

# The Prevalence of Endemic Goiter and Iodine Deficiency and Evaluation of Thyroid Functions in an Area of Central Anatolia

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Endemic goiter and iodine deficiency is an important public health problem particularly in some areas of Turkey as it has been all over the world. We intended to evaluate this problem in Kayseri, where the goiter is endemic.

128 students aged between 10-13 years and 71 adults aged more than 15 years who were living in a rural area of Kayseri were included in the study.

Thyroid gland was evaluated with physical examination and ultrasonography (USG), blood samples were drawn to assess the levels of free T3 (fT3), free T4 (fT4), TSH, thyroglobulin (Tg), anti-microsomal antibody (anti-M) and anti-thyroglobulin (anti-Tg) and spot urine samples were collected from all participants.

Goiter prevalence was 54.8% with palpation and 48.7% with ultrasonography. Thyroid volumes were higher in females than males both in students and adults. fT3 levels were normal or slightly higher, fT4 levels were normal or slightly lower, TSH levels were high and thyroglobulin levels were extremely high.

Mean urinary iodine level was  $11.1 \pm 6.1$  µg/dl and in 53.3% of the participants urinary iodine levels were below the normal level (10 µg/dl). Median urinary iodine level was 9.54 µg/dl indicating mild iodine deficiency.

In conclusion despite the high prevalence of goiter, median urinary iodine level was relatively high suggesting that measurement techniques of iodine level may affect the result. According to chronic iodine deficiency parameter such as thyroglobulin (Tg), it is obvious that the people living at this endemic area need iodine prophylaxis.

**Key words:** Endemic goiter, iodine deficiency, Thyroid function and Central Anatolia

## Introduction

Endemic goiter and iodine deficiency are important public health problems in many countries in the

world (1,2). Different nutritional and environmental factors are responsible for the pathogenesis of goiter but iodine deficiency is the most important factor (2-5).

Recent studies in Turkey demonstrated a high prevalence (up to 82%) of endemic goiter due to iodine deficiency (6-12). Because of the geographical characteristics of Kayseri, iodine deficiency is more common and goiter prevalence was reported as 30% in several studies (6,7,11). But

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these results were obtained only with palpation of thyroid gland. Recently Erdoğan et al. investigated iodine status and goiter prevalence in school-age children in known endemic areas of Turkey including Kayseri. After sonographic thyroid volume and urinary iodine concentration measurement, goiter prevalence and median urinary iodine level was reported as 33% and 25.5 µg/l, respectively (13, 14). Until now, such an extensive evaluation in both school-age children and adults, including thyroid gland USG (ultrasonography), measurements of urinary iodine level, thyroid function test and thyroid antibodies were not performed in this area previously. The aim of this study was to assess all these parameters in primary school students and adults who were living in Tomarza a town of Kayseri and Alakuşak village of Tomarza where goiter prevalence has been reported high.

## Patients and Methods

This study was carried out in Tomarza where the altitude is higher than Kayseri and in Alakuşak (village of Tomarza) which is at the foot of mount Erciyes. Informed consent was obtained from the parents of students.

Heights of Tomarza and Alakuşak from sea level were 2250 meters and 2380 meters, respectively. Populations of Tomarza and Alakuşak were 10113 and 2110 persons, respectively. In Alakuşak primary school students and adults over 15 year old were selected randomly. In Tomarza a school that could represent the town was selected and adults over 15 year old were selected randomly from the district near the school. Table 1 summarizes the age and genders of participants in Tomarza and Alakuşak.

**Table 1.** Classification of adults and primary school students in the study due to gender.

	Female	Male	Total
Tomarza student	33	18	51
Alakuşak student	37	40	77
Tomarza adult	9	7	16
Alakuşak adult	42	13	55
Total	121	78	199

Physical examinations were done and PAHO (Pan American Health Organization) criteria (15) were used to evaluate the thyroid gland by the same endocrinologist (FB). Blood samples were drawn

to assess the serum levels of free T<sub>3</sub> (fT<sub>3</sub>), free T<sub>4</sub> (fT<sub>4</sub>), TSH, thyroglobulin (Tg), anti-M (anti TPO) and anti-thyroglobulin (anti-Tg). Spot urine samples were collected. Blood samples were stored at -20 C° until they assayed. Urine samples were collected deionized tubes and after addition of acidic material stored at -20°. All blood and urine samples were studied at the same time.

