENTS ON CHRONIC HAEMODIALYSIS AT A TERTIARY HOSPITAL IN LIMPOPO PROVINCE,

SOUTH AFRICA

By

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MINI-DISSERTATION

Submitted in partial fulfilment of the requirements for the degree of

MASTER OF MEDICINE IN INTERNAL MEDICINE

In the

FACULTY OF HEALTH SCIENCES

(School of Medicine)

At the

UNIVERSITY OF LIMPOPO

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March 2022

PLAGIARISM DECLARATION

I, Blessing Kudakwashe Muponda, hereby declare that, this research study is my own work and that all sources that I have used or quoted have been indicated and acknowledged by means of in-text citation and list of references. This work has not been submitted for any other degree at any institution.

Signature: BLESSING MUPONDA Date: 17 March 2022

ACKNOWLEDGEMENTS

I would like to take this opportunity to thank the following for their contribution to this dissertation:

- My Lord and Saviour Jesus Christ for giving me life, strength, guidance, wisdom and protection throughout my studies.
- My siblings (Christian, Farai, Bernard, Lovern and Anozivaishe) for their unconditional support, encouragement, and love. As their elder brother, they inspire me to keep leading by example.
- Mosima Phadu, for her assistance with the research proposal.
- My supervisor, Dr Pheto Mangena, for his guidance, support, and encouragement.
- My Co-Supervisor Dr Mokibe Nchabeleng, for his guidance, support, and encouragement.
- Stephina Mokgalaka, for helping me with retrieving patients' files.
- Peter Mphekgwana, for assisting me with data analysis.
- My colleagues in the Internal Medicine department at the Polokwane/ Mankweng Hospital complex for their constructive comments.
- Mmaphoku Nkadimeng, for helping me with technical editing and proof reading of this dissertation.
- Tapiwa Michelle Chitate, for her assistance with proof reading.
- Limpopo Province Department of Health for giving me permission to conduct the study.

DEDICATION

I dedicate this dissertation to my parents (Rachel Muponda and Bernard Muponda) for their endless love, support, and encouragement.

ABSTRACT

Background: Anaemia is a very common cause of morbidity and mortality in patients with chronic kidney disease (CKD) on chronic haemodialysis[7]. The main aetiology of anaemia in CKD among patients on chronic haemodialysis is erythropoietin deficiency [1].

Aim: To determine the prevalence and associations of anaemia among patients on chronic haemodialysis at the PKDC in Limpopo Province, South Africa.

Methods: A retrospective descriptive, cross-sectional quantitative study was performed at a single dialysis centre (PKDC) and included all patients on chronic haemodialysis over a one-year period (01/01/2019 to 31/12/2019). A standardized data collection form created on Epi Info Version 7 was used to collect data from 121 study participants' hospital files. There was no sampling performed as all patients meeting the inclusion criteria were included in the study. The collected data was analysed using the SPSS Version 25.

Results: A total of 121 patients were included in the study. In the final data analysis, 55.5%(n=66) were males and 45.4%(n=55) were females. The overall mean age was 41.9 ± 11.7 years. Using the WHO definition of anaemia (Hb< 13g/dl in males and Hb<12g/dl in females), prevalence of anaemia was 89.3% and 85% in male and female patients, respectively. All 121 (100%) patients were on erythropoietin (EPO). According to the 2012 KDIGO guidelines, the target Hemoglobin (Hb) in haemodialysis patients on EPO is between 10g/dl and 12g/dl. Using a Hb level < 10 g/dl to define anaemia, the overall prevalence of anaemia was 23.1%(n=28). The Chi-square test indicated that there were no associations between anaemia (Hb<10g/dl) and any of the clinical characteristics that were analyzed (all p-values > 0.05). Comparison of the means of two groups (Anaemia: No and Anaemia: Yes) using the t-test it was observed that the p-values were <0.001 and 0.007 for Hb and Albumin respectively. The null hypothesis was rejected, and we concluded that there was a difference between the Hb and albumin levels of patients who have anaemia (Anaemia Yes) and patients who do not have anaemia (Anaemia No), with a 5% significance level. There was no significant mean difference for the other laboratory variables.

Conclusion: This study concludes that there was a low prevalence of anaemia (Hb<10g/dl) among the study population (23%) due to the high rates of EPO use (100%). There was no association between any of the clinical characteristics and anaemia. There was a difference between the Hb and albumin levels of patients who have anaemia (Anaemia Yes) and patients who do not have anaemia (Anaemia No), with a 5% significance level. There was no significant mean difference for the other laboratory variables.

Keywords: *Anaemia, Haemodialysis, Chronic Kidney Disease, Haemoglobin*

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DEFINITION OF CONCEPTS

Anaemia is defined as a haemoglobin (Hb) concentration of less than 13g/dl in adult males and postmenopausal females, and less than 12g/dl in premenopausal females, according to the World Health Organization (WHO)[1]. In this study, the WHO definition was used to define anaemia in patients not on erythropoietin. Haemoglobin concentrations less than 10g/dl were used to define anaemia in patients on erythropoietin since the recommended target haemoglobin is between 10 to 12g/dl in this group of patients [1].

Chronic haemodialysis is a solute clearance process based on transmembrane diffusion generated by a concentration gradient between blood and the dialysate[2]. Chronic haemodialysis patients have three sessions of dialysis per week [2]. In this study, chronic haemodialysis refers to haemodialysis offered to individuals with chronic kidney disease after being accepted into the National Department of Health chronic dialysis program.

End Stage Renal Disease is progressive irreversible chronic renal failure that necessitates the use of renal replacement therapy[3]. For this study, it refers to individuals with CKD stage 5.

Renal Replacement Therapy (RRT) is therapy that replaces the blood filtering functions of the kidneys in individuals with renal failure. Examples of modalities include haemodialysis, peritoneal dialysis, and kidney transplant [2]. For this study, it refers to peritoneal or haemodialysis.

Dialysis means the removal of excess fluid and toxic chemical wastes from the body by extracting solutes through a semipermeable membrane [4]. In this study, the operational definition will be the same as the theoretical definition.

Prevalence is defined as the number of cases of a disease in a certain population at a specific time[4]. For this study, prevalence relates to the number of patients with

anaemia as a proportion of the entire group of patients on chronic haemodialysis from 01/01/2019 to 31/12/2019.

Associations refers to the connection between things where one variable is caused by the other [5]. In this study, this refers to the connection between the different variables that will be collected during the study on anaemia among patients on chronic haemodialysis.

Outcomes are defined as the result or effect of an action or event [5]. In this study, it refers to the clinical consequences of having anaemia in patients on chronic haemodialysis.

Risk Factors refers to one of several things that increase one's chances of developing a certain disease [5]. For this study, it pertains to the various clinical variables that increase the chances of developing anaemia in patients with chronic kidney disease.

LIST OF ACRONYMS AND ABBREVIATIONS

ACEi: Angiotensin converting enzyme inhibitor

ARB: Angiotensin receptor blocker

BMI: Body Mass Index

CKD: Chronic kidney disease

EPO: Erythropoietin

ESA: Erythropoiesis-stimulating agents

ESRD: End stage renal disease

Hb: Haemoglobin

HIV: Human immunodeficiency virus

KDIGO: Kidney Disease Improving Global Outcome

LVMI: Left ventricular mass index

NICE: National Institute for Health and Clinical Excellence

NSAIDS: Non-steroidal anti-inflammatory drugs

PKDC: Polokwane Kidney and Dialysis Centre

PTH: Parathyroid hormone

SPSS: Statistical package for the social sciences

TSAT: Transferrin saturation

URR: Urea reduction ratio

CHAPTER 1:

INTRODUCTION, BACKGROUND AND ORIENTATION TO THE STUDY

1.1. Introduction

Anaemia is defined by the World Health Organization (WHO) as a haemoglobin (Hb) level less than 13 g/dl in adult males and postmenopausal females, and less than 12 g/dl in premenopausal females[1]. A quarter of the world's population suffers from anaemia, which is a major public health concern [6]. According to the South African National Health and Examination Survey (SANHANES-1), anaemia affects 12.2% of adult males and 12.2% of adult females [6].

1.2. Background of the study

Anaemia is a frequent aetiology of poor outcomes in individuals on chronic haemodialysis[7]. Around 75% of CKD patients in third world countries and 22.2% of CKD patients in first world countries are reported to be anaemic [7].

The main aetiology of anaemia in CKD among patients on chronic haemodialysis is relative erythropoietin deficiency, which is the most significant factor [1]. Other potential causes include reduced lifespan of red blood cells (especially in haemodialysis), iron deficiency, blood loss, nutritional deficiencies (namely folate and vitamin B12 deficiencies) and accumulation of metabolic toxins that impede erythropoiesis[7]. This research study sought to identify the prevalence and associations of anaemia among patients with CKD on chronic haemodialysis at the PKDC. No previous study of this nature had been done in Limpopo Province prior to this work (to the best of our knowledge).

Chronic Kidney Disease (CKD) is renal impairment or decreased kidney function occurring over a duration of at least three months[8]. This decreased kidney function is defined using the decline in glomerular filtration rate [8].

This description explicitly alludes to the various stages of CKD, graded according to the degree of glomerular filtration rate decline, and subsequently, these stages influence the type of management that the patient will receive. These different stages of CKD form part of a continuum, and are classified as follows [8]:

1. Stage i: Kidney injury with glomerular filtration rate >90ml/min/1.73m^2
2. Stage ii: Glomerular filtration rate between 60-89 ml/min/1.73m^2
3. Stage iii: Glomerular filtration rate between 30-59ml/min/1.73m^2
4. Stage iv: Glomerular filtration rate between 15-29ml/min/1.73m^2
5. Stage v: Glomerular filtration rate <15ml/min/1.73m^2.

Chronic kidney disease (CKD) stage 5 is also referred to as end stage renal disease (ESRD), and this usually means the patient requires dialysis or kidney transplant to survive. Renal replacement therapy (RRT) may include either haemodialysis or peritoneal dialysis, but where eligibility, availability and resources allow, will ideally constitute a kidney transplant. Patients with CKD often present with hyperkalaemia, metabolic acidosis, water handling abnormalities, anaemia and bone disease following impaired metabolic renal activities. Prompt initiation of RRT is therefore essential in the prevention of complications of CKD that can lead to adverse medical outcomes [8].

The modalities of renal replacement therapy currently being offered at the PKDC include haemodialysis and peritoneal dialysis. Kidney transplantation patients are referred to Charlotte Maxeke Academic Hospital in Gauteng Province.

Aetiologies of CKD include diabetic nephropathy, hypertensive nephrosclerosis, renovascular diseases, glomerular diseases, cystic kidney disease, tubulointerstitial kidney disease, obstructive uropathy and congenital urogenital defects (common in childhood)[3]. Toxins and nephrotoxic drugs may also consequentially lead to CKD [9].

1.3. Problem statement

Due to the National Department of Health policy of rationing dialysis services, only 82 Haemodialysis and 52 peritoneal dialysis patients are currently authorised to be on the Chronic Dialysis program at Pietersburg Hospital [10]. However, allowances are given to exceed this limit due to the increased demand for such therapies. The total number of patients at this unit has since increased from 77 patients in 2007 to 182 patients in

2012, far exceeding the permitted allocated numbers at a rate of close to 20 additional patients each year. In keeping with this trend, unpublished data from the management team of the PKDC also indicates that there were 145 patients on chronic haemodialysis in 2019, exceeding the permitted capacity for such therapies by 18.75%. This is in light of chronic kidney disease reported as being among the top ten causes of mortality in Limpopo province [11]. This again speaks to the public health concern of anaemia, a complication of CKD.

The screening and treatment of anaemia forms a major part of the management and routine care of CKD patients on chronic haemodialysis. Ideally, all patients on chronic haemodialysis should be meeting the recommended target haemoglobin concentration range between 10 and 12g/d [12]. In reality, however, majority of the patients on chronic haemodialysis at the Polokwane Kidney and Dialysis Centre are not meeting this recommended target haemoglobin range due to various reasons, with nutritional determinants of health and comorbidities linked to South Africa's unique burden of disease at the background of most of these reasons. The consequences of not meeting the haemoglobin targets include an increase in negative clinical outcomes in these patients.

This research study sought to identify the prevalence and associations of anaemia among patients on chronic haemodialysis at the PKDC. There is currently no established PKDC local protocol on the management of anaemia among patients with CKD on chronic haemodialysis. This research study forms part of the baseline in improving knowledge on the prevalence and associations of anaemia in this group of patients in a hospital setting. The knowledge that has been obtained from this research study may be used to practically establish and theoretically support local guidelines on the management of anaemia in chronic haemodialysis at the PKDC.

1.4. Significance of the study

The results of this study will assist health care providers at the Polokwane Kidney and Dialysis Centre in Limpopo in obtaining a more comprehensive understanding of the nature and patterns of association of the different demographic characteristics, as well

as clinical and laboratory parameters of anaemia in chronic haemodialysis patients. Such knowledge will serve to improve the management of anaemia in chronic haemodialysis patients at the PKDC by emphasising the importance of prevention care at all stages of treatment. Furthermore, this study may provide useful clinical and scientific data needed by the PKDC and the National Department of Health for the development and implementation of sustainable local guidelines on the management of anaemia in CKD patients.

1.5. Research questions

i. What are the causes of CKD, demographic characteristics, prevalence, and associations of anaemia among patients on chronic haemodialysis at the PKDC?

1.6. Aim of the study

i. The aim of this study was to determine the prevalence and associations of anaemia in patients on chronic haemodialysis at the PKDC in Limpopo Province, South Africa.

1.7. Objectives

The objectives of the study were:

i. To establish the demographic characteristics of the patients on chronic haemodialysis at the PKDC.

ii. To determine the prevalence of anaemia among patients on chronic haemodialysis at the PKDC.

iii. To determine the causes of CKD among patients on chronic haemodialysis at the PKDC.

iv. To demonstrate the association between anaemia and clinical parameters that were collected from the clinical records.

