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DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS

THYROID HORMONE PROFILE IN AMBULATORY HEART FAILURE PATIENTS ATTENDING ADULT OUTPATIENT CLINIC AT KENYATTA NATIONAL HOSPITAL

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DECLARATION

This dissertation is my original work and is being presented as a prerequisite for a master's degree to the Department of Clinical Medicine and Therapeutics, University of Nairobi, Kenya. All resources and materials used or quoted have been acknowledged with reference. It has not been presented for the award of a degree in any other institution.

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LIST OF ABBREVIATIONS AND ACRONYMNS

ACEI	Angiotensin converting enzyme inhibitors
AIH	Amiodarone induced hypothyroidism
AIT	Amiodarone induced thyrotoxicosis
ARB	Angiotensin receptor blockers
ATD	Anti-thyroid drugs
ATP	Adenosine triphosphate
CKD	Chronic kidney disease
DCM	Dilated cardiomyopathy
DNA	Deoxyribonucleic acid
ELISA	Enzyme linked immunosorbent assay
FDH	Familial dysalbuminaemic hyperthyroxinaemia
eGFR	Estimated glomerular filtration rate
HHD	Hypertensive heart disease
HIC	High income countries
HIV	Human immunodeficiency virus
IQR	Interquartile range
KNH	Kenyatta National Hospital
LDL - C	Low density lipoprotein cholesterol
LMIC	Low- and middle-income Countries
NTI	Non-thyroid illness
NYHA	New York Heart Association
RIA	Radioimmunoassay
SCH	Subclinical hypothyroidism
SD	Standard deviation
TKI	Tyrosine kinase inhibitors
TRH	Thyrotropin releasing hormone
TSH	Thyroid stimulating hormone
T3	Triiodothyronine
T4	Thyroxine

ABSTRACT

Background: Thyroid disorder affects 5–10% of the general population and can contribute to heart failure (HF). Hypothyroidism leads to a decrease in the cardiac output by 30–50%. HF affects 23 to 37 million people worldwide. However, despite the known relationship between thyroid dysfunction and HF, there is still a paucity of evidence on the burden of thyroid dysfunction in HF and their association in the Kenyan population. Knowledge of the burden of thyroid dysfunction in HF is essential in guiding clinical decision making and improving outcomes in HF patients.

Objectives: To determine the prevalence of thyroid dysfunction and its correlation with the severity of HF in ambulatory HF patients attending adult outpatient clinic at Kenyatta National Hospital (KNH).

Methods: A descriptive cross-sectional study design of ambulatory patients with HF attending the outpatient cardiac clinic at the KNH. Ambulatory HF patients with a diagnostic label of HF based on Framingham's criteria were consecutively sampled. Patients with structural heart disease based on echocardiogram findings, on amiodarone, and those who declined consent were excluded from the study. The study included patients above 18 years. Chemiluminometric assay was used to measure free triiodothyronine, free thyroxine, and thyroid stimulating hormones (TSH) levels using the Liaison test kits. Thyroid function was defined as either normal or abnormal based on thyroid function test at reference of: fT3 (2.2–4.2) pg/ml, fT4(0.8–1.7) ng/dl, TSH (0.3–3.6) Uiu/ml. The sample was characterised, and overall prevalence, percentages, mean, and standard deviation used. Association between severity of HF based on the New York Heart Association functional class, class 1 and 2 (early HF), class 3 (advanced HF) and thyroid dysfunction were assessed using Pearson's chi-square test.

Results: 304 patients were sampled, 2 declined consent and 302 were recruited into the study. Most of the HFs were caused by Hypertensive heart disease (HHD) (53.3%) and Dilated cardiomyopathy (DCM) (30.8%). 76.2% had HF in class I and II. The overall prevalence of thyroid dysfunction was 36.8% (95% CI: 31.5–42.4). Of those with thyroid dysfunction 66.7% (95% CI: 57.1–75.3) were women and 33.3% (95% CI: 24.7–42.9%) were men. Older adults had a higher prevalence of thyroid dysfunction with 49.6% (95% CI: 39.9–59.2) and 23% (95% CI:

15.9–32.4) among those aged 65–79 years and 50–64 years respectively; 78.4% of patients with thyroid dysfunction are 50 years and above. Prevalence of thyroid dysfunction was 28.8 % (95% CI: 20.6–38.2), 41.4% (95% CI: 32.2–51.2) and 29.7% (95% CI: 21.4–39.1) for patients in HF class III, II and 1, respectively.

Subclinical hypothyroidism (SCH) (18.8%, 95% CI: 14.6–23.8), euthyroid sick syndrome (9%, 95% CI: 6.0–12.7) and primary hypothyroidism (6%, (95% CI: 3.8–9.7) were the most prevalent thyroid dysfunction subtypes. Secondary hyperthyroidism (1.0%, 95% CI: 0.3–3.1), subclinical hyperthyroidism (1.0%, 95% CI: 0.3–3.1), primary hyperthyroidism (0.3%, 95 % CI: 0.1–1.8) and free T3 toxicosis (0.3%, 95% CI: 0.1–1.8) were the least subtypes of thyroid disorders.

There was no significant association between thyroid dysfunction and severity of HF based on NYHA functional class.

Conclusion: Prevalence of thyroid dysfunction in ambulatory HF patients is high. The most common subtype of thyroid dysfunction is hypothyroidism, with SCH being the most prevalent subtype. There is no significant association between thyroid dysfunction and severity of HF based on NYHA functional class.

CHAPTER ONE: INTRODUCTION AND PROBLEM STATEMENT

1.1 Introduction

Heart failure (HF) affects 23 to 37 million people worldwide (1,2). Thyroid disorder affects 5–10% of the general population (3). Thyroid dysfunctions have a higher prevalence among females, but with an increasing prevalence among males with advancing age (3). Among HF patients, 21%–33.3% are estimated to have thyroid dysfunction (4).

Thyroid dysfunction is related to the development of HF (5-7). Hypothyroidism and hyperthyroidism alter cellular and molecular pathways and lead to myocardial remodelling and HF (5). Overt and subclinical hyperthyroidism is linked to an elevated risk of HF and atrial fibrillation (7-10). Exposure of excess thyroid hormones leads to arterial stiffness, decreased blood pressure and increased heart rate (7-10). Hyperthyroidism is correlated with palpitations, tachycardia, exercise intolerance and exertional dyspnoea (11).

Hypothyroidism leads to a 30–50% decrease in cardiac output (12), an increase in hospital admission and deaths among HF patients (13). Overt and SCH are associated with bradycardia, mild hypertension, increased systemic vascular resistance and fatigue (13).

1.2 Problem Statement

Thyroid dysfunction can lead to HF (5-7). It can lead to atrial fibrillation resulting in acute decompensation of the HF (7). Hypothyroidism has been associated with mortality increase and hospitalization among HF patients (13). However, despite the known relationship between thyroid dysfunction and HF, there is still a paucity of evidence on the burden of thyroid dysfunction in HF and their association in the Kenyan population. Knowledge of the burden of thyroid dysfunction in HF is essential in guiding clinical decision making and improving outcomes in HF patients.

CHAPTER TWO: LITERATURE REVIEW

2.1 HF

HF occurs when the heart is unable to pump blood at a rate equal with the metabolic requirements of the body. HF (HF) affects approximately 26 million globally, 5.7 million in the United States (14). Approximately 1936 per 100,000 population have HF in North America and 248 per 100,000 population in Africa (15). The 10 year prevalence of congestive HF is estimated to increase in the Caribbean and Latin America by 44%, 37% in Asia-Pacific and 22% in Europe from 2016. (15). In the UK, the proportion of newly diagnosed HF rose by 12% between 2002 and 2014 with a 23% prevalence during the period (16). The prevalence of HF is high among those above 65 years of age (17). The mean age of HF patients is estimated at 36-62 years in Sub-Saharan Africa (SSA) (18) and 59 years globally (19). In SSA, hypertensive heart disease is the major cause of HF at 39.2%, dilated cardiomyopathy 22.7%, rheumatic heart disease 13.8% and ischemic heart disease 7.2% (18).

