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ORIGINAL RESEARCH

Prevalence and Determinants of Hypothyroidism in Patients on Routine Hemodialysis in Somalia: A Cross-Sectional Study

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Introduction: In recent decades, the relationship between thyroid and kidney disease has drawn considerable attention. We aim to assess the prevalence and the determinants of hypothyroidism in hemodialysis patients in Somalia.

Materials and Methods: This is a cross-sectional study which was conducted in the hemodialysis unit of Mogadishu Somalia Turkish Training and Research Hospital, between June 1 and July, 31 2022. A total of 301 patients who are routinely going to hemodialysis were included in the study. Demographic data including age, gender, and data regarding hemodialysis were extracted from hospital information system (HIS). All participants had their thyroid function test measured before hemodialysis sessions.

Results: A total of 301 patients were examined. Their ages ranged from 40 to 66 years, with the median age being 54 (IQR= 40–66). Males were 167 (55.5%) compared to females 134 (44.5%). Hypertension was the most common comorbidity among the patients with 137 (45.5%). Diabetic kidney disease was the most common cause of renal failure in 138 patients (45.84%) followed by hypertensive kidney disease 100 (33.22%). The prevalence rate of hypothyroidism in hemodialysis patients in our study was 28%. In hypothyroidism patients 57.8% had subclinical hypothyroidism and 42.2% had overt hypothyroidism. 70.8% of our patients were in euthyroid status. Subclinical hypothyroidism was commonly seen in patients with diabetes, hypertension, and heart disease. We found that increasing age, decreased albumin level were related to higher risk of subclinical hypothyroidism. We also found that increasing creatinine levels were associated with lower risk of overt hypothyroidism.

Conclusion: The prevalence rate of hypothyroidism in hemodialysis patients was 28%, with 57.8% showing subclinical hypothyroidism and 42.2% overt hypothyroidism. Increased age and low albumin level was associated with the prevalence of subclinical hypothyroidism in hemodialysis patients. Also low creatinine level was observed in overt hypothyroidism patients.

Keywords: hypothyroidism, overt hypothyroidism, subclinical hypothyroidism, hemodialysis patients, Somalia

Introduction

In recent decades, the relationship between thyroid and kidney disease has drawn considerable attention. Thyroid hormones are required for embryological development and kidney growth. On the other hand, the metabolism, breakdown, and elimination of thyroid hormones are mostly regulated by the kidney.[1] Chronic kidney disease (CKD) is a worldwide public health issue and is described by the National Kidney Foundation's Kidney Disease Outcome Quality Initiative (K/DOQI) as renal disease lasting more than three months with either structural or functional abnormalities, with or without decreased glomerular filtration rate (GFR), reflected by pathological abnormalities or indicators of kidney damage, or by a GFR of less than 60 mL/min/1.73 m2.[2] The definition of end-stage kidney disease (ESKD) is glomerular filtration rate less than 15mL/min and a considerable decline in the kidney's capacity are both indicators of ESKD.[3]

In ESKD patients, primary hypothyroidism is on the rise, and several changes in thyroid function have been well documented. Primary hypothyroidism can only be diagnosed with confidence if a plasma TSH level are elevated; testing

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for free T4 may be helpful, but is not always trustworthy. On the other hand, hyperthyroidism in kidney failure is based on a high T4 concentration in the presence of a suppressed TSH.[4]

A lot of individuals with advanced chronic kidney disease, especially those on dialysis, have problems with their thyroid.[5] Patients receiving regular hemodialysis had decreased levels of thyroid hormones.[6] According to Rhee and coworkers, thyroid function test abnormalities may be linked to cardiovascular morbidity and mortality in CKD and ESKD patients.[7] Patients with ESKD are more likely to develop thyroid abnormalities than healthy individuals with hypothyroidism being the most prevalent regardless of the etiology; however, the precise prevalence varies by location.[7] According to studies, 13% to 25% of the population in the United States and Asia has hypothyroidism.[8]

The objectives of our study were to assess the prevalence of hypothyroidism in hemodialysis patients in Somalia, where no prior research on this topic had been conducted, and to identify any potential risk factors for thyroid abnormalities in this population. The results of this study are predicted to aid practitioners in predicting the prevalence of hypothyroidism among hemodialysis patients. It is also expected to assist in determining if this burden is large enough to warrant the establishment of a regular screening program for the early detection and treatment of this ailment.

