

Research Article

Is There Relationship Between Thyroid Volume, Hyperparathyroidism and Cardiovascular Risk Factors in Patients Under Hemodialysis?

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Abstract

Background: Thyroid dysfunction and hyperparathyroidism are common in with chronic kidney disease (CKD) and under dialysis. It is known that they increase the risk of cardiovascular (CV) diseases in this population.

Objectives: In this study, we aimed to investigate the relationship between thyroid volume, hyperparathyroidism (HPTH), atherogenic index of plasma (AIP), carotis intima-media thickness (CIMT) and uric acid (UA) in hemodialysis (HD) patients.

Methodology: Hemodialysis patients without thyroid dysfunction were divided into three groups as; low (<13.6 pg/mL), target (13.6-61.2 pg/mL) and high (> 61.2 pg/mL) parathyroid hormone (PTH) levels continuing for at least 6 months. Routine laboratory tests, PTH, lipid profile, high sensitive CRP (hs-CRP), TSH, T4, T3, glucose, UA, insulin, C-peptide, AIP, thyroid ultrasonography performed and CIMT were evaluated and recorded.

Results: Total thyroid volume was 21.64 ± 1.83 , 15.01 ± 1.60 , 19.52 ± 1.41 mL respectively in males, females and whole group. Total thyroid volume, AIP, hs-CRP, UA, bilateral CIMT were all lower in low PTH group in comparison with other groups, but statistically significant only for hs-CRP levels. There was positive correlation between total thyroid volume and bilateral CIMT, hs-CRP; and negative correlation between Kt/V and thyroid volume.

Conclusion: In HD patients; thyroid volume may be an indicator of CV risk in harmony with other risk factors.

Keywords: Thyroid volume; Hyperparathyroidism; Uric acid; atherogenic index of plasma; Carotis intima-media thickness; Hemodialysis

1. Introduction

Chronic kidney disease (CKD) is a worldwide public health problem with poor results and increasing incidence. It progresses with reduced glomerular filtration rate (GFR) and affects 10-20% of adults worldwide [1]. In patients with end-stage renal disease (ESRD), as renal replacement therapy (RRT) modalities; kidney transplantation, hemodialysis (HD) and peritoneal dialysis (PD) are among the current options [2]. Thyroid dysfunction is common in patients with CKD and under RRT [3]. While low free T3 hormone levels were associated with arterial stiffness in PD

patients, high TSH levels near the upper limit of normal range were found to be associated with low subendocardial viability rate (arterial stiffness indicator) in euthyroid PD patients [4]. A positive correlation was observed between thyroid volume and creatinine levels in kidney transplant cases [5]. In recent years, factors such as uric acid (UA), hypoalbuminemia, insulin resistance, dyslipidemia, inflammation, oxidative stress and hyperparathyroidism (HPTH) have been frequently used and used as risk factors for the development of cardiovascular diseases (CVD) in patients with ESRD [6]. It is known that secondary HPTH, the most common cause of which is CKD, causes fractures, decreased quality of life and increased risk of CVD [7].

In this study, it was aimed to investigate the relationship between thyroid gland volume, HPTH and atherogenic index of plasma (AIP) and carotis intima-media thickness (CIMT) in the patient population undergoing RRT, and to evaluate the relation between these parameters, each of which is an independent cardiovascular (CV) risk factor.

2. Methodology

This single-center, prospective study was carried out with the approval of the local ethics committee (Erzincan University Ethics Committee; 07-04-2015/ 64593235-050.01.04-E.14331) and informed consent from the participants. The study included 50 ESRD patients without thyroid dysfunction who were followed by our clinic and under HD treatment. Informed consent forms were signed, thyroid volumes and carotis intima media thicknesses of the patients were measured by ultrasound. Biochemical parameters of patients included in the study for the last 6 months were obtained from medical records. Patients under HD treatment due to ESRD divided into three groups as; low (<13.6 pg/mL), target (13.6-61.2 pg/mL) and high (> 61.2 pg/mL) PTH levels. Patients were also evaluated

according to low uric acid and high uric acid levels and low Kt/V and high Kt/V ratios. In addition to the routine laboratory examinations of the patients in the study, laboratory parameters such as parathyroid hormone (PTH), lipid profile, high sensitive CRP, TSH, T4, T3, glucose, UA, insulin, C-peptide, and AIP and also thyroid ultrasonography performed simultaneously by the same Endocrinologist and carotid intima media thickness, which is an indicator of atherosclerosis, was evaluated and recorded.