In SSA, HF contributes to approximately 30% of hospitalisation in cardiovascular unit (20). At KNH 5.7% of patients are admitted in acute HF (21). The mean age of hospitalised patients at KNH is 44 years (21). The mean length of stay is 6.84 days (2-27 days) for patients in Kenya (21). About 45.4% of the HF admissions in SSA are due to hypertension, 14.3% rheumatic heart disease, 7.7% ischaemic heart disease and 18.1% cardiomyopathy (22). Most HF patients in SSA have a median hospital stay of 7 days (5–10 days) (22). In addition, most of the patients present with comorbidities such as renal dysfunction (7.7–11%) (19, 20, 22), diabetes (11.4–29%) (19, 22), HIV (Human immunodeficiency virus) (13%) (22), hypertension (64%) (19), anaemia (15.2%) (22), and atrial fibrillation (18.3%) (22).

Globally, HF is estimated to cause 16.5% of all deaths with 34% and 23% of the deaths being in Africa and India respectively (19). In SSA, HF causes deaths of 3.9%–25.2% of patients in hospital (22-24). At KNH, mortality is 10.7 % among patients with acute HF (21). The 5-year survival rate is estimated at between 50%–60% in most high-income countries (17).

HF is managed using loop diuretics, aldosterone antagonists, angiotensin converting enzyme inhibitors and angiotensin receptor blockers (ACEI/ARBs), digoxin, loop diuretics, beta blockers, angiotensin receptor neprilysin inhibitors (ARNI) (22, 23,25). The management

involves prevention and control of modifiable risk factors like alcohol and tobacco use, elevated blood glucose and blood pressure and physical inactivity (26).

HF costs an estimated $108 billion per annum globally with a per capita cost of $24/annum in 2012 (27). High income countries (HIC) spend more on direct costs while Low and middle income countries (LMICs) on indirect cost (27).

2.2 Thyroid Dysfunction

Five to ten per cent of the general population have thyroid disorder, females have a higher prevalence. Thyroid hormone metabolic dysfunction can lead to HF. Hypothyroidism and hyperthyroidism alter the cellular and molecular pathways and lead to myocardial remodeling and HF.

2.2.1 Prevalence and Patterns of Thyroid Dysfunction

Thyroid dysfunction in Africa occurs in 1.2% - 9.9% of the general population (28). In Ethiopia, the prevalence of thyroid dysfunction among patients with an anterior neck mass is 65.2%, with the most prevalent subtype being SCH at 19.2% (29). In Europe, 6.7% of the population has undiagnosed thyroid dysfunction. All the types of thyroid dysfunctions were more common among females than males (28). In Germany, the prevalence increased from 7.6% to 18.9% between 2000 and 2010 (30). The prevalence of thyroid medication use and goitre in Germany increased from 6.2% to 11.1% and decreased from 35.1% to 29.4% respectively (30). In Cambodia, the prevalence is estimated at 24.5% (31) while the prevalence is estimated at 26% with one male for every five females having a thyroid dysfunction in Nepal (32). The prevalence is estimated at 31.2% in a Nigerian study on patients who underwent a thyroid function test (33).

2.2.2 Hyperthyroidism

Overt primary hyperthyroidism is a low serum TSH concentration and a high serum free thyroxine concentration (34). The age of onset and duration of severity of thyroid hormone dysfunction determines the clinical manifestations (34, 35).

In Europe, a meta-analysis estimated the prevalence of undiagnosed hyperthyroidism at 1.7% and incidence rate at 51 per 100000 per year (36). The prevalence of hyperthyroidism was estimated at 0.6% in Cape Town, South Africa with approximately 67% being undiagnosed cases (37). In Nigeria, the subclinical and overt hyperthyroidism is estimated at 4.1% (0.8% in males and 3.4% in females) and 13.7% (1.5% in males and 3.4% in females) respectively (33). Euthyroid hyperthyroxinaemia and euthyroid sick syndrome is estimated at 0.3% and 1.5% (33).

Hyperthyroid patients are diagnosed using both clinical (history taking and physical examination) and biochemical manifestations of the disease. The thyroid function tests are the main laboratory test needed but some patients require a lipid profile due to tendencies by hyperthyroid patients to have low cholesterol levels (35, 38). Physical examination of a hyperthyroid patient will reveal increased size of the thyroid gland, stare and lid lag, warm and moist skin and tachycardia with tremors and limitation of eye movement (35, 38).

Patients with overt hyperthyroidism have many manifestations that vary ,increased appetite, weight loss, tremors and palpitations, weakness, and anxiety (35, 38). Mild hyperthyroidism shows few localized and one-organ symptoms including weight loss, myopathy, gynecomastia, and menstrual disorders (3, 35-39). Hyperthyroid patients tend to have low total cholesterol, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) due to increased metabolism of lipids and fatty acid clearance (3, 39). Table 1 outlines the diagnostic criteria for different patterns of thyroid dysfunctions.

