AFRICA UNIVERSITY
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Prevalence of thyroid dysfunction among patients with chronic kidney disease attending Diagnostic Laboratory Services, Bulawayo, Zimbabwe 2023.

BY

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A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE (HONOURS) OF MEDICAL LABORATORY SCIENCES IN THE FACULTY OF HEALTH SCIENCES

2024

Abstract

Chronic kidney disease (CKD), can alter thyroid hormone production, distribution, and excretion. Thyroid dysfunctions like hypothyroidism, hyperthyroidism, and euthyroidism are identified in renal failure patients. This study aimed to determine thyroid dysfunction prevalence among CKD patients who attended Diagnostic Laboratory Services in Bulawayo from January to December 2023. The study was analytical and cross-sectional in nature. Archival data collection methods were used to gather information from 118 CKD patients who underwent both thyroid function tests and urea and electrolytes tests. A descriptive and analytical statistic test was used to determine the prevalence of thyroid dysfunction among CKD patients. Chi square test was used to test association between thyroids dysfunction and CKD and associated risk factors. $P< 0.05$ was considered as statistically significant. Thyroid dysfunction prevalence was 53%, increasing with CKD severity, with stage 3B having a high prevalence of 37%. Major types include subclinical hypothyroidism (11%), overt hypothyroidism (16%), and subclinical hyperthyroidism (4.2%), with 36% of females presenting with thyroid dysfunction as compared to 31% of males. Prevalence of thyroid dysfunction increased with an increase in age. Majors risk factosr for CKD in thyroid dysfunction setting were hypertension diabetes and heart failure. In conclusion, there was a high prevalence of thyroid dysfunction (53%) among chronic kidney disease patients.

Keywords: CKD, Thyroid, Dysfunction, Prevalence

Declaration

I declare that this dissertation is my original work except where sources have been cited and acknowledged. The work has never been submitted, nor will it ever be submitted to another university for the award of a degree.

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Acknowledgments

I would like to express my appreciation to Dr. Salissou Maibouge, my academic supervisor, for guiding, advising, and making the final submission of this dissertation possible. I am also grateful to Stanbic Bank Zimbabwe, for sponsoring my education. I would also like to give recognition to Diagnostic Laboratory Services for facilitating my research and the staff members who provided their valuable assistance throughout the process.

Dedication

I dedicate this to my mother, S. Mvula. I would not have been able to complete my studies without your unwavering support and relentless prayers.

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List of Abbreviations

AUREC	Africa University Research and Ethics Committee
CKD	Chronic Kidney disease
DLS	Diagnostic Laboratory Services
eGFR	Estimated Glomerular Filtration Rate
ESRD	End stage renal disease
IL -1	Interleukin
KD	Kidney Disease
SCH	Subclinical Hypothyroidism
T3	Free Triiodothyromine
T4	Free Thyroxine
TD	Thyroid Dysfunction
TFT	Thyroid Function Tests
TSH	Thyroid Stimulating Hormone
TRH	THYROID Releasing Hormone
TNF	Tissue Necrosis Factor

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CHAPTER 1: INTRODUCTION

1.1 Introduction

Thyroid hormones are crucial in the control of kidney function and metabolism. The thyroid gland controls the majority of the body's physiological functions. The kidneys and thyroid are both physically and functionally connected. The thyroid hormone is important in the growth and development of the kidneys, and the kidneys are responsible for its metabolism, degradation, and excretion. Kidney disease, on the other hand, can have an impact on thyroid function by altering thyroid hormone production, distribution, and excretion. Chronic kidney disease (CKD) is now known to disrupt the pituitary-thyroid axis as well as the metabolism of peripheral thyroid hormones. Thyroid dysfunctions such as hypothyroidism, hyperthyroidism, and euthyroidism have been identified in renal failure patients by various researchers (Ansari et al, 2023). The primary goal of this study was to determine the prevalence of thyroid dysfunction among patients with chronic kidney disease attending Diagnostic Laboratory Services in Bulawayo throughout 2023.

1.2 Study Background

Thyroid function problems, particularly hypothyroidism, are significantly more common in people with chronic kidney disease than in the general population, according to epidemiological research. Reports suggest that the progression of CKD is associated with several complications, including thyroid dysfunction, dyslipidemia, and CVD (Thomas et al 2008). Chronic Kidney Disease (CKD) affects 9.1% of the global population and is a growing public health concern worldwide, as per a study by Ogbera in 2023. It is defined as irregularities in the structure or function of one's kidneys that persist for more than three months and pose health risks. CKD increases the risk of all-cause mortality, cardiovascular disease, and progression to end-stage renal disease (ESRD). Therefore,

identifying the risk factors for CKD or a reduction in eGFR can aid in comprehending the mechanisms of CKD and developing new prevention techniques.

The International Journal of Nephrology (2022) reported that CKD can modify thyroid function via non-thyroidal disease, metabolic acidosis, altered hormone catabolism, decreased peripheral conversion, hormonal elimination during HD therapy, and increased iodine storage in the thyroid gland. The burden of CKD coupled with thyroid dysfunction can have serious health consequences (Orgebra, 2023). Chronic Kidney Disease (CKD) affects thyroid function in various ways. It can cause low levels of circulating thyroid hormone, altered metabolism of peripheral hormone, insufficient binding to carrier proteins, reduced thyroid hormone content in tissues, and altered iodine storage in the thyroid gland. In CKD, the hypothalamus pituitary thyroid axis is also affected, leading to impaired thyroid hormone metabolism. Studies have shown that CKD is associated with a higher prevalence of primary hypothyroidism, both overt and subclinical. However, there is no association with hyperthyroidism (Malyszko J et al 2006). Zhang et al (2019) estimated that approximately 13.4% of the general population worldwide may have some form of thyroid dysfunction. In Zimbabwe, the prevalence of thyroid dysfunction has not been extensively studied, and there is limited data available on the specific prevalence rates. Given the reduced thyroid function in CKD patients and the lack of data on thyroid function in the Bulawayo population with CKD, a study was conducted to investigate this population.

1.3 Problem Statement

Renal dysfunctions have been linked to particular changes in thyroid hormone levels. In the past two decades, several researchers have sought to simplify the significance of relationships between kidney illness and thyroid functioning (Srivastava et al, 2018). This knowledge is substantial because it anticipates a connection between two distinct entities. Left unattended, the phenomenon

of the combination of two global public health issues can have a devastating effect on multiple ectors of the economy of any country. Although studies have been done in India, China, Europe and the United States of America, gaps still exist in the literature on the interventions that can be one where the problems exist, particularly in LMICs (Keunmoe, 2019). Up to now, far too little attention has been paid to chronic renal illness and thyroid dysfunction in Zimbabwe, in particular. There is limited data available in Zimbabwe concerning the burden of thyroidal diseases.