Materials and Methods

This cross-sectional study was conducted in the hemodialysis unit of Mogadishu Somalia Turkish Training and Research Hospital, the largest referral and teaching hospital in Somalia.[9] The dialysis unit of our hospital is the largest unit in Somalia with over 360 hemodialysis patients currently on routine hemodialysis in this setting. The study was conducted over a period of 2 months, from 1 June to 31July 2022. It was approved by the research ethics committee of Somali Mogadishu-Turkish Training and Research Hospital (Date of Approval: 09.05.2022/No. of Approval: MSTH/10159).

The data was handled in accordance with the ethical principle of the Declaration of Helsinki privacy protection. Before the study was conducted, each of the study's participants signed a written statement of informed consent. At first, 340 patients who are routinely going to hemodialysis were identified as candidates for the study. Patients with a history of thyroid disease, thyroid and parathyroid surgery, receiving interferon therapy, being exposed to radiation, taking antithyroid medications, or receiving thyroid replacement therapies, patients who have active infection, patients who are clinically unstable, patients who are younger than 18 years old, and patients who refused to participate were excluded from this study. A final number of 301 patients who are routinely going to hemodialysis were included in the study.

Demographic data including age, gender, and data regarding hemodialysis were extracted from hospital information system (HIS). Data regarding comorbid diseases, history of thyroid disease, history of surgery and medication were obtained through face to face questionnaire. All participating patients had their blood drawn through an arterio-venous fistula (or from a venous catheter if they had one), while fasting in before morning session and prior to heparin administration. Thyroid function tests were tested using Roche e411 Immunoassay Analyzer (Roche Diagnostics Corporation, Indianapolis, IN). In our institution, the normal range for thyroid function tests are as follows: TSH 0.35–5.10 mIU/mL, FT4 0.60–1.20 ng/mL, and FT3 1.80–4.20 pg/mL.

The patients were divided into five categories according to the American Association of Clinical Endocrinologists (AACE) and American Thyroid Association (ATA) guidelines:[10] subclinical hypothyroidism, hypothyroidism, euthyroid, subclinical hyperthyroidism, and hyperthyroidism. Hypothyroidism was described in our study as FT4 < 0.60 ng/mL and TSH > 5.1 *m*IU/mL, and subclinical hypothyroidism was defined as normal FT4 level and a TSH > 5.1 *m*IU/mL. Hyperthyroidism was defined as FT4 > 1.20 ng/mL and TSH < 0.35 *m*IU/mL, and subclinical hyperthyroidism as normal FT4 level and TSH < 0.35 *m*IU/mL.

Data were analyzed using SPSS version 26 (IBM Corporation, Armonk, NY, USA). Frequencies and percentages were computed for categorical variables. Numerical variables were first tested for normality assumption using Shapiro–Wilk test. All numerical were non-normal and were summarized as median with inter-quartile range (IQR). Chi-square and Fisher-exact tests were applied to compare categorical variables among patients with euthyroid and hypothyroid. Mann–Whitney *U*-test was applied to compare numerical variables among two groups. Crude odds ratio were calculated using binary logistic regression. Variables with p <0.25 in univariate regression model were put in a final regression model to compute adjusted odds ratio. Hyperthyroidism was excluded from inferential analysis as it was very low frequency.

Results

A total of 301 patients participated in the study, and their ages ranged from 40 to 66 years, with the median age being 54 (IQR= 40–66). The gender ratio in the population that was analyzed showed that there were more males than females overall, with 167 (55.5%) males and 134 (44.5%) females. The clinical characteristics of these patients are presented in Table 1.

Regarding the comorbidities of the participants; 137 out of 301 patients had comorbid conditions, including hypertension in 137 (45.5%), diabetes in 101 (33.6%), heart disease in 43 (14.2), smoking in 4 (1.3%), and ischemic heart disease in 3 (1%) of those patients. We also found that there were a total of 16 patients, or 5.3%, who did not have any known comorbidities.