Thyroid USG was applied, by the same radiologist (NE) with 7.5 mHz high resolution Toshiba sonolayer-L-SAL-77-A equipment and width-length-depth of both thyroid lobes were estimated. Volumes of both lobes of thyroid gland were estimated by the formula of widthXlengthX0.524 and isthmus was not included in the volume (16). Goiter prevalence was defined according to Gutekunst's criteria (17).

Serum fT<sub>3</sub>, fT<sub>4</sub>, TSH, Tg, anti-M and anti-Tg levels were measured with commercial kits (Amerlex-MAB-FT3 RIA, hsTSH Coated Tube Assay IRMA, Thyroglobulin DSL-2500 RIA, TMAb C.T. /BC 1005/IRMA, TGAb IRMA C.T. /BC1006). Normal levels and intra and interassay CV analyses and sensitivities were listed respectively; fT<sub>3</sub> 2.2-4.7 pg/ml, %4.4, %7.6, 0.7 pmol/l, fT<sub>4</sub> 0.77-1.9 ng/dl, %4.4, % 6.1, 0.6 pmol/l, TSH 0.54-4.58 µIU/ml, %2.8, %6.0, 0.04 µIU/ml, Tg 7-38 ng/ml, %4.0, %5.5, 0.8 µg/L, anti-M < 100 IU/ml, %6.3, %11.2, anti-Tg <100 IU/ml, %5.8, 8.3.

Urine samples were analyzed for urinary iodine content according to the method described by Garry PJ et al. (18). Briefly urine samples were incubated with arsenic acid for ten minutes and incubated with ceric ammonium phosphate for ten minutes at 55°C heating-block after dissolving the urine samples at room temperature. This material was analyzed with spectrophotometer at 410 nm compared with distilled water. Results were compared with standard levels and estimated as µg/dl. Urinary iodine levels higher than 10 µg/dl were accepted normal, between 5-10 µg/dl mild, between 2-5µg moderate and lower than 2µg/dl were as accepted severe iodine deficiency.

Statistical analysis were performed by using paired and independent t-test for continuous variables, kappa test for agreement of diagnostic measurements (thyroid palpitation, thyroid USG), Chi-square test for categorical variables and linear regression test for relationships between continuous variables.

## Results

With thyroid palpation goiter prevalence was found as 57,1% in female students, 31.0% in male students and mean prevalence was 45.3%. Goiter prevalence was 86.3% in female adults, 35.0% in male adults and the mean prevalence was 71.8%. The mean goiter prevalence was 54.8% in all persons involved in the study (male 32.1%, female 69.4%).

Thyroid volumes measured with USG at the settlement areas were shown at Table 2. According to these findings thyroid volumes of students and adults in Alakuşak village were significantly higher than in Tomarza (students  $p<0.01$ , adults  $p<0.05$ ). Despite the thyroid volumes (measured with USG) of female students were slightly higher than male students this data was not statistically significant ( $p>0.05$ ), in adults thyroid volumes (measured with USG) of females were significantly higher than males ( $p<0.05$ ).

**Table 2.** Thyroid volumes measured with USG at the settlement areas

	Thyroid volume right (ml)	Thyroid volume left (ml)	Total
Tomarza student	2.38±1.05	2.39±1.08	4.78±2.02
Alakuşak student	6.88±5.86	5.52±3.57	12.40±9.14
Tomarza adult	7.31±2.75	5.74±1.93	13.05±4.19
Alakuşak adult	13.40±9.59	11.65±7.38	25.05±16.18

With USG 55.7% of female students and 50.0% of male students (mean 53.1%) had goiter in iodine deficient areas (17). On the other hand, according to Kurtoğlu's thyroid volume findings, 32.9% of female and 29.3 of males had goiter (19). According to Gutekunst's criteria the mean goiter prevalence in adults was 40.9% (female 52.9%, male 10.0%) (17). The mean goiter prevalence was 48.7% (female 54.5%, male 39.74) in all persons involved in the study (17).

