DRUG THERAPY PROBLEMS AMONG PATIENTS WITH THYROID DISORDERS IN KENYATTA NATIONAL HOSPITAL

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A Research dissertation submitted in partial fulfillment of the Requirements for the award of the degree of Master of Pharmacy in Clinical Pharmacy, School of Pharmacy, in the University of Nairobi

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DEDICATION

I dedicate this work to all practitioners in the pharmaceutical sector whose daily desire and goal is achievement of the best patient centered care.

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ABBREVIATIONS AND ACRONYMS

ALT	Alanine Transaminase
AST	Aspartate Amino Transferase
ATA	American Thyroid Association
ATD	Anti Thyroid Drugs
ADE	Adverse Drug Event
BMI	Body Mass Index
CPK	Creatinine Phosphate Kinase
DTP	Drug Therapy Problem
DTR	Deep Tendon Reflex
FT4	Free Tetra iodothyronine (thyroxine)
FT3	Free Triiodothyronine
Hb	Hemoglobin
Hct	Hematocrit
HTN	Hypertension
HR	Heart Rate
K	Potassium
KNH	Kenyatta National Hospital
LDH	Lactate Dehydrogenase
Na	Sodium
PI	Principal Investigator
PPI	Proton Pump Inhibitors
RAI	Radio Active Iodine
TSH	Thyroid Stimulating Hormone

TRH	Thyroid Releasing Hormone
UoN	University of Nairobi
WHO	World Health Organization

OPERATIONAL DEFINITION OF TERMS

Compliance: It is the willingness and ability of a patient to follow the therapeutic drug regimen as agreed upon between the patient and the prescriber.

Contraindication: It is a factor or a medical condition that renders the use of a certain drug improper and not advisable due to the high risk of an adverse event or a hazard

Dosage: It is the total amount of medication that a patient takes over a specified period of time. It includes the dose, frequency and duration of a regimen

Dose: It is the amount of drug administered to patient at a given time

Dosing interval: It is the time period between administrations of consecutive doses.

Drug: Any substance that interferes with the physiological functioning of the body. It is administered to patients in controlled amounts for treatment, prevention or management of a disease condition

Drug related needs: These are inherent patient's requirements that should be met for optimal medication therapy. They include appropriate indication, effective medication, safe medication and willingness/ability to comply with the regimen.

Drug related morbidity: These are medical conditions or harms leading to illnesses caused by drugs

Drug related mortality: These are deaths or fatalities caused by the use of drugs

Drug therapy problems: These are any undesirable events experienced by patients that involves or is suspected to involve drug therapy and interfere with achievement of desired therapeutic outcomes and require clinical judgement by professionals to resolve.

Goals of therapy: These are the desired outcomes of drug therapy. They can be classified as prevention, cure or management of a disease condition.

Incidence: These are the number of new cases in a given period of time

Indications: These are medical conditions in which certain drugs are recommended for use in specific patients

Practitioner: A professional who uses his/her skills to meet patients demands in accordance to his training and expertise in a certain field.

Prevalence: The number of existing cases or occurrences in a given place during a particular period of time

Thyroid: A gland located on the anterior aspect of the neck below the larynx. It produces both T3&T4

Thyroid hormone: Refers to both T3 and T4hormones produced by the thyroid gland and regulates the basal metabolic rates of the body

ABSTRACT

Background: The prevalence of thyroid dysfunction has been on the rise in sub-Saharan Africa. Patients with thyroid disorders are more likely to present with other comorbidities such as hypertension, diabetes, cardiomyopathies and auto immune diseases. These patients are likely to be on various categories of drugs including those with a narrow therapeutic index such as levothyroxine and others which affects thyroid function. In view of such interventions occurrence of drug therapy problems severely limits achievement of therapeutic goals. Information regarding drug therapy problems in this subset of patients is limited and only mentioned in few inconclusive studies. This study aimed to evaluate the various drug therapy problems that maybe encountered in such patients in Kenya

Study Objectives: The aim of this study was to assess and characterize the various drug therapy problems which occur among patients presenting with thyroid disorders and are being followed up at the endocrinology clinic located within Kenyatta National Hospital.

Methodology: The study adopted a cross-sectional design. A simple random sample of patients presenting with thyroid dysfunctions and who met the inclusion criteria was taken. All relevant patient data was extracted using a questionnaire modified from the Helper and Strand tool. The relevant laboratory reports and medication prescription data was extracted from the patient's files. Assessment of drug therapy problems was done using the Helper and Strand tool. The data obtained was entered in Microsoft excel and analyzed using STATA. Descriptive summary statistics were presented as means with standard deviations for normally distributed data for continuous variables and medians and interquartile ranges for non-normally distributed data. Categorical variables were summarized using frequencies and percentage proportions.

Results

Among the 85 participants recruited, 71 (83%) were females and 14 (17%) were males. The male to female ratio was 1:5. The mean age of participants was 51.4(SD 14.8) with a range of 21-83 years. Hyperthyroidism was the most prevalent thyroid condition (47%) followed by hypothyroidism (25%). The major type of comorbidity was hypertension (36%) followed by both hypertension and diabetes (9%). Eighty seven percent of the participants had a DTP. The most

prevalent type of DTP was noncompliance (38%) followed by dosage too low (25%) and need for additional drug therapy (16%). The most significant risk factors for noncompliance to thyroid medication were level of education (p -0.004), income (p -0.030) and type of drugs (p -0.026).

Conclusion

Hyperthyroidism is the most prevalent thyroid disease condition in KNH. The prevalence of drug therapy problems among thyroid disease patients in KNH is high (87%). Noncompliance to medication regimen is the major type of DTP in the study population. The patient's level of education, income status and type of thyroid medication are the major risk factors for noncompliance to drug regimen.

Recommendations

Introduction of Medication therapy management (MTM) services at the endocrinology clinic would have a positive impact in addressing the high prevalence of DTPs in thyroid disease patients. Further interventional research is needed to access the impact of various solutions applied to solve DTPs. Further research should be done on the DTP related morbidity and mortality in patients with thyroid disease.

CHAPTER ONE: INTRODUCTION

1.1 Background

Thyroid hormone controls the basal metabolic rates of the body. Occurrence of thyroid disorders interferes with multiple body systems which are critical for survival(1). Management of thyroid disorders relies on drugs either as adjuvants to surgery and RAI or as sole therapies which may stretch for a lifetime. Improper drug therapy leads to development of complications such as cardiomyopathies, arrhythmias, myxedema coma, thyroid storm and deranged blood glucose levels(2). Also, the symptoms alone severely limit the quality of life in most patients. Occurrence of other comorbidities such as hypertension, dyslipidemias and diabetes further complicates treatment due to the need for drugs which have been shown to interfere with thyroid function(3). The American Thyroid Association (ATA) has listed drug related problems as a major cause of treatment failure(4). The association in its guidelines recommends research into the influence of medication adherence on management of thyroid conditions. Currently no study has been published in Kenya with regards to drug therapy problems (DTPs) in this subset of patients.

Thyroid disorders can be classified into two broad categories; hyperthyroidism and hypothyroidism. Hyperthyroidism results from excessive production of thyroid hormone (thyrotoxicosis). It can be caused by autoimmune conditions such as Graves ' disease, tumors, drugs and many other factors(5). It presents with heat intolerance, palpitations, increased heart rate, arrhythmias, anxiety, weight loss, increased appetite, menstrual disorders among others. Hypothyroidism results from decreased production of thyroid hormone. It can be caused by iodine deficiency, autoimmune conditions such as thyroiditis, thyroidectomy, thyroid abrasion therapy, drugs such as amiodarone among others(6)(7)(3). Patients present with cold intolerance, tiredness, sluggishness, weight gain, delayed growth and development, menstrual irregularities, decreased heart rate, bradycardia, emotional labilities among other symptoms. The serum levels of thyroid stimulating hormone (TSH) and Ft4, fT3 are used to diagnose these conditions(8)

In a study conducted in KNH, the prevalence of thyroid dysfunction among patients with type II diabetes was 61%; however only 10% of the study subjects had a clinical diagnosis of thyroid disease(9). A systemic review done in Nigeria estimated the general prevalence of thyroid disease

to be about 9% in sub-Saharan Africa(10). Iodine deficiency is the leading cause of thyroid disease followed closely by autoimmune causes. Women are five times as likely as men to have thyroid disorders(11). Malignancies have also been found to contribute to the increased prevalence; in a study done at Kijabe Hospital, the prevalence of cancerous cells was 11.9% in 222 thyroidectomy samples(12).

A drug therapy problem can be defined as any undesirable event or risk experienced by the patient involving or suspected to involve a drug that prevents the patient from achieving the desired outcome of drug therapy and requires a professional to resolve(13). According to Helper and Strand, pharmacy practice has evolved from product centered apothecary practice to patient centered care(14). A 21st century pharmacist is now obligated to meet all the patients drug related needs which include correct indication, effective drug product, safe drug product and willingness /ability to comply. If any of the above drug related needs is not met, ultimately a drug therapy problem (DTP) exists.

The possibility that DTPs are the major cause of treatment failures in thyroid diseases cannot be ruled out. Management of thyroid diseases involve multiple classes of drugs, some to manage the primary disorder such as thioamides and levothyroxine, other classes of drugs are used to manage symptoms such as propranolol, statins, anticonvulsants and antihistamines(15). Changes in BMI can alter achievement of target therapeutic levels of drugs. Drug- drug interactions & drug-food interactions can occur especially in presence of other chronic conditions and in the elderly population(16).

1.2 Problem Statement

The prevalence of thyroid diseases has increased over the recent past(10). All thyroid conditions require therapy with drugs some stretching for a lifetime. Occurrence of complications or comorbidities often requires additional drug therapy(17). Successful control of thyroid hormone levels requires strict drug therapy to achieve positive outcomes. Failure to achieve those outcomes often results in comorbidities and complications which severely limits the quality of life. Among the major causes of treatment failure is presence of a DTP(13).

Information regarding the occurrence of DTPs in these patients is scanty and is often drawn from other studies that examine other causes of failure to achieve target therapeutic outcomes. In addition, the utility of the Helper and Strand tool for diagnosing drug therapy problems in thyroid disease patients has not been assessed.

There are no published studies on DTPs in thyroid disease patients. The lack of information on DTPs in thyroid diseases in the part of healthcare providers may be the cause of observed treatment failures and development of complications which often cause poor quality of life, prolonged hospital stays and increased costs of treatment to the patients.

The study seeks to address this problem by examining the various DTPs and their causes in thyroid diseases using the standardized and validated tool proposed by Cipolle, Linda Strand and Morley(13). The study also seeks to assess the usefulness of that tool if adopted as a standard of diagnosing and treating various causes of DTPs in these patients.

The findings of this study will potentially be useful in the proposed establishment of the medication therapy management (MTM) clinic within the endocrinology unit of Kenyatta National Hospital. It will also inform development and institutionalization of various practices that will lead to better drug therapy management in patients with thyroid disease.

1.3 Purpose of the study

The study seeks to identify DTPs and their possible causes in patients presenting with thyroid diseases. The pharmaceutical care process proposed by Cipolle will be utilized in diagnosing and classifying the various classes of DTPs(13). A survey was carried out at the endocrinology outpatient clinic on all patients presenting with thyroid disorders and then data regarding the type of thyroid condition, the drugs commonly used in treatment, the percentage of patients who achieve the therapeutic outcomes, the various DTPs encountered and much more was assessed. The findings would potentially find use in development of medication therapy management services at the endocrinology clinic and in any other health institution which deals with similar cases(18). It would also inform the suitability of the tools recommended by Cipolle et al for diagnosing DTPs in thyroid diseases.

1.4 Objectives

1.4.1 Broad Objective

To determine the proportions and types of drug therapy problems among patients with thyroid disease at the KNH endocrinology clinic

Specific Objectives

The specific objectives include to

1. Determine the proportions of different types of thyroid disease conditions among patients attending Kenyatta National Hospital endocrinology clinic.
2. Determine the proportions of the selected drug therapy problems among patients with thyroid disease attending KNH endocrinology clinic.
3. Identify the patients and disease related risk factors for selected drug therapy problems among patients attending Kenyatta National Hospital endocrinology clinic.

1.5 Research Questions

1. What are the proportions of different types of thyroid disease conditions among patients attending Kenyatta National Hospital endocrinology clinic?

2. What is the proportion of the selected drug therapy problems among patients with thyroid disease attending KNH endocrinology clinic?

3. What are the patients and disease related risk factors for selected drug therapy problems among patients with thyroid disease attending KNH endocrinology clinic?

1.6 Significance and anticipated output of the study

The control of thyroid hormone levels accurately relies on the precision of drug therapy. Most thyroid diseases persist for a long duration and some may run for a lifetime. The effects of uncontrolled thyroid function are debilitating and can lead to development of life threatening

complications such as myxedema coma or thyroid storm(19). Correct identification of various DTPs can help prevent occurrence of such complications and achievement of various therapeutic outcomes which include cure of the disease, symptom control, reduction in disease progression and disease prophylaxis. This will improve the patient's quality of life, reduce hospital admissions and also reduce the cost of treatment(13).

The study also availed data on the prevalence of thyroid disease in the endocrinology outpatient clinics. This data will inform management strategies and resource allocation budgets in the health sector. The data on occurrence of DTPs and their association with various patient specific variables will also be useful to medical practitioners as well as patients in improving treatment outcomes.