Within the scope of this study, we also investigated the causes of kidney failure among our participants. We observed that diabetic kidney disease was the basis of kidney failure in 138 patients (45.84%), making it the most common cause of kidney failure in our study. In our study, hypertensive kidney disease was the second most common cause of kidney failure among participants. We found that 100 patients or 33.22% of the total patients had hypertensive as their root cause of kidney failure, and was followed by glomerulonephritis, which affected 28 patients (9.3%), polycystic kidney disease, which affected 7 patients (2.3%), and obstructive kidney disease, which affected 13 patients (4.3%), respectively. In addition, we identified that 15 patients (which is 5% of the total) had no discernible explanation for their kidney failure.

Two hundred and thirteen (70.8%) of the 301 patients in our analysis had euthyroid status, 83 (28%) of the patients had hypothyroid condition, and 5 patients (1.7%), had hyperthyroid status. The 83 patients with hypothyroidism, 35 of them (42.2%) had overt hypothyroidism, while the other 48 patients (57.8%) had subclinical hypothyroidism. In spite of the larger number of male participants in our study, the euthyroid state of females was found to be 73.3%, which was slightly higher than the males (70.9%). Subclinical hypothyroidism was the most common type of hypothyroidism seen in patients with diabetes, hypertension, and heart disease. Table 2 shows the comparison of patients' features among those who had euthyroid, hypothyroid and hyperthyroidism. There was a statistically significant difference between the three groups with hypothyroidism in terms of the patients' ages, levels of FT4, albumin, and creatinine. Table 3 illustrates the post-hoc comparisons that reveal significant differences between the three variables.

Table 1 Descriptive Statistics for Clinical Characteristics of Patients

Variables	Frequency (%)
Comorbidity	
No known comorbid	16 (5.3)
Diabetes	101(33.6)
Hypertension	137(45.5)
Heart disease	43(14.2)
Smoker	4(1.3)
Causes of renal failure	
Diabetic kidney disease	138(45.84)
Hypertensive kidney disease	100(33.22)
Glomerulonephritis	28(9.3)
Polycystic kidney disease	7(2.3)
Obstructive kidney disease	13(4.3)
No known cause	15(5)

Table 2 Comparison of Patients' Feature Among Those Who Had Euthyroid and Hypothyroid (n=296)

Variables	Euthyroid n(%)	Sub Clinical Hypothyroid n(%)	Overt Hypothyroidism n(%)	p-value
Age (in years)[#]	52(36.5–65)	59.5(48–70.75)	60(42–72)	0.039*
Gender				
Male	117(70.9)	28(17)	20(12.1)	0.898
Female	96(73.3)	20(15.3)	15(11.5)	
Causes of failure				
Diabetic kidney disease	92(67.6)	24(17.6)	20(14.7)	0.294[ł]
Hypertensive kidney disease	77(77.8)	12(12.1)	10(10.1)	
Glomerulonephritis	22(84.6)	2(7.7)	2(7.7)	
Polycystic kidney disease	6(85.7)	1(14.3)	0(0)	
Obstructive kidney disease	7(53.8)	4(30.8)	2(15.4)	
No known cause	9(60)	5(33.3)	1(6.7)	
Comorbidity				
Diabetes	75(76.5)	12(12.2)	11(11.2)	0.388
Hypertension	93(68.9)	25(18.5)	17(12.6)	0.532
Heart diseases	28(65.1)	8(18.6)	7(16.3)	0.509
Smoker	3(75)	1(25)	0(0)	0.734[ł]
FT4[#] (ng/mL)	0.7(0.6–0.9)	0.6(0.6–0.8)	0.2(0.2–0.3)	<0.001**
BUN[#] (mg/dL)	123(93–152)	114.5(99.25–148)	119(81–148)	0.372
Creatinine[#] (mg/dL)	7.1(5.3–9.5)	7.75(5.25–9.925)	5.6(3.8–7.7)	0.003*
Hemoglobin[#] (g/dL)	8.9(8.4–9.9)	8.8(8.1–9.6)	9.3(8.4–10)	0.216
Calcium[#] (mg/dL)	8.6(8.3–9.2)	8.75(7.75–9.375)	8.6(7.8–9.2)	0.894
Albumin[#] (g/dL)	3.7(3.5–4.2)	3.5(3.125–3.9)	3.7(3.3–4)	0.007**
PTH[#] (pg/mL)	258(178–389)	244.5(160.75–392)	251(149–301)	0.190
Potassium[#] (mEq/L)	4.4(3.85–5.15)	4.7(3.825–5.2)	4.5(3.6–5.2)	0.503
Sodium[#] (mEq/L)	138(135–140)	137.5(135–140)	137(135–139)	0.248
Phosphorous[#] (mg/dL)	4.2(3.2–5.2)	4.45(3.2–5.275)	4.2(3.1–5.2)	0.489
Ferritin[#] (ng/mL)	425(300–625)	529.5(250–628)	515(326–620)	0.831