1.4 Study Justification

To The Researcher

The findings of this study assisted the researcher in contributing efficiently and effectively to the surveillance of chronic renal failure and thyroid dysfunctions, as well as highlighting the effects of this phenomenon on the community. In addition, the researcher learnt more about the impact of deteriorating renal function on thyroid function.

To the community

This study aimed to assess trends and the impact of interventions, particularly on those with chronic kidney disease. It helped to strengthen knowledge. Through quality research, this data helped contribute accurate and reliable information toward preventive measures. This research also assisted with community health education.

To chronic kidney disease patients

This study aided chronic kidney disease patients in learning how to take care of themselves to avoid the potential dangers associated with thyroid dysfunction. Overall, it strengthened public health efforts and interventions while also saving lives.

1.5 Research objectives

1.5.1 Broad objective

This research aimed to investigate the prevalence of thyroid dysfunction among patients with chronic kidney disease attending diagnostic laboratory services from January 2023 to December 2023.

1.5.2 Specific objectives

The specific objectives of this study were as follows:

1. To determine the prevalence of hyperthyroidism among patients with chronic kidney disease attending DLS from January 2023 to December 2023.
2. To determine the prevalence of hypothyroidism among patients with chronic kidney disease attending DLS from January 2023 to December 2023.
3. To determine the distribution, using socio-demographic characteristics, of thyroid dysfunction among patients with chronic kidney disease (according to the different stages) attending DLS from January 2023 to December 2023.
4. To identify potential risk factors for thyroid dysfunction in CKD patients.

1.6 Research Questions

This study was guided by the following questions:

1. What is the prevalence of hyperthyroidism among patients with chronic kidney disease attending DLS from January 2023 to December 2023?
2. What is the prevalence of hypothyroidism among patients with chronic kidney disease attending DLS from January 2023 to December 2023?

3. What is the distribution, using socio-demographic characteristics and risk factors, of thyroid dysfunction among patients with chronic kidney disease (according to the different stages) attending DLS from January 2023 to December 2023?
4. What are the potential risk factors for thyroid dysfunction in patients with CKD?

1.7 Study Limitations

This study was only limited to patients with chronic kidney disease attending Diagnostic Laboratory Services in Bulawayo. Challenges in getting detailed accounts from the holders of data such as the patient records at the institution as a gesture of confidentiality were incurred.

1.8 Study Delimitations

The research covered only a small section of the community as it only focused on the patients attending Diagnostic Laboratory Services thus there is a chance that the result could be biased.

1.9 Chapter Summary

This chapter began with the study's background and problem statement, followed by the study's justification, research objectives, and questions. The chapter concluded with a discussion of the study's limitations and delimitations. The following chapter examines the literature relevant to this study.

CHAPTER 2 LITERATURE REVIEW

2.1 Introduction

This chapter reviewed literature related to the prevalence of thyroid dysfunction among chronic kidney disease (CKD) patients. The aim of this literature review was to provide background information on what is known already on the topic and to draw attention to the most important findings from previous research. The literature was reviewed under the following headings:The prevalence of chronic kidney disease (CKD), The prevalence of thyroid dysfunction ,Literature review on thyroid dysfunction and CKD , A conceptual framework based on thyroid dysfunction and CKD

2.2 Literature review in relation to objectives

2.2.1 The prevalence of chronic kidney disease

Chronic kidney disease (CKD) is a clinical illness caused by a permanent change in the function and/or structure of the kidney, and it is distinguished by its irreversibility and gradual and steady progression. Chronic kidney disease is characterized by elevated levels of serum creatinine and urea, and most importantly, decreased glomerular filtration rate. Another crucial element is that the pathology indicates a higher risk of morbidity and mortality, particularly cardiovascular-related problems.

The American Journal of Nephrology (2022) states that kidney damage is defined by any one of the following findings: a) Pathologic kidney abnormalities b) Persistent proteinuria c) Other urine abnormalities, e.g., renal hematuria d) Imaging abnormalities e) eGFR <60 mL/min/1.73 m2 on two occasions separated by 90 days and that is not associated with a transient, reversible condition such as volume depletion.

An informed interpretation of the estimated glomerular filtration rate (eGFR) is required since the GFR is still considered the best overall index of kidney function in stable, non-hospitalized patients. The eGFR is primarily determined by serum creatinine, and the preferred method for estimating GFR is the body surface area-normalized, 4-variable, Modification of Diet in Renal Disease Study (MDRD) Equation based on serum creatinine, age, gender, and ethnicity.

CKD is categorized into five stages, according to the GFR, as shown in the tables below, as obtained from the BMJ Best Practice Journal, 2023.

Table 1: Stages of CKD

STAGES	GFR	CLASSIFICATION
I	>90	Normal or high
II	60 - 89	Slightly decreased
III A	45 - 59	Mild to moderately decreased
III B	30 - 44	Moderately to severely decreased
IV	15 – 29	Severely decreased
V	<15	Kidney failure

Kidney disease is one of the leading causes of death globally, according to the Centers for Disease Control and Prevention. Chronic Kidney Disease (CKD) is common in the general adult population. Adult prevalence of CKD in the United States is estimated to be 13.1%, which has increased over time. It is estimated that 37 million adults in the United States have CKD, but most of them remain undiagnosed. CKD can lead to kidney failure, early cardiovascular disease, and thyroid problems (Center for Disease Control, 2022). A South African study discovered a high

prevalence of 27.6% new onset thyroid dysfunction (TD) in 163 patients following 369 days of amiodarone treatment for cardiac arrhythmias (Ross et al, 2005). As discovered by Zhang et al (2019) the global estimated prevalence of CKD is reported to be around 13.4%.

2.2.2 Literature review on thyroid dysfunction

British Medical Journal (BMJ) Best Practice (2023) describes thyroid function in the following way: "The thyroid gland produces, stores, and secretes thyroxine (T4) and triiodothyronine (T3) through a negative feedback process involving the hypothalamus and pituitary gland. Thyroid dysfunction can result when any part of this process is affected, and is usually characterized by the presence of high or low levels of thyroid-stimulating hormone (TSH, secreted by the pituitary gland) and free thyroid hormones."