1.7 Delimitations

The study adopted a cross sectional design in which the temporal sequence of events may not be accurately investigated. In patients were excluded and drug therapy problems unique to this patients were not studied. Occurrence of complications of thyroid disease may not have been caused by the underlying thyroid condition.

Medication compliance as a cause of DTPs cannot be conclusively determined due to the cross sectional nature of the study. The study relied on validated tools to assess compliance in the study subjects(20). These tools rely on patient reported information which may be subject to reporting bias.

1.8 Study Limitations

The study was carried out in patient attending outpatient clinics of KNH which is a referral hospital. The hospital drawn cases may not necessarily represent the community drawn cases and may differ on factors such as severity of the disease. As a result, the study results may have limited generalizability.

1.**9 Study Justification**

This study provided data on the prevalence of drug therapy problems in thyroid disease patients. It also availed data on the associations between selected drug therapy problems and patient specific factors. This gave evidence as to whether drug therapy problems could be a cause of treatment failure in these patients. The study also elucidated the types of drug therapy problems and their possible impact on the treatment outcomes.

The results will inform development of various treatment guidelines with regards to possible advice and counselling points when administering therapy to patients. It will also ensure that all threats to safety and effectiveness of drugs used in management of thyroid conditions are addressed beforehand. This will reduce morbidity and mortality associated with drug related problems. It will also reduce the cost of treatments by ensuring optimal drug therapy, reducing frequent hospital visits and reducing costs associated with occurrence of complications.

This study will be of key interest to the Ministry of Health (MoH) which is currently formulating and reviewing guidelines for the management of various endocrine disorders. It will also be of significance to the health care practitioners who specialize in endocrinology as it will inform development of new approaches to medical practice to improve effectiveness. It will also be important to pharmacists in the proposed medication therapy management (MTM) clinic at the endocrinology unit(18). The endocrinology unit is among the pioneer outpatient clinic in KNH to introduce an MTM clinic. Data regarding DTPs in this subset of patients would be of ultimate importance in informing the need for MTM services to patients. The thyroid disease patients will also benefit as this study will seek to address multiple drug related problems that prevent achievement of desired therapeutic goals.

The study also addresses key issues in the Vision 2030 Development Agenda on health(21). The government has cited poor management of chronic noninfectious disease condition as a major impediment to development. To mention but a few, disabilities which result from cretinism are always an economic burden to the government. The money wasted in procuring non effective or unnecessary drugs is a wasted resource. The prevalence data will also be useful to the universal health coverage taskforce committee in estimating the cost of health insurance policies in this subset of patients(22).

1.10 Conceptual/Theoretical Framework

Drug therapy problems in thyroid disease patients can be a function of patient specific factors. These include age which is positively correlated with increased number of comorbidities and increased number of chronic conditions(1). The educational background is an indirect tool for estimation of the literacy levels. This affects how well a patient understands and adheres to instructions regarding a certain regimen(23). It also influences the understanding of drug information(24). The insurance and income status also affects affordability of medications and hence affecting compliance.

Presence of other related comorbidities such as diabetes, cardiovascular disease, autoimmune conditions and dyslipidemias also increases the number of prescribed medication (polypharmacy)(25). This increases the risk of adverse drug events in thyroid disease patients. The number and classes of prescribed drugs also increases the risk of drug interactions and adverse drug events(3). The relationship between the patient specific predictive variables and occurrence of selected DTPs can be summarized as shown in **Figure 1**.

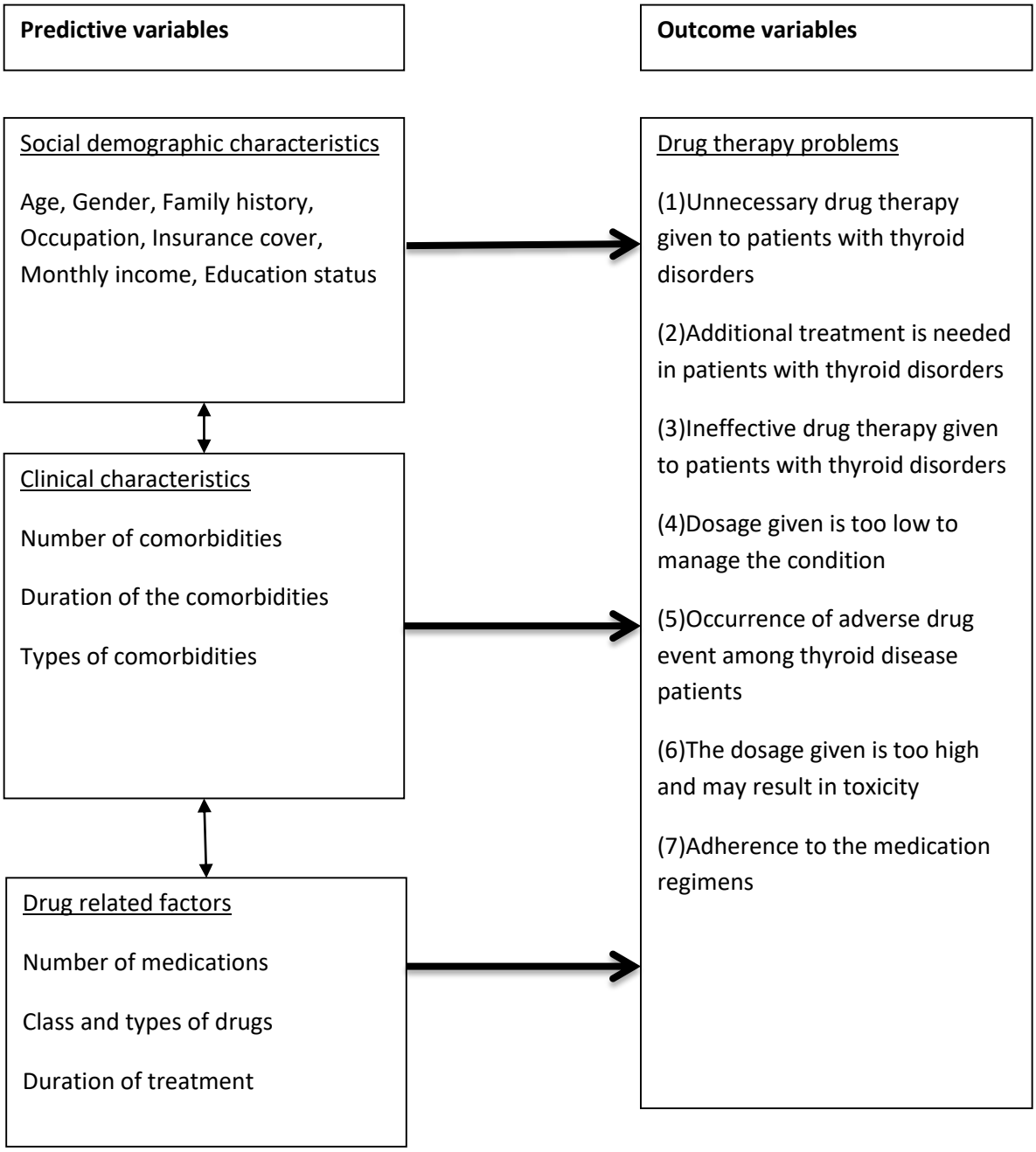

Figure 1 conceptual framework for the risk factors for various types of drug therapy problems

CHAPTER TWO: LITERATURE REVIEW

2.1 Prevalence of Thyroid Disease and Related Comorbidities

The prevalence of thyroid disorders in the past varied with regions depending on iodine supplementation in local diets(26). The rise in malignancies and autoimmune diseases led to prevalence patterns that are independent of iodine deficiency patterns. High prevalence rates are still reported in Middle and Far East countries(27). A systematic review of prevalence studies in Africa notes that the prevalence ranges from 1.2-9.9% with Graves' disease being the leading thyroid related condition(10). Another review noted that determination of the epidemiology of thyroid conditions in Africa was challenging due to lack of population based surveys(28).

Malignancy is one of the causes of thyroid disease. A study in Kijabe hospital in Kenya found that over 220 thyroidectomies were performed in a span of three years and the biopsy of those specimens showed a malignancy rate of 11%(12). With reference to gender, most studies acknowledge that women are 4 times as likely as men to develop a thyroid disorder. Pregnancy increases the risk of thyroid dysfunction(29). However males were found to be three times as likely as females to develop thyrotoxicosis after amiodarone therapy.(27).

Hypothyroidism is positively associated with other comorbidities such as diabetes, celiac disease, rheumatoid arthritis, ankylosing spondylitis, lupus erythematous, psoriatic arthritis and multiple sclerosis(17). subclinical hypothyroidism is associated with poor prognosis in patients with heart failure(30). A survey done in Kenyatta National Hospital found that 60% of patients with type II diabetes had deranged thyroid function tests(9). Table 1 summarizes the prevalence of comorbidities in patients with hypothyroidism.

Table 1: Prevalence of Comorbidities in Patients with Non-iatrogenic Hypothyroidism
(Table obtained from the European journal of endocrinology (17))

	Men		**Women**	
	Prevalence 1000(95%CI)	**OR (95% CI)**	**Prevalence 1000(95%CI)**	**OR (95% CI)**
Type 2 diabetes	145.92 (140.84–151.16)	1.52 (1.46–1.59)	95.74 (94.00–97.51)	1.49 (1.46–1.52)
Type 1 diabetes	10.18 (8.81–11.75)	4.14 (3.56–4.80)	5.93 (5.49–6.40)	3.29 (3.02–3.59)
Gestational diabetes				1.69 (1.71–2.02)
Celiac disease	3.67 (2.88–4.67)	5.80 (4.52–7.44)	5.35 (4.93–5.81)	3.10 (2.84–3.39)
Rheumatoid arthritis	4.34 (3.48–5.41)	1.74 (1.39–2.19)	12.54 (11.89–13.22)	2.08 (1.96–2.20)
Ankylosing spondylitis	0.78 (0.46–1.31)	1.99 (1.17–3.38)	0.53 (0.41–0.68)	1.94 (1.47–2.56)
Lupus erythematosus	0.94 (0.59–1.52)	4.99 (3.06–8.15)	2.60 (2.31–2.92)	2.23 (1.96–2.53)
Psoriatic arthritis	1.95 (1.40–2.71)	1.43 (1.02–1.99	1.95 (1.71–2.24)	1.56 (1.35–1.80)
Multiple sclerosis	1.39 (0.28–2.06	2.07 (1.39–3.08)	2.71 (2.42–3.04)	1.71 (1.52–1.93)

2.2 Genesis of the Helper and Strand Classification of Drug Related Problems

In the 19th century, the industrial revolution changed the concept of the pharmacy practice. Drugs which were formally extracted and purified from plants extracts would now be synthesized in laboratories in bulk. The increase in the number of available drugs also led to increase in drug information. This prompted a change from product centered pharmacy practice to patient centered care. In 1975, a study that focused on the quality of pharmaceutical care in hospitals showed that hospitals which employed full time pharmacists had higher quality of care than those which did not(31). The findings of this study indicated the need proper structured pharmaceutical care. Based on the extensive works of previous pharmacists, Linda Strand was able to publish the first ever classification of drug therapy problems which included eight categories of DTPs in 1990. This was later in 1998 revised by Robert J Cipolle in collaboration with Linda Strand to the current seven categories of DTPs(13). According to this classification, the DTPs can be categorized into four classes based on the four drug related needs; indication, safety, effectiveness and adherence. This classification system is among the four validated DTPs classification systems which have been extensively studied (32). A DTP is any undesirable event experienced by patients that involves or is suspected to involve drug therapy and it interferes with the achievement of desired outcomes of

drug therapy and requires professional judgement to resolve(13). Identification and resolution of DTPs is at the core of patient centered pharmaceutical care(33). This classification system also lists the causes of the DTPs which places it at a practically unique position among the other classification systems.

The Helper and Strand classification tool has been utilized in analysis of drug related problems in various diseases. It has also been used as a model upon which various Medication Therapy Management clinics operate. The tool has been used to classify drug related problems in other endocrine conditions such as diabetes. Premised on earlier success in its use in endocrine conditions, the study will utilize it in describing the occurrence of drug therapy problems in thyroid disease patients.

2.3 Burden of Drug Therapy Problems in Patients with Thyroid Disorders

Iodine supplementation and thyroidectomies were the only treatment modalities for thyroid disease in the eighteenth century. Thyroidectomy was invariably associated with hypo-metabolic syndromes which necessitated development of desiccated thyroid for hormone replacement. Desiccated thyroid was derived from animals such as pigs. The use of desiccated thyroid had two major challenges which eventually led to its withdrawal. First, immunologic reactions triggered by animal proteins caused serious adverse reactions. Secondly there was the problem of precision of dosing; the active component in desiccated thyroid was variable and hence the potency was hard to determine(34). This often resulted to overdose or under dose(35). This medication related problems led to development of newer treatment modalities in the nineteenth century such as the thioamides, radioactive iodine and levothyroxine. The new treatment options were not free from drug therapy problems.

Numerous studies have been done with regard to the safety profiles of thyroid acting drugs. Oral hypoglycemic agents were found to have significant effects on thyroid function(9). In a study done in KNH, thyroid disorders occurred with other comorbidities such as diabetes which often led to the required dose adjustment of the hormone replacement drugs. A recent survey of DTPs in outpatient clinics of KNH reported that 95% of her study participants had at least one DTP(36).