2.1 Statistic analysis

The data was analyzed using SPSS for Windows version 13. All values were presented as mean+ standard error mean (SEM). Normality for continued variables in groups were determined by the Kolmogorov-Smirnov test. The variance homogeneity of the values showing normal distribution was tested by Levene's test. The variables that showed normal distribution and equal variance, were analyzed by Independent-Samples T test and One-Way ANOVA (Scheffe, LSD or Tukey test). The variables that showed normal distribution and unequal variances were analyzed by One-Way ANOVA; Tamhane's T2. The variables that didn't show normal distribution were analyzed by Kruskal-Wallis test and Mann-Whitney U-test (The Bonferroni correction was applied).

3. Results

In our study group; mean age of males and females were 58.94 ± 2.84 and 57.5 ± 4.43 respectively (Table 1). Total thyroid volume was 21.64 ± 1.83 mL in males, 15.01 ± 1.60 mL in females and overall thyroid volume was 19.52 ± 1.41 mL (Table 2). When groups were separated as low (< 13.6 pg/mL), target ($13.6-61.2$ pg/mL) and high (> 61.2 pg/mL) PTH levels continuing for at least 6 months; total thyroid volume, AIP, hs-CRP, uric acid, bilateral CIMT were all lower in low PTH group in comparison with other groups, but statistically significant only for hs-CRP levels (Table 3). When groups were separated as low (< 7 mg/dL) and high (> 7 mg/dL) UA levels continuing for at least 3 months; hs-CRP levels were also high in low UA group, however without statistical significance (Table 4). When groups were separated as low (< 1.2) and high (> 1.2) Kt/V levels for at least 1 year; total thyroid volume ($p < 0.001$), bilateral CIMT ($p < 0.001$) and total cholesterol levels ($p = 0.002$) were all higher in low Kt/V group than high group (Table 5). Also, there was positive correlation between total thyroid volume and left CIMT, right CIMT, hs-CRP; and negative correlation between Kt/V and thyroid volume (Table 6, Figure 1).

	Age	Height	Weight	BMI	BSA
Total (n=50)	58.48 ± 2.37	165.02 ± 1.44	67.78 ± 2.21	24.81 ± 0.73	1.73 ± 0.31
Male (n=34)	58.94 ± 2.84	168.08 ± 1.72	69.63 ± 2.42	24.62 ± 0.76	1.78 ± 0.03
Female (n=16)	57.5 ± 4.43	158.50 ± 1.79	63.85 ± 4.61	25.21 ± 1.67	1.64 ± 0.05

Mean ± SEM; (Body surface area (BSA) was calculated using the Dubois formula)

Table 1: General data of the studied population showing the mean age, weight, height, BMI and BSA.

Subjects (number)	Thyroid volume (mL)	Left lob volume (mL)	Right lob volume (mL)
Males (34)	21.64 ± 1.83*	10.55 ± 0.94**	11.09 ± 0.97
Females (16)	15.01 ± 1.60	6.55 ± 0.77	8.45 ± 0.95
All (50)	19.52 ± 1.41	9.27 ± 0.73	10.25 ± 0.74

Mean ± SEM; * Males total thyroid volume different from females total thyroid volume, p = 0.009; **Males left lob different from females left lob, p = 0.002

Table 2: Volume of thyroid glands in females, males and all cases.

Groups	Total thyroid volume (mL)	AIP	hs-CRP (mg/L)	TAS	TAD	Uric Acid (mg/dL)	Left CIMT (cm)	Right CIMT (cm)
Low PTH (< 13.6 pg/mL) (5)	13.11 ± 2.61	0.59 ± 0.12	2.04 ± 0.52*†	95.00 ± 2.23‡°	64.00 ± 4.00	5.58 ± 0.67	0.64 ± 0.08	0.70 ± 0.06
Middle PTH (13.6-61.2 pg/mL) (13)	18.40 ± 2.31	0.60 ± 0.05	11.05 ± 2.39	120.61 ± 0.26	71.53 ± 2.96	6.23 ± 0.88	0.78 ± 0.19	0.72 ± 0.04
High PTH (> 61.2 pg/mL) (32)	20.98 ± 1.91	0.52 ± 0.03	11.82 ± 1.74	126.00 ± 3.93	75.15 ± 2.30	6.19 ± 0.23	0.75 ± 0.19	0.78 ± 0.04

Mean ± SEM; PTH; Parathyroid Hormone, AIP; Atherogenic Index of Plasma, hs-CRP; High Sensitivity C-Reactive Protein, TAS; Tension arterial systolic, TAD; Tension arterial diastolic, CIMT; Carotid Artery Intima-Media Thickness, *Significantly different from Middle PTH, p = 0.008; †Significantly different from high PTH, p < 0.001; ‡Significantly different from middle PTH, p < 0.001; °Significantly different from high PTH, p = 0.001

Table 3: Total Thyroid Volume, AIP, hs-CRP, TAS, TAD, Uric Acid, Left CIMT And Right CIMT In Patients With Low, Middle And High PTH Levels.

