Original paper

Thyroid Hormone Profile in Ambulatory Heart Failure Patients attending Adult Outpatient Clinic at Kenyatta National Hospital, Nairobi, Kenya

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Abstract

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

Objectives: To determine the prevalence of thyroid dysfunction and it's correlation with the severity of heart failure in ambulatory heart failure patients attending adult outpatient clinic at Kenyatta National Hospital, Nairobi, Kenya..

Design: A descriptive cross-sectional study design of ambulatory patients with heart failure attending the outpatient cardiac clinic at the Kenyatta National Hospital.

Methods: Ambulatory heart failure patients with a diagnostic label of heart failure 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 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 heart failure based on the New York Heart Association functional class, class 1 and 2 (early heart failure), class 3 (advanced heart failure) and thyroid dysfunction were assessed using Pearson's chi-square test.

Results: Three hundred and four patients were sampled, two declined consent and 302 were recruited into the study. Most of the heart failures were caused by Hypertensive Heart Disease (HHD) (53.3%) and Dilated Cardiomyopathy (DCM) (30.8%). Seventy six point two percent had heart failure 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 were 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 heart failure class III, II and 1 respectively.

Subclinical hypothyroidism was 18.8%, (95% CI:14.6; 23.8), euthyroid sick syndrome was 9%, (95% CI: 6.0; 12.7) and primary hypothyroidism was 6%, (95% CI: 3.8; 9.7) were the most prevalent thyroid dysfunction subtypes. Secondary hyperthyroidism was 1.0%, (95% CI: 0.3; 3.1), subclinical hyperthyroidism was 1.0%, (95% CI:0.3; 3.1) , primary hyperthyroidism was 0.3%, (95% CI:0.1; 1.8) and free T3 toxicosis was 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 heart failure based on New York Heart Association functional class.

Conclusion: Prevalence of thyroid dysfunction in ambulatory heart failure patients is high. The most common subtype of thyroid dysfunction is hypothyroidism, with subclinical hypothyroidism being the most prevalent subtype. There is no significant association between thyroid dysfunction and severity of heart failure based on New York Heart Association (NYHA) functional class.

Key words: Ambulatory heart failure, Thyroid dysfunction, Subclinical hypothyroidism, New York Heart Association functional class, Chemiluminometric assay

Introduction

Heart failure affects approximately 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 heart failure patients, 21%–33.3% are estimated to have thyroid dysfunction (4).

Thyroid dysfunction is related to the development of heart failure (5-7). Hypothyroidism and hyperthyroidism alter cellular and molecular pathways and lead to myocardial remodelling and heart failure (5). Overt and subclinical hyperthyroidism is linked to a high risk of heart failure 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 heart failure patients (13). Overt and subclinical hypothyroidism are associated with bradycardia, mild hypertension, increased systemic vascular resistance and fatigue (13). Thyroid dysfunction can lead to heart failure (5-7). It can lead to atrial fibrillation resulting in acute decompensation of the heart failure (7). Hypothyroidism has been associated with mortality increase and hospitalization among heart failure patients (13). However, despite the known relationship between thyroid dysfunction and heart failure, there is still a paucity of evidence on the burden of thyroid dysfunction in heart failure and their association in the Kenyan population. Knowledge of the burden of thyroid dysfunction in heart failure is essential in guiding clinical decision making and improving outcomes in heart failure patients.

Materials and methods

This was a cross sectional study involving 302 patients aged 18 years and above with ambulatory heart failure from the cardiac clinic at Kenyatta National Hospital, and was carried out between November and January 2020. Consecutive sampling was used to recruit patients who met the inclusion criteria. Patients with a diagnostic label of heart failure based on Framingham's criteria were included. Patients with structural heart disease (congenital and rheumatic heart disease), and those on amiodarone were excluded. Written informed consent was obtained from all the participants in the study. A data collection tool was used to collect history from the patients, this included there socio-demographic, medical history and anthropometric measurements. Blood specimen for thyroid function test was collected from the patients. Laboratory measurements of the blood samples for thyroid function test were handled as per the hospital standard operating procedures and delivered to the laboratory and tested within four hours. The blood specimen for thyroid function test was taken to the University of Nairobi Paediatrics Laboratory. This laboratory undergoes both internal and external quality control measures.

The main objective of the study was to determine the prevalence of thyroid dysfunction in ambulatory heart failure patients. The secondary objectives were to determine the subtypes of thyroid dysfunction and the association between thyroid dysfunction and the degree of heart failure based on New York Heart Association functional class (NYHA).

STATA version 15 was used to analyse cleaned data. Median, interquartile ranges and percentages were used for continuous and categorical variables. Thyroid dysfunction was categorized into seven groups ; primary and secondary hyperthyroidism, primary and secondary hypothyroidism, subclinical hypothyroidism, subclinical hyperthyroidism and euthyroid sick syndrome. Association between thyroid dysfunction and severity of heart failure based on NYHA functional class was assessed using the chi square test. The study was approved by the Ethics and Research Committee of the Kenyatta National Hospital and University of Nairobi.

Results

Socio-demographic and clinical characteristics of ambulatory heart failure patients

The mean age of the respondents was 60.3 (SD 14.7) years. Sixty two point six percent of the respondents were female. Eighty eight point seven percent were married. Thirty six percent were overweight and 21% were obese. Seventy six point two percent had heart failure in class I and II. Fifty three point three percent of the patients had hypertensive heart disease with 30.8% having dilated cardiomyopathy.