Notes: [#]Non-normal continuous data is reported as median (inter-quartile range), [ł]Fisher-exact test is reported, *Significant at p<0.05, **Significant at p<0.01.
Abbreviations: FT4, free T4; n, Number of patients; PTH, Parathyroid hormone.

Table 3 Post-Hoc Analysis Among Three Groups of Thyroid Status

Comparison Between Three Groups	Age	FT4	Creatinine	Albumin
Between euthyroid and overt hypothyroid	NS	**	**	NS
Between euthyroid and subclinical hypothyroid	**	**	NS	**
Between subclinical and overt hypothyroid	NS	**	**	NS

Note: **Significant at p<0.01.
Abbreviations: FT4, free T4; NS, non-significant.

Table 4 Univariate Predictor of Hypothyroidism (n=296)

Variables	Subclinical Hypothyroidism OR (95% CI)	p-value	Overt Hypothyroidism OR (95% CI)	p-value
Age (in years)	1.02 (1–1.04)	0.040*	1.02 (0.99–1.04)	0.107
Gender				
Male	1.15 (0.61–2.17)	0.668	1.09 (0.53–2.25)	0.807
Female	Ref		Ref	
Comorbid				
Diabetes	0.61 (0.30–1.24)	0.178	0.84 (0.39–1.81)	0.663
Hypertension	1.40 (0.74–2.62)	0.291	1.22 (0.59–2.49)	0.588
Heart diseases	1.32 (0.56–3.11)	0.524	1.65 (0.66–4.14)	0.284
BUN# (mg/dL)	0.99 (0.99–1.07)	0.867	0.99 (0.98–1)	0.122
Creatinine# (mg/dL)	0.99 (0.99–1.01)	0.878	0.76 (0.65–0.90)	0.001**
Hemoglobin# (g/dL)	0.87 (0.66–1.14)	0.305	1.27 (0.93–1.73)	0.134
Calcium# (mg/dL)	0.90 (0.64–1.28)	0.573	0.87 (0.58–1.29)	0.490
Albumin# (g/dL)	0.39 (0.22–0.70)	0.002**	0.56 (0.28–1.12)	0.100
PTH# (pg/mL)	1 (0.99–1)	0.844	1 (0.99–1)	0.090
Potassium# (mEq/L)	1.27 (0.87–1.84)	0.215	0.99 (0.65–1.53)	0.981
Sodium# (mEq/L)	0.97 (0.90–1.04)	0.380	0.94 (0.86–1.02)	0.143
Phosphorous# (mg/dL)	1.22 (0.99–1.51)	0.068	1.16 (0.91–1.48)	0.238
Ferritin# (ng/mL)	1 (0.99–1)	0.901	1 (0.99–1)	0.757

Notes: #Non-normal continuous data is reported as median (inter-quartile range), *p-value significant at level of 0.05, **p-value significant at level of 0.01.
Abbreviations: BUN, blood urea nitrogen; CI, confidence interval; OR, odds ratio; Ref, Reference category; PTH, parathyroid hormone.

Table 4 shows the association of patients' features with hypothyroidism on univariate analysis. On univariate analysis, increasing age was related to higher risk of subclinical hypothyroidism and increasing albumin levels were associated with lower risk of hypothyroidism. Increasing creatinine levels were associated with lower risk of overt hypothyroidism. Table 5 displays association of patients' features with hypothyroidism on multivariable analysis. On multivariable regression model after adjusting the model with other covariates, the association of age, albumin and creatinine levels still exists.

