Assessment of goiter prevalence, iodine status and thyroid functions in school-age children of rural Yusufeli district in eastern Turkey

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According to previous studies, Turkey has generally been accepted as a moderate endemic iodine deficient country. However, it has recently been reported that there are regions in Turkey where iodine deficiency is more severe than previously known. The current study was aimed at ascertaining the goiter prevalence by thyroid volumes, iodine status and thyroid functions in school-age children living in an area which is suspected to have moderate or severe iodine deficiency.

Overall goiter was found in 47.6% of children, in 22.8% of girls and in 24.8% of boys. Mean thyroid volumes did not differ significantly according to sex. Significant correlation was found between thyroid volume and body surface area and age. There was a negative correlation between the urinary iodine concentration and thyroid volume ($r=0.45$, $p<0.01$). Median urinary iodine concentrations in subjects with and without goiter were 20 μg/dl and 5.2 μg/dl, respectively. While median urinary iodine levels of the subjects with goiter were consistent with severe-moderate iodine deficiency, levels in subjects without goiter were comparable to moderate-mild iodine deficiency. None of the subjects had the signs or symptoms of hyper-or hypothyroidism. The differences in the mean values of thyroid hormones and TSH levels between subjects with or without goiter were not significant ($p>0.05$). No correlation was found between urinary iodine concentrations and thyroid hormone levels. A weak correlation was found between urinary iodine concentration and TSH levels ($r=0.12$, $p=0.05$).

Individuals with goiter were investigated etiologically: biochemical hypothyroidism was detected in 2%, compensated hypothyroidism in 12.6%, autoimmune thyroiditis in 2%, nodular goiter in 3% and isolated high TSH level with autoimmune thyroiditis in 0.08%.

In conclusion, although a salt iodization program has been started in Turkey, our study indicates that some regions with severe iodine deficiency are still present. This research suggests that this program should be re-evaluated for remote areas with self-contained economic systems, and should be expanded and more effectively applied nation-wide.

Key words: iodine deficiency, children, Turkey.

Iodine deficiency is still an important public health issue in Turkey. According to previous studies, Turkey has generally been accepted as a moderate endemic iodine deficiency country[1]. Although salt iodization was started in 1968, the level of utilization of iodized salt has been inadequate to control iodine deficiency. In 1995, the Health Ministry initiated a new national program including standardization of iodized salt and its use nation-wide, and legislation for mandatory iodization of household salt was passed in 1998. However, it has recently been reported that there are regions in Turkey where iodine deficiency is more severe than previously known[2,3].

An inadequate dietary supply of iodine results in the development of a variety of disorders classified under the general heading of iodine deficiency disorders. Endemic goiter is the first and most visible sign of iodine deficiency. The thyroid enlarges as an adaptation to normalize inadequate hormone levels, a reaction mediated by thyrotropin (TSH) stimulation. During this adaptation, deviation in thyroid hormone levels may occur, ranging from compensated hypothyroidism to primary hypothyroidism in respect to the severity of iodine deficiency[4].

The aims of this study were: 1) to determine goiter prevalence by ultrasonography and urinary iodine excretion in school-children aged 7-14 years in a remote area in which goiter is thought to be endemic; 2) to assess the impact of iodine deficiency on thyroid hormone levels of students with or without goiter; 3) to learn how effectively the salt iodization program has been working to improve iodine intake in this remote area.

Material and Methods

The study was performed in the mountain villages of Yusufeli, which is a town in eastern Turkey. Five hundred and eighteen school-children attend the four primary school, and come from the surrounding mountain villages. Of the 518 students, 259 were selected by using systematic sampling method to achieve a homogeneous distribution. Nine subjects were excluded: due to absence of informed consent (n=5), because serum thyroid hormones could not be measured (n=3), and because thyroid ultrasonography could not be performed (n=1). Thus, 250 school-children (126 boys) aged 7-14 years, who were born or living at least for five years in the area, were included in the study. A questionnaire was given to all students participating in the study to be filled out by their families regarding whether or not they used iodized salt in the preparation of food in their homes. All students underwent physical examination and age, gender, weight of the subjects were recorded. Body surface area (BSA in m^2) was calculated suing the formula $BSA=W^{0.425}xH^{0.725}x1.84x10^{-4}$ where W is the weight in kg and H is the height in cm[5]. Thyroid ultrasonic volume measurement was performed by the same radiologist for each student in the supine position with the neck slightly hyperextended. The dimensions of both thyroid lobes were measured with high resolution real-time portable ultrasonic scanner (Corevision, Toshiba, Japan) using a 8 MHz linear transducer (PLF-805ST, Toshiba, Japan). Longitudinal and transverse scans were performed allowing the measurement of the depth (d), the width (w) and the length (L) of each lobe. The volume of each lobe was calculated by the formula: V (ml)=0.479 x d x w x L (cm). The thyroid volume was the sum of the volumes of both lobes. The volume of the isthmus was not included. To define the goiter, thyroid volumes by ultrasound for age and gender were compared with reference thyroid volumes (percentile 97) of children born and living in areas from 12 European countries where iodine intake is normal.