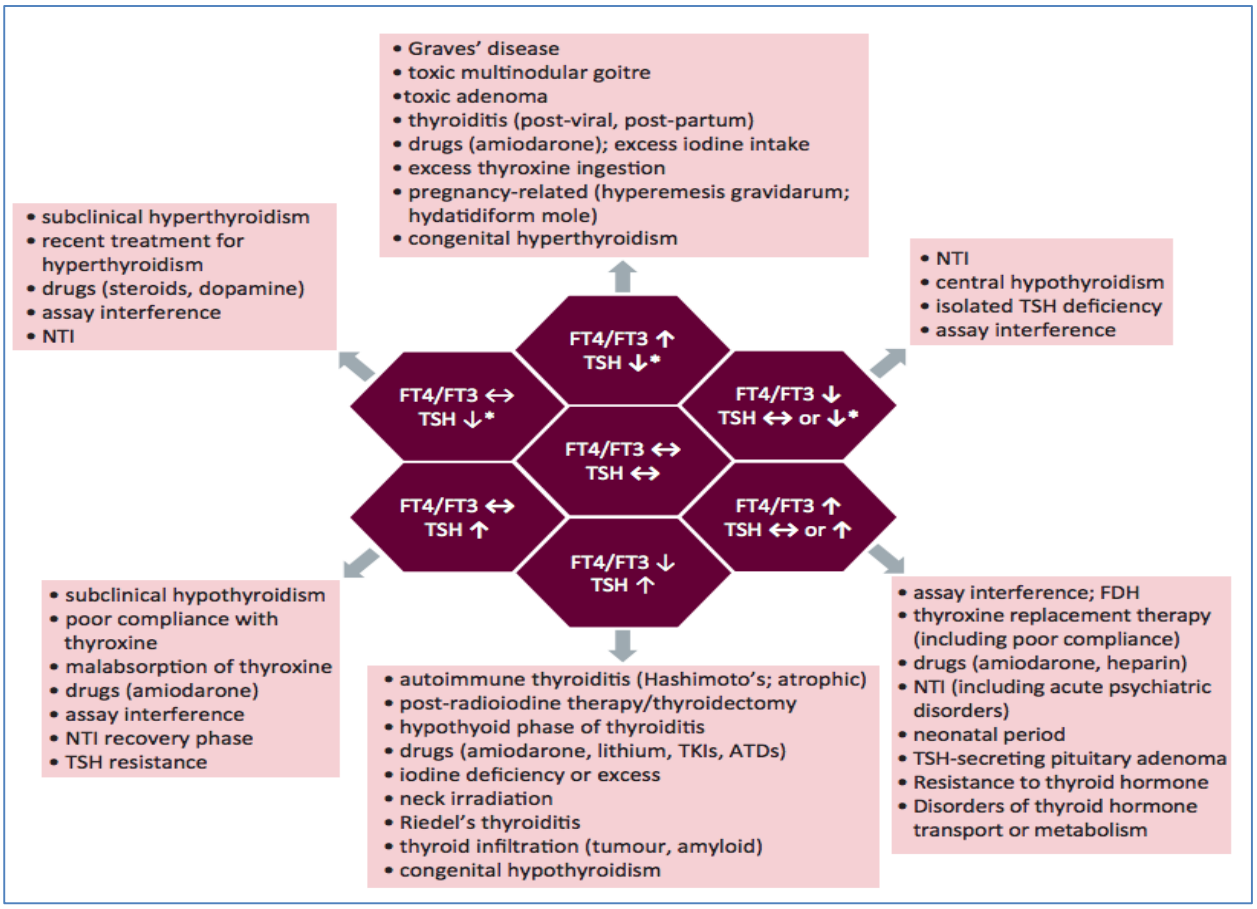


Figure 1. Patterns of thyroid function tests and their causes

Table 1. Diagnostic criteria for hyperthyroidism subtypes

Hyperthyroidism Subtypes	**Diagnostic Criteria**
'Overt hyperthyroidism'	"Low serum TSH; High free T4 and/or T3"
'T3-toxicosis'	"High serum T3"
"T4-toxicosis"	"Low TSH; High serum free T4; Normal T3"
"Subclinical hyperthyroidism"	"Low serum TSH; Normal serum free T4, T3 and free T3"
'TSH-induced hyperthyroidism'	"Normal or high serum TSH; High free T4 and T3"

2.2.3 Hypothyroidism

Overt hypothyroidism has a global cumulative incidence of 33–55% (40). The risk of developing overt hypothyroidism is high among people with history of thyroid problems, those on thyroid dysfunction inducing drugs, older (>60 years), anti-thyroid peroxidase antibody and high initial TSH (>10 mU/L) (41). In a study of prenatal screening for overt hypothyroidism, 2 per 1000 women had overt hypothyroidism (42).

2.2.4.1 Subclinical Hypothyroidism (SCH)

SCH is asymptomatic normal serum free thyroxine concentration in presence of an elevated serum TSH concentration (43). It is caused by Hashimoto's thyroiditis, external radiation therapy in blood cancers, and inadequate T4 replacement therapy (43). In 2–28% of the cases, it progresses to overt hypothyroidism (40, 45), and is associated with coronary heart diseases (10), HF and stroke (44) and cardiovascular mortality (45, 46). It is also associated with abnormalities of the reproductive health system such as amenorrhoea and oligomenorrhoea (47), non-fatty liver disease and neuropsychiatric symptoms (48, 49). In Taiwan, a study found that hypothyroidism is associated with reduced estimated glomerular filtration rate (eGFR) with a higher risk for developing chronic kidney disease (CKD) than euthyroid patients (50).

In a pregnancy loss hypothyroidism study, 8.4% and 3.1% of the women had subclinical and undiagnosed overt hypothyroidism (51). The prevalence of SCH is 30.6% among patients with CKD on haemodialysis in Karachi, being higher among females (46.2%) and those aged 40 years and above (46.2%) (52). Among a sample of 12,900 patients with SCH in the United Arabs Emirates, 6.5% progressed to overt hypothyroidism over 10-years (53).

Treatment of hypothyroidism focuses on improving symptoms, normalizing TSH secretion, reducing the size of the goitre and avoiding overtreatment (54). Synthetic thyroxine is the treatment of choice (54).

2.2.4.2 Drug induced Thyroid Dysfunction

Drug use could result in altered thyroid metabolism and reduce TSH levels in the body. High doses of glucocorticoids, dopamine/dobutamine, imatinib, and octreotide can lower the level of TSH but do not cause clinically significant thyroid dysfunction. Antiepileptic medications such as carbamazepine reduce the triiodothyronine (T3) and thyroxine (T4) half-lives, oestrogens reduce free thyroxine (FT4) availability while glucocorticoids and amiodarone inhibit or impairs the deionisation of T4 to T3 (55, 56). Amiodarone, a drug used to treat cardiac arrhythmias, with a 50-100 days elimination half-life can cause amiodarone-induced thyrotoxicosis or hypothyroidism (12, 57).

2.2.4.3 Laboratory Evaluation of Thyroid Function

The thyroid hormone controls the TSH, which regulates the secretion of thyroxine and triiodothyronine (38). Thyroid function is measured best using the serum TSH since serum free T4 and TSH have a negative log-linear relationship. However, either one or more of the serum TSH, serum total T4, serum total T3 and serum free T4/T3 concentrations could be used to assess thyroid function.

TSH concentration are measured using chemiluminometric assays, which have a detection limits of 0.01mU/L and thus able to detect mild hyperthyroidism and distinguish overt hyperthyroidism from euthyroid patients. The serum total T4 and T3 can be measured using the chemiluminometric assays and RIA (Radioimmunoassay) among other immunoassays. Serum T4 Is bound to thyroxine-binding globulin while serum T3 is bound more on albumin than thyroxine-binding globulin.

The thyroid function test is used clinically to screen patients at risk or strongly suspected to have thyroid dysfunction, monitor treatment of hyperthyroidism, and assess the adequacy of levothyroxine therapy. The thyroid function test helps adjust levothyroxine replacement therapy effectively in patients with primary hypothyroidism and thyroid cancer.

2.3 Thyroid Dysfunction and HF

Hypothyroidism leads to a cardiac output decrease by 30–50% (12). Overt and SCH is linked to bradycardia, fatigue, death and hospital admissions in HF patients (13). A one-fifth to a third of HF patients have thyroid dysfunction (4,58) while 4% to 35% have SCH (4,59). A prospective study of 114 HF patients found a prevalence of 30% in India (60). Patients with HF tend to have a higher prevalence of SCH than hyperthyroidism (4, 5, 58, 60). Table 2 summarises some of the prevalence studies on thyroid dysfunctions among HF patients.

Thyroid hormone has significant effects to the cardiovascular system increasing the heart rate, cardiac output, oxygen consumption in the myocardium and diastolic relaxation (3, 59). The actions of T3 can produce adrenergic effects and inotropic and chronotropic stimulation. Hyperthyroidism causes a reduction of phospholamban and systemic vascular resistance and increases the myocardial sarcoplasmic reticulum calcium-dependent ATP (Adenosine triphosphate) resulting in cardiac output increase, diastolic relaxation, and cardiac contractility (6).

Hyperthyroidism is also related to an increase in other cardiovascular disorders such as hypertension, HF, and angina. Hyperthyroid patients have premature supraventricular depolarizations, and tachycardia. Unmanaged atrial fibrillation in hyperthyroid patients complicates to HF (3, 6, 59).

Table 2. Summary of prevalence studies on thyroid dysfunction in HF patients

Country	Study Design	Sample Size	Prevalence
America (61)	Cross- sectional	132	Thyroid dysfunction – 7% Low T3 syndrome – 34%
Japan (4)	Prospective	274	SCH – 21% Subclinical hyperthyroidism – 2% Low T3 syndrome – 35%
Saudi Arabia (58)	Cross sectional	111	Hypothyroidism – 33.3% SCH – 14.4%
America, Canada, New Zealand (13)	Randomized controlled trial	2225	Thyroid dysfunction – 13% Hypothyroidism – 12% Hyperthyroidism – 1%
India (60)	Prospective	114	Thyroid dysfunction – 30%
China (59)	Prospective	458	Thyroid dysfunction – 19% Low T3 syndrome – 4%

2.3.1 Hyperthyroidism and HF

Hyperthyroidism results in a rate-related cardiomyopathy among patients with HF with no underlying cardiac condition (62). Overt hyperthyroidism has been associated with pulmonary hypertension (44). Hyperthyroidsm increases the risk of atrial fibrillation (7). About 10%–25% of hyperthyroid patients have atrial fibrillation, majority of these being above 60 years (63). Hyperthyroidsm is associated with coagulation abnormalities increasing the risk of cardiac blood clot formation in patients (64).

