

# Thyroid nodules frequency in patients with chronic kidney disease (ckd) who undergoing hemodialysis

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## ABSTRACT

**Objectives:** In our study; we examined the frequency of thyroid nodules, which are very common in the general population, in patients with Chronic Kidney Disease (CKD) who undergoing hemodialysis.

**Methods:** Our study was performed between 01.01.2020 and 01.04.2020 at Van Yuzuncu Yil University Faculty of Medicine, Dursun Odabaş Medical Center. 57 patients with CKD aged between 18-90 years were included in the study. Thyroid ultrasonography were performed on the patients. Subsequently, TSH, fT4 and fT3 laboratory tests, which are the routine tests in all CKD patients, were requested. Presence, number, location, size of thyroid nodules, isthmus thickness and total thyroid volume were recorded.

**Results:** 26 of the patients in our study were female and 31 were male. The mean age of the patients 51,98±18,22. The thyroid volume was 16,57±9,97 mL. Thyroid nodules were detected in 27 (%47,4) of 57 patients. Thyroid nodules were seen to be more common in female gender and with increasing age. Also there was positive correlation between dialysis duration and thyroid nodule. %92,6 of the patients in our study were euthyroid.

**Conclusion:** We found that the frequency of thyroid nodules increased in patients with CKD who undergoing hemodialysis. We found that thyroid nodules were more common in women and with increasing age. In addition, we found that the longer the dialysis duration, the more frequent the thyroid nodule. Routine thyroid USG was recommended to patients with CKD who undergoing hemodialysis.

**Keywords:** Thyroid nodule, Chronic Kidney Disease, Hemodialysis

Thyroid dysfunctions and nodular goiter are more common in patients diagnosed with CKD than in the normal population.<sup>1</sup> Changes in thyroid function occur in patients diagnosed with CKD. These changes are; decrease in free-circulating thyroid hormones, changes in the peripheral metabolism of thyroid hormones, decrease in binding to carrier proteins, decrease in the storage of iodine in the thyroid gland. Euthyroidism, hypothyroidism or sub-

clinical hypothyroidism is more common in patients diagnosed with end-stage renal failure. The decrease in Total T4 (TT4), free T4 (fT4), Total T3 (TT3) and free T3 (fT3) is more common. However, the reason for this situation is still unclear.<sup>2</sup>

Benign and malignant nodules in the thyroid gland are more common in end-stage renal failure than in healthy people.<sup>3</sup> In different studies, thyroid volume was found to be increased in approximately 14% of

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patients diagnosed with end-stage renal failure, and thyroid nodules were detected in 36.8 - 59.4% of patients.<sup>2,3</sup>

## METHODS

Approval was obtained from the Ethics Committee of Van Yüzüncü Yıl University Faculty of Medicine Dursun Odabaş Tıp Merkezi before starting the prospective study, which we plan to conduct to investigate the frequency of thyroid nodules in patients diagnosed with Chronic Kidney Disease (CKD) and receiving hemodialysis treatment (Date: 20/12/2019 Decision No: 03). The study was started after the written informed consent form was received from all the patients. Our study was conducted at Van Yüzüncü Yıl University Faculty of Medicine Dursun Odabaş Tıp Merkezi between 01.01.2020-01.04.2020. A total of 57 patients between the ages of 18 and 90 with a diagnosis of CKD and receiving hemodialysis treatment were included in the study. Through face-to-face interviews, the patients' age, gender, hemodialysis time, whether they have thyroid disease and the medications they use were questioned in detail.

Thyroid ultrasonography (with GE LOGIQ P5 ultrasonography device) was performed by the same endocrinologist at the Endocrinology Clinic of Van Yuzuncu Yil University Faculty of Medicine to all of the patients participating in the study. The dimensions of the thyroid lobes, the thickness of the isthmus, nodules, if any, the location, number and size of nodules of the patients were recorded. The thyroid volume of each lobe was calculated separately. The width (cm) × length (cm) × depth (cm) × 0.479 formula was used when calculating thyroid volume. The total thyroid volume was calculated by summing the volume of both right and left thyroid lobes. The volume of the isthmus was not taken into account when calculating the thyroid volume.