Table 1: Socio-demographic characteristics of ambulatory heart failure 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 2: Clinical characteristics of ambulatory heart failure 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 heart failure (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 heart failure 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

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. Seventy eight point four percent of patients with thyroid dysfunction are 50 years and above. Prevalence 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 heart failure class 3, 2 and 1 respectively.

Figure 1: Prevalence of thyroid dysfunction in ambulatory heart failure patients by age

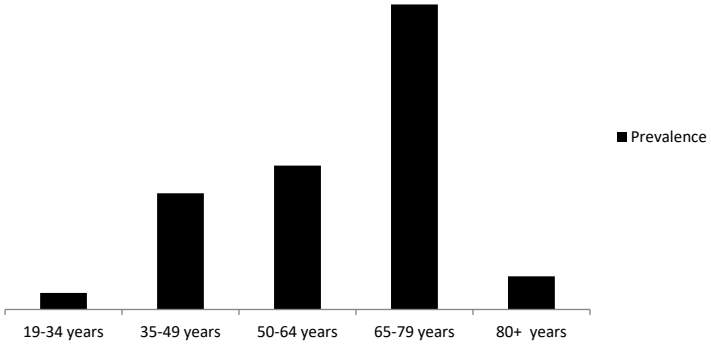

Table 3: Prevalence of thyroid dysfunction in ambulatory heart failure patients according to respondents' socio-demographic and clinical characteristics

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 Heart Failure (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 heart failure n (%)			
Hypertensive heart disease	104(54.5)	57(51.4)	(41.7-60.9)
Dilated cardiomyopathy	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

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.

Table 4. Thyroid dysfunction subtypes

Thyroid dysfunction	(%)	Confidence interval
Subclinical hypothyroidism	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

Association between thyroid dysfunction and heart failure

There is no significant association between thyroid dysfunction and severity of heart failure based on New York Heart Association functional class, class I and II (early heart failure), class III (advanced heart failure).

Table 5. Association between thyroid dysfunction and severity of heart failure in ambulatory heart failure 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

Discussion

The purpose of the study was to determine the prevalence of thyroid dysfunction in ambulatory heart failure patients at KNH. The study was conducted at the KNH outpatient cardiac clinic. Three hundred and two patients with heart failure based on Framingham's criteria, without structural heart disease and not on amiodarone were consecutively sampled. The study population consisted mainly of females at 62.6% with a mean age of 60.3 years and had been diagnosed with heart failure within the last 3 years. Seventy six point two percent of the patients are stable in heart failure class 1 and II and the most common aetiology of heart failure 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 subclinical hypothyroidism 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* (4) in 2016 in a study investigating the prevalence of subclinical hypothyroidism and cardiovascular outcomes in heart failure patients and, Kannan *et al* (7) in 2018 in a study investigating the prevalence of thyroid dysfunction in heart failure and cardiovascular outcomes also used the chemiluminometric assay method. 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* (14) in 2002 in a cross- sectional study investigating the prevalence of thyroid dysfunction in ambulatory heart failure 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, this is almost similar to our prevalence of 37%, however majority of our patients were female . Mahesh *et al* (15) in 2017 in a study to determine the prevalence of thyroid dysfunction in patients with acute decompensated heart failure and six months follow up of subclinical hypothyroidism 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 heart failure patients in our study. The global prevalence of thyroid dysfunction in heart failure is estimated at 21%-33.3% (4,15). There is no recorded data on the prevalence of thyroid dysfunction in ambulatory heart failure patients in sub-Saharan Africa.

Subclinical hypothyroidism, euthyroid sick syndrome and primary hypothyroidism were the most prevalent thyroid dysfunction subtypes in the study. Hayashi *et al* (4) in 2016 in a prospective study investigating the prevalence and prognostic impact of subclinical hypothyroidism and euthyroid sick syndrome in heart failure patients, sampled 274 patients, used the chemiluminometric assay and also found subclinical hypothyroidism and euthyroid sick syndrome as the most prevalent subtypes at 21% and 35% respectively, only 2% of the patients had subclinical hyperthyroidism. Subclinical hypothyroidism is usually asymptomatic (16) and progresses to overt hypothyroidism in only 2 – 28% of the cases (16,17). However, it is associated with coronary heart diseases (10), heart failure and stroke (18) and cardiovascular mortality (19,20). Hypothyroidism leads to a cardiac output decrease by 30–50% (12). Overt and subclinical hypothyroidism is linked to bradycardia, fatigue, death and hospital admissions in HF patients (13).

This study did not find a significant association between severity of heart failure and thyroid dysfunction. This may be due to our smaller size compared to other studies. Unlike our study, Kannan *et al* (7) in a prospective cohort study of ambulatory heart failure 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 heart failure class I-IV and majority were in class II and III heart failure. Chemiluminometric assay method was used for the thyroid function test, significant association was found between thyroid dysfunction and severity of heart failure 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 heart failure patients is high. The thyroid function test should be readily available and affordable to the patients. Patients found to have thyroid dysfunction should be referred to an endocrinologist for specialised care. Early detection and treatment of overt thyroid dysfunction in ambulatory heart failure patients will slow further progression of heart failure and prevent acute decompensation.

Conclusion

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

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