Discussion

Thyroid hormones (T3 and T4) have multiple effects in the body, including metabolism, development, protein synthesis, and the regulation of numerous other vital hormones.[11] The kidney plays a significant role in the metabolism of thyroid hormones, and those with chronic kidney disease and receiving maintenance hemodialysis are more likely to develop thyroid dysfunction than healthy individuals.[11] Chronic kidney disease may impact the hypothalamus-pituitary-thyroid axis and the peripheral thyroid hormone metabolism.[12] It is also considered that the hormonal removal during hemodialysis, decreased T3-binding capacity, changed hormonal catabolism, increased iodine store in thyroid gland, serum thyroid autoantibodies, and decreased peripheral conversion of T4 to T3 contribute hypothyroidism in chronic kidney failure patients.[13]

Table 5 Multivariable Predictor of Hypothyroidism (n=296)

Variables	Subclinical Hypothyroidism OR (95% CI)	p-value	Overt Hypothyroidism OR (95% CI)	p-value
Age (in years)	1.03 (1.01–1.05)	0.014*	1.01 (0.99–1.04)	0.260
Gender				
Male	–	–	–	–
Female	–		–	
Comorbid				
Diabetes	0.27 (0.29–1.25)	0.586	0.87 (0.38–1.97)	0.746
Hypertension	–	–	–	–
Heart diseases	–	–	–	–
BUN[#] (mg/dL)	0.99 (0.99–1)	0.349	0.99 (0.98–1.01)	0.693
Creatinine[#] (mg/dL)	1 (0.99–1.01)	0.748	0.78 (0.64–0.96)	0.016**
Hemoglobin[#] (g/dL)	0.85 (0.64–1.14)	0.286	1.25 (0.88–1.77)	0.216
Calcium[#] (mg/dL)	–	–	–	–
Albumin[#] (g/dL)	0.33 (0.17–0.64)	0.001**	0.61 (0.29–1.30)	0.203
PTH[#] (pg/mL)	1 (0.99–1)	0.688	0.99 (0.99–1)	0.243
Potassium[#] (mEq/L)	1.28 (0.86–1.94)	0.226	1.37 (0.82–2.30)	0.228
Sodium[#] (mEq/L)	0.99 (0.92–1.08)	0.919	0.98 (0.89–1.07)	0.644
Phosphorous[#] (mg/dL)	1.20 (0.96–1.51)	0.115	1.19 (0.92–1.55)	0.182
Ferritin[#] (ng/mL)	–	–	–	–

Notes: [#]Non-normal continuous data is reported as median (inter-quartile range), *p-value significant at level of 0.05, **p-value significant at level of 0.01.
Abbreviations: BUN, blood urea nitrogen; CI, confidence interval; OR, odds ratio; PTH, parathyroid hormone; Ref, Reference category.

In hemodialysis patients, low T3 is the most prevalent laboratory finding and subclinical hypothyroidism is the most common thyroid condition.[12] Some studies pointed that low levels of free T3 have been demonstrated to be an independent predictor of mortality in hemodialysis patients.[14] The prevalence and the patterns of hypothyroidism and the determinants of hypothyroidism among patients receiving routine hemodialysis in Somalia remain unexamined. Therefore, this is the first study which will report the prevalence and the determinants of hypothyroidism in hemodialysis patients in Somalia.

In the presenting study, we found that the prevalence of hypothyroidism in hemodialysis patients is 83 patients (28%). In addition, we described that of the 28 individuals with hypothyroidism, 57.8% had subclinical hypothyroidism and 42.2% had overt hypothyroidism. Hassan-Kadle et al studied 976 patients from Somalia in 2021 to identify the prevalence of thyroid disease in a tertiary hospital. They found that the prevalence rates of primary hypothyroidism and subclinical hypothyroidism were 12.5% and 7.6%, respectively.[15] Another study from Somalia regarding the prevalence of thyroid dysfunction among heart failure patients in 2022 which included 250 patients reported that overt hypothyroidism and subclinical hypothyroidism rated in 25.6% and 33.3%, respectively.[16] A study from Pakistan in 2022 by Memon et al which recruited 140 patients on maintenance hemodialysis reported that 37.9% had hypothyroidism.[17] This number is higher than our findings in this study and it can be attributed to the cultural and nutritional differences between the two populations. A similar study from India in 2021 which analyzed 89 routine hemodialysis patients

concluded that 16.9% had hypothyroidism. The researchers also reported the prevalence of overt hypothyroidism and subclinical hypothyroidism at 8.9% and 7.8%, respectively.[8]