Hypothyroidism is a medical condition that results from a deficiency in two important hormones - T4 and T3. The condition is characterized by various symptoms such as fatigue, cold intolerance, slowed reflexes, hair loss, dry skin, weight gain, constipation, and slowed speech and intellectual function. Hypothyroidism affects women more than men according to the National Institute for Health (2021). The most common cause of hypothyroidism is primary hypothyroidism, which accounts for 95% of thyroid dysfunction. This occurs when the thyroid gland is unable to produce enough hormones due to an iodine deficiency or a thyroid gland abnormality. On the other hand, secondary hypothyroidism is caused by insufficient TSH production, as explained by Naraski et al (2014).

Hyperthyroidism occurs when there is an excess of circulating thyroid hormones (T3 and T4) due to an overactive thyroid gland. This is marked by increased T4 (above 20pmol/l) and T3 (above 8.3 pmol/l) values with a normal TSH (Devereaux and Tewelde (2014)). This is referred to as thyrotoxicosis. Primary hyperthyroidism is a condition where thyrotoxicosis is caused by an

abnormality in the thyroid gland. Graves' disease, which is an autoimmune disorder, is an example of this. On the other hand, secondary hyperthyroidism occurs when a normal thyroid gland is abnormally stimulated. According to BM Best Practice (2023), the major clinical manifestations of hyperthyroidism include nervousness, anxiety, heart palpitations, rapid pulse, fatigue, tremors, and leg weakness, weight loss with increased appetite, heat intolerance, frequent bowel movements, increased perspiration, and often thyroid gland enlargement (goiter).

The most sensitive test in a population at risk for thyroid dysfunction is the serum TSH or T3 and T4 (Demers and Spencer, in press). Physicians rely on these tests to detect, diagnose, and treat diseases caused by thyroid hormones. In most cases of thyroid dysfunction, function can be restored when detected correctly. However, if left untreated, thyroid disorders can lead to serious cardiovascular and neuromuscular complications (Kachawa, 2019).

2.2.3 Literature review on CKD and thyroid dysfunction

Various researchers have observed thyroid dysfunctions like hypothyroidism, hyperthyroidism, and eurothyroid state in renal failure patients. Both the kidneys and thyroid are physiologically and functionally related to each other. The thyroid gland regulates most of the physiological actions of the body. The thyroid hormone is crucial for the growth and development of the kidneys, while the kidneys are responsible for the metabolism, degradation, and excretion of this hormone (Zilstra, 2020).

Chronic kidney disease (CKD) can affect the pituitary-thyroid axis and the peripheral thyroid hormone metabolism. CKD can lead to changes in thyroid function, through non-thyroidal illness, metabolic acidosis, altered hormonal catabolism, diminished peripheral conversion, hormonal removal during HD therapy, and increased iodine stored in the thyroid gland (Zilstra, 2020).

The thyroid gland primarily secretes thyroxine (T4), which is peripherally converted to the more active form of tri-iodothyronine (T3). Local deiodination of T4 in the kidney by the isoform D1 of the enzyme T4-5′-deiodinase leads to the production of the T3 hormone. As CKD progresses, the production of T4-5′-deiodinase decreases, leading to low T3 syndrome and clinical and subclinical hypothyroidism (Drube et al., 2019). There are multiple factors responsible for thyroid disorders seen in CKD patients.

The most prevalent thyroid condition detected in these patients is low T3 and subclinical hypothyroidism. The reason for normal TSH levels is the reduced responsiveness of the pituitary receptor to TRH, which leads to less TSH secretion. TSH's response to TRH is delayed due to a decrease in clearance and a prolongation of the half-life of TSH. (Shakya, 2023).

The thyroid hormone affects the glomerular filtration rate (GFR), proteinuria, and tubular function. Chronic kidney disease leads to the buildup of inflammatory cytokines such as TNF-alpha and IL-1. This leads to decreased peripheral conversion of T4 to T3, again leading to low T3 levels. This is because inflammatory cytokines lead to a decrease in the level of 1 5'-deiodinase, which converts T4 to T3 (Narasaki, vol 41, pp133,2021).

Studies on the spread of thyroid function abnormalities, particularly hypothyroidism, have revealed that the prevalence is considerably greater in individuals with chronic kidney disease compared to the general population. A study conducted in Nepal, South Korea discovered that thyroid dysfunction was found in 38.6% of patients, with subclinical hypothyroidism (27.2%), overt hypothyroidism (TSH levels above the reference range and free thyroxine levels below the reference range) (8.1%), and subclinical hyperthyroidism (3.3%) being the most common types encountered. Subclinical hypothyroidism is defined as an elevated TSH level in conjunction with normal T3 and T4 levels. In North India (Chennai), 66% of CKD patients were reported to have

thyroid dysfunction. Low T3 syndrome accounted for 58% against 8% for hypothyroidism (Keumone, 2019).

In Nairobi, Kenya, it was found that 42% of patients suffer from thyroid dysfunction. Out of the total patients, 14% had a non-thyroidal illness. Subclinical and primary hypothyroidism were responsible for 15% of the patients while different forms of hyperthyroidism accounted for 13%. In advanced CKD, many cases of hypothyroidism may go unnoticed due to symptoms overlapping with uremia and co-existing comorbidities. Hypothyroidism can lead to a decrease in glomerular filtration, hyponatremia, and an alteration of the ability for water excretion (Al Hussaini et al, 2023).