1.8. Overview of the research methods

In this study, the prevalence and associations of anaemia among patients on chronic haemodialysis at a tertiary hospital in Limpopo Province (South Africa) were both explored in a quantitative manner, whereby data was collected from the patients' clinical files in the PKDC. There was no sampling performed. All patients who met the inclusion criteria were included in this study. The study involved 121 patients at Pietersburg Hospital, who met the inclusion criteria. All patients on chronic haemodialysis from 01/01/2019 to 31/12/2019 were included in the study. The recorded data was captured on EPI Info version 7, and was then transferred into SPSS version 25. Descriptive analysis was used to analyse the data thereafter.

1.9. Brief Chapter overviews

In aggregation with the above-mentioned objectives of the research study, the research stays as follows:

Chapter 2 provides a literature review that underlines what has previously been published online about the prevalence and associations of anaemia among patients on chronic haemodialysis.

Chapter 3 offers the research methods that were used to perform this study. The study illustrated centred on the research process, sample, method of data collection, and method of data analysis.

Chapter 4 presents quantitative data analysis and the results that emerged from the SPSS.

Chapter 5 discusses the results that were achieved from the data analysis.

Chapter 6 concludes the study, backed by the study's strengths, limitations, and recommendations for further research.

CHAPTER 2:

LITERATURE REVIEW

2.1. Introduction

Chapter two outlines the academic literature reviewed for this study. This was done using multiple sources, including medical journals, search engines (e.g., PubMed, Google Scholar, Science direct, MedlinePlus, Medscape, BMJ, WebMD, etc.), published volumes and research studies that are not yet published. The following keywords were used “prevalence”, “association”, “anaemia”, “chronic kidney disease” and “haemodialysis”.

2.2. Anaemia among patients on chronic haemodialysis

Anaemia in chronic haemodialysis patients is strongly associated with fatigue, decreased exercise tolerance, poor quality of life, increased incidence of myocardial infarction, left ventricular hypertrophy and congestive cardiac failure [12]. Other negative outcomes associated with anaemia among patients with CKD on chronic haemodialysis include increased risk of hospitalisation and increased length of hospital stay [1]. Anaemia in CKD is the result of composite interactions between stage of CKD, RRT modality, socioeconomic, environmental factors and patient traits [7]. Individualized risk-based treatment of anaemia in patients with CKD is now advocated because of numerous factors that contribute to its development in this group of patients [7].

Most nephrologists use the WHO definition of anaemia although it does not define goals of treatment among patients on chronic haemodialysis [1]. The National Institute for Health and Clinical Excellence (NICE) advocates for assessment of potential aetiologies of anaemia where Hb is less than 11 g/dl and treatment with erythropoietin (EPO) to maintain haemoglobin concentration in the 10 to 12 g/dl range [12].

According to Dmitrieva et al. [12], anaemia is a frequent complication in those with chronic kidney disease, and it's also a risk factor for poor cardiovascular outcomes. Haemoglobin levels decrease as renal function declines. The prevalence of anaemia

in patients with CKD stage 3 is 1%, in CKD stage 4 it is 9%, and in patients with ESRD it is 33%[12]. Anaemia affects more than two-thirds (68%) of patients initiated on haemodialysis; and in addition, 51.1% of men and 49.7% of women with CKD stages 4 and 5 who are not referred to a nephrologist are actually anaemic. [12]. Anaemia in patients with ESRD is associated with decreased ability to exercise; decreased wellbeing, increased rates of myocardial infarction, left ventricular hypertrophy and congestive cardiac failure[12]. Diabetes mellitus (DM) is associated with two-fold increase in the prevalence of anaemia in patients with CKD. There are concerns that angiotensin-converting enzyme inhibitors (ACE-I) might be linked to anaemia [12]. Chronic kidney disease patients are at increased cardiovascular risk, efficacious management of anaemia in these patients improves clinical outcomes[12]. Effective management of anaemia in CKD patients is associated with decrease in left ventricular enlargement, reduced transfusion rates, improved quality of life, delayed progression of renal failure in non-diabetic pre-dialysis patients and improved renal function in patients with heart failure[12]. In the United Kingdom, the NICE guidelines recommend that possible causes of anaemia be assessed when HB< 11g/dl, erythropoiesis stimulants (ESAs) and intravenous iron be administered to maintain Hb levels in the 10-12g/dl range[12].

Ruggajo et al.[13], reported that patients on chronic haemodialysis due to CKD stage 5 experience anaemia complications. They also reported that the occurrence of anaemia underlines some of the symptoms that are linked to fatigue, dyspnoea, depression, reduced kidney function and reduced exercise tolerance. According to Ruggajo *et al*.[13], anaemia has been associated with the worst clinical results; for instance, increased mortality and morbidity because of cardiovascular disease. Therefore, this complication results in an upsurge in the risk of hospitalisation and long period of hospital stay. In turn, the wellbeing of these patients is reduced.

According to Lawler et al. [14], persistent anaemia is a frequent complication CKD patient, mainly as a result of reduced endogenous erythropoietin production. After the addition of erythropoietin (EPO) to available treatments for CKD associated anaemia, there has been a significant reduction in transfusion events in this population. Current guidelines on the management of anaemia recommend treating Hb levels to a range between 10-12 g/dl and using the lowest possible dose of ESA to decrease the need for blood transfusions [14]. Although transfusions are much safer than in the past, there

are still some transfusion associated risks. Risks include secondary haemochromatosis, blood transfusion reactions, transmission of infections, transfusion related acute pulmonary injury, and allogeneic antibody development (which can affect the ability of patients to undergo organ transplantation). In addition, blood transfusions are costly with significant costs arising from storage and acquisition[14].

Individualisation of therapy in patients who may have improvement in the quality of life with Hb greater than 12g/dl is allowed, but targeting Hb above 13g/dl, is not recommended [1]. Treating anaemia with ESA improves clinical outcomes in non-CKD patients with cardiovascular disease [12]. In CKD patients on chronic haemodialysis, ESA showed no benefits in reducing cardiovascular mortality and has been linked to some adverse outcomes (e.g., access thrombosis in patients on chronic haemodialysis), particularly when Hb is above 12 g/dl [(1,12)].

According to Patel et al. [15], CKD affected more than twenty million individuals in the USA. With increasing rates of DM type 2 in addition to demographic aging, chronic kidney disease prevalence has been on the rise. Conversely, CKD patients endure to experience different types of adverse clinical outcomes, which range from fluid overload, electrolyte disturbances, mineral and bone disease in addition to anaemia [15]. Furthermore, recent research studies proposed a possible outcome of deficiency of vitamin D and its metabolites as contributing to anaemia development[15]. Moreover, Patel and colleagues [15] found that their study results were in agreement with preceding research among dialysis patients which showed that supplementing vitamin D increases sensitivity to EPO, as evidenced by reduced doses of EPO required to attain comparable anaemia control[15]. Cardiovascular disease (CVD) was also found to be exceedingly common among individuals with CKD and is still one of the most common aetiologies of mortality[15]. Deficiency in vitamin D and anaemia are reported to be contributory to this increased cardiovascular risk in CKD patients[15].

Remarkably, a major CVD component that is strongly associated with increased adverse clinical outcomes as well as being linked to both anaemia and vitamin D deficiency is left ventricular enlargement[15]. Therefore, it is thought-provoking to postulate whether there might be overlaps between vitamin D deficiency and anaemia

and whether vitamin D use in addition to other traditional anaemia administrations can have mortality benefit by reducing cardiovascular risk in CKD patients[15].

Patel et al. [15] reported that due to the high incidence of anaemia among CKD patients associated with vitamin D deficiency, coupled with the ease and low price it takes to correct this deficiency, their research in context of other discoveries and biological credibility reported to indicate that early vitamin D treatment could contribute to the management of CKD associated anaemia. Subsequently, both calcifediol and calcitriol deficiencies are individually correlated with reduced haemoglobin levels. Patel et al. [15] suggested that potential further research could investigate the comparative erythropoiesis stimulating effects of vitamin D supplementation along with effectiveness of the different types of vitamin D.

The research study by Patel et al. [15] had several vital drawbacks. Considering that their study was cross-sectional, it was impossible to establish a causal association between anaemia and vitamin D deficiency. Furthermore, data regarding iron studies and management of anaemia with ESAs could not be obtained. Nevertheless, earlier research that ensured accuracy in the use of ESAs and iron stores came to the same conclusion[15]. Notably, it was doubtful whether a significant percentage of this chronic kidney disease study population majority of which had early stages of CKD, recruited from primary health care facilities would have been on EPO when the study was conducted[15].

Abdelkarim et al.[17] conducted a study that provided essential data regarding the status of anaemia in CKD stage 5 patients who were dialyzing in Sudan; their study focused on the factors that affected the control of Haemoglobin levels. In this study, a family history of ESRD and period of high blood pressure between “6-9” years were associated with anaemia[17].

In Yaounde Cameroon, Kaze et al. [16] reported that the prohibitive cost of therapies needed in the management of CKD associated anaemia patients e.g., EPO and absence of third-party administrator systems in resource deprived places, strongly implied that the majority of patients in developing countries can’t afford such therapies. In addition, anaemia in places like Sub Saharan Africa is possibly more common in individuals with CKD as a result of local geographic factors such as nutritional insufficiencies, parasitic diseases and hemoglobinopathies[16]. Management of

anaemia in this setting relies heavily on packed red cell transfusions, a contradiction due to the lack of safe blood products in these locations due to the multiple endemic infectious diseases[16]. However, not much is known about anaemia prevalence in patients receiving haemodialysis in Africa and its evolution in the context of packed red cell transfusion reliant management [16] In Cameroon, the care of chronic kidney disease patients in need of haemodialysis has improved recently due to government sponsored dialysis grants [16]. However, these government grants do not cover the costs of managing comorbidities such as anaemia. Therefore, treatment of anaemia in dialysis patients in Cameroon relies on packed red cell transfusions, despite the lack of organized blood bank facilities.

2.3. Causes of chronic kidney disease

Chronic kidney disease is more prevalent in developing countries, as compared to developed countries[18]. The most common aetiologies of CKD in developing countries are hypertension and disorders of the glomeruli (chronic glomerulonephritis). The most common aetiology in Japan, Europe and the USA is diabetic nephropathy. Diabetic nephropathy is now the most frequent aetiology of ESRD in most developed countries[18]. The main reasons behind this upward trend includes increases in the number of diabetic patients, improvement in survival rates of diabetic patients and increased acceptance of geriatric multimorbid patients into dialysis programs in these countries[18].

One of the issues liable for regional discrepancies in the prevalence of ESRD between the developing and the developed countries is competing mortality. Males and females in Sub-Saharan Africa (SSA) have an average life expectancy of 48.4 and 50.1 years, respectively, compared to 73.4 and 50.1 years in developed countries[18].This low life expectancy in developing countries precludes a lot of people from developing DM and DM related ESRD since the prevalence of Type 2 DM increases with increasing age[18].

In India and Pakistan, chronic glomerulonephritis is the principal aetiology of CKD being liable for at 33% of the cases, whilst diabetic kidney disease is responsible for at least 25% of all the patients suffering from CKD[18]. In other countries in southeast Asia, CKD most commonly occurs as a result of glomerulonephritis, nephrolithiasis as well as completed acute kidney injury due to a variety of causes[18]. Every year,

approximately 5000 kidney transplants are performed in China[18]. Immunoglobulin A nephropathy (IgAN) is the principal aetiology of CKD amongst the primary aetiologies of glomerular disease, and systemic lupus erythematosus is the most common etiology amongst the secondary glomerulonephritis group. In Brazil, glomerulonephritis is the most frequent aetiology of CKD[18].

In Nigeria, the most frequent causes of CKD are chronic glomerulonephritis, hypertension, DM and obstructive uropathy[18]. Interstitial nephritis (14 to 32%), glomerulonephritis (11 to 24%), Diabetic nephropathy (5 to 20%), and hypertensive nephrosclerosis (5 to 21%) are the principal aetiologies of CKD in North Africa. Obstructive uropathy secondary to bilharzia is a frequent aetiology in Egypt (7%), Libya and Algeria[18].

According to the South African Renal Registry (SSAR), there were 9,937 people on chronic kidney replacement therapy in South Africa in December 2019. This represents a prevalence of 169 per million people[19]. The majority of the patients were on haemodialysis (83.4%). The most common reported cause of CKD was hypertensive kidney disease (36%) followed by unknown causes (31.7%). Other reported causes included diabetic kidney disease (14.4%), glomerulonephritis (10.2%), polycystic renal disease (3%), and obstructive nephropathy (1.8%)[19].

Similar to the SSAR report, a Sudanese study reported similar causes of CKD with the most common cause being reported as hypertension (55.6%), followed by diabetes mellitus (25.3%), obstructive uropathy (14.8%), other causes (15.2%), treatment (7.5%), unknown cause (6.9%), glomerulonephritis (6.9%), pyelonephritis (6.9%) and hereditary nephropathy (0.6%)[17].

In another study that was done in Saudi Arabia by Afshar *et al*[20] at Mustafa Khomeini Hospital in Tehran Iran, the most common aetiologies of CKD were DM (49.1%), hypertensive nephrosclerosis (28.3%), glomerulonephritis (17.1%) and cystic renal disease (5.6%)[20].

2.4. Prevalence of anaemia in chronic haemodialysis

Anaemia is a serious complication of CKD and it is also a risk factor for cardiovascular disease among chronic kidney disease patients. The prevalence of anaemia among

CKD patients in South Africa is largely unknown[7]. Around 78% of CKD patients in middle and low-income countries were reported to be anaemic compared to only 22% in high income countries[7].

According to Macdougall et al. [21], anaemia is very common in CKD patients and it is linked to serious adverse outcomes. CKD associated anaemia usually develops before dialysis is needed, although it is often initially inadequately controlled or managed. The majority of CKD patients start haemodialysis with haemoglobin levels lower than recommended targets despite improvements in anaemia care. In reality, maintaining anaemia management in CKD patients cumbersome and carries a significant burden on scarce medical resources. With the rising prevalence of CKD, the demand for dialysis units is expected to increase [21].