Among the seven DTPs, the need for additional drug therapy was the most frequent (73%). The prevalence of DTPs in thyroid disease patients is unknown.

2.4 Categories of Drug Therapy Problems

According to the fore mentioned Helper and Strand classification system, DTPs arise from the four drug related needs which are common to all medical conditions(13). These needs include right indication, effectiveness safety and compliance.

2.4.1 Indication

A drug indication is defined as a recommended use of a drug product for management or prevention of a medical condition. Indications are based on peer reviewed studies and adopted by a panel of experts. The recommendations are compiled to form treatment guidelines based on best current available literature. In thyroid disease, various professional associations have developed treatment guidelines that guide treatment selection. The study will rely on the American Thyroid Association (ATA) guidelines since there are no validated thyroid treatment guidelines in Kenya or in the African region. The ATA guidelines are the most preferred guidelines among the KNH endocrinologists because they are up to date(4). Two DTPs can result from errors of commission or omission with regards to indication; unnecessary drug therapy or need for additional drugs.

2.4.1.1 Unnecessary Drug Therapy

Unnecessary drug therapy refers to a scenario where the drug therapy is not needed since the patient does not have any indication for use of the drug product. This can have several causes including; duplicate therapy where multiple drugs are used for a condition that requires only single drug therapy. Lack of a valid medical diagnosis can lead to improper indication. Further to this, prescribing drugs for conditions where non drug therapy is recommended leads to unnecessary drug use. Use of recreational drug use also amounts to improper drug therapy. Treating avoidable or self-limiting adverse drug reactions is also termed as unnecessary drug therapy. The Minnesota Pharmaceutical Care Project found a very low prevalence of this DTP in patients transiting from

hospital to home care(37). The study in KNH found that unnecessary drug therapy was among the least common DTP accounting for only 1.7% of the problems identified(36). However when developing treatment guidelines for thyroid disease, the panel of experts in the American Thyroid Association noted that improper diagnosis of a thyroid condition can prompt unnecessary drug use(4). A study conducted at KNH endocrinology clinic reported that subclinical hypothyroidism was highly prevalent(9). The American Thyroid Association does not recommend levothyroxine replacement therapy for subclinical hypothyroidism(38). Based on this argument occurrence of this DTP cannot be ruled out in this patients.

2.4.1.2 Need for Additional Drug Therapy

This refers to the recommended obligation to add new drugs in a treatment regimen so as to manage symptoms or prevent complications. Additional drugs may be needed for synergy with current drugs, or for treating underlying medical conditions. This is attributed to factors such as presence of an untreated condition which requires drug therapy, need for preventive drug therapy and finally the need synergistic or additive effects(13). This type of DTP had the highest prevalence according to the Minnesota Pharmaceutical Care Project(37). It has also been cited as the leading DTP in cardiovascular disease management(39). The study done in KNH outpatient clinics also found the omission of drug therapy to be the leading type of DTP(36). Since the thyroid hormone controls the basal metabolic rates of the body, derangement of thyroid functions presents with a myriad of symptoms as summarized in the tables 2 and 3.(5)

Table 2: Clinical Presentation of Hypothyroidism (Table obtained from Applied Therapeutics by Koda and Kimble 10th edition(5))

Symptoms	Physical findings	Laboratory values
1. General: weakness. Tiredness. Lethargy. Fatigue Cold intolerance 2. Headache 3. Loss of taste/smell Deafness 4. Hoarseness No sweating 5. Modest weight gain 6. Muscle cramps. Aches. Pain 7. Dyspnea 8. Slow speech Constipation 9.Menorrhagia 10. Galactorrhea	I. Thin brittle nails II. Thinning of skin Pallor III. Puffiness of face and eyelids. Yellowing of skin IV. Thinning of outer eyebrows. Thickening of tongue. Peripheral edema V. Pleural/peritoneal/pericardial effusions VI. "Myxedema heart" VII. ↓ DTRs VIII. Hypertension Bradycardia (↓ HR) IX. Goiter (primary hypothyroidism)	A.↓ TT4 B. ↓ FT4I ↓ TT3 ↓ FT4 ↓ FT3I C. Positive antibodies (in Hashimoto's) D. ↑ TSH E. ↑ Cholesterol F. ↑ LDH G. ↓ Na ↑ CPK H. ↓ Hct/Hgb I. ↑ AST J. AST

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Symptomatic management of hypothyroidism improves the patients quality of life(38). Hormonal management with levothyroxine takes a duration of more than two weeks for resolution of symptoms in hypothyroid patients(40). Within that duration, prompt symptomatic management is advised. Omission of such remedies indicates a need for additional drug. Hyperthyroid patients also present with various symptoms as shown in Table 3.

Table 3: Clinical Presentation of Hyperthyroidism (Table obtained from Applied Therapeutics by Koda and Kimble 10th edition(5))

Symptom	Physical findings	Laboratory values
1. Heat intolerance 2. Palpitations 3. Weight loss common, or weight gain caused by ↑ appetite 4. Pedal edema Diarrhea/frequent bowel movements 5. Amenorrhea/light menses 6. Tremor. Weakness. Fatigue 7. Nervousness. Irritability. Insomnia	I. Thinning of hair (fine) II. Proptosis. Lid lag. Lid retraction. Stare III. Chemosis. Conjunctivitis. Periorbital edema. Loss of extraocular movements IV. Diffusely enlarged goiter. Bruits. Thrills V. Wide pulse pressure VI. Pretibial myxedema VII. Plummer nails. Flushed moist skin. Palmar erythema VIII. Brisk DTRs	A.↑ TT4 B.↑ FT3I/FT3 C.↑ FT4I/FT4 D,↑ TT3 E. Suppressed TSH F. TSI present TgAb present TPA present RAIU >50% G.↑ Calcium H .↑Alkaline phosphatase ↓ Cholesterol I.↑ Calcium ↑Alkaline phosphatase ↑ AST

The American Thyroid Association recommends symptomatic management of those symptoms. A specific example in hyperthyroidism, ATA recommends the use of non-selective beta blockers in patients with increased heart rates(4). Omission of such symptomatic management drugs leads to a drug therapy problem. Some studies have reported positive benefits and advantages of combined symptomatic treatments as opposed to single drug therapy(41). However there are no published studies which independently examine the presence of this DTP in patients.

2.4.2 Effectiveness

The unmet need for effective drug can be caused by two main factors, the use of ineffective drugs and under dosing.(13)

Use of an ineffective drug can be caused by the following factors, availability of more effective drug in the market, a medical condition being refractory to the drug, inappropriate dosage form of a drug product, presence of a contraindication, and drug product not appropriate for the condition being treated. The use of ineffective drug products has been cited as a leading cause of treatment

failure especially in hormone replacement therapies(38). In the context of thyroid disease, use of ineffective drug includes switching brands of levothyroxine. ATA does not recommend switching between different brands of levothyroxine. Different brands have been shown to vary in effectiveness even if the indicated potency is similar because of lack of bioequivalence(23).

A second form of ineffective drugs in the context of thyroid disease is occurrence of treatment resistant hypothyroidism. A study done in Italy found that cases of levothyroxine resistant hypothyroidism exist and such cases require higher levothyroxine doses(42). The possible causes of levothyroxine refractory hypothyroidism are non-compliance, switching to generics with different bioavailability and other causes such as pregnancy and gastro intestinal conditions(42).

Under dosing is giving ineffective dose which leads to failure to attain the minimum effective concentration of the drug in plasma. Also in specific cases, under dosing includes failure to conduct additional monitoring to determine if the dose is appropriate. Another cause is inappropriate frequency where the dosage interval is too infrequent to produce the desired response. Incorrect administration in that the dose was not administered through the correct route or method can cause an under dose.

Drug interactions which lead to decreased bioavailability or increased rates of metabolism. Many drugs have been shown to reduce the bioavailability of levothyroxine and antithyroid drugs especially when administered together(3). They include calcium and iron containing supplements, antacids, PPIs among many others(6). Combined oral contraceptives also increase the thyroid binding proteins in blood(43). Drug interactions have been implicated as a leading cause of treatment failure by the American Thyroid Association. Administration of a drug for shorter duration than the recommended is also a possible cause of a dosage too low. The association also acknowledges the lack of consensus on whether to adjust levothyroxine dosage in patients who have achieved target TSH levels but with residual symptoms(38). Studies have also shown that increase in weight often renders the constant levothyroxine dosages below the minimum effective levels(42). The Minnesota pharmaceutical care project also noted that dosage too low was the second most common type of DTP(37). This can be attributed to the fact that most prescribers do not take into consideration the dose determining parameters specific to the patients. Levothyroxine has a long half-life of more than 6days, hence the effects of a low dose may take a few weeks to present(44). Persistent low doses increase the risk of complications such as myxedema coma,

bradycardia and dyslipidemias(2). A recent study showed that 40% of the patients on drugs for various thyroid diseases had deranged TSH levels, this indicates that they are either over treated or undertreated(45). Findings from the same study indicated that transient elevations in TSH levels were strongly correlated to changes in lipid profiles which are a major risk to cardiovascular diseases(45).

2.4.3 Safety

Safety concerns makes a large proportion of every patients drug related needs. Morbidity and mortality have been reported from use of unsafe drugs. Drugs with a narrow therapeutic window such as levothyroxine require strict monitoring(44). Safety of a particular drug product is determined by the drug molecule itself, the excipients and the patient specific factors. Two DTPs can arise from the safety need(13). They include adverse drug events and dosage too high.

The types of adverse drug events includes undesirable drug reactions which are not dose related, unsafe drug product based on patient specific risk factors, drug interactions which results in undesirable reactions, incorrect administration resulting in adverse reactions, allergic reactions to the drug or drug product and drug reactions resulting from rapid increase in dose(13). Use desiccated thyroid in treatment hypothyroidism was abolished due to immunogenicity of the animal proteins.(34). Hypersensitivity to antithyroid drugs and levothyroxine has been reported. However the prevalence is still unknown in Kenya(46). Methimazole and Carbimazole are contraindicated in the 1st trimester of pregnancy due to the risk of teratogenicity(47). Thionamides also carry a myriad of side effects the most serious being agranulocytosis. American Thyroid Association recommends cessation of therapy upon development of agranulocytosis and blood counts for monitoring(25). The adverse effects of thioamides include pharyngitis, purpuric rash, arthralgia, fatigue, nausea and fever among others. The American Thyroid Association also gives a green light on the use of antihistamines to manage cutaneous reactions due to antithyroid drugs(25). Propylthiouracil can cause elevation of serum transaminase and hence liver function tests should be done routinely. If there is sustained elevation of transaminase levels, discontinuation of propylthiouracil therapy is recommended(25). Levothyroxine has serious side effects such as atrial fibrillation and osteoporosis and hence monitoring of therapy is recommended in the elderly and post-menopausal women(2). The use of radioactive iodine is always associated

with development of hypothyroidism and should not be used in pregnancy due to teratogenicity(40).

Dosage too high is a scenario where actual amounts of drug in each dose are too high causing toxicity. The frequency at which each dose is given may be too short hence causing accumulation of the drug to toxic concentrations. The duration of therapy may be too long leading to toxic effects. In some cases there is need for additional monitoring of drug levels in patients at high risk of toxicity. Further to that drug interaction which results to decreased metabolism or elimination of other drugs can cause toxicity(13). This is the most infrequent DTP in the general population according to the Minnesota Pharmaceutical Care Project(37). However its occurrence in the endocrine conditions may be higher than the general population due to variability of potency between brands and the pharmacokinetic profiles of the hormones. In hyperthyroidism, the progressive weight loss may lead to transient high doses. The American Thyroid Association recommends dose adjustments in nephropathy and liver diseases so as to minimize overdosing(38).

2.4.4 Adherence

The main causes of non-adherence in patients include(13); failure by the patients to understand instructions. Also, the cost of drug products may influence its affordability for patients hence directly affecting compliance. In addition to that patients may prefer not to take the drug based on personal reasons. The patient may also forget to take the drug which is common especially in elderly patients. The prescribed drug product may be unavailable in the market. Finally the patient may not be able to swallow or administer the drug as intended. Non adherence has been sighted as a possible cause of treatment failure by the American Thyroid Association(38). Further to that the association recommends further research into that as there are few studies. In a study done in Italy, the Morisky Medication Adherence Scale (MMAS) was used to assess adherence to levothyroxine liquid and tablet formulation(48). Among other findings, the study reported higher rates of adherence in patients using the liquid formulation as opposed to the solid tablets. In another study, almost half of the study subjects reported non adherence to levothyroxine therapy, literate patients had a higher percentage of non-adherences than illiterate patients. Forgetfulness was cited as the leading reason for non-adherence(23). A similar survey published by the American Thyroid Association cites forgetfulness as a major cause of non-adherence among pregnant hypothyroid

women(49). A study in Lebanon showed that presence of comorbidities, smoking and alcohol intake increased the risk of non-adherence to levothyroxine regimens(50). The same study recommended implementation of doctor-pharmacist to patient educational programs since this was shown to increase adherence. In addition to the above studies, numerous surveys to check adherence to antithyroid drugs have been done. A retrospective study found that patients with higher medication adherence index to antithyroid drugs had lower risk of ischemic stroke(51). A randomized control trial to examine the influence of an educational booklet on thyroxine adherence in patients with hypothyroidism found that although the intervention group had minimal improvement there was no statistically significance difference hence provision of information booklets would not be a solution to promote adherence(52). There are no published studies on adherence to thyroid disease medications in Kenya and the African region at large.