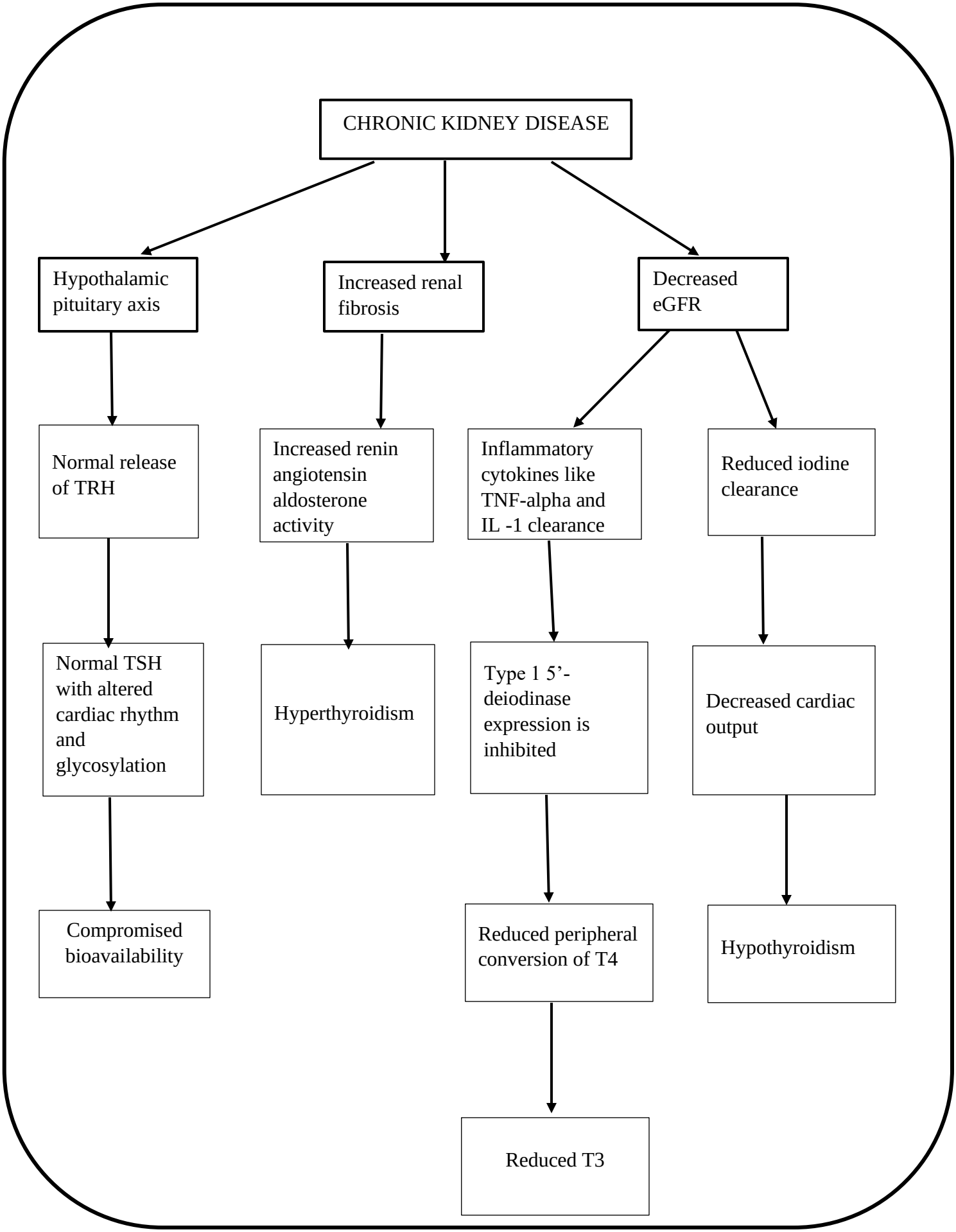
An excess of TH can cause an increase in glomerular filtration rate and renal plasma flow. Renal disease can cause significant changes in thyroid function, and various types of glomerulopathies have been associated with both hyper and hypofunction of the thyroid. There have also been some reports of tubulointerstitial disease being linked to functional thyroid disorders, although this is less common. In cases of nephrotic syndrome, the loss of protein in the urine can lead to changes in TH concentrations (Sinjari et al, 2022).

Severe hypothyroidism may result in reduced cardiac function, which can worsen kidney function over time. This means that thyroid dysfunction can lead to increased morbidity and cardiovascular mortality in CKD patients. Additionally, low T3 syndrome has been found to be an independent predictor of cardiovascular mortality in this patient population.

2.2.4 Conceptual framework based on CKD and thyroid dysfunction

A conceptual framework illustrates what is expected to be found through research. It gives a picture of how the variables of the study relate to each other (Swaen, 2015). This concept was guided by the International Journal of Nephrology (Volume, 2014).

Figure 1 shows the correlation between thyroid dysfunction and chronic kidney disease.


CHRONIC KIDNEY DISEASE
Hypothalamic pituitary axis
Increased renal fibrosis
Decreased eGFR
Normal release of TRH
Increased renin angiotensin aldosterone activity
Inflammatory cytokines like TNF-alpha and IL -1 clearance
Reduced iodine clearance
Normal TSH with altered cardiac rhythm and glycosylation
Hyperthyroidism
Type 1 5'-deiodinase expression is inhibited
Decreased cardiac output
Compromised bioavailability
Reduced peripheral conversion of T4
Hypothyroidism
Reduced T3

KEY

TRH	Thyroid Releasing Hormone
TNF	Tissue Necrosis Factor
IL -1	Interleukin

2.3 Chapter Summary

This chapter reviewed the related literature about thyroid dysfunction and chronic kidney disease. The literature review gives a baseline to this study. The next chapter will outline the research methodology that will be employed in this study.

CHAPTER 3 RESEARCH METHODOLOGY

3.1 Research Design

The study was analytical cross sectional in a retrospective manner. This study design was appropriate because it elicited information from reviewed records of patients who CKD presented to Diagnostic Laboratory Services for thyroid function tests.

3.2 Study Population

This study population comprised all chronic kidney disease patients who attended Diagnostic Laboratory Services from January 2023 to December 2023.

3.3 Exclusion Criteria

The study excluded CKD patients without thyroid function tests. The study also excluded chronic kidney disease patients on hemodialysis and those on drugs altering thyroid profile and those with incomplete data.

3.4 Inclusion Criteria

This study focused on CKD patients who were screened for thyroid function. The results were stratified according to the different stages of chronic kidney disease.

Cases definitions:

Thyroid dysfunction was considered if the patients thyroid hormones fell outside the physiological reference range; free T3 (4.0– 8.3 pmol/L), free T4 (9.0–20.0 pmol/L), and TSH (0.25–5 mIU/L).

Euthyroid was considered if thyroid hormone levels fell within the reference range.

Overt hypothyroidism was defined as TSH > 5 mIU/L free T3 < 4.0 pmol/L and free T4 < 9.0 pmol/L.

Overt hyperthyroidism was defined as TSH <O.25 and free T3 and Free T4 above normal range.

Subclinical hypothyroidism was considered if TSH > 5 mIU/L and free T3 and free T4 within reference range.

Subclinical hyperthyroidism was defined as TSH < 0.25 mIU/L and free T3 and free T4 within reference range.

Chronic Kidney Disease we used in this study as a documented evidence of CKD in the client s medical chart including parameter of having an e-GFR < 60 mL/ min/1.73m using Cockcroft Gault equations as indicator of CKD with a persistent abnormality in kidney structure or function (eg, glomerular filtration rate [GFR] <60 mL/min/1.73 m^2 or albuminuria ≥30 mg per 24 hours) for more than 3 months.