After that, TSH, fT4 and fT3 laboratory tests, which are routinely requested in all CKD patients, were re-

quested. TSH levels were studied with the Architect ci16200 TM device. Reference range was accepted as 0.35-4.94  $\mu$ IU/mL for TSH.

As a result of thyroid ultrasonography, according to the recommendations of the "American Thyroid Association" (ATA) guidelines, it was recommended to perform a thyroid fine needle aspiration biopsy on nodules with a high potential for malignancy. Those with subnormal TSH were again offered radionuclide thyroid screening in accordance with the recommendations of the ATA manual.

Those who were not within the specified age range at the time of diagnosis, did not have the diagnostic criteria for CKD disease, had previously undergone thyroid surgery, had any malignancies at the time of diagnosis and pregnant women were not included in the study.

## RESULTS

A total of 57 patients diagnosed with CKD and undergoing hemodialysis, including 26 (45.61%) women and 31 (54.39%) men, were included in our study. The mean age of the patients in our study group was 51.98 $\pm$ 18.22. There was a significant difference between the mean ages of male and female patients ( $p=0.036$ ) (table 1).

When looking at Table 2, it was seen that 47.4% of the kidney failure patients included in the study (27 patients) had thyroid nodules. When the evaluation was performed according to gender, 16 (61.5%) female and 11 (35.5%) male patients were found to have thyroid nodules. It was found that there was significant difference between gender and whether thyroid nodule ( $p=0.05$ ). As a result of the analysis, it was found that the patients with nodules were the most female patients.

74.1% of the patients included in the study (20 patients) had one nodule and 25.9% (7 patients) had more than one nodule. In this case, it was found that the vast majority of the patients included in the study

**Table 1. The Average Age of the Patients Participating in the Study According to Their Gender**

Gender	Number	Age Average	Standart Deviation	Minimum	Maximum	P value
Female	26	57,46	17,813	18	91	
Male	31	47,39	17,536	20	80	
Total	57	51,98	18,221	18	91	0,036

**Table 2. The Relationship between Gender and Whether There is a Thyroid Nodule or Not**

			The detected of a thyroid nodule		Total
			Detected	Not detected	
<b>Gender</b>	<b>Female</b>	Number	16	10	26
		Gender%	61,5%	38,5%	100,0%
	<b>Male</b>	Number	11	20	31
		Gender%	35,5%	64,5%	100,0%
<b>Total</b>		Number	27	30	57
		Gender%	47,4%	52,6%	100,0%

**P value: 0.05**

had a nodule (Table 3). It was found that the average age of hemodialysis patients with thyroid nodules included in the study was  $57.96 \pm 16.07$  and the average age of hemodialysis patients without thyroid nodules was  $46.6 \pm 18.61$ . It was found that there was a significant difference between age and thyroid nodule ( $p=0.02$ ). In the current study, hemodialysis patients with a thyroid nodule were found to have one nodule, two nodules, or three nodules. The average size of the first nodules of the patients was  $8.70 \pm 5.10$  mm, the average size of the second nodules was  $16 \pm 11.81$  mm and the average size of the third nodules was  $8.50 \pm 2.12$  mm.

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the third nodules was  $8.50 \pm 2.12$  mm.

The average TSH values of the patients included in the study were  $1.69 \pm 1.05$  and the average ST4 values were  $0.82 \pm 0.29$ . There were no differences when considering the status of thyroid nodule or absence of TSH, ST4 values ( $p=0.61$ ;  $p=0.09$ ). The average ST3 values of patients were 2.50. The average ST3 values of patients who had thyroid nodules were 2.37. The average ST3 values of patients who didn't have thyroid nodules were 2.62. ST3 values of patients with thyroid nodules and those without thyroid nodules differ ( $p=0.05$ ). It was found that the ST3 values of hemodialysis patients with nodules were lower (Table 4)

The average hemodialysis time of all patients was  $5.96 \pm 5.27$ , the average hemodialysis time of patients with thyroid nodules was  $8.11 \pm 5.90$  and the average of patients without thyroid nodules was  $4.03 \pm 3.77$ . It was found that there was a significant difference between hemodialysis patients with a thyroid nodule and without a thyroid nodule. The hemodialysis time of patients with thyroid nodule detection is longer than in patients without thyroid nodule detection ( $p=0.00$ ). The average thyroid volume of all patients was  $15.29 \pm 8.16$ , the average thyroid volume of pa-