Groups	Total thyroid volume (ml)	AIP	hs-CRP (mg/L)	TAS	Weight (kg)	Cholesterol (mg/dL)
Low Uric Acid (<7 mg/dL) (39)	19.77 ± 1.58	0.53 ± 0.03	11.43 ± 1.63	121.05 ± 3.48	65.17 ± 2.32*	155.56 ± 4.29**
High Uric acid (> 7 mg/dL) (11)	18.63 ± 3.23	0.59 ± 0.06	7.85 ± 1.50	124.72 ± 3.88	77.04 ± 5.06	198.90 ± 16.44

Mean ± SEM; *Significantly different from High Uric Acid p= 0.025; **Significantly different from High Uric Acid p= 0.026

Table 4: Total Thyroid Volume, AIP, hs-CRP, TAS, Weight and Cholesterol in Patients With Low And High Uric Acid Levels.

Groups	Total thyroid volume (ml)	Left CIMT (cm)	Right CIMT (cm)	Insulin (uU/mL)	Cholesterol (mg/dL)	TSH (mIU/L)
Low Kt/v (< 1.2) (11)	27.09 ± 1.84*	0.81 ± 0.05**	0.82 ± 0.04°	9.27 ± 0.95†	183.49 ± 8.06††	0.77 ± 0.13‡
High Kt/v (> 1.2) (39)	16.62 ± 1.26	0.69 ± 0.02	0.70 ± 0.02	23.46 ± 2.72	153.05 ± 4.23	1.63 ± 0.20

Mean ± SEM; *Significantly different from high Kt/v p < 0,001; **Significantly different from high Kt/v p=0,020; °Significantly different from high Kt/v p=0,014;

†Significantly different from high Kt/v p < 0,001; ††Significantly different from high Kt/v p=0,002; ‡Significantly different from high Kt/v p=0,001

Table 5: Total Thyroid Volume, Left CIMT, Right CIMT, Insulin, Cholesterol and TSH in Patients with Low, and High Kt/v Levels.

	Volume left (mL)		Volume right (mL)		Total thyroid volume (mL)		k/vt		Left CIMT (cm)		Right CIMT (cm)		hs-CRP (mg/L)		Weight (kg)		TSH (mIU/L)		
	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	
n=50																			
Volume left	1		0.866	0	0.843	0	-0.376	0.007	0.328	0.02	0.394	0.005	0.257	0.072	0.398	0.004	-0.558	0	
Volume right	0.866	0	1		0.828	0	-0.306	0.031	0.334	0.018	0.402	0.004	0.299	0.035	0.425	0.002	-0.639	0	
Total thyroid volume	0.843	0	0.828	0	1		-0.36	0.01	0.353	0.012	0.422	0.002	0.292	0.039	0.433	0.002	-0.627	0	
k/vt	-0.376	0.007	-0.306	0.031	-0.36	0.01	1		-0.157	0.275	-0.162	0.262	-0.036	0.803	-0.554	0	0.138	0.339	
Cimleft	0.328	0.02	0.334	0.018	0.353	0.012	-0.157	0.275	1		0.787	0	0.245	0.086	0.26	0.068	-0.375	0.007	
Cimright	0.394	0.005	0.402	0.004	0.422	0.002	-0.162	0.262	0.787	0	1		0.292	0.04	0.274	0.054	-0.397	0.005	
hs-CRP	0.257	0.072	0.299	0.035	0.292	0.039	-0.036	0.803	0.245	0.086	0.292	0.04	1		0.438	0.001	-0.101	0.486	
Weight	0.398	0.004	0.425	0.002	0.433	0.002	-0.554	0	0.26	0.068	0.274	0.054	0.438	0.001	1		-0.075	0.605	
TSH	-0.558	0	-0.639	0	-0.627	0	0.138	0.339	-0.375	0.007	-0.397	0.005	-0.101	0.486	-0.075	0.605	1		

Bold written ones; correlation is significant (2-tailed). r=Pearson or Spearman correlation, and p=significant/p value

Table 6: Correlation of Thyroid Volume with Kt/v, Left CIMT, Right CIMT, hs-CRP, Weight and TSH in all Patients.