3.5 Sample Size

The study used the census methods through the total population sampling to get a sample size of 118 cases which represent all patients admitted during the year 2023 to Diagnostic Laboratory Services for a urea and electrolyte test panel simultaneously with complete thyroid function tests during the study period.

3.6 Sampling Procedure

Convenience sampling method was used in this study. This was a sampling method in which cases that fall within a specific time frame were chosen. This sampling method was used because it enabled to obtain data that was relevant to the period of interest.

3.7 Study Setting

This study was conducted in a natural setting at Diagnostic Laboratory Services in the City of Bulawayo. The Laboratory Scientists from this hospital have the experience of conducting the tests

for a large number of patients in Bulawayo. Therefore it was easier to get an adequate sample from this setting.

3.8 Data Collection Procedure

The data was retrieved without the inclusion of any patient names or personal information. The data collected included TFT test results, creatinine levels and eGFR, age, sex and patients' previous medical history such as existence of comorbidities such as Diabetes and cardiovascular disease (CVD).

3.9 Data Analysis

The data was captured using Microsoft Excel and all statistical analyses was done using the Grap-Pad (Prism version 6). A descriptive statistic test of frequency was used to establish the prevalence of thyroid dysfunction among CKD patients Chi square test was used to test association between dependent and independent variables, at $P < 0.05$ and Odd ratio and confidence interval were determined.

3.10 Ethical Considerations

Permission to conduct the study was sought from the Africa University Research Ethics Committee (AUREC) and Diagnostic Laboratory Services. Ethical principles of research which include non-maleficence, beneficence, justice, advocacy and confidentiality were considered and maintained throughout the study. No harm was caused to the patient be it physical, emotional or mental damage.

CHAPTER 4: RESULTS

4.1 Biochemical characteristics of the study population

Of the 118 CKD patients, all of them had complete thyroid profile tests, and the ones with one or no thyroid function tests at all were not included in the study. The mean and standard deviation were calculated to determine how the data collected varied from the average value of each variable studied. Table 1 presents the minimum, maximum, standard deviation, and average values for the variables utilized in this research. Most of the participants were elderly, with the mean age being 56. While the mean Egfr was below the normal ranges stipulating CKD however the means for the biochemical parameters: T3, T4 and TSH were mostly within normal range.

Table 1: Biochemical characteristics of study participants (N=118)

Parameters	**Age**	**Egfr**	**T3(mmol/l)**	**T4(mmol/l)**	**TSH(mmol/l)**
N	118	118	118	118	118
Mean	55.6	84.8	5.6	12.35	4.17
Std. Deviation	18.2	22.02	7.83	4.98	6.64
Minimum	4	33.3	0.4	0.8	0.003
Maximum	90	160	87.0	32.3	42.8
Physiological Ranges	n/a	>90	4.0 – 8.3	9.0 – 20.	0.25 – 5.

4.2 Socio-Demographic characteristics of study participants

A total of 118 urea and creatinine profile reports for subjects between the ages of 4 to 90 years were screened for thyroid dysfunction. Of this, 77% were female and 23% were male. More females (36%) than males (30%) had thyroid dysfunction. Table 2 below shows the distribution of thyroid dysfunction between males and females. The participants were aged between 4 and 90

years. The mean age was 55, the median was 58 and most participants were aged 68. The prevalence of thyroid dysfunction increased with an increase in age (Table 3)

Table 2: Distribution of Thyroid Dysfunction by Age (N=118)

AGE RANGE (years)	Total (n)	%WITH TD	%WITHOUT TD
0 - 14	3	33	67
15 - 29	5	20	80
30 - 44	22	31	69
45 - 59	32	37	63
60 - 74	41	31	69
75 and above	15	46	54
Total (N)	**118**	**53**	**47**

4.3 The prevalence of thyroid dysfunction by stages of KD

The prevalence of thyroid dysfunction was 53% (table3) and was found to increase with the severity of KD, with stage 3B having a high prevalence of 37 %.Stages of CKD are usually categorized from stage 1 to stage 5, with stage 1 being the mildest form and stage 5 being the most severe(Table 3). Of the study participants, none had stage 4 and stage 5 chronic kidney disease. The majority of the patients fell in Stages 1 and 2. However Chi square test show no statistical significance between CKD stages and TD (Table 3)

Association between Thyroid Dysfunction and Stages of KD

Table 3: Chi square test for Association between TD and Stages of CKD (N=118)

Stages of CKD	**Egfr**	**TD Cases**	**No TD cases**	**Total**	**% of TD**	**OR , 95 % CI**	**P Value two sided**
Stage 1	>90	15	35	50	30	0.69(0.318-1.507	0.43
Stage 2	60-89	21	31	52	40	1.55(0.72-3.34)	0.33
Stage 3a	45-59	2	6	8	25	0.6(0.11-3.15)	0.54
Stage 3b	30-44	3	5	8	37	1.13(0.25-5.0)	0.86
Totals	Na	41	77	118	53		

OR Odd Ratio, CI: Confidence Interval

4.4 Prevalence and Spectrum of the major types of thyroid dysfunction among CKD patients

The major types of thyroid dysfunction were Subclinical Hypothyroidism (13%), overt hypothyroidism (20%), overt Hyperthyroidism (3%), and subclinical Hyperthyroidism (5%). The most prevalent being Hypothyroidism (Figure 1).