Kuragano et al. [22] reported that current large-scale medical research has shown that maintaining a high haemoglobin target level is not closely linked with favourable clinical outcomes in chronic haemodialysis patients. Moreover, patients who required high doses of EPO to sustain the recommended haemoglobin levels and patients who responded poorly to EPO, commonly have a guarded prognosis. Kuragano and colleagues assessed the association of CKD related anaemia treatments, particularly EPO and iron therapy, with adverse events and prognosis in chronic haemodialysis patients in a sub-analysis of the Prospective Study of Treatment for Renal Anaemia on Prognosis in haemodialysis (TRAP) trial [22].One of characteristic aspects of their study was an observed rise in blood ferritin levels after administration of iron; which might influence the prognosis of patients on chronic haemodialysis that display ferritin levels that are in ranges lower than the KDIGO guidelines recommended targets[22]. Furthermore, Kuragano et al.[22] demonstrated that maintenance haemodialysis patients who maintained a constant focus on haemoglobin level had a lower risk of adverse events than those who did not maintain a constant focus on haemoglobin level. Kuragano and colleagues[22] discovered that individuals receiving higher EPO doses had significantly higher chances of hospitalization and infection than those on lower doses. Furthermore, patients with increased serum ferritin, as well as individuals with high-amplitude changes in ferritin level, had significantly higher risks of death, hospitalisation, infection, and CCVD[22].

In a study among chronic haemodialysis patients in one of the main dialysis units in Yaounde Cameroon, anaemia was defined as haemoglobin less than 9g/dl as this was the threshold for blood transfusion in this dialysis unit[16]. Microcytosis and macrocytosis were defined by mean corpuscular volume (MCV) less than 80fl and greater than 100fl, respectively[16]. Hypochromia and normochromia were defined by mean corpuscular haemoglobin (MCH) less than 27pg and greater than 27pg, respectively[16]. Only 29.5% of patients on dialysis were on erythropoietin (EPO), with the remaining 70.5% being neither on EPO nor IV iron [16]. The prevalence of anaemia was found to be 79% and the anaemia was mainly microcytic hypochromic [16]. The very high prevalence of anaemia in this study from Yaounde, Cameroon can be explained by the lack of erythropoietin use in the patients recruited for this study. According to unpublished data by the management team at the PKDC, more than 90% of patients on chronic haemodialysis were on EPO in 2019.

In a similar study done in Tunisia with patients on chronic haemodialysis, anaemia was classified as Hb levels below 12g/dl [23]. Anaemia was observed in 87.8% of the patients in the study, and 73% of these cases showed a normochromic and normocytic morphology picture [23]. Iron deficiency was found in 21.6% of anaemic individuals, with iron deficiency anaemia being defined as TSAT below 20% [23]. Due to financial reasons, 89.2% of the patients were found to not be on EPO and 38% required regular blood transfusions [23].

In another study that was conducted at Mustafa Khomeini Hospital in Tehran Iran, anaemia was defined using the 2006 NFK-K/DOQI guidelines for CKD anaemia; Hb< 13.5 in men and less than 12g/dl in women [20]. Out of the 54 patients on chronic haemodialysis, 90.7% received EPO subcutaneously three times per week[20]. This was warranted by the presence of a high prevalence of anaemia in chronic haemodialysis patients of 85%, with 80% of those cases showing a normocytic normochromic morphological picture [20]. The high prevalence of anaemia in this study can be attributed to the definitions used to define anaemia in this study which don't define the goals of therapy in this group of patients.

In Khartoum Sudan, Abdelkarim et al[17], anaemia among patients on chronic haemodialysis was classified as haemoglobin levels below 12g/dl in both females and males. All patients (n=534,100%) had anaemia (using this definition), but only sixty-

point-eight percent (60.8%, n=325) of patients in this study were on erythropoietin (EPO). Sixty seven percent (67%, n=358) of patients in this study had Hb levels less than the recommended 10g/dl (anaemia). The limited use of EPO in this study might have led to the high prevalence of anaemia.

2.5. Associations of anaemia among CKD patients on chronic haemodialysis

Many comorbidities, which include parasitosis, malnourishment, hemoglobinopathies, and HIV, contribute to the worsening of anaemia in patients with ESRD on chronic haemodialysis in developing countries[23]. Low GFR, race, iron supplementation, hypocalcaemia, hypoalbuminemia, and other comorbidities including diabetes mellitus (DM) have all been found to be risk factors for anaemia development in CKD patients[7]. Previous research has linked angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARBs) to the development of anemia[7]. Both ACEi and ARBs are commonly used in all stages of CKD to manage proteinuria and hypertension. Elevated levels of parathyroid hormone (PTH) have been shown to reduce erythropoiesis, promote haemolysis, and cause bone marrow fibrosis in patients with CKD [7].

According to Meremo et al. [24], anaemia increases the risk of cardiovascular disease and lowers the quality of life in CKD patients. Anaemia in CKD is associated with memory loss, disturbances in sleep, CKD progression, CVD co-morbidities and higher mortality rates. The reduction in quality of life (e.g., fatigue, depression, reduced productivity) is even more marked in patients with anaemia. In a study in South Africa, primary hypertension was reported to occur in a quarter of patients with CKD, and was the putative aetiology of ESRD among a larger proportion of the patients. Since anaemia is widespread among individuals with renal diseases and is linked with increased mortality rates, most studies have clinically focused on anaemia among patients who have CKD[24].

Stancu et al. [25] reported that iron deficiency is widespread in CKD patients and that venofer is an established treatment modality for anaemia in chronic haemodialysis patients, especially those treated with EPO. According to several studies, iron deficiency as indicated by bone marrow iron tests, is common in individuals with CKD prior to dialysis initiation[25]. The prevalence of iron deficiency in bone marrows varied

greatly in the reported series, ranging from 23% to 90%. Although 38-68% of patients have been found to have a positive response to intravenous iron without the use of EPO, the significance of iron therapy in non-dialysis patients with CKD is much less obvious than in haemodialysis patients.[25].

The prevalence of anaemia among CKD patients was 43.18 % in a cross-sectional study of pre-dialysis patients at Charlotte Maxeke Academic Hospital[7]. In this study, pre-dialysis CKD patients with DM exhibited a threefold greater likelihood of developing anaemia compared to non-diabetic CKD patients[7]. Additionally, hypoalbuminemia was linked to anaemia [7]. In this study ACEIs and ARBs predicted anaemia which was consistent with previous studies[7].

In a study among chronic haemodialysis patients in one of the main dialysis centres in Yaounde Cameroon by Kaze et al [16], being on EPO was associated with 1.1g/dl higher levels of Hb, 2.6fl higher level of MCV and 0.9pg higher levels of MCH [16]. Each ten-month period on haemodialysis was associated with 0.3g/dl higher Hb levels, while iron supplementation was associated with 0.5g/dl higher Hb levels[16]. In a similar study conducted in Tunisia among chronic haemodialysis patients, the significance of dialysis quality was demonstrated by a positive correlation between Hb levels and the urea reduction ratio, and a similar relationship was identified with Kt/V[16]. In a Tanzanian study by Ruggajo et al[13] in CKD patients on haemodialysis, low transferrin saturation less than 30% (P-value <0.0001) and the presence of more than one comorbidity (P-value=0.04) were associated with the presence of anaemia[13]. In a Sudanese study by Abdelkarim et al in CKD patients on haemodialysis, the clinical characteristics associated with anaemia (HB<10g/dl) included family background of end stage renal disease [OR=0.57, (0.35-0.94)] and hypertension duration of 6-9 years[17]. Anaemia was observed in 87.8% of patients and 73% of these cases showed a normochromic and normocytic morphological picture[17]. Iron Deficiency was found in 21.5% of anaemic participants [OR=0.47, (0.25-0.87)] [17].

Very few South African studies on the prevalence of anaemia in the healthy community and pre-dialysis CKD patients have been published. The prevalence of anaemia among patients on chronic haemodialysis remains largely unknown. This shortage of studies on this topic in South Africa led the author to conduct this study to fill the gap in knowledge on this topic.

2.6. Pathophysiology of anaemia in chronic kidney disease (CKD)

The processes underlying anaemia linked to CKD are numerous and intricate[32]. They include, among other things a reduction in the generation of endogenous erythropoietin (EPO), absolute and/or functional iron deficiency and inflammation with elevated hepcidin level, red cell lifespan reduction, systemic inflammation caused by CKD and its accompanying comorbidities, diminished response of the bone marrow to EPO as a result of uremic toxins, vitamin B12 or folic acid deficiencies[32].Patients are often treated with erythropoiesis stimulating agents (ESA) and oral or intravenous iron supplementation[32]. However, these treatments come with potential hazards and occasionally don't work well enough[32]. Nonetheless, there have been some significant developments in the management of CKD-related anaemia in recent years, which have generated great expectations[32]. A brand-new class of medications called hypoxia inducible factor prolyl hydroxylase inhibitors has been developed (HIF-PHIs) [32]. These agents improve iron availability, lower hepcidin levels, and promote endogenous EPO production, among other effects[32]. Recent clinical trials have elucidated important aspects of iron supplementation, which may change the treatment targets in the future[32].

A glycoprotein called EPO, which has a molecular weight of 30.4 kDa, binds to its receptor on the surface of erythroid progenitor cells, which are found mostly in the bone marrow[32]. EPO is an important stimulant of red cell survival, proliferation, and differentiation. EPO is produced primarily by the fibroblast-like interstitial peritubular cells of the kidneys, and in a much lesser proportion, by the perisinusoidal cells in the liver, in response to variations in tissue oxygen saturations[32]. EPO production is regulated at the EPO gene transcription level[32]. The hypoxia inducible factor (HIF) system, whose activity is dependent on tissue oxygen levels, is one of the most critical elements that regulate EPO expression[32]. More specifically, under hypoxic or anaemic stress, HIF1 binds to the EPO gene and promotes its expression[32].

2.7. Conclusion

This chapter emphasized the literature that was conducted by other researchers. The following chapter will go into the methods used to answer the research questions and fulfil the study's objectives.

CHAPTER 3:

METHODS

3.1. Introduction

This chapter discusses the methodology used in this research study. This chapter describes the research philosophy, research design, motivation for using quantitative method, study population and sampling, data collection tools for the study, data analysis, reliability and validity and concludes with ethics that were considered in the study. The study aimed to determine the prevalence and associations of anaemia among chronic haemodialysis patients at the Polokwane Kidney and Dialysis Centre in Limpopo Province.

3.2. Research Design

A retrospective cross-sectional, non-experimental quantitative study, performed at a single dialysis centre (Pietersburg Kidney and Dialysis Centre) including all patients on chronic haemodialysis over a one-year period (01/01/2019 to 31/12/2019). Cross-sectional studies are also known as one-shot or status studies [26]. This study design is best suited for a study that seeks to ascertain the prevalence of a problem, situation, issue, relationship, or phenomenon. They help to get the overall picture at the time of the study [26].

3.3. Motivation for the use of a quantitative research design

3.3.1. Strengths

According to Queirós, Faria, and Almeida [27], quantitative research refers to the study of data that can be measured. The results are treated as if they represented a broad and properly full perspective of the entire population because the samples are usually large and deemed to be representative of the entire population[27]. Mathematicians and statisticians, for example, assume a fundamental significance in the process of analysis and generalization of the conclusions gained[27]. Quantitative research is based on objectivity and is especially useful when it is possible to obtain quantifiable measures of variables in addition to inferences from population samples[27]. As a result,

quantitative research embraces well-organized data collection approaches and strict methods. The information collected is gathered systematically and objectively [27].

Following data collection, statistical techniques are used to analyse quantitative data, most commonly using software like STATA or SPSS. Quantitative data is information that can be computed and is typically gathered through surveys from a large number of randomly selected respondents[27]. In quantitative research, secondary data such as government statistics, census data, and health system indicators (just to mention a few) are frequently used[27]. Statistical approaches are used to analyse quantitative data. Quantitative methodologies are best suited for answering who, when, and what inquiries, but are not suited for how and why inquiries[27]. The information is presented in descriptive terms and can be utilized to build graphic patterns that are easier to understand and apply to a large number of people[27]. Quantitative approach allows the detection of latent structure among the studied variables [27].

3.3.2. Weaknesses

Quantitative research approach has some limitations. With this research approach, the understanding of the context of the problem is limited compared to that gained from a qualitative approach. It is difficult to understand the context of a phenomenon when using quantitative research approach and the data obtained might not be reliable enough to clarify complicated issues or contextual nuances. When looking at secondary data, sometimes it is inaccessible or difficult or impossible to get existing data [27].

Furthermore, in quantitative studies natural dependent variables tend to be abnormally distributed. All variables having communality values greater than 0.5 are recommended to be eliminated, and hence some results might be lost[27]. To validate and confirm the instrument scale, distinct and randomised samples are required, which may increase the study duration[27].

3.4. Study Setting

This study was carried out at Pietersburg Hospital's kidney and dialysis centre which is in Polokwane [10]. Pietersburg hospital is a five hundred bed hospital located in Limpopo, South Africa providing comprehensive specialist clinical and surgical services [11]. This hospital serves the province of Limpopo's 5.8 million people, who are spread across five districts. [11]. These high-level services are offered to the people of Limpopo through well-defined referral systems across all the regional and district hospitals. This dialysis centre is the only public sector facility in Limpopo providing dialysis services [10]. As of November 2019, there were 1159 health workers at Pietersburg Hospital, according to the hospital's human resource registry. There were 276 medical practitioners, 729 nurses and 154 Allied health practitioners among these personnel. However, this staff complement fluctuates monthly because of new appointments, resignations, retirements, and deaths.