2.5 Literature Gap

There are no studies that explicitly report the prevalence of the entire spectrum of drug therapy problems in thyroid disorders. The only published studies in this area are skewed towards compliance, suboptimal therapy and side effects of therapy.

This study aimed to fill the gap by providing the data on prevalence of selected DTPs in thyroid disease patients in Kenya.

CHAPTER THREE: METHODOLOGY

3.1 Introduction

This chapter describes the components and the methods that were used to carry out the study. The sections include research design, location of the study, target population and study population, sample, research instruments, pilot study or pretesting, validity, reliability, data collection techniques, data analysis, logistical and ethical considerations, work plan and budget

3.2 Study Design

The study was a hospital based cross sectional survey of adult patients with thyroid disease with or without any comorbidities and being followed up in the KNH endocrinology outpatient clinic. The study was conducted within a period of three months. The design was selected as it can be used to determine the prevalence of health related conditions in a given point in time.

3.3 Location of the Study

The study was conducted at Kenyatta National Hospital (KNH) endocrinology clinic. KNH is the largest referral hospital in Kenya. It is located in the Upper Hill Area of the Nairobi about 4km west of the Nairobi central district. It has a bed capacity of about 2000 beds and serves about 75000 inpatients daily. It also has 23 outpatient clinics that serve around 550000 patients annually. The hospital serves the local population in Nairobi cosmopolitan as well as referral cases from across Kenya and the East African region. It offers diagnostic, preventive and curative services. The staff at KNH includes clinical pharmacists, specialist doctors, nurses, pharmacists, clinical officers among others. The endocrinology clinic is located next to the proposed cancer center and opposite the government chemist. It runs daily from Monday to Friday with the major clinic being on Friday. It serves patients with endocrinology disorders such as diabetes and thyroid disease. The largest proportion of patients is the diabetic patients and thyroid disease patients are ranked second. Each major clinic day the endocrinology clinic serves about 20 patients with thyroid disease.

3.4 Target and study Populations

The target population was adult thyroid disease patient in Kenya. The study population was the adults with thyroid disease attending outpatient endocrinology clinic in Kenyatta National Hospital in the duration between September to December 2020.

3.5 Inclusion and Exclusion Criteria

Patients were included if they meet the following criteria

1 Diagnosed with any thyroid disease with or without any comorbidities
2 Aged above 18years
3 Treated and followed up at KNH endocrinology clinic for at least 2 months.
4 Gave informed consent to participate in the study

Patients who fail to meet any of the above conditions were excluded from the study

3.6 Sample

There are no previous studies which examine DTPs in thyroid disease patients. A study among medical patients in KNH reports that each of the 60 study subjects had at least one medication related problem (MRP) resulting in a prevalence of 100%(53). Assuming a 5% error, the lowest possible prevalence of 95% will be used. Hence a prevalence of 95% was used to estimate the sample size.

The sample size was calculated using the Cochran formula(54)

$$N = \frac{Z^2 * p(1-p)}{d^2}$$

Where

N – Minimum sample size required

Z – a two sided level of alpha at 95% (standard value of 1.96)

P – Estimated prevalence of drug therapy problems from in KNH medical patients(53) (95%)

D – Margin of error (0.05)

$$N = \frac{1.96^2 \text{ X } 0.95(1-0.95)}{0.05^2}$$

N = 73

The calculated sample size is 73. However to cater for non-response bias the sample was inflated by 10% to yield a minimum sample size of 80. The study participants were randomly selected. This was done using a computer generated simple random sequence.

3.7 Research Instruments

3.7.1 Screening for eligibility

The inclusion criterion which guided the Principal Investigator on recruiting study participants is presented (Appendix 1). Based on this tool, the principal investigator assessed whether the patient is above 18years based on the patient reported date of birth. The investigator also assessed whether the patient had any clinical diagnosis for a thyroid disorder based on the records.

3.7.2 Informed consent form

These forms were used to obtain informed consent for those patients who met eligibility criteria. The first form issued to the eligible patients was the consent explanation form (Appendix 2A). Then the consent declaration form followed after that (Appendix 2B). The two forms were in English and Kiswahili for the patients who were Kiswahili literate only.

3.7.3 Data Collection Tool

The data collection tool was an interviewer guided structured questionnaire (Appendix3) modified from the Helper and Strand tool and the Adherence Estimator Tool(55). These are validated tools and were used to collect all relevant patients' data. The laboratory reports and the medication data was obtained from the patient files using the questionnaire (Appendix 3) as a guide.

3.8 Pre-Testing the data collection tool

The questionnaire was pretested on 10% of the study sample (8 patients) to test the completeness, relevance, applicability and reliability of the data collection tool. This pretest was done at the endocrinology clinic during the clinic days. Corrections and rectifications were done on the identified areas of weakness.

3.9 Validity

To ensure validity the questions in the data collection tool were structured in a way that they captured all the data required to answer the study objectives. The questions were precise and

straight to the point. The questionnaire also used a simple and well understood language free from complex medical terms. The sample size was optimal to enhance representativeness to the target population. Simple random sampling of participants also ensured that the sample is representative of the target population to allow generalization. The pilot study was also used to verify the internal validity of the data collection tools

3.10 Reliability

The reliability of the data collection tool was assessed by performing the pilot study. This allowed adjustment of parameters to ensure that tool is reliable and applicable. The questionnaire were also based on the helper and strand tool whose validity and reliability have been proven in similar studies

3.11 Data Collection Techniques

The study was conducted at the endocrinology clinic of KNH during the outpatient clinic visits. The principal investigator was assisted by research assistants who were fellow pharmacists, nurses and medical officers working at the endocrinology clinic. The techniques for data collection included first screening for eligibility of randomly selected patients. This was guided by the eligibility screening form (Appendix 1). After that the eligible patient was presented with the consent explanation form (Appendix 2A) followed by the consent declaration form (Appendix 2B) which was filled in duplicate. Then the consenting participants were allocated a unique code to ensure confidentiality. The principal investigator then conducted the participants' interview guided by the questionnaire (Appendix 3) while filling in the relevant answers to in the questionnaire. The interviewer guided questions were filled in a private place so as to protect the patient's privacy. The questions included the biodata, medication history, family history as guided by the helper and strand tool and questions regarding medication adherence obtained from the Adherence Estimator tool. The interview was carried out by the principal investigator. The next step involved abstraction of data from the patient's files. This included data on the most recent thyroid functions tests, biodata and medication data. The data was filled into the relevant slots in the data collection tool (Appendix 3). The consent form and the questionnaire were then be allocated a unique code to replace the patient specific identifiers so as to ensure confidentiality. The principal investigator then stored all the patients' data under a lock and key to ensure data security and confidentiality.

3.12 Data Analysis

The data was entered into Microsoft excel 2010 and analyzed using STATA version 13.0 software. Descriptive summary statistics were presented as means with standard deviations for normally distributed data on continuous variables and medians and interquartile ranges for non-normally distributed data on continuous variables. Categorical variables were summarized using frequencies and percentage proportions. Binary and multi variable logistic analysis was used to control for confounders. Chi squared (X^2) test statistic was used to measure the associations between DTPs and patient specific factors. The prevalence ratios and odds ratios were generated. The odds ratios will be used as measures of associations. All qualitative data obtained was analyzed by identification of common themes, patterns and relationships within a sample group.

3.13 Logistical and Ethical Considerations

3.13.1 Ethical approval

Clearance from the University of Nairobi and Kenyatta National Hospital Ethics and Research committee was granted (Ref KNH-ERC/A/295) (Appendix 4). The researcher also got authorization from the Kenyatta National Hospital administration. The participation in this research was voluntary and was only guaranteed after understanding and filling of the consent declaration forms.

3.13.2 Informed consent

All eligible participants were taken through a brief description of the nature of the study (Appendix 2A); all aspects of the study were explained to them in the language they understand. The willing participants will be presented with the consent declaration form to sign (Appendix 2B). This was signed in duplicate whereby one copy was given to the patient and the other copy remained with the principal investigator.

3.13.3 Risks and benefits

The study as outlined did not involve any foreseeable risk since there are no invasive procedures. However the researcher collaborated with other medical colleagues to address any eventuality. The study participants benefited from drug information and medical advice given upon discovery of potential DTPs

3.13.4 Privacy and Confidentiality

The documents containing patient's data and the signed consent forms were stored under a lock and key accessible only to the researcher. The patients identifier data was not be shared with anyone else but only the principal investigator. The patient's identifiers were replaced with patient specific codes on the data collecting tools. All interviews were conducted in secluded rooms to ensure privacy.

CHAPTER FOUR: RESULTS

4.1 Introduction

A total of 139 thyroid disease patients were identified from the clinic bookings. Nine patients were excluded for failing to meet the required age of 18 years and above. Twenty patients failed to give an informed consent and were also excluded from the study. Ten patients never attended the clinic on the booking day. Fifteen patients were newly diagnosed and a clear diagnosis was yet to be

made and hence they were not on any medication. The recruitment process is as summarized in **figure 2**

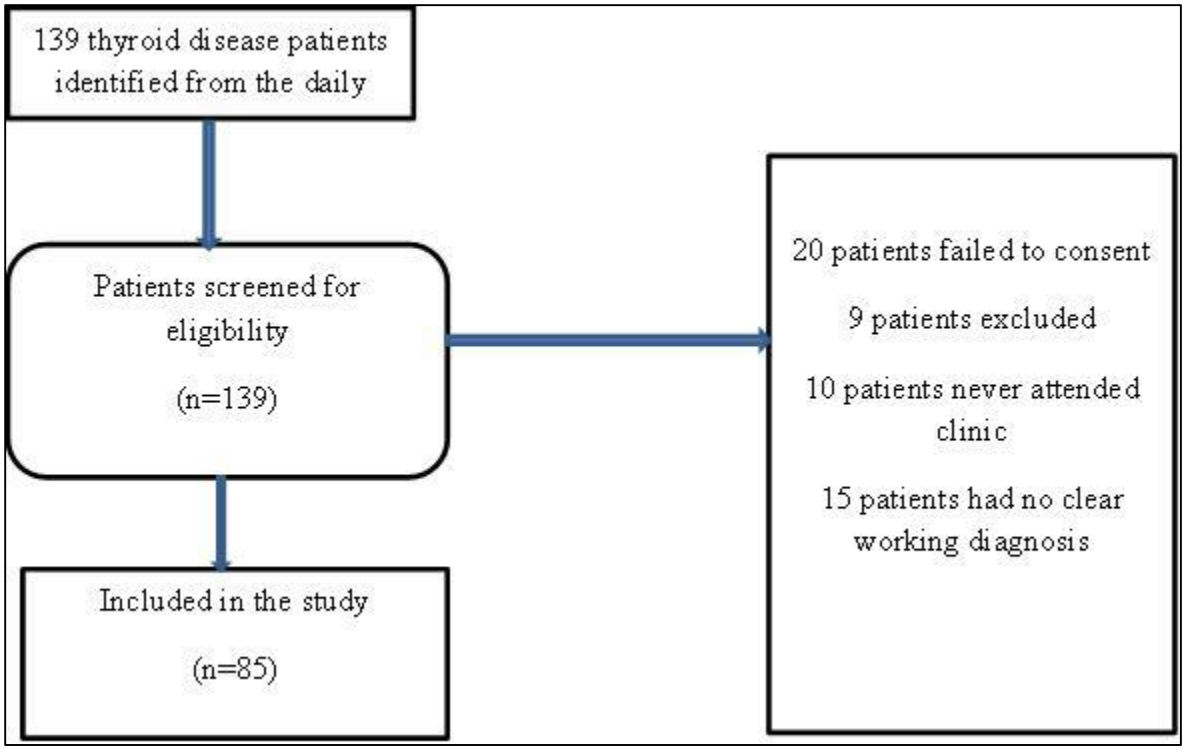

Figure 2 Consort Diagrams of Participants Included in the Study

4.2 Social Demographic Characteristics of the Study Participants

A total of 85 patients with thyroid disease participated in the study out of which 71(84%) were female and 14 (16%) were males. The average age of the patients was 51.4 (±14.8 years) with a range of 21 to 83 years. Majority of the patients were between the ages of 40 and 70 years. Females had a mean age of 49.8 years (SD 14.53). The mean age among males was 59.9 (SD 13.6) years. The range of ages in males was 42 - 80years hence males are more likely to present with thyroid disease at later age than females.

Eighteen (21%) of the study participants were single, 63(74%) were married, 2(2%) were widowed and 2(2%) were divorced. Seventeen (20%) had attained a primary level of education, 32(38%) had a secondary level, 31(36%) had a college level and 5(6%) had never attended any school. A majority of the participants were Christians 83(98%) and the rest were Muslims 2(2%). Six (7%)

patients were currently consuming alcohol or had done so in the past. A majority 79(93%) have never used alcohol. All the other social demographics were summarized as shown in **Table 4**.