2.3.2 Hypothyroidism and HF

Hypothyroidism causes a 30–50% decrease in cardiac output (12), increased mortality and hospitalization in HF patients (13). Hypothyroidism almost has an opposite effect on the heart compared to hyperthyroidism. Reduced cardiac contractility in hypothyroid patients results in reduced ventricular diastolic relaxation and decreased cardiac output (12, 62, 63). Patients with hypothyroidism show the following clinical manifestations of cardiovascular disease: bradycardia, non-pitting oedema, pericardial effusions, hypertension and exertional dyspnoea and exercise intolerance (12, 62, 63).

Furthermore, the hypothyroid patients tend to have high cholesterol levels. The elevated cholesterol levels as well as the diastolic hypertension among other factors increase the likelihood of coronary heart disease (64, 65). Hypothyroid patients have decreased LDL catabolism. These patients also have increased oxidation of LDL, and decreased cholesterol secretion into bile and transfer of cholesteryl ester (64).

2.3.3 Outcome of Thyroid Dysfunction in HF

The risk of mortality is increased 1.58 times in patients with symptomatic HF and abnormal thyroid function (13) relative to those without thyroid dysfunction. Also, HF patients are known to have poor prognosis when diagnosed with SCH (7, 66). A study found that the likelihood for mortality and admissions to hospital is increased in patients with SCH and HF (67). HF progression is increased significantly among patients with hypothyroidism (68).

2.4 Study Purpose

The aim of the study was to determine the burden of thyroid dysfunction and its association with the severity of HF in ambulatory HF patients attending adult outpatient cardiac clinic at KNH.

2.5 Study Significance

The proportion of HF patients has increased over the years forming 5.7% of all medical admissions at KNH (21). The rates of thyroid dysfunction are also high especially as a comorbidity. Several studies have shown that thyroid dysfunction and HF are related. However, in Africa and Kenya specifically, little has been done to study this relationship. The lack of local evidence to inform national clinical guidelines on the burden and the management of thyroid dysfunction in HF is of concern necessitating this study. The study contributes to evidence on thyroid dysfunction in HF by highlighting the magnitude of thyroid dysfunction among HF patients, which could inform review or development of clinical guidelines based on local evidence.

2.6 Scope of the Study

The study assessed the thyroid function in ambulatory HF patients attending cardiac clinic at KNH. It involved measurement of the thyroid function test and collection of sociodemographic data and clinical history of HF patients.

2.7 Research Question

What is the burden of thyroid dysfunction in ambulatory HF patients attending adult outpatient cardiac clinic at KNH?

2.8 Study Objectives

2.8.1 Broad Objective

To determine the prevalence of thyroid dysfunction and its association with the severity of HF in ambulatory HF patients attending adult outpatient cardiac clinic at KNH.

2.8.2 Specific Objectives

The primary objective of the study was:

i) To determine the prevalence of thyroid dysfunction in ambulatory HF patients attending the adult outpatient cardiac clinic at KNH.

The secondary objectives of the study were:

i) To determine the subtypes of thyroid dysfunction in ambulatory HF patients attending adult outpatient cardiac clinic at KNH.
ii) To determine the association between thyroid dysfunction and the severity of HF based on New York Heart Association functional class, early HF (class I and II), advanced HF (class III).

CHAPTER THREE: METHODOLOGY

3.1 Study Design

A descriptive cross-sectional study design.

3.2 Study Area

The study was conducted at the outpatient cardiac clinic of the KNH. KNH is the level six national referral hospital with an 1,800-bed capacity, offering both inpatient and outpatient services including specialized care.

3.3 Study Population

Ambulatory HF patients on follow-up at the KNH cardiac clinic, based on Framingham's criteria

3.4 Eligibility Criteria

3.4.1 Inclusion Criteria

- diagnosed with HF
- above 18 years
- written informed consent

3.4.2 Exclusion Criteria

- structural heart disease as the aetiology of HF based on echocardiogram findings.
- patients on amiodarone therapy.

3.5 Sample Size

A sample size for a single proportion was used (69) using an estimated prevalence of thyroid dysfunction as 30% based on an Indian study (60) (a 5% error margin and 95% confidence level. Due to a small study population, the sample will be adjusted for infinite population and a 20% non-response rate to ascertain the correct sample. The sample size was determined as follows: $\mathbf{n= (z^2\, p\, q)/d^2}$

Where:

n = minimum sample size

Z = standard deviation correspondence to 95% confidence level (1.96)

p = thyroid dysfunction prevalence among ambulatory HF patients (30% in India)

d = 0.05 (Level of precision at 5%)

n = $(1.96)^2$ x 0.30 x (1–0.30) / 0.05^2 = 329

The sample size is adjusted for the smaller study population of 4000

n (adj)= (Nxn)/(N+n) = **304 patients**

3.6 Sampling Techniques

On the day of the clinic patients' files were reviewed, those with a diagnostic label of HF based on Framingham's criteria were consecutively sampled, those with structural heart disease based on echocardiogram findings and on amiodarone treatment were excluded.

3.7 Data Collection Tool

A structured, researcher-administered tool with three sections; demographic data, clinical history and anthropometric and laboratory test was used.

3.8 Data Collection Procedures

All the consecutively sampled and consenting patients were provided with information about the study including the purpose, benefits and risks involved by taking part in the study. The patients then signed a written informed consent after reading and asking questions.

The data collection tool was administered to the patient by the researcher. Anthropometric measurements were taken using calibrated clinic equipment and recorded. The patients were informed of the thyroid function test and how it will be performed. A sample of whole blood was then drawn using aseptic techniques and collected through a venepuncture. The sample

was labelled appropriately and tested at the UoN paediatrics laboratory in KNH for thyroid function tests.

All the tests were performed as per the standard operating procedures for specimen collection, preparation, and storage at KNH. Both internal quality control measures (using liaison test control kits done daily) and external quality control measures (done quarterly) were performed to assure the results of the study.

3.8.1 Thyroid Function Test

Chemiluminometric assay was used to measure thyroid hormone T_3, T_4, and TSH levels using the Liaison test kits. Chemiluminometric assays, have a detection limit of 0.01mU/L and thus able to detect mild hyperthyroidism and distinguish overt hyperthyroidism from euthyroid patients. Aseptically collected whole blood through venepuncture and centrifuged at 3000 rpm was used to determine hormones concentration in human serum/plasma. Reference values: fT3 (2.2–4.2) pg/ml, fT4(0.8–1.7) ng/dl, TSH (0.3–3.6) Uiu/ml.

3.9 Case Definition

Patients diagnosed based on Framingham's HF criteria (70) to have HF as recorded in the medical files were included.

The elevated levels of the hormones T_3, T_4, and TSH was based on the following cut-offs: fT3 (2.2–4.2) pg/ml, fT4 (0.8–1.7) ng/dl, TSH (0.3–3.6) Uiu/ml. The thyroid dysfunction was categorised into seven groups (subclinical hyper- and hypothyroidism; overt hyper- and hypothyroidism; secondary hyper- and hypothyroidism, and euthyroid sick syndrome) as highlighted in Table 3.

Table 3. Classification of Thyroid Dysfunction

Thyroid dysfunction	Characteristics of failure
SCH	"Increased TSH and normal fT3 and fT4"
Primary (overt) hypothyroidism	Reduced fT3 and fT4 and increased TSH
Secondary hypothyroidism	"Reduced TSH, fT3 and fT4"
Subclinical hyperthyroidism	"Reduced TSH and normal fT3 and fT4"
Primary (overt) hyperthyroidism	Reduced fT3 and fT4 and reduced TSH
Secondary hyperthyroidism	Increased TSH, fT3 and fT4
Euthyroid sick syndrome	Normal TSH and fT4 and reduced fT3

3.10 Study Variables

3.10.1 Dependent Variable

The dependent variable is thyroid dysfunction.

3.10.2 Independent Variables

The independent variable is the NYHA functional class.

3.11 Data Entry, Validation, Handling and Storage

Completed data collection tool were reviewed for accuracy and data entered in Microsoft Excel worksheet that was protected using a password known to researcher only. The anonymised data is accessible to the research team and all the signed consent forms and data were placed under lock and key within a room with limited access for a minimum period of five years.