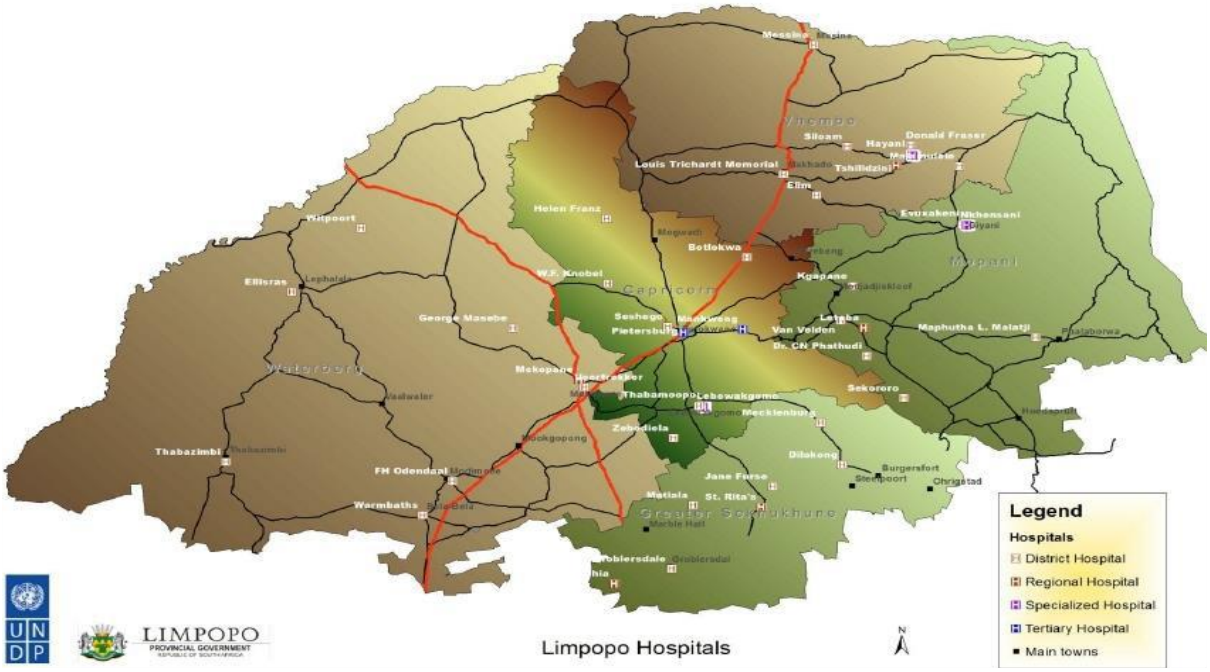

Figure 3.4.1 Map of hospitals in Limpopo Province(South Africa Department of Health, 2016)

3.5. Study population

The study population was drawn from CKD patients who were already on chronic haemodialysis at the Polokwane Kidney and Dialysis Centre (PKDC). This study involved day-care patients registered at this dialysis centre. According to unpublished data from the PKDC, there were 145 patients on chronic haemodialysis in 2019. Majority of patients who received chronic dialysis at the PKDC were unemployed, black Africans from rural parts of Limpopo province and have very poor socio-economic backgrounds [10].

3.6. Sampling procedure and sample size

There was no sampling done in this study. This study included all patients who met the inclusion criteria. A detailed accounting of all the individuals in a sample is known as a census survey[28]. It can be presumed that in this inquiry all subjects are covered; no element is left to chance and utmost accuracy is achieved [28].

3.6.1. Inclusion criteria

All Patients on chronic haemodialysis from 01/01/2019 to 31/12/2019 were included in the study. These were the patients who were accepted into the National Department of Health chronic dialysis program with the long-term goal of getting them a kidney transplant. These patients got renal replacement therapy via haemodialysis at the PKDC three times per week with most of them travelling from district hospitals in Limpopo province.

3.6.2. Exclusion criteria

The following groups of patients routinely managed at the PKDC were excluded from this study*:* Post kidney transplant patients, pre-dialysis CKD patients and patients on peritoneal dialysis were excluded from this study because they were not on chronic haemodialysis. Patients on acute haemodialysis were excluded from this study because they were on haemodialysis for maximum duration of up to 8 weeks. Patients who were not on chronic haemodialysis for the full duration of the year 2019 were

excluded because they were not on haemodialysis for full duration of the study period between 01/01/2019 to 31/12/2019.

3.7. Method of data collection

A data collection form was created in Epi info Version 7 by the author. Data was collected from the patients' clinical files in the PKDC. The author recorded data from the patients' files on the data collection forms. According to unpublished data from the PKDC, laboratory tests were obtained every 3 months from patients who were on chronic haemodialysis. The mean of the 4 laboratory parameters obtained during the year 2019 was entered into the data collection form as the patient's laboratory parameter. All the parameters that were recorded on the forms were exported into SPSS version 25 via Microsoft excel for analysis.

3.8. Method of Data analysis

The data was captured into EPI info version 7 and then exported to SPSS version 25. Normally distributed continuous variables were presented as mean ± standard deviation. Non-normally distributed continuous variables were presented as median ± Interquartile range. Categorical variables were presented as numbers, percentages, and charts. Demographic and clinical parameters were compared between anaemic and non-anaemic patients using Pearson's chi-square test and student's t-test.

3.8.1. Reliability, validity, and bias

3.8.1.1. Reliability

Reliability is the dependability and consistency of the research instrument in measuring a variable, equivalence and internal consistency [28]. To ensure reliability, a pilot study was conducted at the PKDC. When a study is carried out to investigate the possibility of doing it on a larger scale and to simplify the main study methods and procedures, this is known as a feasibility study or pilot study [26]. Such a study might bring to light the weaknesses of the research instrument or research technique [28]. Some studies suggest 30 samples per group whilst others suggest 12 samples per

group to pilot a clinical study [29]. For this study, 12 patients' files that meet the inclusion criteria at the PKDC were used to pilot the study.

3.8.1.2. Validity

The validity of an instrument is how accurately it measures what the researcher is looking for [28]. The degree to which a measuring tool provides adequate coverage of the subject under research is referred to as content validity [28]. To ensure content validity in this study, a comprehensive literature review was done prior to the development of the data collection tool.

The data collection tool was subsequently reviewed by the supervisor who is an expert in the field of study. The supervisor evaluated the tool to assess if it adequately covered what the researcher intended to find out. The university's biostatistician was consulted to evaluate the research proposal and data collection instrument. The data collection tool was found to answer the research questions. Validity was ensured by collecting data from the patients' clinical files as they are formal medico-legal documents.

3.8.1.3. Bias

Any disposition that precludes unprejudiced assessment of a topic is defined as bias[30]. This occurs when a systematic inaccuracy is introduced into sampling or analysis by favouring or encouraging one possible outcome over the others[30]. Bias can develop at any point in the clinical trial process, including research design, collection of data, data analysis, and publishing of the trial [30]. Selection bias can occur during identification of the study population [30]. Sampling bias is a type of selection bias that occurs when a study's population is not randomly selected. This can result in some participants being less likely to be included in the study than others. In this study sampling bias was mitigated by including the whole target population in the study instead of sampling. Data was obtained from the medical records of all the individuals who met the inclusion criteria, and the principal researcher did not have any prior knowledge of the patients' clinical information.

Information bias is any systematic discrepancy from facts that arises when information is collected, recorded, recalled, and processed in a study, including how missing data

are handled[30]. There was information bias in this study. There was some missing patient data due to poor registration quality or missing records. To mitigate this issue, a pilot study was conducted prior to the main study to identify these unexpected issues that could occur during the main study and reduce the amount of missing data.

3.9. Ethical considerations

Ethical approval was obtained from the school of medicine Senior Degrees Committee (SSDC) followed by the faculty of health higher degrees committee for approval by the Turfloop Research Ethics Committee (TREC). Further approval for data collection was obtained from the Limpopo Department of Health Ethics Committee and Pietersburg Hospital Ethics Committee. Permission to conduct the study was obtained from Pietersburg hospital CEO.

Confidentiality concerns the ethical obligation of clinicians not to disclose information about patients or study participants without authorization[31]. In this study, patients' files were allocated specific codes and unique numbers to protect the identity of the patients. Patient files were kept safe at the Pietersburg hospital records section throughout the duration of the study. These files are medicolegal documents and are stored as medical records for a minimum of 10 years. Data collected from the patients' files will be kept in the principal researcher's password protected google drive account for at least 10 years after final publication of the research findings.

3.10. Conclusion

This chapter concentrated on the methods that were used in the research, that aided to answer the research questions. The methods of data collection procedure were explained. This chapter discussed the ethical considerations, reliability, and validity. A statistical analysis of patients' data is presented in the chapter that follows.

CHAPTER 4:

PRESENTATION AND INTERPRETATION OF RESULTS

4.1. Introduction

This chapter presents the results that were obtained from the methods used in this study. This results section begins with a presentation of demographic characteristics of the participants, followed by geographical location, duration on haemodialysis, clinical characteristics of study population, causes of chronic kidney disease, haemoglobin distribution, associations between anaemia and clinical characteristics, Associations between anaemia and laboratory parameters. The summary of the descriptive statistics for the data captured in SPSS version 25 is presented in Annexure B.

4.2. Demographic characteristics of the participants

This study included a total of 121 participants. Of the total participants, 26% of the participants were above the age of 50 years and 74% were below the age of 50 years, as demonstrated in Figure 4.2.1. below. All 121 patients in the study were black.

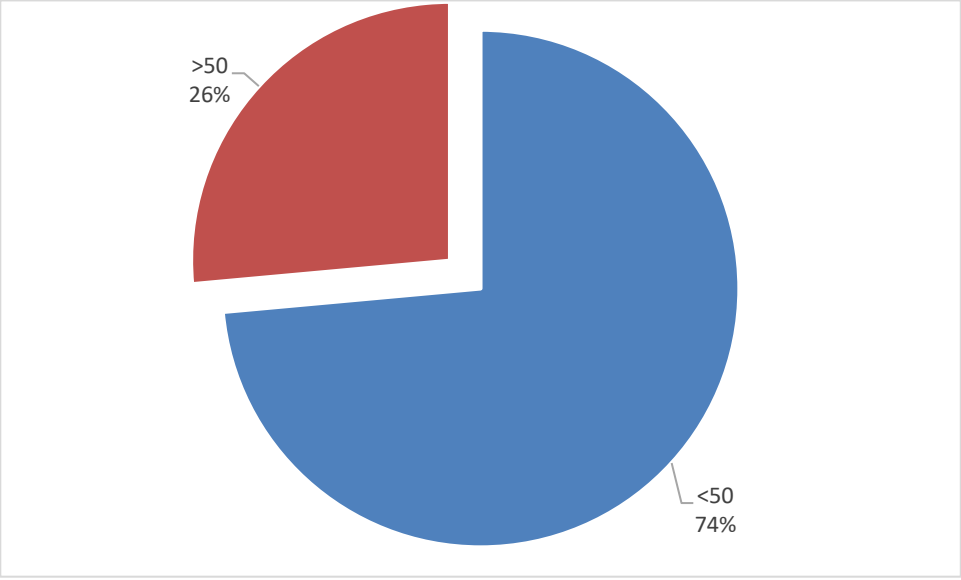

Figure 4.2.1 : Age distribution of the participants (n=121)

Moreover, figure 4.2.2. below demonstrates the age groups of participants in percentages. The highest percentage of participants were between the ages of 41 and 50 years, making up 28% of the study population. The age distributions were as follows: 26% of participants were between the ages of 31 and 40 years, 23% of participants were between the ages of 51 and 60 years, 17% of participants were between the ages of 21 and 30 years, and furthermore, 4% of participants were over the age of 60 years. Participants aged between 11 and 20 years old were the lowest group making up only 2% of the study population. The overall mean age was 41.9 ± 11.7 years (Range 20 to 69 years).

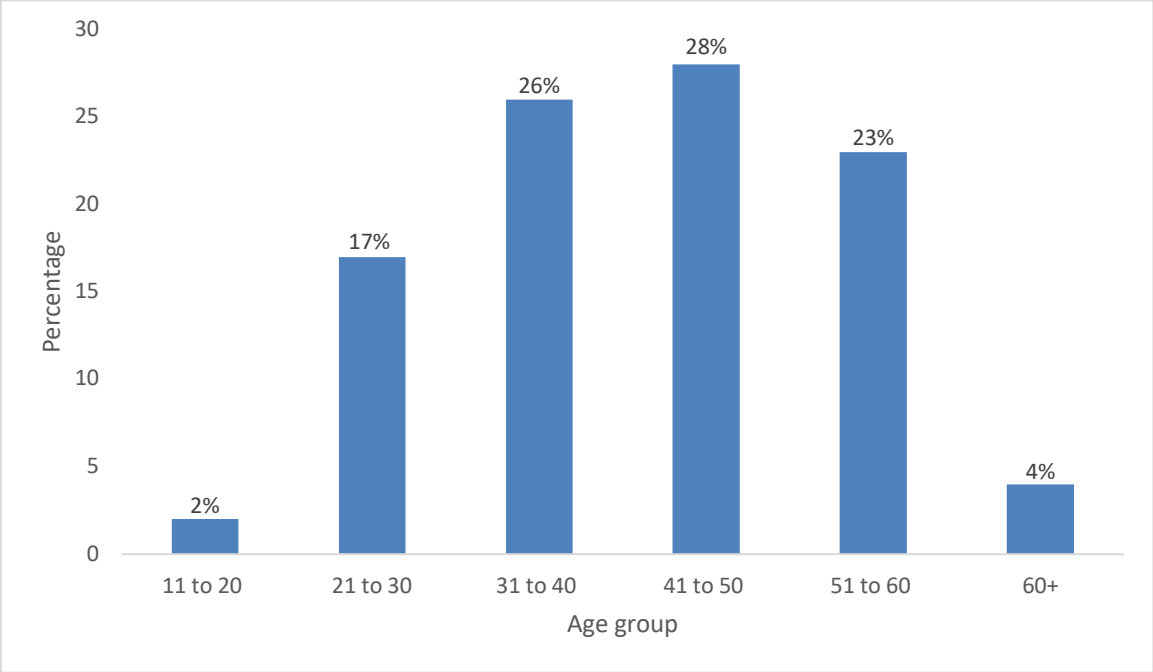

Figure 4.2.2 : Age distribution of patients (n=121)

The figure 4.2.3 below demonstrates the gender of participants who were included in the study. Majority of participants were male patients making up 55% of the total number of participants, whereas 45% of participants were female patients.