Students with nonpalpabl thyroid glands had significantly higher  $fT_3$ ,  $fT_4$  levels than students with palpable thyroid glands ( $p<0.05$ ). Also we found that TSH, Tg levels and thyroid volumes were significantly higher in students with palpabl thyroid gland than students with nonpalpabl thyroid gland ( $p<0.05$ ). Despite BMI, age, and anti-Tg were higher in students with palpable thyroid gland than in students with nonpalpable thyroid gland, no statistically significant difference was demonstrated ( $p>0.05$ ) (Table 3). Adults with palpable thyroid glands had higher  $fT_3$ , TSH, anti-M, anti-Tg levels, and adults with nonpalpable thyroid glands had higher BMI, and  $fT_4$  levels but these differences were not significant. Adults with palpabl thyroid glands had significantly higher thyroid volumes than nonpalpable thyroid glands ( $p<0.05$ ) (Table 3).

$FT_3$ , TSH, Tg, antiTg and thyroid volumes were significantly higher in students who have goiter

**Table 3.** Comparison of some parameters (all students and adults) due to palpation of thyroid gland.

	Thyroid	Students			P	Thyroid	Adults			P
		N	X±SD				N	X±SD		
$FT_3$ (pg/ml)	Non-palpabl	70	3.80±0.62	0.026		Non-palpabl	20	3.37±0.66	0.511	
	Palpabl	58	3.56±0.58			Palpabl	51	3.51±0.81		
$FT_4$ (ng/dl)	Non-palpabl	70	1.55±0.39	0.010		Non-palpabl	20	1.58±0.50	0.413	
	Palpabl	58	1.27±0.54			Palpabl	51	1.47±0.47		
TSH (μIU/ml)	Non-palpabl	70	3.17±1.70	0.080		Non-palpabl	20	2.74±1.51	0.580	
	Palpabl	58	4.05±2.04			Palpabl	51	2.96±1.46		
Tg (ng/ml)	Non-palpabl	70	47.93±40.01	0.001		Non-palpabl	20	27.64±27.95	0.001	
	Palpabl	58	75.43±44.48			Palpabl	51	77.00±48.43		
Anti-Tg (IU/ml)	Non-palpabl	70	71.97±20.53	0.151		Non-palpabl	20	77.63±25.00	0.238	
	Palpabl	58	77.31±21.30			Palpabl	51	87.25±31.77		
Anti-M (IU/ml)	Non-palpabl	70	5.39±7.76	0.589		Non-palpabl	20	4.11±1.73	0.430	
	Palpabl	58	4.81±2.45			Palpabl	51	6.73±14.31		
BMI (kg/m <sup>2</sup> )	Non-palpabl	70	16.25±2.36	0.068		Non-palpabl	20	24.24±4.60	0.862	
	Palpabl	58	17.03±2.43			Palpabl	51	24.02±4.72		
Age (year)	Non-palpabl	70	10.97±0.80	0.163		Non-palpabl	20	45.21±18.98	0.576	
	Palpabl	58	11.19±0.96			Palpabl	51	42.48±17.79		
Thyroid volume (ml)	Non-palpabl	70	6.01±3.14	0.001		Non-palpabl	20	12.89±4.87	0.010	
	Palpabl	58	13.41±10.18			Palpabl	51	25.80±16.23		

N: number of patients, X±SD: mean ±standard deviation

with USG than normal students. FT<sub>4</sub> levels were significantly higher in the students who have not goiter than students who have goiter (measured with USG) ( $p < 0.001$ ) (Table 4). It was demonstrated that in adult participants with goiter FT<sub>3</sub>, anti-M levels were slightly but not significant, but Tg, anti-Tg, thyroid volumes were significantly higher than adult participants without goiter. Although it did not reach a significant level some parameters such as BMI, fT<sub>4</sub> and TSH were higher in adults with goiter (Table 4).