3.12 Statistical Analysis

The data entered on a Microsoft Excel worksheet were imported onto STATA 15 (College Station, TX, USA) for further analysis. To characterize the sample, median and interquartile range and percentages were used for continuous and categorical variables. The overall prevalence was estimated. The relationship between severity of HF-based on the NYHA functional class, class I and 11 (early HF), class 111 (advanced HF) and thyroid dysfunction were assessed using chi-square test.

3.13 Quality control procedures

The quality assurance was run intermittently as data entry was ongoing. The research assistants were trained on the interview process, data abstraction and study procedures prior to commencement of the project work. Five millilitres of blood were aseptically drawn from the patients into a well labelled plain bottle. Samples were put into a cool box and transported to the UoN Paediatrics laboratory at KNH. Internal quality control measures (using liaison test control kits done daily) and external quality control measures (done quarterly) were performed to assure the results of the study, with supervision from a Senior Lecturer at the department of Human Pathology, UoN.

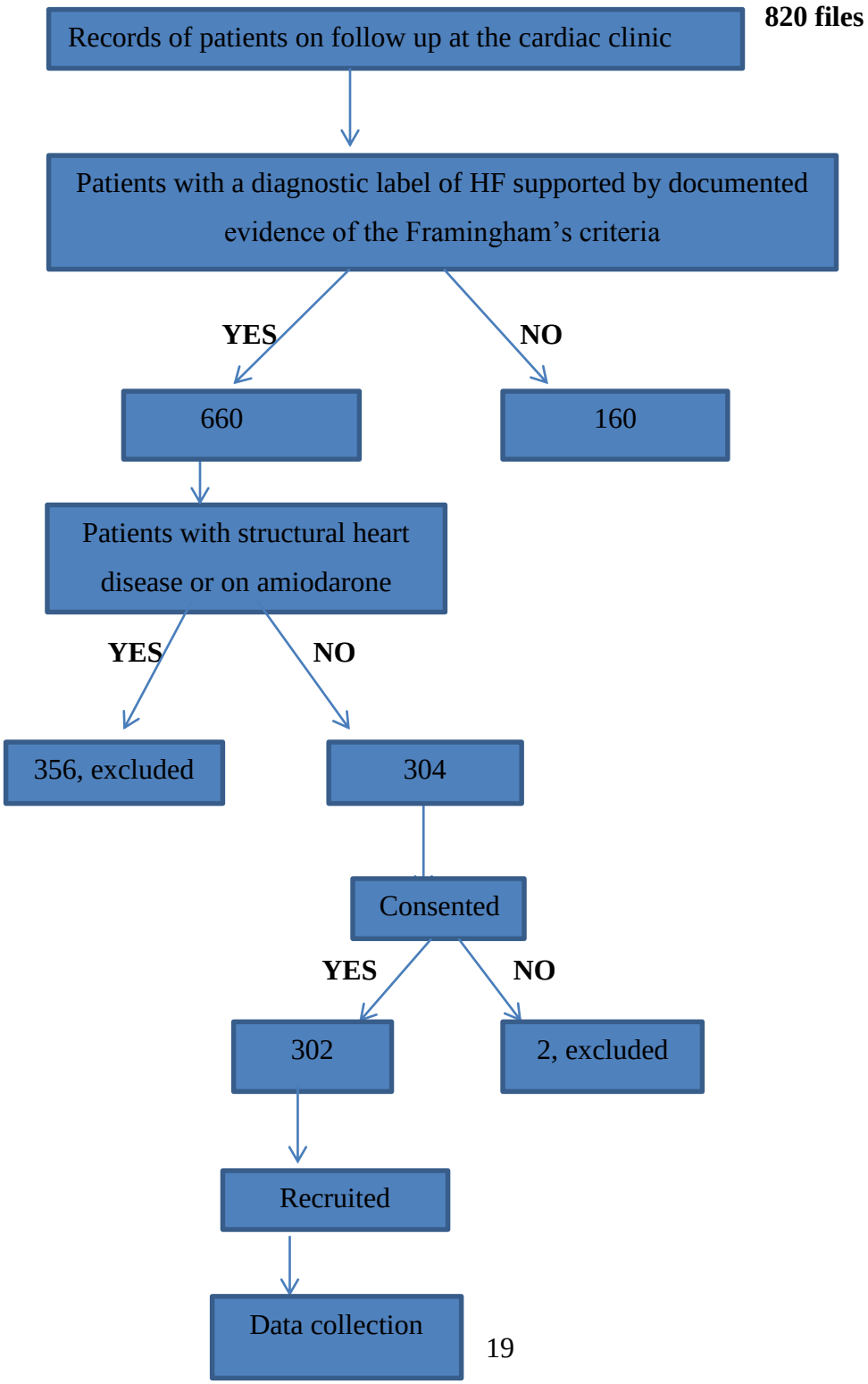
3.14 Ethical Considerations

The KNH / UoN Ethical Review Committee approved the study protocol. All study participants signed a written informed consent after understanding the information provided on the study, its purpose, benefits, and risks. Importantly, the study participants were informed of their rights to voluntarily take part in the study and right to stop taking part in the study without a need to provide a reason at any point during and after the study among other rights. Laboratory tests results were provided to the patients with a copy filed in their records. Patients with thyroid dysfunction were given an earlier appointment date to the cardiac clinic and referred to the endocrinology clinic for follow up. All the data collection tools used were serialized and no information that could identify the patients were collected.

Only the researcher kept and has access to a recruitment log with details of all patients contacted and included in the study while identified data is accessible by the research team.

CHAPTER FOUR: RESULTS

4.1 Recruitment Flowchart



4.2 Sociodemographic and clinical characteristics of ambulatory HF patients

The mean age of the respondents is 60.3 (SD 14.7) years. 62.6% of the respondents are female. 88.7% are married. 36% are overweight and 21% are obese. 76.2% have HF in class I and II. 53.3% of the patients had hypertensive heart disease with 30.8% having dilated cardiomyopathy.

Table 4. Sociodemographic characteristics of ambulatory HF patients

Variables	**Total N=302**	**Male N=113**	**Female N=189**
Age, mean (SD), years	60.3 (14.7)	60.0 (14.9)	60.4 (14.6)
19–34 **n (%)**	15 (5.0)	7 (6.2)	8 (4.2)
35–49	60 (19.9)	20 (17.7)	40 (21.2)
50–64	88 (29.1)	33 (29.2)	55 (29.1)
65–79	121 (40.1)	48 (42.5)	73 (38.6)
80+	18 (6.0)	5 (4.4)	13 (6.9)
Marital status n (%)			
Yes	268 (88.7)	104 (92.0)	164 (86.8)
Occupation n (%)			
Farming	91 (30.1)	34 (30.1)	57 (30.2)
Business	69 (22.9)	31 (27.4)	38 (20.1)
Unemployed	101 (33.4)	22 (19.5)	79 (41.8)
Formal employment	41 (13.6)	26 (23.0)	15 (7.9)
Family History of thyroid disease n (%)			
Yes	23 (7.6)	5 (4.4)	18 (9.5)

IQR: Interquartile range; SD: Standard deviation

Table 5. Clinical characteristics of ambulatory HF patients

Variables	Total N=302	Male N=113	Female N=189
Body Mass Index n (%)			
Underweight	13 (4.3)	5(4.4)	8(4.2)
Normal	119(39.4)	40 (35.4)	79 (41.8)
Overweight	108 (35.8)	50 (44.3)	58(30.7)
Obese	62(20.5)	18 (15.9)	44(23.3)
Severity of HF (NYHA) n (%)			
I	109 (36.1)	44 (38.9)	65 (34.4)
II	121 (40.1)	44 (38.9)	77 (40.7)
III	72 (23.8)	25 (22.1)	47 (24.9)
Causes of HF n (%)			
Hypertensive heart disease	161(53.3)	52(46.2)	109(57.7)
Dilated cardiomyopathy	93 (30.8)	39 (34.5)	54 (28.6)
Ischaemic heart disease	38 (12.6)	19(16.8)	19(10.1)
Cor Pulmonale	9(3.0)	4(3.5)	5(2.7)
Pericarditis	1 (0.3)	1 (0.9)	0
Medication n (%)			
ACEI	165 (54.6)	63 (55.8)	102 (54.0)
Digoxin	74 (24.5)	27 (23.9)	47 (24.9)
Beta Blockers	223 (73.8)	79 (69.9)	144 (76.2)
Aldosterone	103 (34.1)	37 (32.7)	66 (34.9)
Duration since Diagnosis, median (IQR)	3 (1-5)	3 (1-5)	3 (1-5)