**Table 3. Having a single or multiple nodule in patients with a thyroid nodule**

Number of thyroid nodules			Detected		Not detected	
			Detected	Not detected	Detected	Not detected
<b>0 nodule</b>		Number	0	30	30	
		Total%	0,0%	100,0%	52,6%	
<b>1 nodule</b>		Number	20	0	20	
		Total%	74,1%	0,0%	35,1%	
<b>2 nodules</b>		Number	5	0	5	
		Total%	18,5%	0,0%	8,8%	
<b>3 nodules</b>		Number	2	0	2	
		Total%	7,4%	0,0%	3,5%	
<b>Total</b>		Number	27	30	57	
		Total%	100,0%	100,0%	100,0%	

**P value: 0,000**

**Table 4. Descriptive Statistics And Comparative Results of Thyroid Nodule Absence Status**

	Thyroid nodule	Number	Average	Standart Deviation	Minimum	Maximum	P value
TSH	Detected	27	1,6141	1,04493	0,08	4,54	0,613
	Not detected	30	1,7563	1,06113	0,08	5,45	
	Total	57	1,6889	1,04651	0,08	5,45	
fT4	Detected	27	0,7478	0,33104	0,04	1,55	0,087
	Not detected	30	0,8780	0,22886	0,09	1,50	
	Total	57	0,8163	0,28689	0,04	1,55	
fT3	Detected	27	2,3737	0,52320	1,05	3,66	0,051
	Not detected	30	2,6200	0,40733	1,93	3,39	
	Total	57	2,5033	0,47792	1,05	3,66	
Duration of hemodialysis(year)	Detected	27	8,11	5,899	1	20	0,003
	Not detected	30	4,03	3,774	1	19	
	Total	57	5,96	5,268	1	20	
Thyroid volum (mL)	Detected	27	18,2122	9,90283	5,10	40,30	0,009
	Not detected	30	12,6637	5,06279	5,70	23,70	
	Total	57	15,2919	8,16190	5,10	40,30	

tients with thyroid nodules was  $18.21 \pm 9.90$  and the average thyroid volume of patients without thyroid nodules was  $12.66 \pm 5.06$ . There were differences between patients with thyroid nodules and those without thyroid nodules ( $p = 0.01$ ). It was found that kidney failure patients with thyroid nodules had higher thyroid volumes (Table 4)

## DISCUSSION

Thyroid nodules constitute the most common group of diseases belonging to the thyroid gland in society. The clinical importance of thyroid nodules is the functional status of the nodule, whether it is malignant, whether it causes pressure symptoms and signs.<sup>4</sup>

Both environmental and genetic factors play a role in the formation of thyroid nodules.<sup>5</sup> The prevalence of nodular goiter may vary depending on the iodine intake of the society in which the research was conducted, as well as depending on techniques such as palpation or USG used in scans.<sup>6</sup> In this study, we investigated the frequency of thyroid nodules in patients diagnosed with CKD and undergoing hemodialysis.

There are numerous studies investigating the frequency of thyroid nodules in our country.<sup>7,8</sup> In Erzurum province, one of the iodine-deficient regions, the prevalence of thyroid nodules in the adult population was found to be 2.1% by palpation and 18% by ultrasonography.<sup>7</sup> In the 2023 thyroid diseases diagnosis and treatment (TEMĐ) guideline, it was reported that the frequency of thyroid nodules detected by

ultrasonography in our country was 23.5% between the ages of 18-65 and 37.4% over the age of 65.<sup>4</sup>

The relationship between thyroid gland and kidney function has been known for a long time.<sup>9</sup> According to numerous studies, it has been found that CKD affects the metabolism of thyroid hormones and the thyroid gland structurally. These structural changes can be in the form of diffuse goiter, single thyroid nodule or multinodular goiter. Benign and malignant thyroid nodules are observed more frequently in patients with CKD than in the normal population.<sup>10-13</sup> According to studies in the literature, thyroid nodules were detected in 36.8 - 59.4% of patients diagnosed with CKD and undergoing hemodialysis.<sup>14-16</sup> According to a study conducted by Kutlay S and his colleagues in our country, thyroid nodules were detected in 36.8% of hemodialysis patients in areas with moderate iodine deficiency.<sup>14</sup> In a study conducted by Pakfetrat M *et al.* in Iran, the rate of thyroid nodules in patients undergoing hemodialysis was found to be 43.7%.<sup>16</sup> In two different studies conducted by Miki H *et al.* and Lin C *et al.*, the thyroid nodule rate in hemodialysis patients was found to be 55% and 59.8%.<sup>15,17</sup> Similar to other studies in our study, we detected a thyroid nodule in 47.4% of patients diagnosed with CKD who underwent hemodialysis.