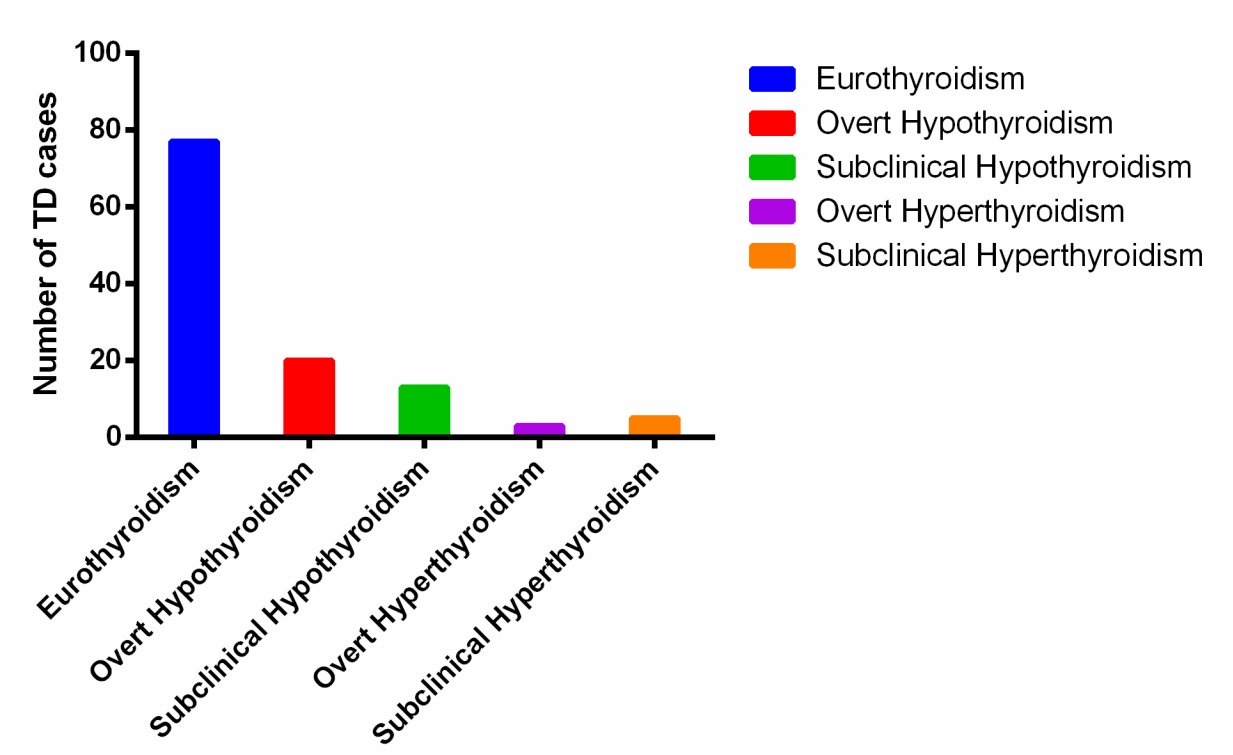


Figure 1 Stratified prevalence of all type of TD among CKD Patients.

4.5 Risk factors associated with thyroid dysfunction among CKD patients

It is important to identify the risk factors that are associated with thyroid dysfunction and to understand how they influence the development and progression of this condition. Heart failure, diabetes mellitus and Hypertension were the most dominant significant risk factors for Thyroids Disorders in CKD patients ($P < 0.05$) while others factors were not associated with TD (Table 4) ($P > 0.05$).

Table 4: Chi square: thyroid dysfunction and associated risk factors among CKD patients (N=118).

Associated Risk Factor	CKD No TD	CKD + TD	Total	OR,95%CI	P value two sided
Sex					
Male	19	8	27	1.35(0.53-3.42)	0.52
Female	58	33	91		
Age					
Age < 45 years	21	9	30	1.33(0.54-3.2)	0.53
Age > 45 years	56	32	88		
Hypertension					
Yes	4	9	13	5.133(1.47-17.9)	0.018
No	73	32	105		
Diabetes Mellitus:					
Yes	2	7	9	7.72(1.52-39.1)	0.0082
No	75	34	109		
High BMI :					
Yes	2	3	5		0.34
No	75	38	113	2.96(0.47-18.4)	
Sob ,Fatigue					
Yes	4	2	6		1.00
No	73	39	112	0.93(0.16-5.34)	
Heart Failure					
Yes	5	8	13		0.03
No	72	33	105	3.49(1.06-11.49)	
Palpitations					
Yes	2	2	4	1.92(0.26-14.1)	0.51
No	75	39	114		

CHAPTER 5: DISCUSSION

5.1 Prevalence of thyroid dysfunction among chronic kidney disease patients

The major types of hypothyroidism were Subclinical Hypothyroidism (13%), and overt hypothyroidism (20%), being the most prevalent form of thyroid dysfunction among the study participants. According to Shakaya (2023), the most prevalent thyroid condition detected in these patients is low T3 and subclinical hypothyroidism. Severe hypothyroidism can result in reduced cardiac function and lead to a gradual decline in kidney function. This means that thyroid dysfunction can aggravate the morbidity of patients with chronic kidney disease (CKD) and increase their risk of cardiovascular mortality. Similarity in finding in term of prevalence in a study conducted on 100 CKD patients by (Apoorva, 2019) was found where 53 patients had thyroid dysfunction which accounted for 53% while in the same study there was disparity with our finding which documented Subclinical Hypothyroidism (13%), overt hypothyroidism (20%), overt Hyperthyroidism (3%), and subclinical Hyperthyroidism (5%) (Apoorva, 2019). A study found prevalence of SCH was 33% the discrepancy could be attributed to study design or sample size which differ among the two studies(Apoorva, 2019).

5.2 Socio-demographic distribution of thyroid dysfunction among CKD patients

L E Zijlstra et al (2019) mentions that older patients are at risk of being affected by thyroid dysfunction and CKD. This is due to the dilapidating effects of aging. In this study, most participants were 63 years of age, with known CVD conditions and CKD. The younger population did not present with requests for thyroid function screening. Although further research can be carried out, the elderly were presenting with problems of thyroid dysfunction and kidney failure.

77% of the study population was female. More females than males presented with cases of thyroid dysfunction and renal failure. As a result, sex could be a factor in the development of hypothyroidism. As observed by Asanari et al (2023), as age advances, there is reduced deiodination of T4 to form T3 levels. The levels of antithyroperoxidase and anti-thyroglobulin antibodies rise with age, commonly seen in women above 60 years of age, contributing to the decline in levels of T3.

5.3 Risk factors associated with thyroid dysfunction among CKD patients

CKD can lead to serious complications, such as end-stage renal disease, cardiovascular disease, and death. Therefore, it is important to identify and manage the risk factors for CKD and prevent its progression. Some of the most common risk factors for CKD are diabetes and hypertension, which can impair the blood flow and function of the kidney cells. Although both diabetes and hypertension can be controlled their pathophysiology can worsen the state of the patient and contribute to thyroid dysfunction. In this study patients presented with clinical data such as hypertension, diabetes, cardiovascular accidents, and abnormal weight gain and loss. A substantial number of these patients suffered from some form of thyroid dysfunction Risk factors analysis by chi square test show significant association between Heart failure , hypertension and diabetes mellitus in CKD patients with TD this findings corroborate with study by Mohamedali et al 2024 (Mohamedali, Reddy Maddika, Vyas, Iyer, & Cheriyath, 2014) where Hypertension and Diabetes mellitus were reported as potential risk factors, however in this present study stages of CKD were not associated with occurrence of thyroid disorders.