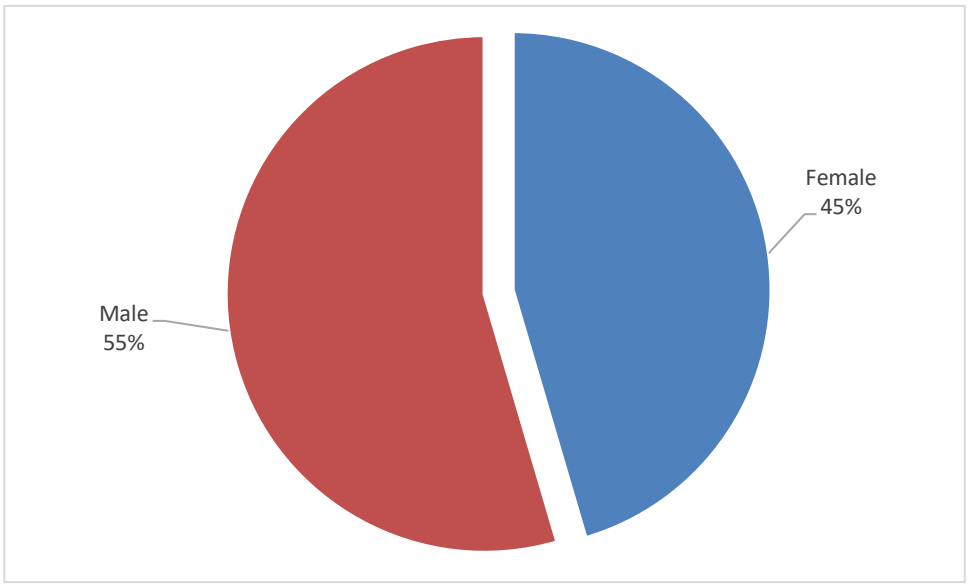

Figure 4.2.3: Gender distribution of the participants (n=121)

4.3. Geographical location

Most participants were from Capricorn district (31%), followed by 26% of participants from Vhembe district. Comparatively, 21% of participants were from Mopani district and 12% of participants were from Sekhukhune district. The district that had the lowest number of participants was Waterberg comprising only 9%. This is demonstrated in Figure 4.3.1 below.

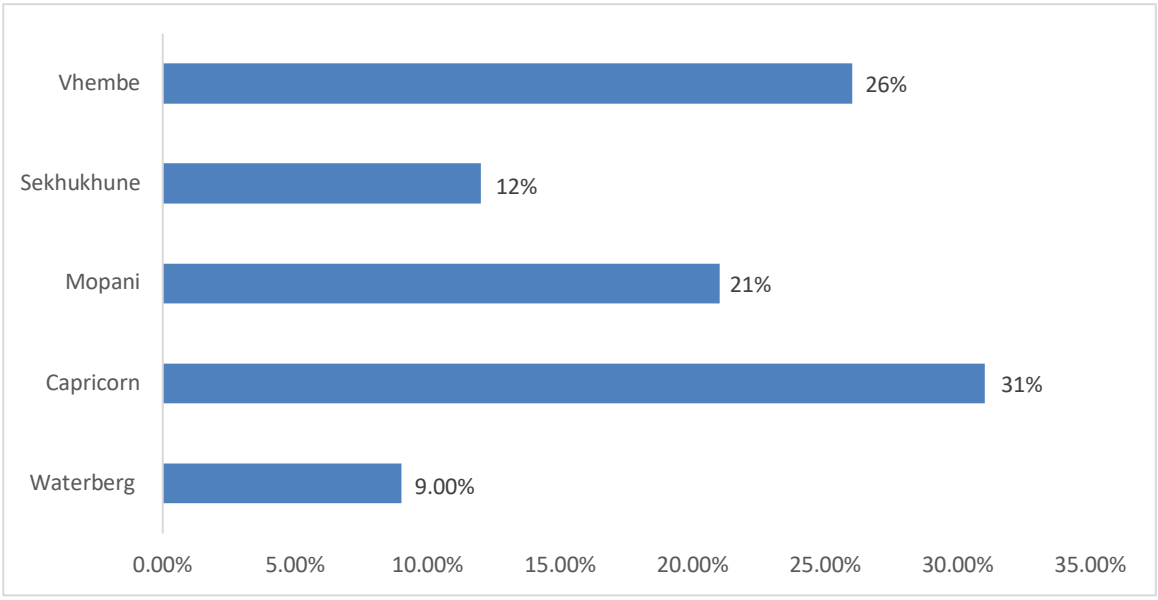

Figure 4.3. 1: Distribution of participants by Limpopo province district (n=121)

4.4. Haemodialysis

The Figure 4.4.1 below demonstrates the duration patients have been on haemodialysis. A total of 55% of the participants had been on haemodialysis for less than 5 years, whereas 45% of participants had been on haemodialysis for more than 5 years.

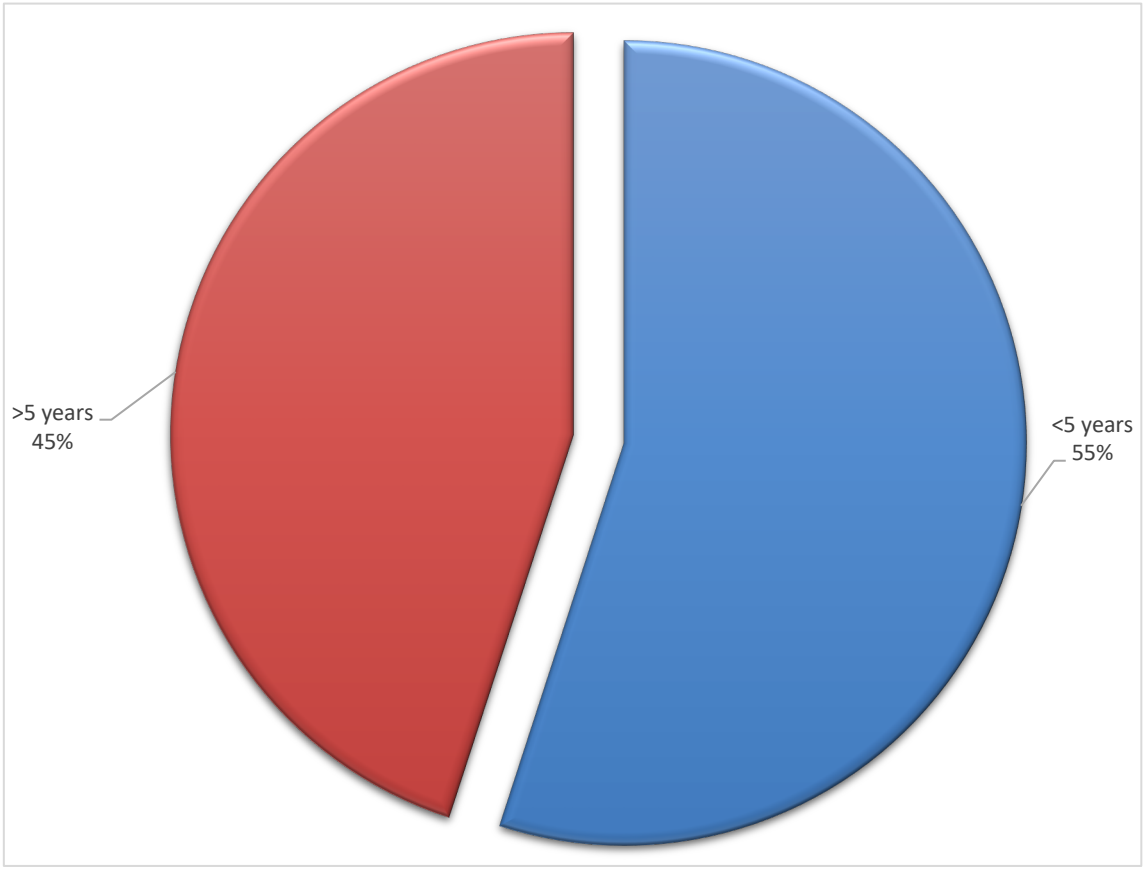

Figure 4.4.1: Duration on haemodialysis (n=121)

4.5. Clinical characteristics of study population

The Table 4.5.1 below demonstrates the clinical characteristics of the study population frequencies in percentage (%) that were obtained from descriptive statistical analysis; 12 variables were used. Firstly, IV Access (with AV Fistula was 37.2% and with permanent catheter was 62.8%) and secondly, ACEI (without ACEI was 17.3% and with ACEI was 82.6%). Thirdly, ARB (without ARB was 86.77% and with ARB was 13.2%) and fourthly, NSAIDS (without NSAIDS was 66.9% and with NSAIDS was 33.1%). Fifthly, Diabetes Mellitus was considered (without Diabetes Mellitus was 87.6% and with Diabetes Mellitus was 12.4%), followed by HIV (without HIV was 90.1% and with HIV was 9.9%), and hypertension (without Hypertension was 9.9% and with Hypertension was 90.1%). Moreover, Hyperparathyroidism was evaluated (without Hyperparathyroidism was 27.2% and with Hyperparathyroidism was 72.7%), as well as Peptic Ulcer Disease (without Peptic Ulcer Disease was 94.2% and with Peptic Ulcer Disease was 5.8%). Furthermore, Hepatitis B was assessed (without Hepatitis B was 95.9% and with Hepatitis B was 4.1%), and then Anaemia was finally evaluated (without Anaemia was 76.9% and with Anaemia was 23.1%). All the patients in the study were on EPO (with EPO was 100% and there were no participants not on EPO).

Table 4.5. 1: Clinical characteristics of study population

	Frequency	Percentage (%)
IV Access		
AV Fistula	45	37.20
Permanent Catheter	76	62.80
ACEI		
No	21	17.35
Yes	100	82.64
ARB		
No	105	86.77
Yes	16	13.22
NSAIDS		
No	81	66.9
Yes	40	33.1
Diabetes Mellitus		
No	106	87.6
Yes	15	12.4
HIV		
No	109	90.10
Yes	12	9.90
Hypertension		
No	12	9.90
Yes	109	90.10
Hyperparathyroidism		
No	33	27.27
Yes	88	72.72
Peptic Ulcer Disease		
No	114	94.2
Yes	7	5.8
Hepatitis B		
No	116	95.90
Yes	5	4.10
Anaemia (Hb<10)		
No	93	76.90
Yes	28	23.10
EPO		
Yes	121	100
No	0	0

4.6. Causes of chronic kidney disease

The Figure 4.6.1 below demonstrates the causes of chronic kidney disease that were reported. It was evident that 58.68% had an unknown cause of chronic kidney disease. Hypertensive kidney disease (11.57%), obstructive uropathy (8.26%), Diabetic nephropathy (6.61%), Glomerulonephritis (4.96%), HIVAN (3.31%) and Polycystic kidney disease (1.65%) were among the causes of chronic kidney disease. In contrast, only 0.83% of causes were Lithium toxicity, Lupus nephritis, Nephrectomy post gunshot, Preeclampsia, Renal artery stenosis and Takayasu arteritis.

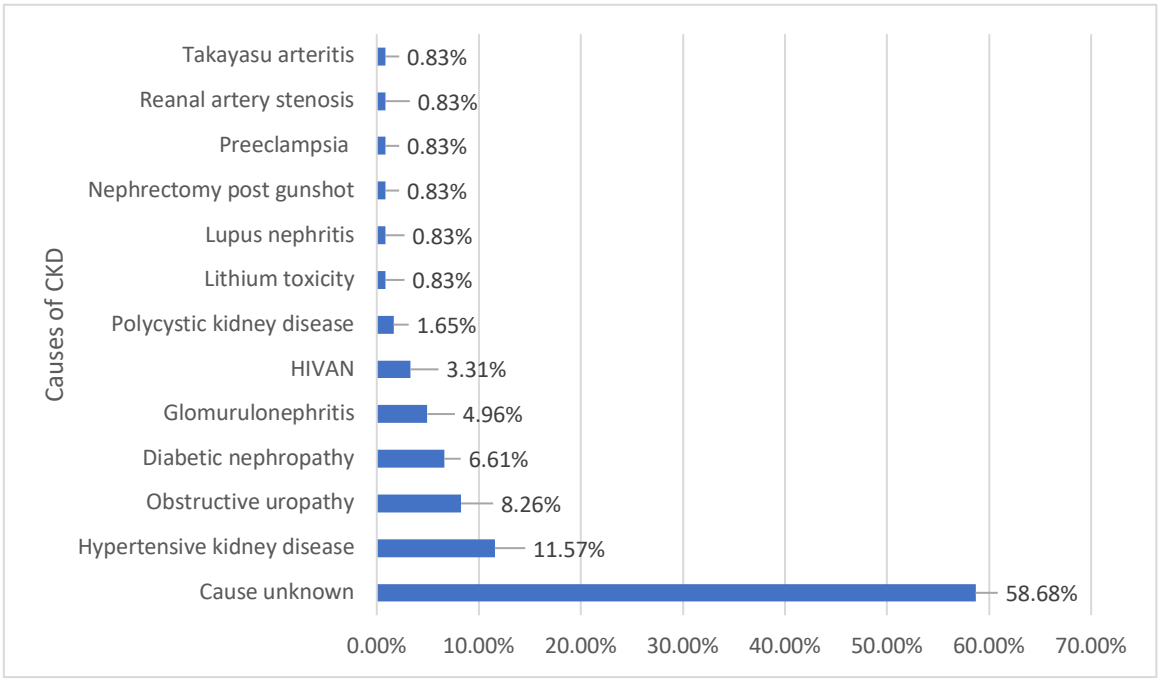

Figure 4.6. 1: Reported causes of chronic kidney disease among study population(n=121)

4.7. Prevalence of anaemia

The Figure 4.7.1 below demonstrates the haemoglobin (Hb) distribution that was seen among the study participants using the 2012 KDIGO guidelines recommended Hb target levels among patients using erythropoietin on chronic haemodialysis. In this study all 121 participants were on erythropoietin. The overall mean Hb was 10.6 ± 1.68g/dl (range 5.9 to 14.8g/dl). It was found that 23%(n=28) of participants had anaemia with hemoglobin levels below 10g/dl. Those that were above the

recommended target were 13%(n=15), with hemoglobin levels that were more than 12g/dl, and those that had hemoglobin levels within the recommended target were 64%(n=78), with hemoglobin levels between 10g/dl and 12g/dl. Figure 4.7.2 below shows that there were more females (53.5%, n=15) with anaemia than males (46.4%, n=13). Figure 4.7.3 below demonstrates the hemoglobin (Hb) distribution among the study participants using the WHO definitions of anaemia (Hb<13g/dl in male patients and Hb< 12g/dl in female patients). The prevalence of anaemia using the WHO definitions were 89.3% and 85% in male and female patients, respectively. These WHO definitions however do not define the goals of treatment among patients on chronic haemodialysis on erythropoietin, and thus, the 2012 KDIGO guidelines recommendations are used for this population group (Hb target 10g/dl -12g/dl).