Table 4 Social Demographic Characteristics of Study Participants (n=85)

Variables		**Frequency (n)**	**Percentage (%)**
Sex	Male	14	16.5
	Female	71	83.5
Marital status	Single	18	21.3
	Married	63	74.2
	Divorced	2	2.3
	Widowed	2	2.3
Religion	Christian	83	97.7

	Muslim	2	2.3
Level of education	Primary	17	20.0
	Secondary	32	37.7
	College/university	31	36.5
	None	5	5.9
Alcohol use	Used alcohol	6	7.0
	Never used alcohol	79	93.0
Occupation	Formal	12	14.1
	Informal	43	50.6
	Unemployed	24	28.2
	Retired	6	7.1
Average income	<5000	10	11.8
	5000-10000	26	30.6
	10000-30000	10	11.8
	>30000	2	2.4
	Fluctuating*	37	43.5
Insurance policy	Have a health policy	32	37.7
	No health policy	53	62.3
Place of drug purchase	Chemist	37	43.5
	Hospital	48	56.5

* These include the inconsistent incomes and the seasonal incomes

4.3 Types of Thyroid Disease, Duration of Illness and Comorbidities

Hyperthyroidism was the most prevalent thyroid disorder among the study participants (47%) followed by hypothyroidism at 25% and thyroid cancers had the lowest prevalence 1.2%. Majority of the participants (29%) had been diagnosed less than three years ago. A total of nine patients (10.6%) had a positive family history of thyroid disease. The most frequent comorbidity was hypertension (36.5%) followed by both diabetes and hypertension (9%). A majority of patients (41%) did not have any comorbidity and were purely been followed up for thyroid disease alone. The various types of thyroid disease and other comorbidities are summarized in **Table 5**.

Table 5 Types of thyroid disease and comorbidities in patients seen at the endocrinology clinic of Kenyatta National Hospital

Thyroid condition	**Frequency**(n=85)	**Percentage** (%)
Hyperthyroidism	40	47.0
Subclinical hyperthyroidism	10	11.8
Hypothyroidism	22	25.9
Subclinical hypothyroidism	8	9.4

Thyroid cancer	1	1.2
Others	4	4.7
Duration of the illness		
Less than one year	16	18.8
One to three years	25	29.4
Three to five years	20	23.5
Greater than five years	24	28.2
Comorbidity		
Diabetes	4	4.7
Hypertension	31	36.5
Diabetes and Hypertension	8	9.4
Cancer	1	1.2
None	35	41.2
Others*	6	7.1

*these include Arthritis, Asthma, and cardiomyopathies

4.3.1 Relationship between Gender and Thyroid Disease

The female to male ratio was 5:1 which showed a greater female predominance. This means that females are five times as likely as males to present with thyroid disease. The distribution of various thyroid conditions by gender was summarized in **Figure 3.** For all disease condition, females were over represented.

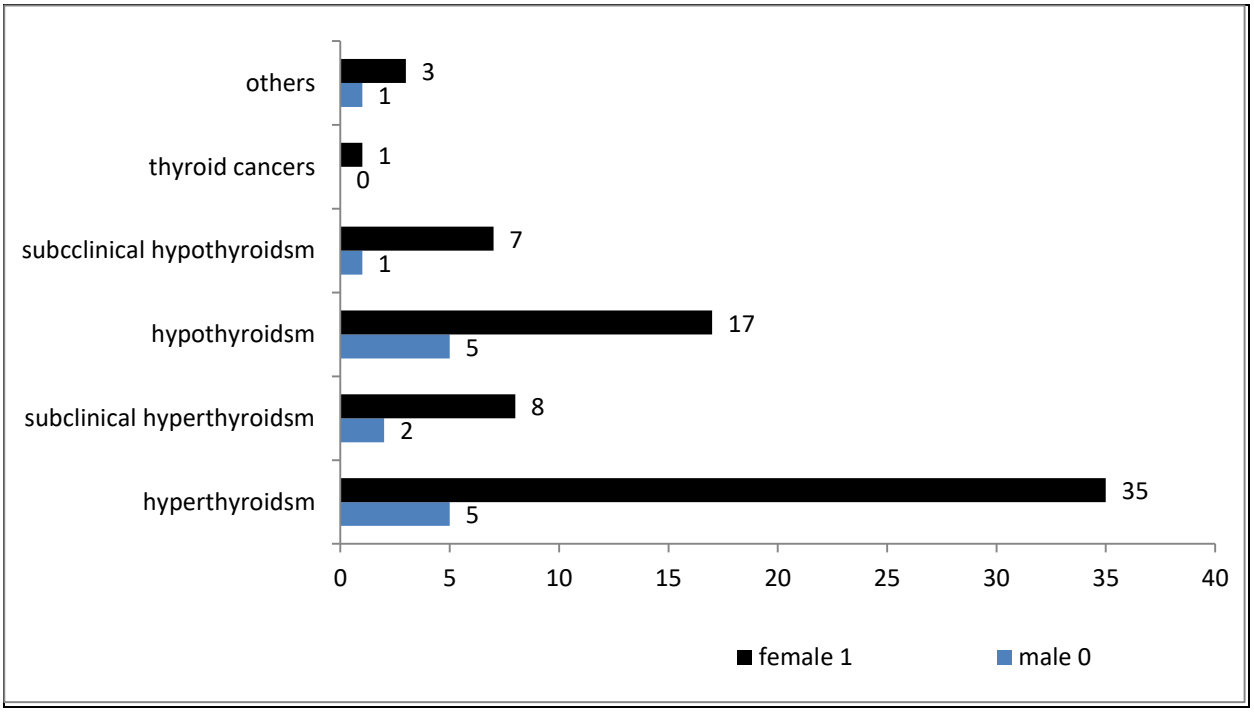

Figure 3 Distribution of Thyroid Conditions according to Sex

4.4 Pharmacological and Surgical Management of Thyroid Disease

Surgical procedures such as thyroidectomy had been done in 7 (8.2%) of patients out of the 85 sampled. The commonly used antithyroid drugs are summarized in **Figure 4**. The most frequently used drug was carbimazole because the most prevalent disorder was hyperthyroidism. Six patients (75%) with subclinical hypothyroidism were on levothyroxine while only twenty one patients (95%) with clinical hypothyroidism were on levothyroxine. Thirty six patients (90%) with hyperthyroidism were on carbimazole while nine patients (90%) with subclinical hyperthyroidism were on carbimazole

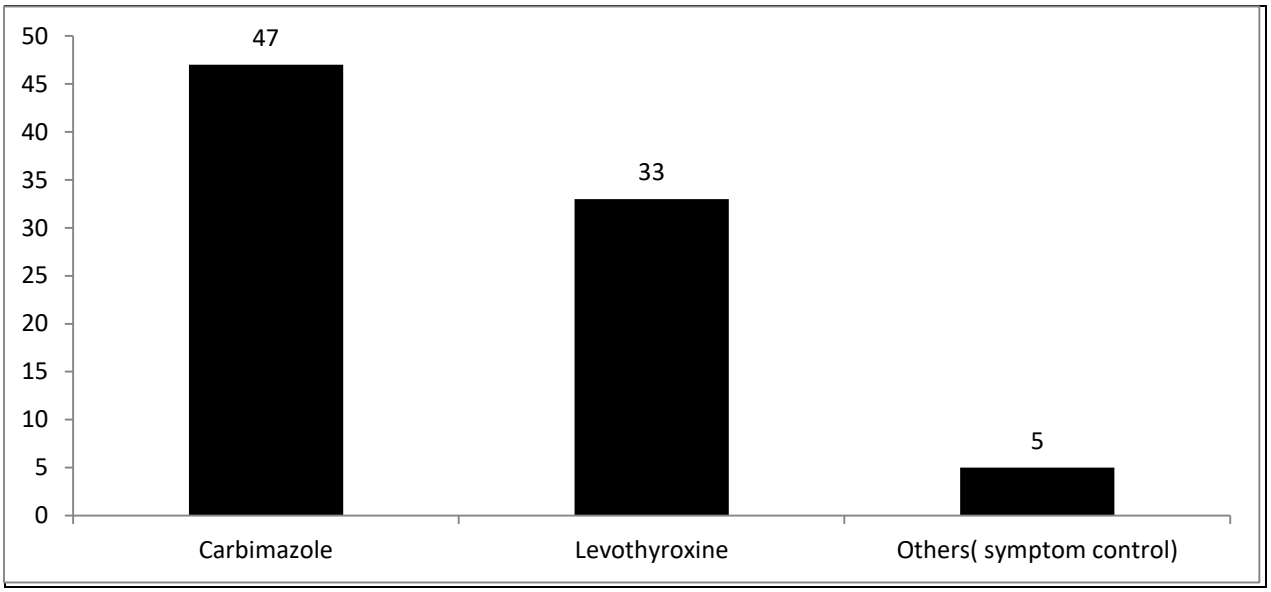

Figure 4 Drugs used for management of thyroid disorder in Kenyatta National Hospital

Drugs used for symptom control include propranolol, prednisone, vitamin(C, D&E) and paracetamol (antipyretic).

4.4.1 Drugs used in Management of Comorbid Hypertension and Diabetes

Nineteen patients (22.3%) were on propranolol for symptomatic control of hyperthyroidism. A majority of hypertensive patients were on losartan (24%), followed by amlodipine (9.4%. seven

patients (8.2%) were on carvedilol. Other antihypertensive such as spironolactone, atenolol, enalapril, nifedipine and methyldopa accounted for less than 2% each. Four patients (4.7%) were on metformin and only one patient (1.1%) was on insulin Mixtard.

4.5 Drug Therapy Problems in Patients with Thyroid Disease in Kenyatta National Hospital

A total of 74(87.1%) of the patients had at least one DTP. This prevalence was very high. The prevalence was evaluated by gender, type of thyroid condition and drug. The results are presented in **Table 6**. The prevalence did not vary significantly with these variables.

Table 6 Prevalence of Drug Therapy problems by gender, thyroid condition and drug

Variable	Prevalence (%)	P value
Gender		0.577
Male	12(85%)	
Female	62(87.2%)	
Thyroid condition		0.458
Hyperthyroidism	34(85%)	
Hypothyroidism	20(90.9%)	
Thyroid cancers	1(100%)	
Drugs		0.760
Carbimazole	41(87.2%)	
Levothyroxine	29(87.8%)	

4.5.1 Types of Drug Therapy Problems

The drug therapy problems were summarized using the Helper and Strand tool as shown in **Figure 5.** Noncompliance was the most prevalent type of drug therapy problem.

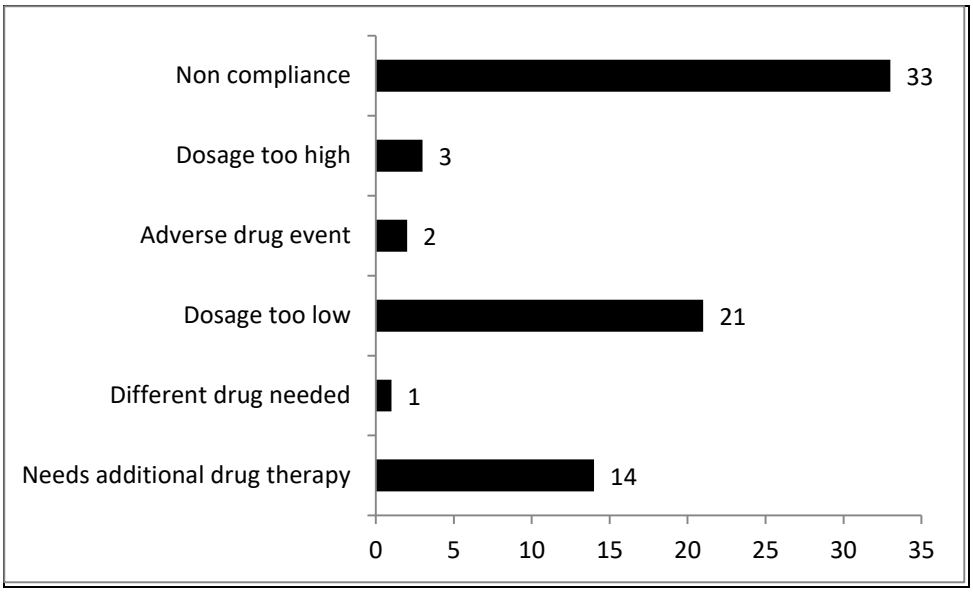

Figure 5 Proportions of different classes of drug therapy problems using the Helper and Strand classification

The major subtypes of the drug therapy problems were analyzed per each category of DTP as shown in **Table 7**. The leading cause of noncompliance was affordability of medication. Presence of an untreated condition was the major indicator for the need for additional drug therapy.

Table 7 Subtypes and causes of drug therapy problems in patients with thyroid disease in Kenyatta National Hospital

DTPs	Cause of DTP	Frequency	Percentage
Needs additional drug therapy	Untreated condition	12	14.1
	Synergistic/potentiating drug needed	2	2.4
Different drug needed	Condition refractory to the drug	1	1.2
Dosage too low	Ineffective dose	10	11.8
	Drug interaction reduces the amount of active drug	11	12.9
Adverse drug event	Allergic reactions	2	2.4
Dosage too high	Dose too high	3	3.5
Non compliance	Unknown cause of non-compliance	1	1.2
	Patient does not understand instructions	7	8.2
	Patient prefers not to take	10	11.8
	Cannot afford drug product	12	14.1
	Drug product not available	3	3.5

4.6 Patients Understanding of Drug Therapy.

Analysis of patients understanding of drug regimen versus occurrence of DTP revealed that 83.9% of patients with a correct understanding of drug regimen had at least one DTP. 95% of patients with incorrect understanding of dosage regimen had at least one DTP. The exact p value was 0.275 hence not a significant association.