The prevalence of hypothyroidism is somewhat directly related to the estimated GFR level of the patients. For instance, it was previously observed that subclinical hypothyroidism rate increased from 7% to 17.9% in patients whose GFR reduced from 90 mL/min to 60 mL/min.[18] The prevalence of hypothyroidism was 5.4%, 10.9%, 20.4%, 23.0%, and 23.1% among those with eGFRs of ≥ 90, 60–89, 45–59, 30–44, and 30mL/min/1.73m2, respectively, according to the third National Health and Nutrition Examination study in a study which included data from 14,623 participants.[19]

In our analysis, we found that increasing age was related to higher risk of development of subclinical hypothyroidism. We did not find any statistically correlation between age and overt hypothyroidism. This is consistent with the Whickham survey, first population-based study to evaluate the presence of thyroid dysfunction in community-dwelling individuals, which observed that TSH levels increased with age in women after the age of 45 years.[20] Another study from Netherlands in 2016 which analyzed 10,318 individuals older than 45 years reported that the prevalence of subclinical hypothyroidism was 9.1% compared to overt hypothyroidism 0.8%.[21]

In the present investigation, a low blood albumin level was deemed to be a risk factor for subclinical hypothyroidism in hemodialysis patients. Our patients with subclinical hypothyroidism showed lower serum albumin levels than the euthyroid patients. In line with our findings, a cross-sectional study of 137 ESKD patients from south India by Shantha et al concluded that decreased serum albumin level was significantly associated with subclinical hypothyroidism.[22] In opposite to both of these studies, Kang et al found in their cohort study of 51 ESRD patients on continuous ambulatory peritoneal dialysis that patients with subclinical hypothyroidism had substantially increased serum albumin levels than patients with normal serum TSH levels.[23] These differences can be explained that the former two studies involved hemodialysis patients and the later study focused on patients with ambulatory peritoneal dialysis. According to Shah and coworkers, hypoalbuminemia is an important predictor for cardiovascular disease in patients with early stages of kidney failure and may be used to identify populations at increased risk for cardiovascular disease.[24]

Interestingly in our analysis, we also found that lower creatinine level was associated with higher risk for developing overt hypothyroidism. Our patients who had overt hypothyroidism had lower creatinine level compared to the euthyroid and subclinical hypothyroid patients. This contradicts the findings of prior studies,[25–28] which suggested that a higher creatinine level is consistent with overt hypothyroidism, and warrants for additional investigation into its authenticity. This difference can be explained by a number of factors, including the fact that these mentioned studies analyzed a smaller sample size than our study, patients with a history of hypothyroidism, and patients who are not routinely going to hemodialysis.

Our study has several limitations that need to be considered; first it is a cross-sectional study and only focused in a single tertiary hospital. The sample size is relatively small and the findings may not represent the whole country of Somalia. A large national-based cohort study is needed to determine the prevalence of hypothyroidism in hemodialysis patients in Somalia. In contrast, as strength, our findings are the first to be reported from Somalia about the prevalence of hypothyroidism in hemodialysis patients and will offer a framework for future research.

Conclusion

Our study has shown 28% prevalence rate of hypothyroidism in hemodialysis patients. In hypothyroidism patients 57.8% had subclinical hypothyroidism and 42.2% had overt hypothyroidism. Increased age and low albumin was associated with the prevalence of subclinical hypothyroidism in hemodialysis patients. We also observed lower creatinine level in overt hypothyroidism patients.

Abbreviations

AACE, American Association of Clinical Endocrinologists; ATA, American Thyroid Association; CKD, chronic kidney disease; ESKD, end-stage kidney disease; GFR, glomerular filtration rate; HIS, hospital information system; IQR, inter-quartile range; K/DOQI, Kidney Disease Outcome Quality Initiative; SPSS, Statistical Package for the Social Sciences; TSH, thyroid stimulating hormone.

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Disclosure

The authors declare no competing interests in relation to this study.

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