IQR: Interquartile range; SD: Standard deviation

4.3 Prevalence of Thyroid Disorders

The overall prevalence of thyroid dysfunction is 36.8% (95% CI: 31.5–42.4). Of those with thyroid dysfunction 66.7% (95% CI: 57.1–75.3) were women and 33.3% (95% CI: 24.7–42.9%) were men. Older adults have a high prevalence of thyroid dysfunction with 49.6% (95% CI:39.9–59.2) and 23% (95% CI: 15.9–32.4) among those aged 65–79 years and 50-64 years. 78.4% of patients with thyroid dysfunction are 50 years and above. Prevalence is 28.8 % (95% CI: 20.6–38.2), 41.4% (95% CI: 32.2–51.2) and 29.7% (95% CI: 21.4–39.1) for patients in HF class 3, 2 and 1, respectively.

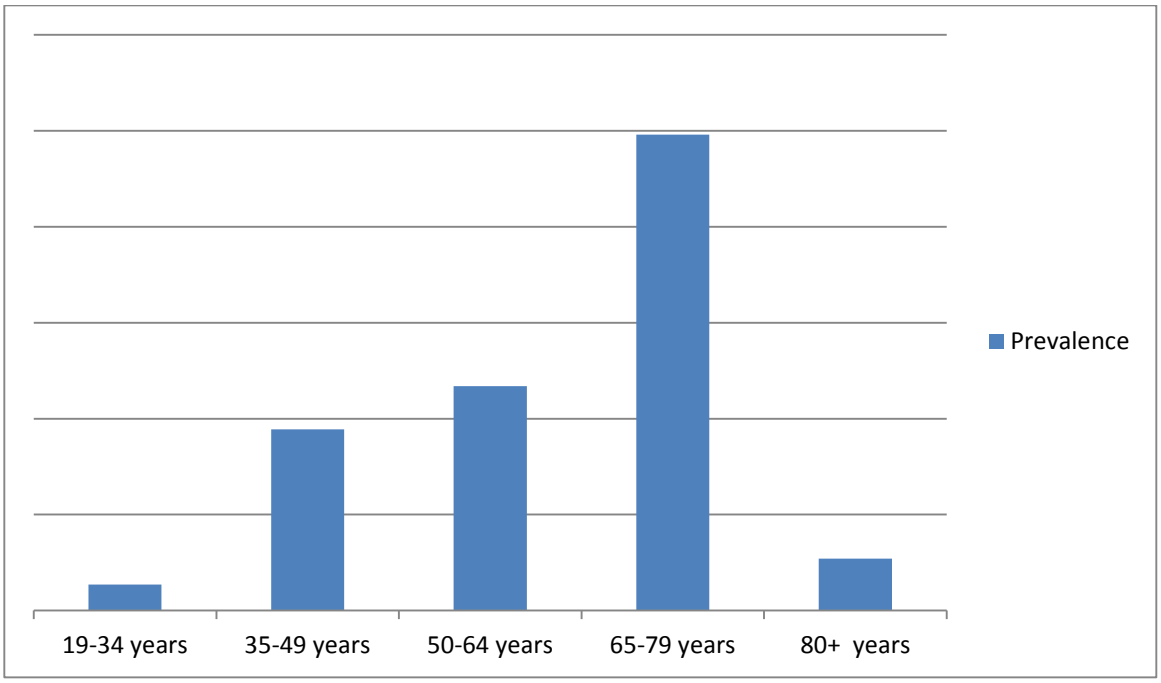


Figure 2: Prevalence of thyroid dysfunction in ambulatory HF patients by age

Table 6. Prevalence of thyroid dysfunction in ambulatory HF patients according to respondents' sociodemographic and clinical characteristics.

Variables	Thyroid Dysfunction		95 % Confidence Interval
	No N=191	Yes N=111	
Age, mean (SD), years	59.0 (15.1)	62.4 (13.8)	
19–34 **n (%)**	12 (6.3)	3 (2.7)	(0.2-2.9)
35–49	39 (20.4)	21 (18.9)	(12.1-27.5)
50–64	62 (32.5)	26 (23.4)	(15.9-32.4)
65–79	66 (34.6)	55 (49.6)	(39.9-59.2)
80+	12 (6.3)	6 (5.4)	(2.0-11.4)
Sex n (%)			
Male	79 (39.8)	37 (33.3)	(24.7-42.9)
Female	115 (60.2)	74 (66.7)	(57.1-75.3)
Body Mass Index n (%)			
Underweight	8 (4.2)	5 (4.5)	(1.48-10.2)
Normal	74 (38.7)	45 (40.5)	(31.3-50.3)
Overweight	73 (38.2)	35 (31.5)	(23.0-41.0)
Obese	36 (19.0)	26 (23.4)	(15.9-32.4)
Severity of HF (NYHA) n (%)			
I	76 (39.8)	33 (29.7)	(21.4-39.1)
II	75 (39.3)	46 (41.4)	(32.2-51.2)
III	40 (20.9)	32 (28.8)	(20.6-38.2)
Causes of HF n (%)			
HHD	104(54.5)	57(51.4)	(41.7-60.9)
DCM	60 (31.4)	33 (29.7)	(21.4-39.2)
Ischemic heart disease	25(13.1)	13(11.7)	(6.4-19.2)
Cor pulmonale	8(4.2)	1(0.9)	(0.00-4.9)
Pericarditis	1 (0.5)	0 (0.0)	(0)

SD: Standard deviation

4.4 Thyroid Dysfunction Subtypes

Subclinical hypothyroidism (18.8%, 95% CI: 14.6–23.8), euthyroid sick syndrome (9%, 95% CI: 6.0–12.7) and primary hypothyroidism (6%, 95% CI: 3.8–9.7) are the most prevalent thyroid dysfunction subtypes. Secondary hyperthyroidism (1.0%, 95% CI: 0.3–3.1), subclinical hyperthyroidism (1.0%, 95% CI: 0.3–3.1), primary hyperthyroidism (0.3%, 95 % CI: 0.1-1.8) and free T3 toxicosis (0.3% 95% CI :0.1-1.8) are the least subtypes of thyroid disorders.

Thyroid dysfunction	**Percentage**	**Confidence interval**
SCH	18.8%	95% CI :14.6-23.8
Euthyroid sick syndrome	9%	95% CI: 6.0-12.7
Primary hypothyroidism	6%	95% CI: 3.8-9.7
Secondary hyperthyroidsm	1%	95% CI: 0.3-3.1
Subclinical hyperthyroidsm	1%	95% CI: 0.3-3.1
Primary hyperthyroidsm	0.3%	95% CI: 0.1-1.8
Free T3 toxicosis	0.3%	95% CI: 0.1-1.8

Table 7. Thyroid dysfunction subtypes

4.5 Association between Thyroid Dysfunction and HF

There is no significant association between thyroid dysfunction and severity of HF based on NYHA functional class, class I and II (early HF), class III (advanced HF).

Table 8. Association between thyroid dysfunction and severity of HF in ambulatory HF patients.