4.7 Risk Factors for Selected Drug Therapy Problems

The relationship between patient's gender, type of thyroid disease, type of drugs with occurrence of a need for additional therapy, dosage too low and non-compliance was summarized as shown in **Table 8.** There was a significant association between the type of drugs and noncompliance (0.023). The rates of non-compliance to levothyroxine were very high. Slightly over half the patients were non-compliant (51.1%). Out of the drugs, levothyroxine was the most likely to be under-dosed (36.4%). Also patients on levothyroxine were more likely to need additional therapy (21.2%) compared to patients on carbimazole (10.6 %). Overall, patients on levothyroxine were more prone to experiencing non-compliance, under-dosing and need for additional therapy. Participants with an income level of Kshs. 5000- 10000 and those with variable incomes had significantly higher chances of presenting with noncompliance than those of income ranges greater than 10000ksh.

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Table 8 Association between participants gender, type of thyroid disease and thyroid drugs with occurrence of low dose, need for additional drug and noncompliance

Variable	Low dose	Need for additional drug	Non compliance
	n (%)	n (%)	n (%)
Gender			
Male	3 (21%)	1(7.1%)	7 (50%)
Female	18 (25%)	13(18.3%)	26 (36.6%)
P value	**0.527**	**0.227**	**0.259**
Type of thyroid disease			
Hyperthyroidism	7 (17.5%)	5 (12.5%)	20(50%)
Subclinical hyperthyroidism	5 (50%)	1 (11.1%)	3 (30%)
Hypothyroidism	7 (31.8%)	5 (22.7%)	7 (31.8%)
Subclinical hypothyroidism	1 (14.2%)	2 (25%)	1 (12.5%)
P value	**0.278**	**0.683**	**0.208**
Type of drugs			
Carbimazole	9 (19.4%)	5 (10.6%)	24 (51.0%)
Levothyroxine	12 (36.3%)	7 (21.2%)	7 (21.2%)
P value	**0.094**	**0.120**	**0.023**
Income			
<5000	2 (20.0%)	1 (10%)	1 (10%)
5000-10000	8 (30.7%)	4 (15.3%)	9 (34.6%)
10000-30000	2 (20%)	1(10%)	4 (40%)
>30000	1 (50%)	1(50%)	0 (0%)
Variant	8 (21.6%)	7 (18.9%)	19 (51.3%)
P value	**0.763**	**0.659**	**0.109**
Place of purchase			
Chemist	10 (27%)	5 (13.5%)	14 (37.8%
Hospital	11 (22.9%)	9 (18.7%)	19 (39.5%)
P value	**0.426**	**0.367**	**0.525**
Education			
Primary	1 (5.8%)	3 (17.6%	12 (70.5%)
Secondary	11 (34.3%)	3 (9.3%)	12 (37.5%)
Tertiary	9 (29.0%)	6 (19.3%)	8 (25.8%)
None	0 (0%)	2 (40%)	1 (20%)
P value	**0.087**	**0.246**	**0.017**
Duration of illness			
Less than one year	1(6.2%)	2 (12.5%)	9 (56.2%)
One-three years	5(20%)	5 (20%)	8 (32%)
Three –five years	8(40%)	3 (15%)	6 (30%)
Greater than five years	7(29.1%)	4 (16.6%)	10 (41.6%)
P value	**0.113**	**0.957**	**0.371**
Comorbidities			
Diabetes	2(50%)	1(25%)	1(25%)
Hypertension	4(12.9%)	7(22.5%)	15(48.3%)

Diabetes and hypertension	2(25%)	1(12.5%)	3(37.5%)
P value	**0.076**	**0.730**	**0.845**

4.8 Binary Regression Analysis of Risk Factors for Non-compliance amongst patients with thyroid disease

Bi-variable regression analysis was done by regressing each of the variables listed in **Table 9** against non-compliance. Then a forward stepwise model building was used to come up with a parsimonious model. Income status, level of education and type of drugs were significant predictors to occurrence of noncompliance.

There was a negative association between non-compliance and education (AOR 0.422; 95% CI 0.227, 0.781). This implied that patients who were more educated were more likely to be compliant. There was a significant negative association between types of drug and non-compliance (AOR 0.683, 95% CI 0.504, 0.925). It was noted that patients was levothyroxine were most likely to be non-compliant than patients on carbimazole. Though the effect of income was significant on bi-variable analysis, it lost significant after adjusting for confounding for education on multivariable analysis.

Table9: Logistic regression Analysis for predictors of Noncompliance in patients with thyroid disease

Predictors	**Bi-variate regression analysis**		**Parsimonious model on multivariate regression analysis**	
	Crude Odds Ratio (95% CI)	**P values**	**Adjusted Odds Ratio (95% CI)**	**P values**
Sex	0.577 (0.182-1.831)	0.351		
Age	0.997 (0.968-1.027)	0.871		
Marital status	0.462 (0.189-1.128)	0.090		
Education	0.429 (**0.239-0.767**)	**0.004**	0.422 (0.227-0.781)	0.006
Recreational drug use	1.291 (0.223-7.480)	0.775		
Occupation	1.005 (0.583-1.731)	0.984		
Income	1.385 (**1.031-1.86**)	**0.030**	1.32 (0.960-1.820)	0.087
Insurance	0.718 (0.293-1.760)	0.470		
Place of drug purchase	1.076 (0.446-2.597)	0.870		
Thyroid condition	0.742 (0.523-1.053)	0.095		
Duration of thyroid disease	0.874 (0.584-1.308)	0.514		
Comorbidities	0.959 (0.872-1.055)	0.393		
Knowledge of regimen	2.129 (0.805-5.633)	0.128		
Type of drugs	0.725 (**0.546-0.963**)	**0.026**	0.683 (0.504-0.925)	0.014

4.9 Binary Regression Analysis of Risk Factors for Need for additional drug amongst patients with thyroid disease

Bi-variable regression analysis was done by regressing each of the variables listed in **Table 10** against need for additional drug. Then a forward stepwise model building was used to come up with a parsimonious model. There was a positive association between recreational drug use and needs for additional drug therapy AOR 1 (0.120-0.383). Participants with a current or past recreational drug use were at a significantly high risk of presenting with a need for additional drug therapy.

Table10: Logistic regression Analysis for predictors of Need for additional drug therapy in patients with thyroid disease

Predictors	**Bi-variate regression analysis**		**Parsimonious model on multivariate regression analysis**	
	Crude Odds Ratio (95% CI)	**P values**	**Adjusted Odds Ratio (95% CI)**	**P values**
Sex	2.913 (0.349-24.299)	0.323		
Age	1.02 (0.986-1.068)	0.197		
Marital status	2.154 (0.795-5.838)	0.131		
Education	1.443 (0.723-2.881)	0.298		
Recreational drug use	1 (0.120-0.383)	0.000	1 (0.120-0.383)	0.000
Occupation	1.521 (0.748-3.095)	0.246		
Income	1.157 (0.794-1.686)	0.447		
Insurance	2.531 (0.648-9.878)	0.181		
Place of drug purchase	1.476 (0.449-4.849)	0.520		
Thyroid condition	1.237 (0.841-1.819)	0.279		
Duration of thyroid disease	1.032 (0.608-1.750)	0.907		

Comorbidities	0.923 (0.814-1.045)	0.209		
Knowledge of regimen	2.382 (0.724-7.835)	0.153		
Type of drugs	1.362 (0.970-1.913)	0.074		

4.10 Binary Regression Analysis of Risk Factors for Low dosing amongst patients with thyroid disease

Bi-variable regression analysis was done by regressing each of the variables listed in **Table 11** against low dosing. Then a forward stepwise model building was used to come up with a parsimonious model. No significant association was found between any of the selected variables and occurrence of low dose.

Table 11 Logistic regression Analysis for predictors of Low dosing in patients with thyroid disease

Predictors	Bi-variate regression analysis		Parsimonious model on multivariate regression analysis	
	Crude Odds Ratio (95% CI)	P values	Adjusted Odds Ratio (95% CI)	P values
Sex	1.245 (0.312-4.969)	0.756		
Age	0.977 (0.944-1.012)	0.202		
Marital status	0.804 (0.323-2.002)	0.640		
Education	1.200 (0.699-2.152)	0.540		
Recreational drug use	0.633 (0.107-3.733)	0.614		
Occupation	0.934 (0.504-1.732)	0.831		
Income	0.938 (0.683-1.289)	0.697		
Insurance	0.975 (0.353-2.692)	0.961		
Place of drug purchase	0.802 (0.298-2.159)	0.663		
Thyroid condition	1.059 (0.747-1.502)	0.744		
Duration of thyroid disease	1.581 (0.973-2.567)	0.064		
Comorbidities	1.047 (0.937-1.169)	0.412		
Knowledge of regimen	0.366 (0.096-1.388)	0.140		
Type of drugs	1.124 (0.842-1.502)	0.425		

CHAPTER FIVE: DISCUSSION, CONCLUSION AND RECOMMENDATION

5.1 Introduction

This chapter discusses the results obtained from the study and compares them to other studies done in different populations. The first part discusses the patient social demographic characteristics and compares them with results from other studies. The second part discusses the disease related factors among study participants and the final part discusses study outcomes including significant associations and compares them with outcomes from other studies. It also gives recommendation for practice and further research.

5.2 Social Demographic Characteristics of the Study Participants

Majority of the patients with thyroid disease were females (84%) while (16%) were males. The female to male ratio was 5:1 which agrees perfectly with other studies done in Europe(56). Another study done in Norway reported a prevalence ratio of 4:1(57). Females have higher chances of developing thyroid disease than males. Majority of the patients were between the ages of 40 and 70years. The elderly have a higher predisposition to development of thyroid disease(28). Females had a mean age of 49.8 years (SD 14.53). Post-menopausal women had higher odds of presenting with thyroid disease than any other population group. The mean age among males was 59.9(SD 13.6) years. Males are more likely to present with thyroid disease at later age than females. This demographics largely agreed with other studies done in the African continent(10)

5.3 Types of Medications

A majority of patients were on carbimazole (55%) which tallied well with hyperthyroidism being the most prevalent condition. The second commonly used drug was levothyroxine (38%). Other drugs used for symptomatic management such as propranolol accounted for 5% only.

5.4 Proportions of Thyroid Conditions and Comorbidities

Hyperthyroidism was the most prevalent thyroid disorder among the study participants (47%) followed by hypothyroidism at 25% and thyroid cancers had the lowest proportion 1.2%. This findings slightly differed from the results of a prevalence study done in patients with diabetes at the same clinic(9). In the said study, subclinical hypothyroidism had the highest proportion. Females had a higher proportion in all types of thyroid conditions. The observed discrepancy was due to the fact that the mentioned study focused on patients with diabetes only. Majority of the patients had the thyroid condition for less than three years hence they were recently diagnosed.

The major comorbidity in all participants was hypertension (36%) followed by both hypertension plus diabetes (9%). The Rotterdam study found a significant association between thyroid function and life expectancy in people with cardiovascular disease(58). A majority of patients (22.3%) were on propranolol for control of hyperthyroid tremors which agreed with findings of a study in Europe(41).

5.5 Proportions of DTPs

Non-compliance, under-dosing and need additional drug therapy were the most common DTPs. Noncompliance had the highest proportion. The proportion of these three DTPs was highest in patients on levothyroxine. This agrees with findings from other studies done in KNH outpatient clinics(36). It shows that medication related problems can be a possible cause of treatment failures in KNH. Implementation of policies on mandatory provision of drug information services would go a long way in ensuring resolution of medication related problems.

5.6 Risk Factors for Noncompliance – Effects of Income and Education.

The study established a significant association (p value-0.030) between patient's income levels and noncompliance to medication on bi-variable regression analysis. This agrees with other studies that puts income as a significant predictor of adherence to drugs(23). This is because patients with higher incomes can afford medications and also have access to specialized services. The effect of income lost significance after adjusting for confounding for education. Education status was a significant predictor of noncompliance. We found a negative association between education and non-compliance. Educated people are more likely to understand the disease condition and related drug information and therefore more likely to comply with the dosage regimen. This disagrees

with the findings of a study done in Lebanon where increased education levels were found to negatively impact compliance(23). In the said study, patients with higher levels of education were found to disregard drug information services than those with lower levels. In the Kenyan population, the stakeholders in health should put more emphasis on education as it was shown to improve compliance.

5.7 Association between Type of Drugs and Non-compliance

There was a very significant association between the type of drug and noncompliance (p value 0.03). Patients on carbimazole had a 0.5 chance of presenting with dosage too low than patients on levothyroxine. Slightly over half of the patients on levothyroxine were non-compliant. This can be attributed to the high cost of levothyroxine compared to carbimazole.

A positive history of recreational drug use had no significant association with noncompliance to medication regimen. This goes against the findings of an earlier study which established a significant association between cigarette smoking and deranged thyroid hormone levels(59). In our study the number of smokers was very small and therefore it was not possible to identify any associations between smoking and non-compliance. No significant association was found between number of comorbidities and noncompliance unlike in a systematic review done in Nigeria where a clear association was found(11). This can be attributed to larger sample sizes in the said study.