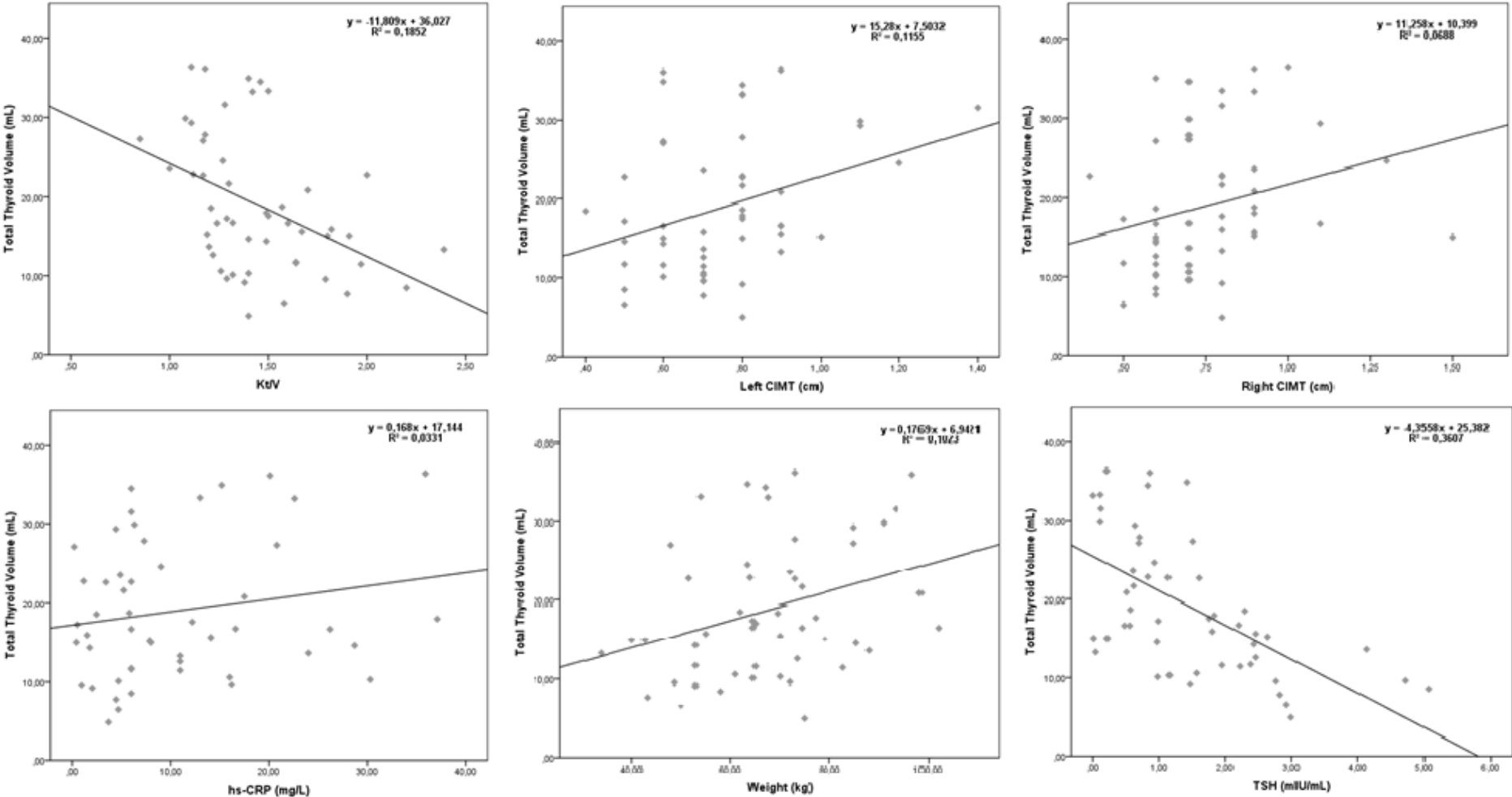


Figure 1: Scatter Plot for Total Thyroid Volume Against Kt/v, Left CIMT, Right CIMT, hs-CRP, Weight and TSH in all Patients.