Variables /NYHA	I N=109	II N=121	III N=72	p-value*
Thyroid Dysfunction n (SD)				
No	76 (69.7)	75 (62.0)	40 (55.6)	0.143
Yes	33 (30.3)	46 (38.0)	32 (44.4)	

SD: Standard deviation; * Chi square test of association

CHAPTER FIVE: DISCUSSION

The purpose of the study was to determine the prevalence of thyroid dysfunction in ambulatory HF patients at KNH. The study was conducted at the KNH outpatient cardiac clinic. 302 patients with HF based on Framingham's criteria, without structural heart disease and not on amiodarone were consecutively sampled. The study population consisted of females at 62.6% with a mean age of 60.3 years and had been diagnosed with HF within the last 3 years. 76.2% of the patients are stable in HF class 1 and II and the most common aetiology of HF was hypertensive heart disease at 53.3%. We found a prevalence of thyroid dysfunction of 37%, higher among females at 66.7% and those above 65 years at 55%. The most common subtypes of thyroid dysfunction are SCH at 18.8%, euthyroid sick syndrome at 9% and primary hypothyroidism at 6%.

Chemiluminometric assay was used to measure thyroid hormone fT_3, fT_4, and TSH levels using the Liaison test kits. Chemiluminometric assays, have a detection limit of 0.01mU/L and thus able to detect mild thyroid dysfunction accurately. This is similar to studies done in the west , Hayashi et al in 2016 in a study investigating the prevalence of SCH and cardiovascular outcomes in HF patients and, Kannan et al in 2018 in a study investigating the prevalence of thyroid dysfunction in HF and cardiovascular outcomes also used the chemiluminometric assay method (4, 7).The chemilumminometric assay method is more specific and sensitive than previously used radioimmunoassay (RIA) and enzyme linked immunosorbent assay (ELISA) methods with detection limits of 0.1mU/L, hence unlikely to underestimate our results. The method was chosen for our study as it is readily available and accurate. The reference ranges used were fT3 (2.2–4.2) pg/ml, fT4 (0.8–1.7) ng/dl, TSH (0.3–3.6) Uiu/ml, this is in keeping with global reference ranges. Internal and external quality control measures were adhered to.

Ascheim et al in 2002 in a cross- sectional study investigating the prevalence of thyroid dysfunction in ambulatory HF patients, sampled 132 patients, using the chemiluminometric assay method, the prevalence of thyroid dysfunction was 41%, the mean age of the patients was 67 years and majority were males (61), this is almost similar to our prevalence of 37%, however, majority of our patients were female. Mahesh et al in 2017 in a study to determine

the prevalence of thyroid dysfunction in patients with acute decompensated HF and six months follow up of SCH and low T3 syndrome, sampled 114 patients, used the chemiluminometric assay method, and found a prevalence of 30%, the mean age of the patients was 57 years , this is almost similar to the prevalence in ambulatory HF patients in our study. The global prevalence of thyroid dysfunction in HF is estimated at 21%-33.3% (4, 60), there is no recorded data on the prevalence of thyroid dysfunction in ambulatory HF patients in SSA.

Sub-clinical hypothyroidism, euthyroid sick syndrome and primary hypothyroidism were the most prevalent thyroid dysfunction subtypes in the study. Hayashi et al in 2016 in a prospective study investigating the prevalence and prognostic impact of SCH and euthyroid sick syndrome in HF patients, sampled 274 patients, used the chemiluminometric assay and found SCH and euthyroid sick syndrome as the most prevalent subtypes at 21% and 35% respectively, only 2% of the patients had SCH (4). Subclinical hypothyroidism is usually asymptomatic (43) and progresses to overt hypothyroidism in only 2–28% of the cases (40, 43). However, it is associated with coronary heart diseases (10), HF and stroke (44) and cardiovascular mortality (45, 46).

Hypothyroidism leads to a cardiac output decrease by 30–50% (12). Overt and SCH is linked to bradycardia, fatigue, death and hospital admissions in HF patients (13).

This study did not find a significant association between severity of HF and thyroid dysfunction. This may be due to our smaller size compared to other studies. Unlike our study, Kannan et al in a prospective cohort study of ambulatory HF patients to determine the prevalence of thyroid dysfunction and associations with cardiovascular outcomes, recruited 1365 patients between 2003 and 2011, mean age of the patients was 57 years, the study included patients in HF class I–IV and majority were in class II and III HF. Chemiluminometric assay method was used for the thyroid function test, significant association was found between thyroid dysfunction and severity of HF based on NYHA functional class (7). This study had a smaller sample size, and this may explain the difference in the results.

Use of drugs such as amiodarone could increase the risk of thyroid dysfunction, but patients using amiodarone were excluded from this study.

The prevalence of thyroid dysfunction in ambulatory HF patients is high. The thyroid function test should be readily available and affordable to the patients. Patients with thyroid dysfunction should be referred to an endocrinologist for specialised care. Early detection and treatment of overt thyroid dysfunction in ambulatory HF patients will slow further progression of HF and prevent acute decompensation.

5.1 Study Limitations

1. The lack of a second confirmatory blood test after the baseline test, hence unable to exclude the possibility of transient changes in thyroid function, which may have led to the diagnosis of more patients with euthyroid sick syndrome hence increasing the prevalence or a reduction in the prevalence with resolution of thyroid dysfunction.
2. The study is cross- sectional in nature hence causation cannot be inferred.
3. Small sample size, hence unable to make a concise conclusion on the association between thyroid dysfunction and severity of HF based on NYHA functional class.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

Prevalence of thyroid dysfunction in ambulatory HF patients is high. The most common subtype of thyroid dysfunction is hypothyroidism, with SCH being the most prevalent subtype. There is no significant association between thyroid dysfunction and severity of HF based on NYHA functional class.

6.2 Recommendation

Based on the findings of the study, the following is the recommendation:

1. Thyroid function testing for ambulatory HF patients, focused more on females and those above 65 years.

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APPENDICES

Appendix I A: Patient Information Sheet

Introduction

My name is Dr. Beryl Muyodi. I am a postgraduate student of Internal Medicine at the University of Nairobi. The purpose of this statement is to inform you about a research study I am carrying out. I am doing a study on the prevalence of thyroid dysfunction in ambulatory heart failure patients attending adult outpatient clinic at Kenyatta National Hospital. The purpose of this study is to determine how many heart failure patients have thyroid dysfunction.

Procedures to be followed in the study

Participation in the study is voluntary. Should you accept to take part, the following is a summary of what the study involves:

1) Obtaining your personal information and information on heart failure and any other medical condition you have.

2) Blood pressure and anthropometric measurements will be recorded.

3) A blood sample for thyroid function test will be collected.

This will take 30 minutes of your time.

Risks and costs incurred: There will be minimal pain while withdrawing the blood sample for the laboratory test. No costs will be incurred.

Your rights as a participant: Your participation in this research is voluntary and if you refuse to take part your treatment will not be affected. If you choose to take part and not to answer certain questions you are free to do so. You are free to end the interview and withdraw from the study at any time. You are free to ask questions before signing the consent form.

Assurance of confidentiality

All your responses as well as results will remain confidential. Your individual responses will be stored in a locked place under my control and will be seen by the statistician and I the principal investigator.

Benefits: All the above examination and procedures, shall be done free of charge (the principal investigator shall bear the cost of the laboratory investigations). The results of the thyroid function tests will be put in your file, and if found to have thyroid dysfunction your

primary health physician will be informed, and you will be referred to an endocrinologist for further management.

Compensation

Participants will not receive any monetary compensation for taking part in this study.

Contacts

If you have any questions, please do not hesitate to ask, clarifications may be sought from:

Dr. Beryl Muyodi,

P.O.BOX 81464-80100

Mombasa

Tel: 0711844003

The Secretary

KNH/UON Ethics and Review Committee

Tel: 2726300 Ext: 44102

Appendix I B: Jarida la Maelezo ya Mgonjwa

Utangulizi

Jina langu ni Dr. Beryl Muyodi. Mwanafunzi wa uzamili, idara ya Internal Medicine katika chuo kikuu cha Nairobi. Ninataka kukueleza madhumuni ya utafiti ninayofanya**.** Madhumuni ni kujua mzigo wa ugonjwa wa tezi na uwiano wake na kiwango cha ukali wa ugonjwa wa moyo, miongoni mwa wagonjwa wa moyo wanaohudumiwa katila kliniki ya nje katika hospital ya Taifa ya Kenyatta.