5.8 Association between Recreational Drug Use and Need for Additional Drug Therapy

Recreational drug use was a significant predictor of a need for additional drug therapy (p- 0.000). Participants with a past or current recreational drug use had a higher risk of presenting with a need for additional drug therapy. This can be explained by frequent complications associated with recreational drugs such as cardiovascular disease(60).

5.9 Strengths and Limitations of the Study

Being the first study to be done on the subject of drug therapy problems in thyroid disease patients in Kenya, the results obtained are crucial in shaping the practice in management of thyroid disease.

It also points out the critical role medication therapy management clinic would serve under trained clinical pharmacists. The study was able to identify statistically significant predictors of occurrence of DTPs in thyroid disease patients. The study was hospital based and hence the results obtained would not be generalized to the general population. Being a cross-sectional study, the study would not report on the incidence of DTPs. It also relied on patient's information to judge compliance to medication which made it prone to reporting bias.

5.10 Conclusion

The prevalence of DTPs was 87%. Noncompliance, under dosing and need for additional drug therapy were the most frequent drug therapy problems particularly in patients on levothyroxine. A significant association was found between income status, level of education and type of antithyroid drugs versus occurrence of noncompliance. There was a significant association between recreational drug use and occurrence of the need for additional drug. Upon bi-variable regression analysis of the selected risk factors, no significant predictors were found for low dosing.

5.11 Recommendation for Practice

1. Intervention by a clinical pharmacist would positively influence chemotherapeutic management of thyroid disease.
2. Drug information services also need to be implemented as most DTPs would be evaded by providing patients with the correct information regarding drugs.
3. A majority of DTPs occurred in the low income groups due to unaffordability of medications, affordable health insurance policy targeting this population of patients would go a long way in improving therapeutic outcomes.

5.12 Recommendation for Future Research

1. Prospective studies should be done to assess the impact of various interventional solutions to DTPs in thyroid disease patients.
2. A prospective case control study should be done to access morbidity and mortality rates due to DTPs in thyroid disease patients.

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APPENDICES

APPENDIX 1 SCREENING AND ELIGIBILITY FORM

All subjects must meet the eligibility criteria based on the inclusion/exclusion criteria in the application approved by the KNH/UON Ethics and Research Committee.

I STUDY INFORMATION

Study title: Drug therapy problems in patients with thyroid disorders and related comorbidities in Kenyatta National Hospital.

Principal investigator: Simon Kigoro Kamau

Signature…….

Date of screening…….

II PATIENT INFORMATION

Patient code……..

Gender Male… Female…

III INCLUSION/EXCLUSION CRITERIA

Inclusion criteria (answered 'yes' for inclusion)	Yes	No
1. Patient above 18years		
2. Patient has a documented clinical diagnosis for a thyroid condition		
3. Patient is being treated and followed up at KNH endocrinology clinic for at least two months		
Exclusion criteria (answered 'no' for inclusion)		
1. Patient declines to give consent		

APPENDIX 2A CONSENT EXPLANATION FORM

Patient …… care giver……

Relation to patient…….

Study title: drug therapy problems in patients with thyroid disorders and related comorbidities in Kenyatta National Hospital

Institution: department of pharmaceutics and pharmacy practice, school of pharmacy, university of Nairobi P.O Box 30197- 00400, Nairobi

Principal investigator: Dr Simon Kigoro Kamau masters student (clinical Pharmacy) P.O Box

48917 -00100 Nairobi

Supervisors: Dr Sylvia Opanga, Senior Lecturer, Department of Pharmaceutics and Pharmacy Practice, University of Nairobi

Prof Faith Okalebo Senior Lecturer, Department of Pharmacology and Pharmacognosy, University of Nairobi

I am Dr Simon Kigoro conducting the above study to partly fulfil the requirements for a master's degree in clinical pharmacy of the University of Nairobi

Ethical approval

Kenyatta National Hospital/University of Nairobi Ethics and Research Committee.

What is the purpose of the study?

The study you are being asked to participate in aims at assessing the drug therapy problems that occur in thyroid disease patients being treated at Kenyatta National Hospital. It also aims to find out the prevalence of thyroid disorders and the associations between the drug therapy problems and patient specific factors.

Why have I been invited to participate?

You have been invited to participate since you are an adult over 18yrs on treatment for a thyroid disorder and being followed up at KNH endocrinology clinic.

What is expected of me as a participant?

Should you agree to participate in the study you will be interviewed using a structured questionnaire to collect social demographic data and medical history. This will take less than an hour of your time.

Who will have access to collected the data?

All data collected from you will be coded and entered in a password protected computer without access from the public in order to protect your identity. Only the research investigator will have access to the personal information. However ethics review committee members may access the information if need be to inspect the research records. At the end of the study there will be no way to link your name with the collected data. Any published work arising from the study will not bear your name or any other personal identifiers.

Must I participate?

Your participation is completely voluntary. If you decide to participate you are completely free to withdraw or refuse to answer any question at any time without jeopardy to your treatment at KNH. You will not be required to give any reason for such withdrawal or refusal.

Are there any benefits for participation?

Immediate benefit to you as a participant is that is any serious drug therapy problem is identified

in the course of the study; such will be communicated to your physician for review. The research will also identify the drug therapy problems in thyroid disease patients. This will help to improve future treatment services in KNH and other health facilities.

What are the risks associated with my participation?

No risks are associated with your participation. No invasive procedures will be done on you. In case of any unforeseen risks, the researcher will collaborate with the medical personnel on duty during that day so as to respond to the emergency. The data obtained from you will be treated with utmost confidentiality.

What will happen to the study findings?

Study findings will form part of the master's degree in clinical pharmacy project dissertation. This will further be published in a peer reviewed journal. The study will also be shared with the University of Nairobi College of health sciences administration, KNH administration and in presentations at scientific conferences.

What do I do in case of a problem?

You are free to raise any concerns about your rights as a participant in this study to me or KNH/UON ethics and research committee who have approved this study

……..

If patient only understands Kiswahili use the section below

MGONJWA……. **MLEZI……..**

UHUSIANO NA MGONJWA……

Kuhusu utafiti huu. Tathmini ya matatizo ya matatizo yanayo tokea kwa matumizi ya dawa katika matibabu ya tezi kwenye hospitali kuu ya Kenyatta.

Taasisi. idara ya pharmaceutics and pharmacy practice, shule ya pharmacy, chuo kikuu cha Nairobi

Mtafiti mkuu. Dkt Simon Kigoro Kamau, mwanafunzi uzamili (utabibu wa dawa) S.L.P 48917-00100 Nairobi

Wasimamizi. Dkt Sylvia Opanga, mhadhiri mkuu, idara ya pharmaceutics and pharmacy practice, chuo kikuu cha Nairobi.

Prof Faith Okalebo, mhadhiri mkuu, idara ya pharmacognosy and pharmacology, chuo kikuu cha Nairobi

Mimi ni Dkt Simon Kigoro, nafanya utafiti huu kutimiza sehemu ha mahitaji ya ukamilifu wa shahada kuu katita utaalam wa utabibu wa dawa, chuo kikuu cha Nairobi.

Idhini ya kimaadili

Kamati ya maadili na utafiti ya hospitali kuu ya Kenyatta- chuo kikuu cha Nairobi

Nini madhumuni ya utafiti?

Utafiti huu unalenga kutathmini kiwango cha matatizo yanayo husiana na dawa katita matibabu ya wagonjwa wa tezi wanaotibiwa kwenye hospitali kuu ya Kenyatta. Pia utafiti huu unalenga kutathmini kiwango cha ugonjwa wa tezi hapa nchini. Pia utafiti huu unalenga kutathmini uhusiano wa matatizo ya dawa na hali binafsi ya wagonjwa wa tezi.

Mbona mimi nimealikwa kushiriki?

Umealikwa kushiriki kwa maana wewe umetimiza umri wa mtu mzima na pia unatibiwa ugojwa wa tezi katika hospitali kuu ya Kenyatta.

Nini kinachotarajiwa kutoka kwangu kama mshiriki?

Ukikubali kuwa mshiriki utahojiwa kupitia nakala za dodoso kukusanya ujumbe kuhusu hali yako, jamii na historia za matibabu ya dawa. Shughuli hii haitachukua Zaidi ya dakika therathini.

Nani watakuwa na uwezo wa kuangalia ujumbe utakao kusanywa?

Nakala yoyote ya ujumbe itakayo kusanywa kutoka kwa mgonjwa itahifadhiwa kwa siri na itatumika kwa utafiti huu pekeyake. Baada ya kumaliza utafiti ujumbe unaohusiana na mgonjwa binafsi hautaweza kuunganishwa na nakala yake. Ujumbe utakao chapishwa kutoka kwa utafiti huu hautakuwa na kitambulisho cha mgonjwa binafsi.

Lazima nishiriki?

Kushiriki kwa utafiti huu ni kwa hiari yako. Hata utakapo amua kushiriki bado unahaki ya kujiondoa kutoka kwa utafiti huu. Pia una haki ya kutojibu maswali au swali lolote bila hofu ya kutopewa matibabu kamili hospitalini. Sio lazima upeane sababu ya kutoshiriki katika utafiti huu.

Kuna faida ya kushiriki?

Faida kuu itakayo tokana na kushiriki kwako ni kuwa mtafiti akigundua shida kuu itokanayo na dawa unazotumia ataweza kuarifu muuguzi wako aweze kurekebisha. Pia ujumbe utokanao na

utafiti huu utaweza kusaidia hospitali kuu ya Kenyatta katika kuboresha huduma za dawa kwa wagonjwa wa tezi.

Nini hatari ya kushiriki?

Hakuna hatari yoyote itakayo tokana na kushiki katika utafiti huu. Utafiti huu hautahusu maelekezo yanayo ingilia mwili wa mgonjwa kwa njia yoyote. Iwapo hatari isiyotarajiwa itawadia, wauguzi waliohitimu watakuwa tayari kushughulikia mgonjwa.

Nini kitafanyika na matokeo ya utafiti?

Matokeo ya utafiti yatakuwa sehemu ya ukamilifu wa shahada kuu ya utabibu wa dawa. Matokeo pia yatachapishwa kwenye jarida linalo angaziwa na wataalamu. Matokeo yatawasirishwa kwa usimamizi wa hospitali kuu ya Kenyatta. Pia yatawasilishwa kwenye chuo kikuu cha nairobi na kwenye kongamano tofauti za kisayansi.

Nifanye nini kama kuna shida?

Uko huru kuwasilisha malalamishi yoyote yanayo husiana na haki zako kama mshiriki kwangu ama kwa kamati ya maadili na uttafiti ya hospitali kuu ya Kenyatta ikishirikiana na chuo kikuu cha Nairobi ambayo imepitisha utafiti huu.

APPENDIX 2B: CONSENT DECLARATION FORM

Informed consent

PATIENT…….

CARE GIVER…….. RELATION TO PATIENT…….....

I, the undersigned, willingly agree to participate in this study. I have read and understood the nature of the study, my responsibility as the participant, the inconveniences associated with voluntary participation in the study and that all my questions and concerns relating to the study have been answered satisfactorily. I understand that I may choose to leave the study at any time

and will not be prejudiced or penalized in any way. I understand that the information gathered will be used for the purpose of this study only and maximum confidentiality will be maintained.

I will receive a copy of this signed consent document to take away and keep

Respondent name……

Signature……..

Date……..

Witness (colleague)……..

Sign……. Date…….

Investigators statement

I, the undersigned, have explained the information in this document to this participant and encouraged them to ask questions which I took time to answer. I am satisfied that the participant understands all aspects of the research as discussed in the consent process information document above.

……

Name and sign of the person obtaining consent

In case of any concern you may contact the following principal investigator on email simonkigoro@gmail.com/ Tel 0708701317 or KNH-UON Ethics and Research Committee secretary: Email uonknh_erc@uonbi.ac.ke

If patient understands Kiswahili only use the section below

Ridhaa

MGONJWA…….

MLEZI…….. UHUSIANO NA MGONJWA……

Mimi, mtiaji sahihi, kwa hiari yangu nimekubali kushiriki katika utafiti huu. Nimesoma na kuelewa asili ya utafiti, majukumu yangu kama mshiriki, usumbufu unao husiana na hiari yangu kushiriki katika utafiti huu na maswali pamoja na wasiwasi kuhusu utafiti huu yamejibiwa kwa

kuridhisha. Nimeelewa kuwa naweza acha kushiriki katika utafiti huu wakati wowote bila kuweka matibabu yangu hatarini yoyote. Nimeelewa kuwa taarifa yoyote kutokana na utafiti huu itatumika kwa utafiti huu pekee na usiri utahakikishwa wakati wote.

Nitapata nakala yangu ya ridhaa iliyowekwa sahihi nichukue niweke

Jina la anayejibu……

Sahihi……..

Tarehe……..

Shahidi(mwenzangu)

Sahihi…… tarehe……..

Kauli ya mtafiti

Mimi, mtiaji sahihi, nimeelezea taarifa iliyomo katika hati hii kwa mshiriki na kumhimiza kuuliza maswali yenye nimemjibu. Nimeridhika kuwa mshiriki anaelewa vizuri vipengele vinavyohusiana na utafiti kama ilivyo elezewa katika mchakato wa ridhaa uliyo hapo juu

…….