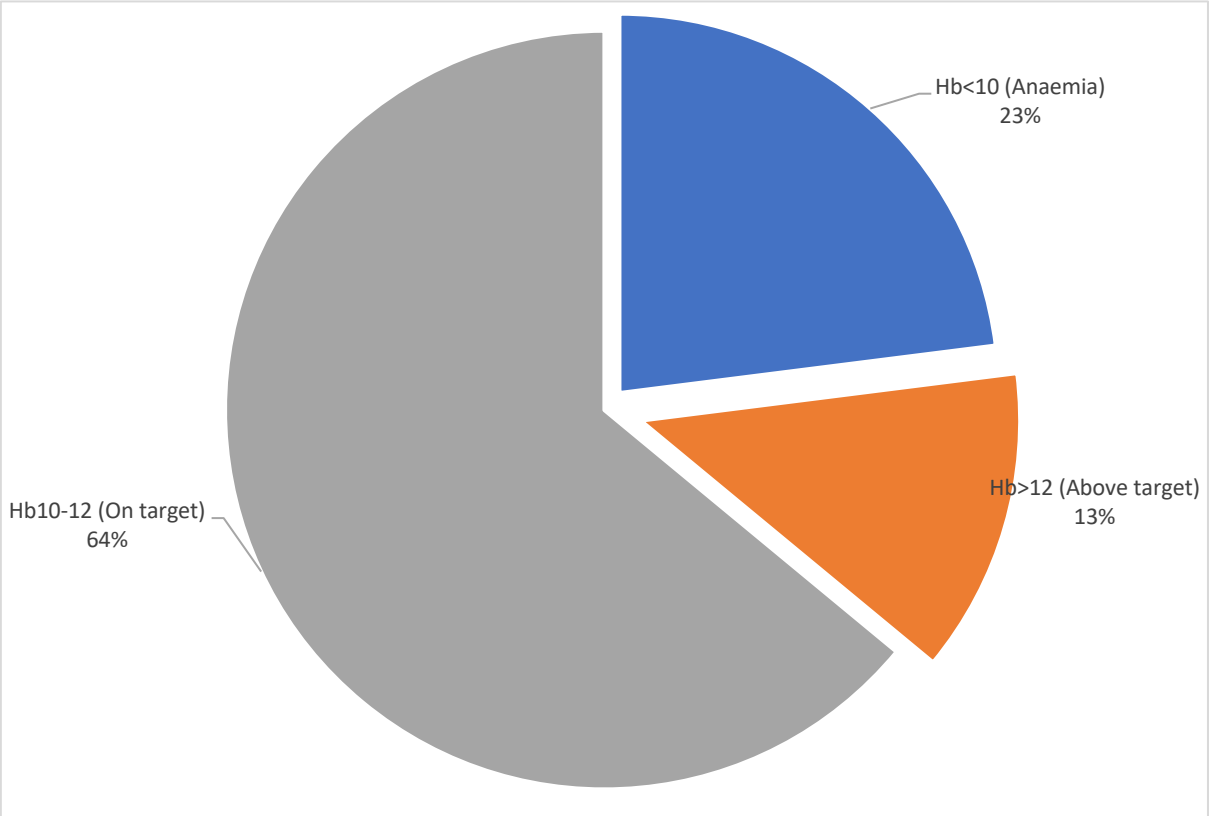

Figure 4.7. 1: Hemoglobin distribution seen in study population (KDIGO)(n=121)

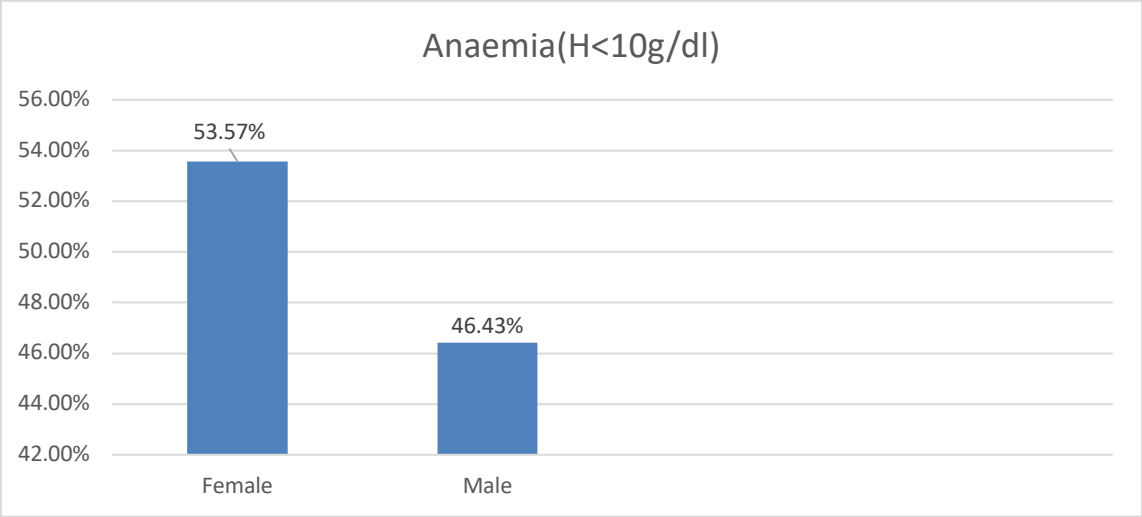

Figure 4.7. 2: Prevalence of anaemia (HB<10g/dl) by gender

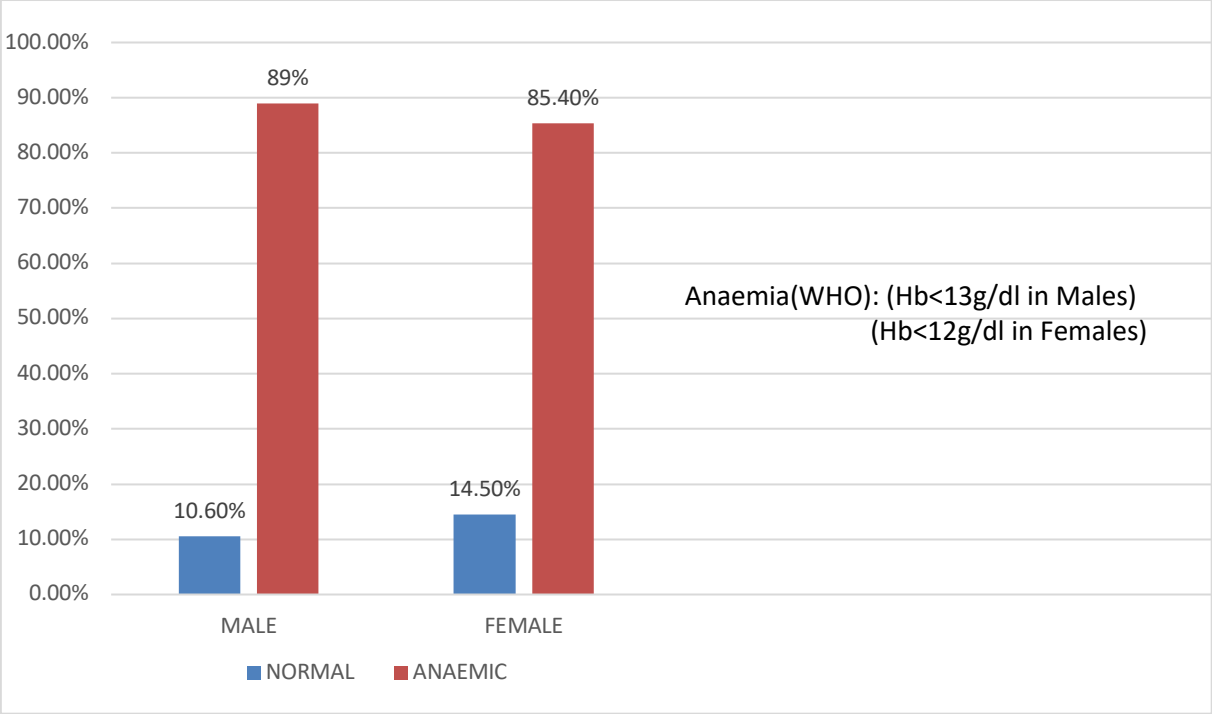

Figure 4.7. 3: Prevalence of anaemia in study population (WHO definitions)

4.8. Association between anaemia and clinical characteristics

The Table 4.8.1 below demonstrates the Chi-square test values of association between anaemia and clinical characteristics of the study participants. The Chi-square test indicated that there were no associations between anaemia (Hb<10g/dl) and any of the clinical characteristics that were analyzed (all p-values > 0.05).

Table 4.8. 1: Associations between anaemia and clinical characteristics

	Anaemia		
	No	Yes	P-value
ACEI			0.637
No	14(15.1%)	6(21.4%)	
Yes	78 (83.9%)	22(78.6%)	
ARB			0.303
No	82(88.2%)	22(78.6%)	
Yes	10(10.8%)	6(21.4%)	
NSAIDS			0.424
No	64(68.8%)	17(60.7%)	
Yes	29(31.2%)	11(39.3%)	
Diabetes Mellitus			0.336
No	80(86%)	26(92.9%)	
Yes	13(14%)	2(7%)	
HIV			0.575
No	83(89.2%)	26(92.9%)	
Yes	10(10.8%)	2(7.1%)	
Hypertension			0.575
No	10(10.8%)	2(7.1%)	
Yes	83(89.2%)	26(92.9%)	
Hyperparathyroidism			0.591
No	25(26.9%)	5(17.9%)	
Yes	66(71%)	22(78.6%)	
Peptic Ulcer Disease			0.567
No	87(93.5%)	27(96.4%)	
Yes	6(6.5%)	1(3.6%)	
Hepatitis B			0.865
No	89(95.7%)	27(96.4%)	
Yes	4(4.3%)	1(3.6%)	

4.9. Mean difference between anaemia and laboratory parameters

Table 4.9.1 below shows the comparison of means of two groups (Anaemia: NO and Anaemia: Yes) using the t-test. From the table below, it was observed that the p-values are < 0.001 and 0.0007 for Hb and Albumin, respectively. We rejected the null hypothesis and concluded that there was a difference between the mean Hb and albumin of having anaemia and not having anaemia at 5% significance level. For other variables the t-test did not show any significant mean difference.

Table 4.9. 1 Association between anaemia and laboratory parameters

	Anaemia		**P-value**
	No mean±SD	**Yes mean±SD**	
Calcium	2.25±0.25	2.19±0.19	0.258
Phosphate	1.17±0.52	1.26±0.60	0.459
Albumin	36.09±3.16	33.46±4.46	0.0007
PTH	54.27±65.96	56.85±62.22	0.854
Ferritin	834.39±854.97	867.75±514.34	0.845
TSAT	38.12±19.71	35.67±18.17	0.558
URR	77.04±3.78	76.75±4.57	0.735
Kt/V	1.633±0.174	1.64±0.189	0.733

4.10. Conclusion

This chapter highlighted the data that was obtained from the participants. The chapter that follows will discuss the results and conclude this research study by highlighting the strengths, limitations, and suggestions for future research.

CHAPTER 5

DISCUSSION, CONCLUSION, RECOMMENDATIONS AND LIMITATIONS

5.1. Introduction

This chapter discusses the study results presented in Chapter 4 with consideration of previous studies and literature on the prevalence of anaemia and its associations in patients on chronic haemodialysis. In addition, limitations, recommendations, and the conclusion of the study will be discussed. The aim of the study was to determine the prevalence and associations of anaemia among patients on chronic haemodialysis at a tertiary hospital in Limpopo Province, South Africa.

This Chapter is subdivided into:

1) Demographic characteristics of the study participants
2) Geographical location of the study participants
3) Causes of chronic kidney disease
4) Prevalence of anaemia
5) Association between anaemia and clinical characteristics
6) Associations between anaemia and laboratory parameters
7) Conclusion
8) Recommendations
9) Limitations

5.2. Discussion

5.2.1. Demographic characteristics of the study participants

The results of this study revealed that majority of patients on chronic haemodialysis in Limpopo Province were male (55%). This was in agreement with national and Sub-Saharan epidemiological trends of CKD patients needing renal replacement therapy being more commonly males than females. The South African Renal Registry Report, 2019 indicated that they were more males (60%) on chronic renal replacement than females (40%). In a study conducted in Yaounde, Cameroon by Kaze et al, it was

found that there were more male patients (70.5%) than female patients (29.5%) on chronic haemodialysis.