5.4 Limitations of the study

Diabetes mellitus, dyslipidaemia, and other diseases that can affect thyroid hormone levels might have been present in the subjects that were not investigated in the current study. This study was a

retrospective prevalence study carried out between January to December 2023, the available information at that particular period was collected. During this period, there were no patients who presented with stage 4 and 5 chronic kidney disease. Clinical information that would have been used to determine the severity of illness in patients was not available. The location and time when the data for research was collected are not guaranteed to be a true representative of the chronic kidney disease population in Zimbabwe

5.5 Recommendations for Research

To corroborate the study's conclusions, the sample size should be greater and more representative of Zimbabwe's population. This study's evidence could be reinforced by testing thyroid function in CKD patients at all stages. Establishing thyroid disease registries is crucial for determining the burden of these disorders in CKD patients, as well as documenting shifting patterns to improve patient management.

5.6 Conclusion

In this study, there was a high prevalence of thyroid dysfunction (53%) among chronic kidney disease patients. The most prevalent form of thyroid dysfunction was overt hypothyroidism (20%). Thyroid dysfunction increased with age, mostly in females. Hypertension, diabetes mellitus were the most significant risk factor with thyroid dysfunction among chronic kidney disease patients.

References

Al Hussaini, H. A., Al Sahlawi, M. A., Alhussain, F., Alja'afari, L. A., Aljohar, H. I., Al-Ramadhan, M. S., ... & Al-Ramadan, M. S. (2023). *Prevalence of Hypothyroidism Among Dialysis Patients in Eastern Region, Saudi Arabia.* Cureus, 15(1).

Ansari, I., Kumar, S., Acharya, S., Agrawal, S., & Saboo, K. (2023). *Thyroid dysfunction at different stages of chronic kidney disease: a cross-sectional study at a rural teaching college in central India*. Cureus, 15(7).

Apoorva,S.,S, Sripriya, S. Kumar, B.S., & Satyanarayana, (2019) *Prevalence study on synergism of Thyroid Disorders and Type 2 Diabetes Mellitus*, Journal of Cardiovascular Disease Research.

BMJ Best Practice. *Overview of thyroid dysfunction*. May 2023.

Crawshaw, & Chambers. (2001). Significance tests for Correlation coefficients . In Crawshaw, & Chambers, A concise course in Advanced Level Statistics Fourth Edition (p. 605). United Kingdom: Nelson Thornes Limited.

Devereaux, D., & Tewelde, S. Z. (2014). Hyperthyroidism and thyrotoxicosis. *Emergency Medicine Clinics*, *32*(2), 277-292.

Drube, J., Wan, M., Bonthuis, M., Wühl, E., Bacchetta, J., Santos, F., ... & European Society for Paediatric Nephrology Chronic Kidney Disease Mineral and Bone Disorders, Dialysis, and Transplantation Working Groups. (2019). *Clinical practice recommendations for growth hormone treatment in children with chronic kidney disease*. Nature Reviews Nephrology, 15(9), 577-589.

Garmendia Madariaga, A., Santos Palacios, S., Guillén-Grima, F., & Galofré, J. C. (2014). The incidence and prevalence of thyroid dysfunction in Europe: a meta-analysis. *The Journal of Clinical Endocrinology & Metabolism*, *99*(3), 923-931.

Hobby, G. P., Karaduta, O., Dusio, G. F., Singh, M., Zybailov, B. L., & Arthur, J. M. (2019). *Chronic kidney disease and the gut microbiome*. American Journal of Physiology-Renal Physiology, 316(6), F1211-F1217.

Kachhawa, P., & Sinha, V. (2019). *Assessment of thyroid dysfunction, dyslipidemia, and oxidative stress in hypertensive end stage chronic renal disease patients in a teaching hospital in Western Uttar Pradesh*. Asian Journal of Medical Sciences, 10(5), 13-18.

Keunmoe, P., Halle, M. P., & Nguedia, J. C. A. (2019). *Correlation Between Biomarkers of Thyroid Function Abnormalities and Stages of Chronic Kidney Disease in Cameroon*. J Med-Clin Res & Rev, 3(6), 1-8.

Khassawneh, A. H., Al-Mistarehi, A. H., Zein Alaabdin, A. M., Khasawneh, L., AlQuran, T. M., Kheirallah, K. A., Saadeh, N. A., Beni Yonis, O., Shawkat, M., & Obeidat, N. (2020). *Prevalence and Predictors of Thyroid Dysfunction Among Type 2 Diabetic Patients: A Case-Control Study. International journal of general medicine*, 13, 803–816. https://doi.org/10.2147/IJGM.S273900

Li, L. Z., Hu, Y., Ai, S. L., Cheng, L., Liu, J., Morris, E., ... & Fu, P. (2019). *The relationship between thyroid dysfunction and nephrotic syndrome: a clinicopathological study*. Scientific reports, 9(1), 6421.

Malyszko J, Malyszko J, Wolczynski S, Mysliwiec M. *Adiponectin, leptin and thyroid hormones in patients with chronic renal failure and on renal replacement therapy: are they related?* Nephrol Dial Transplant. 2006;21(1):145-52

Matsuoka-Uchiyama, N., Tsuji, K., Sang, Y., Takahashi, K., Fukushima, K., Takeuchi, H., ... & Wada, J. (2022). *The association between hypothyroidism and proteinuria in patients with chronic kidney disease: a cross-sectional study. Scientific reports*, 12(1), 14999.

Mohamedali, Mohamed & Maddika, Srikanth & Vyas, Anix & Iyer, Viswanathan & Cheriyath, Pramil. (2014). *Thyroid Disorders and Chronic Kidney Disease*. International journal of nephrology. 2014. 520281. 10.1155/2014/520281

Narasaki, Y., Sohn, P., & Rhee, C. M. (2021, March). *The interplay between thyroid dysfunction and kidney disease*. In Seminars in Nephrology (Vol. 41, No. 2, pp. 133-143). WB Saunders.

National Institute for Health and Care Excellence. *Clinical knowledge summary. Hypothyroidism –Definition*. May 2021

Ross, I. L., Marshall, D., Okreglicki, A., Isaacs, S., & Levitt, N. S. (2005). Amiodarone-induced thyroid dysfunction. *South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde*, *95*(3), 180–183.

Shakya, S., Kumar, S., Verma, V., Gupta, H., Sonkar, S. K., & Atam, V. (2023). *Evaluation of Interactions Between Thyroid Dysfunction in End-Stage Renal Disease Patients: A Cross-Sectional Study*. Cureus, 15(2).