FT<sub>3</sub> levels were measured higher than upper limit in 7.34% of all participants and less than the lower limit in 3% of the same group. fT<sub>4</sub> levels were measured higher than upper limit 19.1% of all participants and lower than lower limit in 5.5% of the same group and TSH levels of 22.1% of all participants were found as higher than upper limit but neither of the values were lower than lower limit. Tg, anti-M, anti-Tg levels were found higher than upper limit 64.8%, 0.5%, 16.6% of all participants respectively.

In the diagnosis of goiter correlation between the palpation method and USG method was 76% in students ( $k=0.760$ ) and 43% in adults ( $k=0.426$ ).

Mean urinary iodine level was estimated as  $11.1 \pm 6.1$  µg/dl and in 53.3% of all participants urinary iodine levels were under the normal level (10 µg/dl). Median urinary iodine level was estimated as 9.54 µg/dl. Table 5 summarizes the urinary iodine levels due to settlement areas.

**Table 5.** Urinary iodine levels at the settlement areas

	2 ↓ (µg/dl)	2-5 (µg/dl)	5-10 (µg/dl)	10 ↑ (µg/dl)
Alakusak student	–	4	31	42
Tomarza Student	4	9	21	17
Alakusak Adult	–	5	23	27
Tomarza Adult	–	1	8	7
Total	4	19	83	93
%	2,01	9,55	41,71	46,73

## Discussion

Iodine deficiency and its consequences are important public health problems in Turkey. Many studies had been done in Turkey and in Central Anatolia to evaluate this problem (1,2,4,5,20-22) but most of them did not establish the relation between urinary iodine level and the goiter prevalence.

**Table 4.** Comparison of some parameters (all students and adults) due to thyroid gland USG.

	Students			Adults		
	Goiter N	X±SD	P	Goiter N	X±SD	P
FT <sub>3</sub> (pg/ml)	- 60	3.02 ± 0.67	0.001	-42	3.47 ± 0.66	0.979
	+ 68	3.48 ± 0.46		+ 29	3.48 ± 0.91	
FT <sub>4</sub> (ng/dl)	- 60	1.66 ± 0.39	0.001	-42	1.57 ± 0.42	0.127
	+ 68	1.18 ± 0.45		+ 29	1.40 ± 0.54	
TSH (µIU/ml)	- 60	2.84 ± 1.69	0.001	-42	2.92 ± 1.40	0.914
	+ 68	4.23 ± 1.86		+ 29	2.88 ± 1.59	
Tg (ng/ml)	- 60	38.01 ± 30.68	0.001	-42	43.19 ± 39.98	0.001
	+ 68	80.77 ± 44.84		+ 29	93.62 ± 45.66	
Anti-T (IU/ml)	- 60	69.84 ± 19.39	0.019	-42	78.69 ± 24.73	0.044
	+ 68	78.52 ± 21.64		+ 29	93.34 ± 35.47	
Anti-M (IU/ml)	- 60	4.44 ± 3.86	0.218	-42	4.29 ± 3.14	0.152
	+ 68	6.75 ± 7.34		+ 29	8.55 ± 18.78	
BMI	- 60	16.26 ± 2.74	0.118	-42	24.33 ± 4.78	0.586
	+ 68	16.92 ± 2.05		+ 29	23.71 ± 4.54	
Thyroid volume (ml)	- 60	4.76 ± 1.56	0.001	-42	14.12 ± 3.97	0.001
	+ 68	13.63 ± 9.23		+ 29	34.26 ± 17.50	

N: number of patients, X±SD: mean ± standard deviation

Thyroid gland palpitation is noninvasive and easy, it has been used in many epidemiological studies. Although this method is reliable in adults, in children and newborns thyroid palpation method has limitations. In Turkey goiter prevalence had been reported between 30.5-82% in different studies (9, 12). The goiter prevalence was approximately 40.2 % - 43.8% in Kayseri (7,11). We found a higher prevalence of goiter (54.8% with palpation) than other studies. Female/male ratio was calculated as 2,17 in our study.