In a similar study by Abdelkarim et al. (2020) in Khartoum Sudan, there were also more male patients (57.5%) on chronic haemodialysis than there were female patients. In another conducted in Tanzania by Ruggajo et al. (2019), they had more male patients (65.2%) than female patients (34.8%) on chronic haemodialysis. The studies discussed above -including the current study- revealed that CKD requiring renal replacement therapy is more common in males than females. This reflects the gender disparities in the epidemiology of CKD in Sub-Saharan Africa. The reasons for these disparities are yet to be explored.

The results of this study revealed that patients on chronic haemodialysis in Limpopo province were younger than patients in similar studies in Sub-Saharan Africa. Twenty six percent (26%) of the participants were above the age of 50 years whereas seventy four percent (74%) of the participants were below the age of 50 years (Figure 4.2.1). The mean age was 41.9 ± 11.7 years which is considerably younger than the mean ages of patients in similar studies done in other developing countries. Different from the current study, the 2019 South African Renal Registry Annual Report stated that the median age of patients receiving chronic renal replacement therapy as 53.1 years (IQR 42.4 to 62.6). The patients in the 2019 South African Renal Registry Report were older likely because of inclusion of patients from private sector dialysis units where there is no rationing of dialysis services based on age and comorbidities, unlike that which occurs in the public sector.

In the Cameroonian study, the age of patients ranged from 18 to 75 years with a mean age of 47.6±14.3 years. This mean age was older than that of the patients in the current study. In the Sudanese study, the mean age was 48.7±16.1 years, which was also older than the current study. In the Tanzanian study, the mean age was 51.4±14.2 years which again, was older than the present study. Patients on chronic haemodialysis in Limpopo province were younger than those in other similar studies. This is due to the rationing and selection criteria applied at the Polokwane Kidney and Dialysis Centre, due to scarcity of resources. Patients above the age of 60 years presenting with end stage renal disease requiring chronic haemodialysis are

automatically excluded from the renal replacement program. Patients with diabetes mellitus at presentation above 50 years are also automatically excluded from chronic haemodialysis.

5.2.2. Geographic location

This study involved participants from all the districts of Limpopo province, South Africa. Currently, there is only one dialysis centre in the province located in Polokwane, which is in the Capricorn District. This study revealed that most patients on chronic haemodialysis were from Capricorn district (31%), followed by 26% of participants from Vhembe district. The other 21% of participants were from Mopani district and 12% of participants were from Sekhukhune district. The district that had lowest percentage of participants was Waterberg, with only 9% (Figure 4.2.3). Waterberg District had the lowest number of patients on chronic haemodialysis because it is the least populated district in Limpopo Province, whilst Capricorn is the most populated district. Therefore, the higher percentage of patients on dialysis from Capricorn district is largely explained for by population distribution. Currently, all patients are required to travel for dialysis three times per week from other districts to Polokwane, which is in the Capricorn district, and these travelling costs are incurred by the Limpopo Department of Health. According to Malatjie et al. (2019), the average yearly cost per patient on haemodialysis was R212 286 in 2012. This is likely to have significantly gone up due to inflation. Contributing to these costs is transporting patients from their respective districts to Capricorn district for haemodialysis. Decentralization haemodialysis services to districts with higher patient volumes (i.e., Vhembe (26%) and Mopani (21%)) will likely reduce the overall annual expenditure costs of the Limpopo department of health with regards to patients on chronic haemodialysis.

5.2.3. Causes of chronic kidney disease

In this study, the aetiologies of CKD in the study population were explored. It was evident that the majority (58.68%) of patients had an unknown cause of their chronic kidney disease. Hypertensive kidney disease (11.57%), Obstructive uropathy (8.26%), Diabetic nephropathy (6.61%), Glomerulonephritis (4.96%), HIVAN (3.31%) and Polycystic kidney disease (1.65%) were among the causes of chronic kidney disease.

In contrast, only 0.83% of causes were attributable to Lithium toxicity, Lupus nephritis, Nephrectomy post gunshot, Preeclampsia, Renal artery stenosis and Takayasu arteritis. In contrast, according to the 2019 South African Renal Registry report, the most reported cause of chronic renal failure was hypertensive nephrosclerosis (36%), followed closely by unknown causes (31.7%) and diabetic kidney disease (14.4%). Glomerulonephritis accounted for only 10.2%, cystic kidney disease constituted for even less at 3%, and obstruction and reflux only contributed 1.8% to causes of CKD. The Sudanese study reported contrasting causes of CKD, with the most common cause being reported as hypertension (55.6%), followed by diabetes mellitus (25.3%), obstructive uropathy (14.8%), other causes (15.2%), treatment (7.5%), unknown cause (6.9%), glomerulonephritis (6.9%), pyelonephritis (6.9%) and hereditary nephropathy (0.6%). In a similar study done in Saudi Arabia by Afshar et al. at Mustafa Khomeini Hospital in Tehran Iran, the most common aetiologies of chronic kidney disease were diabetes kidney disease (49.1%), hypertensive nephrosclerosis (28.3%), glomerulonephritis (17.1%) and cystic kidney disease (5.6%) [19]. The high prevalence of CKD of unknown cause (58.68%) in Limpopo province were likely due to patients presenting late with kidneys that were not suitable for kidney biopsy, a requirement for a definitive diagnosis of the cause of CKD. Hypertension(n=109,90%) was a very common comorbidity in most of the patients in the current study. It is very plausible that most of the patients listed as CKD of unknown cause actually had primary, undiagnosed hypertension as the cause of their CKD instead of the hypertension being secondary to the CKD. Diabetic nephropathy (6.61%) was not a common cause of CKD in Limpopo province compared to the other similar studies. This is due to the strict criteria for enrolling patients with diabetes mellitus into the renal replacement program in public hospitals in Limpopo province, which excludes diabetic patients from dialysis if they are older than 50 years on first presentation.

5.2.4. Prevalence of anaemia

This study revealed that all patients on chronic haemodialysis at the PKDC were on erythropoietin (n=121, 100%). The overall mean Hb was 10.6 ± 1.68g/dl. According to the 2012 KDIGO guidelines, the goals of therapy in terms of Hb management in patients on EPO on chronic haemodialysis should target Hb levels between 10g/dl and

12g/dl. It was found that 23%(n=28) of patients had anaemia with haemoglobin levels below target (less than 10g/dl), 13%(n=15) had Hb levels above the recommended target (with haemoglobin levels above 12g/dl), and 64%(n=78) had Hb levels on target (haemoglobin levels between 10g/dl and 12g/dl) (Figure 4.3.1). Using the WHO definitions of anaemia (Hb<13g/dl in male patients and Hb< 12g/dl in female patients), this study revealed that the prevalence of anaemia was 89.3% in male patients and 85% in female patients. The WHO definitions of anaemia are however not used to define the goals of treatment among patients on chronic haemodialysis on erythropoietin. Thus, the 2012 KDIGO guideline recommendations are used for this group of patients (Target Hb 10g/dl -12g/dl).

In Khartoum, Sudan, Abdelkarim et al, anaemia was defined as Hb levels less than 12g/dl in both males and females. All patients(n=534,100%) had anaemia using this definition. Only sixty-point-eight percent (60.8%, n=325) of patients in this study were on erythropoietin. Sixty seven percent (67%, n=358) of patients in this study had Hb levels less than the recommended 10g/dl(anaemia). The lower prevalence of anaemia in the present study (23%) can be attributed to the higher usage of erythropoietin (100%) in patients with CKD compared to lower usage (60.8%) in the Sudanese study.

Additionally, in another study at the Mustafa Khomeini Hospital in Tehran Iran, anaemia was defined using the 2006 NFK-K/DOQI guidelines for CKD anaemia (Hb< 13.5g/dl in males and below 12g/dl in females [19]). Out of the 54 patients on chronic haemodialysis, 90.7% received EPO subcutaneously three times per week[19]. The prevalence of anaemia in chronic haemodialysis patients was 85%[19]. Similarly, our present study showed a prevalence of anaemia of 89.3% in male patients and 85% in female patients using the WHO definitions (Hb<13g/dl in male patients and Hb< 12g/dl in female patients). Ruggajo et al in Tanzania defined anaemia using the WHO definitions. The overall mean Hb levels were 11g/dl, and 74% of females and 64% of males had anaemia. The percentage of patients on EPO was not mentioned. The high levels of anaemia in both studies can be attributed to the definitions used to define anaemia in both studies (2006 NFK-K/DOQI and WHO). These definitions of anaemia are not used to define the goals of treatment among patients on chronic haemodialysis on erythropoietin. The 2012 KDIGO guideline recommendations are the goals of treatment in this group of patients (Hb target 10g/dl -12g/dl).

In Yaounde, Cameroon, in a study by Kaze et al with a similar patient profile to the present study. Only 29.5%(n=28) of the 95 patients recruited for this study were on EPO with only 39%(n=11) of these patients on EPO using it regularly. Anaemia was defined using the K-DOQI guidelines Hb levels< 11g/dl. In contrast to our current study which had mean Hb of 10.6 ± 1.68g/dl, the mean Hb values in the Cameroon study were 8.6g/dl (Range 3.3-14g/dl) and the prevalence of anaemia was 79%(n=75). The very high prevalence of anaemia in this study can be attributed to the low usage of EPO in that setting (29.5%), which is in stark contrast to the present study which had all patients on EPO. This just proves the importance of EPO in the management patients on chronic haemodialysis in the prevention and treatment of anaemia.

5.2.5. Associations between anaemia and clinical characteristics

In the present study using the Chi-square test, there were no associations between anaemia (Hb<10g/dl) and any of the clinical characteristics that were analysed (all p-values > 0.05). In contrast, in the Tanzanian study by Ruggajo P et al, low transferrin saturation of less than 30% (P-value <0.0001) and the presence of more than one comorbidity(P-value=0.04) were associated with the presence of anaemia. Angiotensin Converting Enzyme Inhibitors(ACEIs), Angiotensin Receptor Blockers(ARBs) and comorbidities such as diabetes mellitus have been associated with anaemia in previous studies (Nalado et al., 2019). In the Sudanese study by Abdelkarim et al, the clinical characteristics associated with anaemia (HB<10g/dl) included family history of ESRD [OR=0.57, (0.35-0.94)] and the duration of hypertension of 6-9 years [OR=0.47, (0.25-0.87)]. A plausible explanation to why there were no associations between anaemia and clinical characteristics in the current study could be due to the low prevalence of anaemia (Hb<10g/dl) in this study group (23%) compared to other studies. Data analysis for associations of anaemia used an Hb<10g/dl instead of the values that other similar studies used for data analysis. This could have affected the results.

5.2.6. Mean difference between anaemia and laboratory parameters

Comparison of the means of two groups (Anaemia: NO and Anaemia: YES) using t-test as shown in Table 4.9.1. It was observed that the p-value were < 0.001 and 0.0007 for Hb and albumin, respectively; the null hypothesis was rejected, and we concluded that there was a difference between the mean Hb and Albumin of having anaemia and not having anaemia at 5% significance level. The other laboratory parameters did not show any significant mean difference (Table 4.9.1).

Multiple studies have identified hypalbuminaemia, hypocalcaemia, and hyperparathyroidism as risk factors for anaemia in CKD patients (Nalado et al 2019). Patel et al. [16] found that anaemic CKD patients had lower GFR, lower serum albumin, lower calcium and low 1,25 vitamin D levels, as well as higher serum phosphate and higher PTH levels than nonanemic subjects. Square p-value= 0.8.

5.3. Conclusion

From this study, the prevalence of anaemia among patients on chronic haemodialysis was low (23%) using the 2012 KDIGO guidelines recommended goals of therapy (Target Hb10g/dl-12g/dl). Using the WHO definitions of anaemia (Hb<13g/dl in male patients and Hb< 12g/dl in female patients), this study revealed that the prevalence of anaemia was 89.3% and 85% in male and female patients, respectively. All patients on chronic haemodialysis in Limpopo province were on erythropoietin. There were no associations between anaemia and the patient's clinical characteristics.

5.4. Recommendations

There is a need for protocols to be put in place for routine screening of haemoglobin levels and transferring saturation to enable early diagnosis and appropriate treatment of anaemia in patients on chronic haemodialysis.

Decentralization of haemodialysis services to districts with a lot of patients i.e., Vhembe (26%) and Mopani (21%) will likely reduce the overall annual costs the department of health Limpopo province spends on patients on chronic haemodialysis.

Future studies should involve multiple dialysis centres across South Africa to accommodate even more patients on chronic haemodialysis to further explore this topic from a larger sample size.

5.5. Limitations

This was a retrospective study, therefore it had limitations due to information bias. There were 24(16.5%) missing patient records that met the inclusion criteria. These files could not be found at the hospital records section. Most of these files were of patients that had demised before the study was commenced.

Folate, vitamin B12 levels and MCVs were not obtained because they are not routinely measured at the PKDC. These are very important in determining the cause of anaemia.

The study was done in a single dialysis centre (PKDC) which may limit its generalisability to the whole of South Africa.