Sinjari, H. Y., & Ibrahim, J. M. (2022). *Thyroid Function Disorders in Patients with Chronic Kidney*. Medical Journal of Babylon, 19(1), 77.

Srivastava, S., Rajput, J., Shrivastava, M., Chandra, R., Gupta, M., & Sharma, R. (2018). *Correlation of Thyroid Hormone Profile with Biochemical Markers of Renal Function in Patients with Undialyzed Chronic Kidney Disease. Indian journal of endocrinology and metabolism*, 22(3), 316–320. https://doi.org/10.4103/ijem.IJEM_475_17

Swaen, B. (2015, December 7). *Constructing a conceptual framework*. Retrieved from Scribbr: https://www.scribbr.com/dissertation/conceptual-framework/

Thomas R, Kanso A, Sedor JR. *Chronic kidney disease and its complications*. Prim Care. 2008;35(2):329–44.

Wilkinson, D. (2021, March 8). The Researcher's Toolkit. Retrieved from https://libguides.wits.ac.za/c.php?g=693518&p=4914913#:~:text=Research%20methodology%20is%20the%20specific,study%27s%20overall%20validity%20and%20reliability.&text=How%20was%20it%20analyzed%3F

Lv JC, Zhang LX. Prevalence and Disease Burden of Chronic Kidney Disease. *Adv Exp Med Biol*. 2019;1165:3-15. doi:10.1007/978-981-13-8871-2_1

Zijlstra, L. E., van Velzen, D. M., Simsek, S., Mooijaart, S. P., van Buren, M., Stott, D. J., ... & Trompet, S. (2020). *The kidney, subclinical thyroid disease and cardiovascular outcomes in older patients. Endocrine Connections*, 9(1), 55.

Appendix 1

Work Plan

January to April 20204

	JANUARY					FEBRUARY					MARCH					APRIL				
	2	9	16	23	30	6	13	20	27		6	13	20	27		3	10	17	24	
PROJECT WEEK	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**
Preparation and Submission of Proposal to AUREC																				
Pretesting																				
Data collection																				
Data Processing and Analysis																				
Project Writing																				
Project Submission to Africa University																				

Appendix 2

Budget

Item	**Unit Cost (US$)**	**Multiplying factor**	**Total Cost (US$)**
Bond paper	5	1 (rim)	5
Printing costs	10	1	10
Binding costs	1	10	10
Travelling costs	10	2	20
Airtime	10	1	10
Stationery	1	5	5
Total	**-**	**-**	**60**

Appendix 3

Data Abstraction Template

	A	B	C	D	E	F	G	H
1	**Lab Number**	**Sex**	**Age**	**eGFR**	**T3 in pmol/L**	**T4 in pmol/L**	**TSH in pmol/L**	
2								
3								
4								
5								
6								
7								
8								
9								
10								
11								
12								
13								
14								
15								
16								
17								
18								
19								
20								
21								
22								
23	**Key**							
24	**eGFR** : calculated glomrular filatration rate							
25	**pmlo/L** : picomoles per litre							
26								

RISK FACTORS	**Urea**	**Creatinine**	**GFR**
Stage1			
Stage2			
Stage3			
Stage4			
Stage 5			
Hypertension			
Diabetes			

Appendix 4

DLS Approval Letter

DLS Diagnostics Laboratory Services

Commitment to Quality

Mater Dei Hospital
Burns Drive, Malindela
P.O.Box 2133
Bulawayo
Tel: +263 292 241132
+263 292 241191

No 2 Fairbridge Avenue
Belgravia
Harare
Tel: +263 782 609 658

www.dls.co.zw

Date: 20 November 2023

From: DLS Lab Manager Nohlanhla Nyoni

REF: Approval to conduct Research study at DLS

Dear Lindiwe Angela Sibanda

This letter serves to grant you permission to conduct your research; **An investigation on the prevalence of thyroid dysfunction among patients with chronic kidney disease attending Diagnostic Laboratory Services, Bulawayo, Zimbabwe 2023.**

You will be permitted to collect the data from our system for the purposes of analysis of this information only.

Yours sincerely

Nohlanhla Nyoni (Laboratory Manager) Signature

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BURNS DR. MALINDELA
DIAGNOSTICS
LABORATORY SERVICES
TEL: +263 29 2241132, CELL: +263 [illegible]
P. O. BOX 2133, BULAWAYO

Appendix 5

Investing in Africa's future

AFRICA UNIVERSITY RESEARCH ETHICS COMMITTEE (AUREC)

P.O. Box 1320 Mutare, Zimbabwe, Off Nyanga Road, Old Mutare-Tel (+263-20) 60075/60026/61611 Fax: (+263 20) 61785 Website: www.africau.edu

Ref: AU3104/24

14 February, 2024

LINDIWE ANGELA SIBANDA
C/O Africa University
Box 1320
MUTARE

RE: AN INVESTIGATION ON THE PREVALENCE OF THYROID DYSFUNCTION AMONG PATIENTS WITH CHRONIC KIDNEY DISEASE ATTENDING DIAGNOSTIC LABORATORY SERVICES, BULAWAYO, ZIMBABWE 2023

Thank you for the above-titled proposal that you submitted to the Africa University Research Ethics Committee for review. Please be advised that AUREC has reviewed and approved your application to conduct the above research.

The approval is based on the following.

a) Research proposal

- **APPROVAL NUMBER** AUREC 3104/24
  This number should be used on all correspondences, consent forms, and appropriate documents.
- **AUREC MEETING DATE** NA
- **APPROVAL DATE** February 14, 2024
- **EXPIRATION DATE** February 14, 2025
- **TYPE OF MEETING:** Expedited
  After the expiration date, this research may only continue upon renewal. A progress report on a standard AUREC form should be submitted a month before the expiration date for renewal purposes.
- **SERIOUS ADVERSE EVENTS** All serious problems concerning subject safety must be reported to AUREC within 3 working days on the standard AUREC form.
- **MODIFICATIONS** Prior AUREC approval is required before implementing any changes in the proposal (including changes in the consent documents)
- **TERMINATION OF STUDY** Upon termination of the study a report has to be submitted to AUREC.

AFRICA UNIVERSITY RESEARCH ETHICS COMMITTEE (AUREC)
APPROVED
P.O. BOX 1320, MUTARE, ZIMBABWE

Yours Faithfully

MARY CHINZOU
ASSISTANT RESEARCH OFFICER: FOR CHAIRPERSON
AFRICA UNIVERSITY RESEARCH ETHICS COMMITTEE