Taratibu za kufuatwa katika utafiti

Ushiriki wako katika utafiti ni kwa hiari yako.Iwapo utakubali kushiriki yanayofuata ni muhtasari ya kile utafiti unahusisha:

1) maelezo yako ya kibinafsi na maelezo kuhusu ugonjwa wa moyo na ugonjwa yoyote mwingine ulionao utachukuliwa.

2) Kipimo cha shinikizo la damu, urefu na uzito wako utachukuliwa

3) Damu ya kupima homoni ya tezi itachukuliwa kwa njia stadi.

Utafiti utachukia dakika 30 ya muda wako

Hatari na gharama: Maumivu kidogo wakati wa kutoa damu, hakuna gharama yoyote kwa mgonjwa.

Haki yako kama mgonjwa: Ushiriki wako katika utafiti ni kwa hiari, na iwapo utakataa kushiriki matibabu yako haitakatizwa. Ukiamua kushiriki na kutojibu maswali fulani uko na uhuru, uko na uhuru wa kusimamisha mahojiano na kujiondoa kutoka kwa utafiti wakati wowote. Uko na haki ya kuuliza maswali kabla ya kutia saini fomu hii.

Usiri: Habari unayotoa na majibu yako yatashughulikiwa kisiri. Habari yako itafungiwa mahali salama na itadhibitiwa na mimi mchunguzi mkuu

Faida: Uchunguzi na taratibu zote zinafanywa bila malipo yoyote kwa mgonjwa (mchunguzi mkuu atagharamia). Majibu yako ya homoni ya tezi yatawekwa katika faili na anayepatikana

na shida ya homoni ya tezi, daktari wako katika kliniki atajulishwa na atatumwa kwa daktari mtaalamu apate matibabu.

Malipo: Hakuna malipo ya kushiriki katika utafiti huu.

Contacts:

Ukiwa na swali yoyote usiogope kuuliza. Utapata ufafanuzi kutoka kwa:

Dr. Beryl Muyodi,

P.O.BOX 81464-80100

Mombasa

Tel: 0711844003

Katibu

KNH/UON Ethics and Review Committee

Tel: 2726300 Ext: 44102

Ukitia saini hapa chini unadhihirisha ya kwamba umesoma fomu hii ya ridhaa ya utafiti na umekubali kushiriki katika utafiti huu kwa hiari yako. Kama hutaki kushiriki tafadhali rudisha fomu ya ridhaa.

Appendix II A: Consent Form

Study Title: Thyroid hormone profile in ambulatory HF patients attending adult outpatient clinic at Kenyatta National Hospital.	
Principal Investigator: Dr. Beryl Muyodi	Study site: Kenyatta National Hospital

If you agree with each statement, please INITIAL the box provided	
1.I confirm I have read or been explained to and understood the information sheet dated…… for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2.I understand that participation in this study is voluntary and I am free to withdraw consent at any time, without giving a reason, without any penalties	
3. I understand that data collected during the study may be looked at by individuals from KNH, UON and from regulatory authorities. I give permission for these individuals to have access to my records	
4.I understand that if I change my mind about taking part in this study, I can withdraw at any time and this will not have any consequences	
5. I hereby declare that I have not been subjected to any form of coercion in giving this consent	

6.I agree to the data about me collected in this study being stored for further use in the future	
7. I agree that I will receive no incentives to take part in the study	
8. I agree to take part in this study	

Signing this declaration does not affect your right to decline to take part in any future study

Name of

Participant…… Date……..Signature……

Name of

Person taking consent…….....Date……...Signature……

Appendix II B: Fomu ya Idhini

Jina la utafiti: Homoni ya tezi miongoni mwa wagonjwa wa moyo wanaohudhuria kliniki katika hospitali ya Taifa ya Kenyatta.	
Mpelelezi mkuu:Dr. Beryl Muyodi	Eneo la utafiti:Hospitali ya Taifa ya Kenyatta

Ikiwa unakubaliana na kila kauli tafadhali idhinisha kwenye sanduku	
1.Ninadhibitisha kuwa nimesoma au nimeelezwa na kuelewa karatasi ya habari iliyooidhinishwa……kwa utafiti huu. Nilikuwa na fursa ya kuzingatia habari, kuuliza maswali, na kupata majibu ya kuridhisha	
2. Ninaelewa kuwa kushiriki katika utafiti huu ni kwa hiari na niko huru kujiondoa wakati wowote, bila kutoa sababu, bila adhabu yoyote	
3.Ninaelewa kwamba data zilizokusanywa wakati wa utafiti zinaweza kuonekana na watu kutoka KNH,UON, na kutoka kwa mamlaka ya udhibiti. Ninawapa ruhusa watu hawa kuwa na upatikanaji wa rekodi zangu	
4.Ninaelewa kuwa iwaapo nitabadili maoni yangu kuhusu kushiriki katika utafiti huu, naweza kujondoa wakati wowote nah ii haitakuwa na matokeo yoyote	
5.Mimi natangaza kwamba sijalazimishwa kwa njia yoyote kutoa ridhaa hii	
6. Nakubaliana na data kunihusu zilizokusanywa katika utafiti huu kuhifadhiwa kwa matmizi zaidi baadaye	
7.Nakubali ya kwamba sitapokea msukumo wa kushiriki katika utafiti	
8. Nakubali kushiriki katika utafiti huu	

Kutia saini kauli hii hakuathiri haki yako ya kukataa kushiriki katika utafiti wowote ujao

Jina la mshiriki……Tarehe…….Sahihi

Jina la anayechukua ……Tarehe…….Sahihi

Idhini

Appendix III A: Data Collection Tool

1. Patient file number	
2. Patient contact number	
3. Age (years)	
4. Sex	Male Female
5. Marital Status	Yes/No
6. Occupation	
7. Current weight(kg)	
8. Current height(cm)	
9. Family History of Thyroid Disorder	Yes / No
10. Current medications	ACEI Digoxin Beta blockers Aldosterone Amiodarone Others (specify)_____
11. Duration (years) since HF diagnosis	
12. Causes of HF	
13. NYHA functional class	I II III IV
14. Symptoms of thyroid dysfunction (weight loss/gain, diarrhoea/constipation, heat or cold intolerance, anxiety, irritability, fatigue, low mood, hyperactivity.	Yes/No
15. History of thyroid dysfunction	Yes/No
16. Duration of thyroid dysfunction(years)	
17. Thyroid function test results FT3- FT4- TSH-	

Appendix III B: Chombo cha Kukusanya Habari

1.Nambari ya faili ya mgonjwa	
2.Nambari ya simu ya mgonjwa	
3.Umri (Miaka)	
4.Jinsia	Kiume Kike
5.Hali ya ndoa	Ndiyo/Hapana
6.Kazi	
7.Uzito(kilo)	
8.Urefu(sentimita)	
9.Historia ya familia ya ugonjwa wa tezi	Ndiyo/Hapana
10. Dawa unazotumia kwa sasa	ACEI Digoxin Beta blockers Aldosterone Amiodarone Others (specify)_____
11.Muda (miaka) tangu kutambuliwa kwa ugonjwa wa moyo	
12.Chanzo cha ugonjwa wa moyo	
13.Ukali wa ugonjwa wa moyo (NYHA)	I II III IV
14. Dalili za ugonjwa wa tezi (kuongeza/kupunguza kilo,kuhara/kuvimbiwa,shida ya joto au baridi,uchovu,wasiwasi,hasira,huzuni,uharibifu	
15.Historia ya ugonjwa wa tezi	Ndiyo/Hapana
16.Muda (miaka) wa ugonjwa wa tezi	
17.Matokeo ya kipimo ya homoni ya tezi FT3- FT4- TSH-	