According to the 2023 TEMĐ guideline, the incidence of thyroid nodules in female is higher than in male.<sup>4</sup> In studies conducted by Lin C *et al.* and Kaptein EM *et al.*, it was found that thyroid nodule is more common in female hemodialysis patients.<sup>15,18</sup> In our study, when the evaluation was made according to

gender, we detected thyroid nodules in 16 (61.5%) female and 11 (38.5%) male patients. As a result of our analysis, we found that the patients who were found to have nodules, similar to the other studies, were the most female patients ( $p=0.05$ ).

In the 2023 TEMD guideline and other studies, it has been observed that the frequency of thyroid nodules increases with age.<sup>4,19</sup> We found that the average age of kidney failure patients with thyroid nodules included in our study was  $57.96\pm 16.07$ , and the average age of kidney failure patients without thyroid nodules was  $46.6\pm 18.61$ . We found that there was a significant difference between age and thyroid nodule ( $p=0.02$ ). In our study, similar to the TEMD guideline and other studies, we found that the frequency of thyroid nodules increases with increasing age.

When looking at the TSH values in different studies, it was found that hypothyroidism is often found in hemodialysis patients. However, there are also studies that have found euthyroidism.<sup>14,20</sup> In a study conducted by Ibrahim Ihab A and his colleagues, it was found that the TSH values of hemodialysis patients were in the normal range.<sup>12</sup>

In our study, we have found that TSH values between 0-0,34 mIU/L (7,4%) and between 0,35-5,47 mIU/L (92,6%) who have had thyroid nodules. And we have found that TSH values between 0-0,34 mIU/L (3,3%) and between 0,35-5,47 mIU/L (96,7%) who haven't had thyroid nodule. In our study, we found that the majority of patients' TSH values were in the normal range who had thyroid nodule.

In the studies conducted by Kutlay S *et al.* and Lebkovska U *et al.*, it was found that the frequency of diffuse goiter and nodular goiter increases when the duration of dialysis increases.<sup>14,21</sup> In our study, when we looked at the relationship between the duration of hemodialysis of patients and the thyroid nodule, we found that there was a significant relationship. In our study, similar to the other studies, we found that thyroid nodule is observed more frequently when the duration of dialysis increases.

## CONCLUSION

In our study, we detected thyroid nodules in 27 (47.4%) of 57 hemodialysis patients. In addition, we found that a thyroid nodule is more common in female than in male and a thyroid nodule is more common with increase age. The frequency of thyroid nodules by gender and age, were similar to the thyroid nod-

ule studies in hemodialysis patients performed in our country and around the world.

In our study, we found that there is a significant relationship between the duration of dialysis and a thyroid nodule. We found that the incidence of thyroid nodules increased as the duration of dialysis increased.

When we looked at the TSH values of the patients in our study, we found that our patients had more euthyroidism.

Due to the high frequency of thyroid nodules in hemodialysis patients, we found that it is appropriate to routinely screen patients undergoing dialysis for the presence of nodules using thyroid ultrasonography.

## Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Ethical Approval

The protocol of the study was approved by the Medical Ethics Committee of Yüzüncü Yıl University İstanbul, Turkey. (Decision number: 06, date: 18.12.2019).

## Authors' Contribution

Study Conception: MA, MA, YD; Study Design: MA, MA, YD; Supervision: MA, MA, YD; Funding: MA, MA; Materials: MA, MA; Data Collection and/or Processing: MA, MA; Analysis and/or Data Interpretation: MA, MA; Literature Review: MA, MA; Critical Review: MA, MA, YD; Manuscript preparing: MA, MA, YD.

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