USG is recommended method in epidemiological studies for the diagnosis of goiter. Particularly for detecting goiters with small volumes, it is a reliable and accepted as a standard method for measuring thyroid volumes (21, 16, 23). Aydın et al. reported that when compared with areas without iodine deficiency, all of the children had goiter and according to Kurtoğlu's criteria goiter prevalence was found as 76.7% (11). In our study according to Gutekunst's thyroid volume findings 55.7% of female student and 50,0% of male student (mean 53.1%), according to Kurtoğlu's thyroid volume findings from mild iodine deficient areas (19) 32.9% of female students 29.3 of male students (mean %31.3) had goiter with USG. Recently by measuring sonographic thyroid volumes, Erdoğan et al. has reported goiter prevalence as 33% in school-age children living in our region. In this study, recommended normative values for thyroid volume in European schoolchildren, has been used to define goiter (14). The mean goiter prevalence in adults, with USG according to Gutekunst's criteria (17), was found as 40.9% (female 52.9%, male 10.0%). Thyroid volume measurements with USG reveals that female students had 1,1 times more goiter than males and this ratio was found 5,3 in adults; totally female/ male ratio was estimated as 1,37.

Various studies from our country and other countries with different results have been reported about the relation between gender and thyroid volumes (11,24-27). In our study thyroid volumes in females detected with USG were higher than males in students and in adults. In students (male and female) and in male adults right thyroid volumes were larger than left. In female adults left thyroid volumes were larger than right. These findings were correlated with some of the recent literatures (19,27, 29).

85-90% of daily iodine intake is excreted via urine so urinary iodine level is one of the most important parameter that reflects iodine level of an area. To determine the iodine level of an area minimally 40-50 urine samples needed. Also to reflect the chronic iodine effect thyroid gland volumes and Tg levels are good criteria's (28). In most European countries inverse ratio between urinary iodine level and goiter prevalence has been reported (29-31). A study from our country showed the similar data (32), but another study has demonstrated that there were no differences between urinary iodine levels of pregnant with goiter, pregnant without goiter and normal females without goiter (33).

Aydın et al. showed that 94.6% of children had lower than normal urine levels in our region (11). We demonstrated 46.7% of adults had lower than normal urine levels. Furthermore we determined median urinary iodine as 9.54 µg/dl indicating mild iodine deficiency. Erdoğan et al. has reported moderate iodine deficiency (median urinary iodine level, 2.55 µg/dl) (14). In our study, the median urinary iodine concentration was not comparable with the severity of goiter prevalence, and according to high goiter prevalence the median urinary iodine level was more than expected suggesting that measurement techniques of iodine level may interfere with the results. Moreover urinary iodine levels reflect iodine intake but thyroid volume and Tg level reflect chronic effects of iodine deficiency.

It is known that in iodine deficient areas  $ft_3$  levels are normal or high,  $ft_4$  levels are low-normal or low and TSH levels are generally normal or slightly high. Because of the adaptation mechanisms due to iodine deficiency TSH levels increase and thyroid volumes increase due TSH levels. Ando et al. (30) and Martino et al. (21) reported that  $ft_4$ ,  $TT_4$  and  $ft_3$ ,  $TT_3$  and TSH levels were not significantly different between endemic and control areas but in both studies its demonstrated that Tg levels were higher in endemic areas. Also anti-M and anti-Tg positivity were found 3% and 6.2% respectively. Hintze et al. showed that the persons with goiter had low TSH levels and high Tg levels (27). Many studies revealed different results between goiter prevalence and thyroid fuctions, TSH levels, thyroid antibody positivity and iodine levels (34-37). In normal population Koloğlu reported that anti-M positivity as 2%, but in endemic areas this

parameter was reported as 20.5% (38). Keleştimur et al. reported postpartum anti-M positivity as 0.2% (39). In our study we detected similar values as anti-M positivity as 0.5%, and high anti Tg level as 16,6%.

It is accepted that increase of Tg level is the most important parameter which shows chronic iodine deficiency and generally this is positively correlated with TSH levels (40, 41). In our study we detected positive correlation between increased Tg levels, TSH levels and goiter in students but in adults we could not demonstrate these relations.

In conclusion despite the high prevalence of goiter, median urinary iodine level was relatively high, suggesting that measurement techniques of iodine level may affect the results. According to chronic iodine deficiency parameter such as Tg, it is obvious that the people living at this endemic area need iodine prophylaxis.

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