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7. APPENDICES

7.1. ANNEXURE 1: TREC ethics approval

University of Limpopo
Department of Research Administration and Development
Private Bag X1106, Sovenga, 0727, South Africa
Tel: (015) 268 3935, Fax: (015) 268 2306, Email:
makoetja.ramusi@ul.ac.za

TURFLOOP RESEARCH ETHICS COMMITTEE

ETHICS CLEARANCE CERTIFICATE

MEETING: 17 February 2021

PROJECT NUMBER: TREC/16/2021: PG

PROJECT:

Title: Prevalence and associations of anaemia among patients on chronic *haemodialysis* at a tertiary hospital in Limpopo Province, South Africa

Researcher: BK Muponda
Supervisor: Dr P Mangena
Co-Supervisor/s: Dr M Nchabeleng
School: Medicine
Degree: Master of Medicine in Internal Medicine

PROF P MASOKO
CHAIRPERSON: TURFLOOP RESEARCH ETHICS COMMITTEE
The Turfloop Research Ethics Committee (TREC) is registered with the National Health Research Ethics Council, Registration Number: **REC-0310111-031**

Note:

i) **This Ethics Clearance Certificate will be valid for one (1) year, as from the abovementioned date. Application for annual renewal (or annual review) need to be received by TREC one month before lapse of this period.**

ii) **Should any departure be contemplated from the research procedure as approved, the researcher(s) must re-submit the protocol to the committee, together with the Application for Amendment form.**

iii) **PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES.**

Finding solutions for Africa

7.2. ANNEXURE 2: Limpopo Department of Health approval

LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

Department of Health

Ref	:	LP_2021-03-006
Enquires	:	Ms PF Mahlokwane
Tel	:	015-293 6028
Email	:	Phoebe.Mahlokwane@dhsd.limpopo.gov.za

PERMISSION TO CONDUCT RESEARCH IN DEPARTMENTAL FACILITIES

Your Study Topic as indicated below;

Prevalence and associations of anaemia among patients on chronic haemodialysis at a tertiary hospital in Limpopo province, South Africa

1. Permission to conduct research study as per your research proposal is hereby Granted.
2. Kindly note the following:
   a. Present this letter of permission to the institution supervisor/s a week before the study is conducted.
   b. In the course of your study, there should be no action that disrupts the routine services, or incur any cost on the Department.
   c. After completion of study, it is mandatory that the findings should be submitted to the Department to serve as a resource.
   d. The researcher should be prepared to assist in the interpretation and implementation of the study recommendation where possible.
   e. The approval is only valid for a 1-year period.
   f. If the proposal has been amended, a new approval should be sought from the Department of Health
   g. Kindly note that, the Department can withdraw the approval at any time.

   Your cooperation will be highly appreciated

pp **Head of Department** **Date** 19/04/201

Private Bag X9302 Polokwane
Fidel Castro Ruz House, 18 College Street. Polokwane 0700. Tel: 015 293 6000/12. Fax: 015 293 6211.
Website: http/www.limpopo.gov.za

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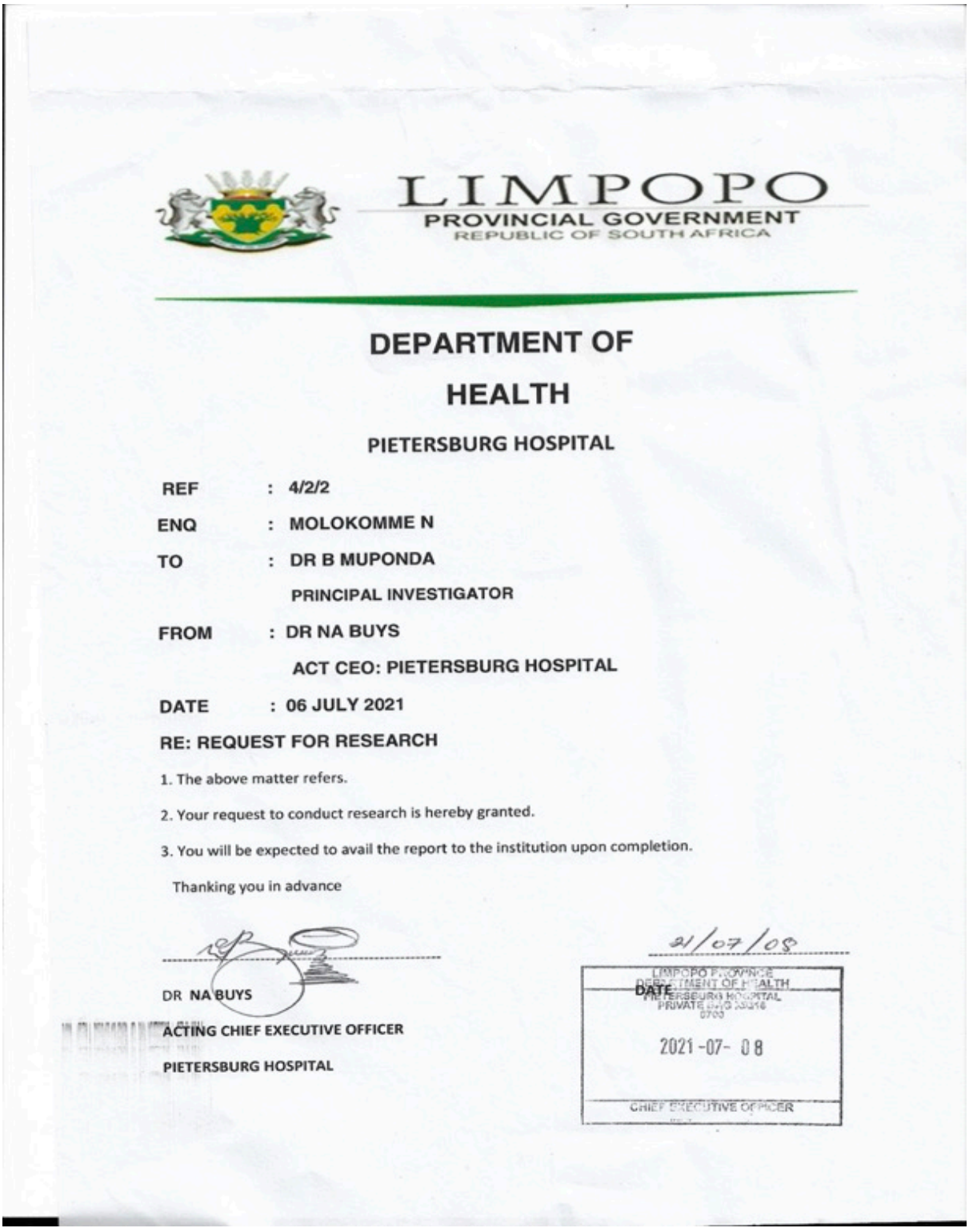
7.3. ANNEXURE 3: Pietersburg Hospital approval



LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

DEPARTMENT OF

HEALTH

PIETERSBURG HOSPITAL

REF : **4/2/2**

ENQ : **MOLOKOMME N**

TO : **DR B MUPONDA**
PRINCIPAL INVESTIGATOR

FROM : **DR NA BUYS**
ACT CEO: PIETERSBURG HOSPITAL

DATE : **06 JULY 2021**

RE: REQUEST FOR RESEARCH

1. The above matter refers.
2. Your request to conduct research is hereby granted.
3. You will be expected to avail the report to the institution upon completion.

Thanking you in advance

DR **NA BUYS**
ACTING CHIEF EXECUTIVE OFFICER
PIETERSBURG HOSPITAL

21/07/08
DATE

LIMPOPO PROVINCE
DEPARTMENT OF HEALTH
PIETERSBURG HOSPITAL
PRIVATE BAG X9612
0700
2021-07-08
CHIEF EXECUTIVE OFFICER

7.4. ANNEXURE A: Data collection sheet

Annexure A: Data Collection Sheet

Demographic Information

Patient unique number | DOB | Age | Age Group

Gender | District | Race

Clinical Information

Dry weight | EPO(Units/Kg/week) | Duration on RRT

Date Started on RRT | Iron | Type of IV Access

Aetiology of CKD | NSAIDS | ACE-I | ARB

Cormobidities

Peptic Ulcer Disease | Diabetes Mellitus | HIV

Hepatitis B | Hypertension | Hyperparathyroidism

Laboratory Data

Mean MCH | Mean Hb | Mean PTH | Mean cCa2+ | Mean Albumin

Mean MCV | Kt/V | Mean PO4 | Mean Ferritin | Mean TSAT(%)

7.5. Annexure B Descriptive Statistics Results

```
. ttest MeanHb, by(Anaemia)

Two-sample t test with equal variances
```

Group	Obs	Mean	Std. Err.	Std. Dev.	[95% Conf.	Interval]
0	93	11.3828	.1157594	1.116343	11.15289	11.6127
1	28	8.346429	.1894354	1.002398	7.957739	8.735118
combined	121	10.68017	.1530661	1.683727	10.37711	10.98323
diff		3.036367	.2352932		2.570463	3.502271

```
    diff = mean(0) - mean(1)                                      t =  12.9046
Ho: diff = 0                     degrees of freedom =      119

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 1.0000         Pr(|T| > |t|) = 0.0000          Pr(T > t) = 0.0000

. ttest MeanCorrectedCalcium, by(Anaemia)

Two-sample t test with equal variances
```

Group	Obs	Mean	Std. Err.	Std. Dev.	[95% Conf.	Interval]
0	93	2.254516	.0264485	.2550597	2.201987	2.307045
1	28	2.195	.037496	.1984103	2.118064	2.271936
combined	121	2.240744	.0221506	.2436567	2.196887	2.2846
diff		.0595161	.0524604		-.0443607	.163393

```
    diff = mean(0) - mean(1)                                      t =   1.1345
Ho: diff = 0                     degrees of freedom =      119

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0.8706         Pr(|T| > |t|) = 0.2589          Pr(T > t) = 0.1294

. ttest MeanPO4, by(Anaemia)

Two-sample t test with equal variances
```

Group	Obs	Mean	Std. Err.	Std. Dev.	[95% Conf.	Interval]
0	93	1.176559	.0547764	.5282446	1.067768	1.28535
1	28	1.263929	.1138357	.6023616	1.030357	1.4975
combined	121	1.196777	.0495384	.5449223	1.098694	1.294859
diff		-.0873694	.1176848		-.3203972	.1456583

```
    diff = mean(0) - mean(1)                                      t =  -0.7424
Ho: diff = 0                     degrees of freedom =      119

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0.2297         Pr(|T| > |t|) = 0.4593          Pr(T > t) = 0.7703
```

```
. ttest MeanAlbumin, by(Anaemia)

Two-sample t test with equal variances
```

Group	Obs	Mean	Std. Err.	Std. Dev.	[95% Conf.	Interval]
0	93	36.09677	.3282921	3.165935	35.44476	36.74879
1	28	33.46429	.8443434	4.467845	31.73184	35.19674
combined	121	35.4876	.3330127	3.66314	34.82826	36.14695
diff		2.632488	.7553317		1.136856	4.128121

```
    diff = mean(0) - mean(1)                                      t =   3.4852
Ho: diff = 0                                     degrees of freedom =      119

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0.9997         Pr(|T| > |t|) = 0.0007          Pr(T > t) = 0.0003

. ttest MeanPTH, by(Anaemia)

Two-sample t test with equal variances
```

Group	Obs	Mean	Std. Err.	Std. Dev.	[95% Conf.	Interval]
0	93	54.27957	6.840334	65.9658	40.69408	67.86506
1	28	56.85714	11.76002	62.2282	32.72756	80.98672
combined	121	54.87603	5.897618	64.8738	43.19916	66.55291
diff		-2.577573	14.04097		-30.3801	25.22495

```
    diff = mean(0) - mean(1)                                      t =  -0.1836
Ho: diff = 0                                     degrees of freedom =      119

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0.4273         Pr(|T| > |t|) = 0.8547          Pr(T > t) = 0.5727

. ttest MeanFerritin, by(Anaemia)

Two-sample t test with equal variances
```

Group	Obs	Mean	Std. Err.	Std. Dev.	[95% Conf.	Interval]
0	93	834.3978	88.65706	854.9777	658.3173	1010.478
1	28	867.75	97.20263	514.348	668.3067	1067.193
combined	121	842.1157	71.5904	787.4944	700.3717	983.8597
diff		-33.35215	170.4382		-370.8368	304.1325

```
    diff = mean(0) - mean(1)                                      t =  -0.1957
Ho: diff = 0                                     degrees of freedom =      119

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0.4226         Pr(|T| > |t|) = 0.8452          Pr(T > t) = 0.5774
```

```
. ttest MeanTSAT, by(Anaemia)

Two-sample t test with equal variances
```

Group	Obs	Mean	Std. Err.	Std. Dev.	[95% Conf.	Interval]
0	93	38.12903	2.044515	19.71659	34.06845	42.18962
1	28	35.67857	3.434209	18.17213	28.63216	42.72499
combined	121	37.56198	1.756722	19.32395	34.0838	41.04017
diff		2.450461	4.176938		-5.820293	10.72121

```
    diff = mean(0) - mean(1)                                      t =   0.5867
Ho: diff = 0                     degrees of freedom =      119

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0.7207         Pr(|T| > |t|) = 0.5585          Pr(T > t) = 0.2793

. ttest URR, by(Anaemia)

Two-sample t test with equal variances
```

Group	Obs	Mean	Std. Err.	Std. Dev.	[95% Conf.	Interval]
0	93	77.04086	.3925029	3.785161	76.26132	77.8204
1	28	76.75	.8649173	4.576712	74.97534	78.52466
combined	121	76.97355	.3603541	3.963895	76.26008	77.68703
diff		.2908602	.8576334		-1.40734	1.98906

```
    diff = mean(0) - mean(1)                                      t =   0.3391
Ho: diff = 0                     degrees of freedom =      119

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0.6325         Pr(|T| > |t|) = 0.7351          Pr(T > t) = 0.3675

. ttest KTV, by(Anaemia)

Two-sample t test with equal variances
```

Group	Obs	Mean	Std. Err.	Std. Dev.	[95% Conf.	Interval]
0	93	1.633333	.0181117	.1746632	1.597362	1.669305
1	28	1.646429	.0358134	.1895065	1.572946	1.719912
combined	121	1.636364	.0161348	.1774824	1.604418	1.668309
diff		-.0130952	.0384001		-.0891313	.0629408

```
    diff = mean(0) - mean(1)                                      t =  -0.3410
Ho: diff = 0                     degrees of freedom =      119

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0.3668         Pr(|T| > |t|) = 0.7337          Pr(T > t) = 0.6332
```