Jina na sahihi ya mwenye kuchukua ridhaa

Kwa maelezo Zaidi wasiliana na mtafiti mkuu kwa barua pepe: simonkigoro@gmail.com/ simu ya rununu 0708701317 ama KNH-UON kamati ya maadili na utafiti barua pepe: uonknh_erc@uonbi.ac.ke

APPENDIX 3 QUESTIONAIRE
SECTION A: PATIENT SURVEY

Code number of the participant…….

I BIODATA

1. Age_____ years Date of birth_____

2. Sex Male___(0) Female ___(1)

3. County of residence_____

3. Weight _____kg Height in cm_____

4. BMI_____

BMI CATEGORY	CODE
18.5 and below (underweight)	0
18.5-25.9(healthy weight)	1
25-29.9(over weight)	2
30 and above obesity	3

5. Marital status Single (0) Married (1) Divorced (2)

6. Pregnancy status Yes (0) No (1) Due date_____

7. Religion Christian (0) Muslim (1) Others (2)

8. Level of education: Primary (0) Secondary (1) College/University (2) None (3)

9. Recreational drug use status.

Substance	**History of use**	**Substance**	**History of use**
Tobacco use (0) No tobacco use (1)	(0) 0-1 packs per day (1)> 1 pack per day (2) Uses other forms of tobacco (e.g. chewing, e-cigarettes) (3) Previous history of smoking (4)Interested in quitting	Alcohol use (0) No alcohol use (1)	(0)<2 drinks per week (1)2-6 drinks per week (2)> 6 drinks per week (3) Past alcohol use
Caffeine (0) No caffeine use (1)	(1) <2 cups per day (2) 2-6 cups per day (3) >6 cups per day	Recreational drug use (include substance and frequency of use)	(1) Yes (2) N0 (3) Other

II OCCUPATION

10. What is your employment status? Formal (1) informal (2) unemployed (3) retired (4) other

(5)

11. On average how much do you make per month?_____

12. Category of monthly income (Ksh) <5000 (0) 5000-10000 (1) 10000-30000 (2) >30000(3)

13. Do you have a health insurance policy? Yes (0) No (1)

14. Where do you purchase your medications from?

Chemists (0)

Hospital (1)

Private clinics (2)

Others……. ……..(3)

15. How do you pay for the medications? Through insurance (0) Cash based transfer (1) Other (2)

III THYROID DISEASE CONDITION

16. Which thyroid disorder are you being treated for?

CONDITION	CODE
Hyperthyroidism	1
Subclinical hyperthyroidism	2
Hypothyroidism	3
Subclinical hypothyroidism	4
Thyroid cancer	5
Other	6

17. When did this condition begin?

DURATION OF THYROID DISEASE	CODE
Less than one year	1
Less than three years	2
Less than five years	3

Greater than five years	4

18 Do you have other ailments? Yes (0) No (1) Other (2)

If yes to question 3 above, list in the following table

CONDITION	CODE
Diabetes	0
Hypertension	2
Kidney disease	3
Cancer	4
HIV	5
TB	6
Other infectious diseases	7
GIT conditions	8
Autoimmune diseases	9
Others	10
TOTAL TALLY OF THE CONDITIONS	

IV PAST MEDICAL HISTORY

19. Have you ever been admitted in a hospital due to thyroid disease? Yes (0) No (1) Other (2)

20. Have you ever had a thyroidectomy? Yes (0) No (1) Other (2)

21. Have you ever had a blood transfusion? Yes (0) No (1) Other (2)

22. Have you ever used any complementary or alternative medicine to manage thyroid condition? Yes (0) No (1) Other (2)

V MEDICATION HISTORY

23. Are you taking any medication for the thyroid condition? Yes (0) No (1) Other (2)

Medication Experience

24. Do you like taking medications? Yes (0) No (1) Other (2)

25. If no to question 1 above, what is the reason?

Drugs don't work Yes (0) No (1)

Drugs cause more problems Yes (0) No (1)

I don't take medications Yes (0) No (1)

The cost of drugs Yes (0) No (1)

Availability of drugs yes (0) no (1)

Other (2)

26. What do you expect from the medications you use? Cure (0) Relief (1) Other (2)

27. Do you have any concerns regarding your medications? Yes (0) No (1) Other (2)

28. If yes to question 4 above what are your concerns?

The number of pills Yes (0) No (1)

The number of times you take the drugs Yes (0) No (1)

Side effect of the medication Yes (0) No (1)

29. Do you currently suffer from any side effects of the medication? Yes (0) No (1) Other (2)

30. Do you choose to take medications without being compelled? Yes (0) No (1) Other (2)

31. Do you choose to refill your prescriptions? Yes (0) No (1) Other (2)

32. When you feel that your condition is under control do you sometimes stop taking the medications for a while? Yes (0) No (1) Other (2)

Patients Understanding of the Thyroid Disease Medication.

33. Do you know the dose(s) of the medication(s) you are using? _____

Correct (0) incorrect (1)

34. How many times do you take in a day?_____

Correct (0) incorrect (1)

35. Do you know the duration within which you should take your drugs?_____

Correct (0) incorrect (1)

36. How should you take this medication with regard to food? With food (0) After food (1) Before food (3) I don't know (4)

37. Do you know why you are using this medication? _____

Correct (0) Incorrect (1)

38. Do you hold any cultural or religious beliefs for or against the use of certain medications?

Yes (0) No (1)

Fill in the patients reported info in this table to assist in assessment

DRUG	dosage form	Dose	frequency	Drug drug interraction Yes(0) No (1)	Indication	taking with food(1) without food(2)	possibility of drug-food interraction yes(0) no (1)	overdose(0) underdose (1)
Carbimazole(1)								
PTU(2)								
Methimazole(3)								
Levothyroxine(4)								
RAI(5)								
Others(6)								

VI FAMILY HISTORY

39. Is there any member of your family who also has a thyroid condition? Yes (0) No (1) Other (2)

VII REVIEW OF SYSTEMS

A. General system

40. Fever? Yes (0) No (1) Other (2)

41 Malaise? Yes (0) No (1) Other (2)

42. Are you experiencing pain anywhere? Yes (0) No (1) Other (2)

43. Do you have any weight change? Yes (0) No (1) Other (2)

B. Special senses

Eyes

44. Do you have any problem with the eyes? Yes (0) No (1) Other (2)

If yes which problem?

45. Impaired visual acuity? Yes (0) No (1) Other (2)

46. Pain in the eyes? Yes (0) No (1) Other (2)

47. Itching? Yes (0) No (1) Other (2)

48. Swelling? Yes (0) No (1) Other (2)

Ears

49. Do you have any problem with your ears? Yes (0) No (1) Other (2)

If yes, which is the problem?

50. Loss of hearing? Yes (0) No (1) Other (2)

51. Loss of balance? Yes (0) No (1) Other (2)

52 Ringing in the ears? Yes (0) No (1) Other (2)

C.Throat

53. Do you have any problem with your throat?

If yes which is the problem?

54. Pain while swallowing food? Yes (0) No (1) Other (2)

D. Respiratory System

55. Do you have any problem with your respiratory system? Yes (0) No (1) Other (2)

If yes, which is the problem?

56. Chest pain? Yes (0) No (1) Other (2)

57. Shortness of breath? Yes (0) No (1) Other (2)

58. Wheezing? Yes (0) No (1) Other (2)

59. Coughing? Yes (0) No (1) Other (2)

E. Digestive system

60. Do you have any problem with your digestive system? Yes (0) No (1) Other (2)

If yes, which is the problem?

61. Pain in the abdomen? Yes (0) No (1) Other (2)

62. Poor appetite? Yes (0) No (1) Other (2)

63. Heart burn? Yes (0) No (1) Other (2)

64. Difficulty in swallowing? Yes (0) No (1) Other (2)

65. Diarrhea? Yes (0) No (1) Other (2)

66. Hard stool? Yes (0) No (1) Other (2)

67. Nausea? Yes (0) No (1) Other (2)

F. Genitourinary system

68. Do you have any problem with your genitourinary system? Yes (0) No (1) Other (2)

If yes, which is the problem?

69. Pain when urinating? Yes (0) No (1) Other (2)

70. Decreased sexual drive? Yes (0) No (1) Other (2)

71. Increased frequency of urination? Yes (0) No (1) Other (2)

72. Irregular menses? Yes (0) No (1) Other (2)

73. Painful menses? Yes (0) No (1) Other (2)

74. Heavy menses? Yes (0) No (1) Other (2)

G. Neurologic system

75. Do you have any problem with your neurologic system? Yes (0) No (1) Other (2)

If yes, which is the problem?

76. Feeling dizziness? Yes (0) No (1) Other (2)

77. Feeling drowsiness? Yes (0) No (1) Other (2)

78. Experiencing memory loss? Yes (0) No (1) Other (2)

79. Experiencing mood changes? Yes (0) No (1) Other (2)

80. Lack of sleep? Yes (0) No (1) Other (2)

81. Head ache? Yes (0) No (1) Other (2)

H. Musculoskeletal System

82. Do you have any problem with your musculoskeletal system? Yes (0) No (1) Other (2)

If yes, which is the problem?

83. Back ache? Yes (0) No (1) Other (2)

84. Joint pain? Yes (0) No (1) Other (2)

85. Joint stiffness? Yes (0) No (1) Other (2)

86. Difficulty in walking? Yes (0) No (1) Other (2)

87. Swelling of joints? Yes (0) No (1) Other (2)

I. Integumentary System

88. Do you have any problem with your skin? Yes (0) No (1) Other (2)

If yes, which is the problem?

89. Itchiness? Yes (0) No (1) Other (2)

90. Rashes? Yes (0) No (1) Other (2)

91 Dry skin? Yes (0) No (1) Other (2)

SECTION 2 MEDICAL RECORDS REVIEW

92. The following data should be abstracted from the medical records.

Lab parameter	Previous reading	Current reading	Status	Remarks

Heart rate				
Blood pressure				
Fasting blood glucose				
HbA1c				
Body temperatures				
Weight				
TSH levels				
T3 levels				
T4 levels				
Full hemogram				
Coagulation profiles				
Sodium				
Potassium				
Creatinine				
Urea				
AST				
ALT				
ALP				

93 Summary of prescribed drugs and indications and identified DTPs.

Condition	Drugs	Dosage	Goals	Current results	Outcome status	Drug therapy problem	Cause

SECTION 3 EVALUATIONS OF DTPs

94. Did the patient have any DTP? Yes (0) No (1)

95. If yes to question 1, classify the DTP according to the table shown below

DTP	CODE	CAUSE	CODE	COMMENT
Unnecessary drug therapy	1	Not available	0	
		No valid medical indication	1	
		Duplicate therapy	2	
		Non drug therapy indicated	3	
		Treating avoidable ADR	4	
		Addictive or recreational drug	5	
Needs additional drug therapy	2	Not available	6	
		Untreated condition	7	
		Preventive	8	
		Synergistic/potentiating	9	
Different drug needed	3	Not available	10	
		More effective drug available	11	
		Dosage form inappropriate	12	
		Condition refractory to the drug	13	
		Contraindication present	14	
		Drug not effective for the	15	

		condition		
Dosage too low	4	Not available	16	
		Ineffective dose	17	
		Needs additional monitoring	18	
		Frequency inappropriate	19	
		Drug interaction reduces the amount of active drug	20	
		Duration inappropriate	21	
ADR	5	Not available	22	
		Undesirable effect	23	
		Unsafe drug for the patient	24	
		Dosage administered or changed too soon	25	
		Drug interactions causes undesirable reactions	26	
		Allergic reactions	27	
		Contraindication present	28	
Dosage too high	6	Not available	29	
		Dose too high	30	
		Needs additional monitoring	31	
		Frequency too short	32	
		Duration too long	33	
		Drug interaction results in toxicity	34	
Non compliance	7	Not available	35	
		Patient does not understand instructions	36	

		Patient prefers not to take	37	
		Cannot afford drug product	38	
		Patient forgets to take	39	
		Drug product not available	40	
		Cannot administer	41	

96. Develop a final analysis of DTPs present in this patient and summarize them in the table below.

NO	DTP	STATUS	
1	Unnecessary drug therapy	Yes (0)	No (1)
2	Needs additional drug	Yes (0)	No (1)
3	Different drug needed	Yes (0)	No (1)
4	Dosage too low	Yes (0)	No (1)
5	Adverse drug event	Yes (0)	No (1)
6	Dosage too high	Yes (0)	No (1)
7	Non compliance	Yes (0)	No (1)

APPENDIX 4; KNH-UON ETHICS APPROVAL

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Ref: KNH-ERC/A/295

8th September 2020

KENYATTA NATIONAL HOSPITAL APPROVED 08 SEP 2020 KNH/UoN-ERC P. O. BOX 20723 - 00202 NAIROBI

Simon Kigoro Kamau
Reg. No.U56/11110/2018
Dept.of Pharmaceutics and Pharmacy Practice
School of Pharmacy
College of Health Sciences
University of Nairobi

Dear Simon

RESEARCH PROPOSAL – DRUG THERAPY PROBLEMS AMONG PATIENTS WITH THYROID DISORDERS IN KENYATTA NATIONAL HOSPITAL (P103/ 02/2020)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 8th September 2020 – 7th September 2021.

This approval is subject to compliance with the following requirements:

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