4. Discussion

The increased frequency of thyroid dysfunction in CKD patients and the increase of thyroid gland volume has been demonstrated with previous studies [3]. In a previous study on healthy adult Turkish population, thyroid volume of males was 14.53 ± 2.55 ml and 12.9 ± 2.05 ml in females, and in all study group was determined as 12.98 ± 2.53 ml and these values are especially recommended as a reference value for Turkey's south-eastern regions [8]. In our study; we found total thyroid volume as 21.64 ± 1.83 mL in men, 15.01 ± 1.60 mL in women and 19.52 ± 1.41 mL in the whole group. We also found that in our HD patient population, thyroid volume increased as serum PTH level increased.

Thyroid diseases are common in CKD. It was found that morphological, functional and autoimmune thyroid diseases are more common in patients with hemoglobin levels below 125 g/ dL in CKD patients under HD treatment [3]. It was found that the average thyroid volume increased in HD patients. There was no significant relationship between the history of HD and thyroid volume. The most common thyroid pathologies in the HD patient population were diffuse and multinodular goiter. In the same patient group, a positive correlation was found between TSH levels and thyroid volume [9]. While low free T3 hormone levels were associated with arterial stiffness in PD patients, high TSH levels near the upper limit of normal range were found to be associated with low subendocardial viability rate in euthyroid PD patients [4].

In a study evaluating 143 patients in Japan, 14% of patients under HD had goiter (thyroid volume > 20 ml), and 59.4% of them, especially in women, had nodular lesions in the thyroid gland [10]. Thyroid hormones have been reported to

be effective on kidney function. For this purpose, thyroid hormone and thiamazol, an antithyroid agent, were applied to the rats with renal failure. At the end of 22 weeks, the survival rate was 100% in the thiamazol group, while it was 62.5% in the group given thyroid hormone. Thyroid hormone aggravated tubular changes and interstitial volume increase triggered by adriamycin [11].

Thyroid dysfunction is frequently observed in cases under RRT. In kidney transplant cases, thyroid volume was found higher than HD and SAPD cases; while goiter and thyroid nodules were most frequently observed in transplantation, then HD and at least PD cases. A positive correlation was observed between thyroid volume and creatinine levels in kidney transplant cases [5].

Cardiovascular diseases are the main cause of morbidity and mortality in ESRD patients. When this patient group is evaluated in terms of CV risk factors; in addition to traditional risk factors, we encounter factors such as bone and mineral metabolism disorders, chronic inflammation, oxidative stress and hyperuricemia [12]. High PTH levels are blamed for the etiology of vascular calcification. Increased PTH acts as a uremic toxin; contributes to bone loss, vascular and cardiac valve calcification, anemia, cardiomyopathy, hypertension and glucose intolerance [13]. In studies conducted in the general population, HPTH has been shown to be associated with CV disease [14]. In CKD patients, some studies have shown that there is a higher risk of death due to CVD with increased PTH levels [15], while others have reported that low PTH is associated with a greater risk for CVD [16].

In our study; when groups were separated as low (< 13.6 pg/mL), target (13.6-61.2 pg/mL) and high (> 61.2 pg/mL)

PTH levels continuing for at least 6 months; cardiovascular risk factors such as AIP, hs-CRP, uric acid, bilateral CIMT were all lower in low PTH group in comparison with other groups. Serum UA level has been defined as an independent risk factor for future cardiovascular mortality in the general population [17]. In the literature, there are contradictory data about the role of UA in ESRD patients and its relationship with cardiovascular events, and some studies have found high UA levels [18], and some other studies associated low UA levels with cardiovascular events [19].

In our study group; when groups were separated as low (<7 mg/dL) and high (> 7 mg/dL) uric acid levels continuing for at least 3 months; , hs-CRP levels were also high in low uric acid group. When our patient groups were separated as low (<1.2) and high (> 1.2) Kt/V levels for at least 1 year; total thyroid volume ($p<0.001$), bilateral CIMT ($p<0.001$) and total cholesterol levels ($p=0.002$) were all higher in low Kt/V group than high group as suggesting that adequate dialysis is also important in order to reduce cardiovascular risks.

5. Conclusions

In HD patients; thyroid volume, hyperparathyroidism, uric acid and atherogenic index of plasma may be an indicator of CV risk in harmony with other risk factors. Clinicians should evaluate these parameters during their clinical practices.

Ethics and Consent

Institutional Review board allowed for the project, and informed consent was taken from each participant.

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There is no source of funding; the project has been run on its own.

Competing Interests

There are no competing interests.

Authors Contribution

All authors contributed to designing the project, data collection, and interpretation, literature review, and gave the final evaluation.

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