Urinary iodine concentrations were measured in randomly collected urine samples by Sandhell-Kolthoff reaction. Urine was first digested with chloric acid in a heating block and iodine was determined by its catalytic reduction of ceric ammonium sulfate in the presence of arsenious acid. Mean urinary iodine excretion lower than 1.9 μg/dl was accepted as severe, levels between 2.0-4.9 μg/dl as moderate and levels between 5.0-9.9 μg/dl as mild iodine deficiency[6].

Serum free thyroxine (FT_4), total thyroxine (TT_4), free triiodothyronine (FT_3), total triiodothyronine (TT_3) and thyroid stimulating hormone (TSH) concentrations were determined by chemiluminometric method using ACS 180 (Chiron Diagnostic). Serum anti-thyroid antibodies were studied using enzyme-linked immunoassay (ELISA) method (Clark Laboratories Inc., New York, USA). The results of thyroid hormones were compared with the reference values in the same ages in the literature in which chemiluminometric method was used[7,8]. Cut-off levels for anti-thyroperoxidase and anti-microsomal antibodies were >0.527 and >0.460, respectively.

This study was approved by the Atatürk University Ethical Committee and informed consent forms were obtained from families of all children recruited for the study. Statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS). Student's-t test was used in comparisons. Chi-square test was used where appropriate.

Results

According to questionnaire responses, 62.8% (158/250) of the subjects were consuming uniodized salt, termed "rock salt".

Clinical characteristics, mean and median thyroid volumes of subjects by age and sex, and the upper limits of reference thyroid volumes are shown in Table I. When compared with the upper limits of the reference thyroid volumes by ultrasonography, goiter was found in 47.6% (119/250) of all children, in 22.8% (57/250) of girls, and in 24.8% (62/250) of boys. Although goiter prevalence was slightly higher in boys, the difference was not statistically significant ($p>0.05$). Mean thyroid volumes did not differ significantly by sex ($p>0.05$). Significant correlations were found between thyroid volume and body surface area (BSA) ($r=0.99$, $p<0.05$) and age ($r=0.96$, $p<0.05$).

Median urinary iodine concentrations of subjects with and without goiter were 2.0 µg/dl and 5.2 µg/dl, respectively (Table II), and the difference was statistically significant ($p<0.05$). While median urinary iodine levels of the subjects with goiter were consistent with severe-moderate iodine deficiency, the levels in subjects without goiter were comparable to moderate-mild iodine deficiency[6]. The correlation between urinary iodine excretion and thyroid volume is depicted in Figure 1. There was a negative correlation between them ($r=0.45$, $p<0.01$).

Table III shows the serum thyroid hormone levels in subjects with and without goiter. None of the subjects had the signs or symptoms of

Table I. Characteristics of the Subjects with Goiter by Age and Sex

				Thyroid volume (ml)				
Age	Sex	N	BSA* (m^2)	Mean±SD	Range	Median	ULN** (97%)	No of subjects with goiter (%)
7	F	11	0.8	6.9±4.1	3.6-10.2	5.2	5.9	4 (36.4)
	M	5	0.8	5.7±2.0	3.6-10.6	5.4	5.7	2 (40)
8	F	11	0.9	7.2±3.0	3.9-10.5	5.8	6.9	7 (63.6)
	M	15	0.9	7.0±2.5	3.9-9.8	6.7	6.1	9 (60)
9	F	14	1.0	8.0±2.7	5.1-0.9	7.7	8.0	7 (50)
	M	14	1.0	7.4±2.1	5.1-10.4	8.1	6.8	8 (57.1)
10	F	12	1.1	9.6±2.6	5.4-11.7	8.3	9.2	6 (50)
	M	12	1.0	8.5±4.2	5.4-11.7	6.6	7.8	5 (41.7)
11	F	15	1.2	12.7±6.4	9.9-15.5	11.8	10.4	7 (46.6)
	M	23	1.1	10.7±5.9	9.9-13.0	9.0	9.0	10 (43.3)
12	F	24	1.3	13.1±8.9	10.9-15.3	10.2	11.7	9 (37.5)
	M	22	1.2	12.6±5.0	10.9-14.9	10.9	10.4	10 (45.4)
13	F	18	1.3	13.8±6.3	10.2-15.3	11.7	13.1	6 (33.3)
	M	19	1.4	13.1±7.4	10.2-15.8	11.8	12.0	8 (42.1)
14	F	19	1.4	15.6±5.4	13.1-18.1	17.1	14.6	11 (57.9)
	M	16	1.5	17.0±5.4	10.2-19.6	16.2	13.9	10 (62.5)
Total		250						119 (47.6)
	F/M	124/126						57/62 (45.9/49.2)

* Body surface area, ** Upper limit of normal thyroid volume.

Table II. Mean and Median Urinary Iodine Concentrations of Subjects with and without Goiter

		UIC* (µg/dl)		
	n	Mean±SD	Median	Range
Subjects with goiter	119	2.9±3.3	2.0	0.0-17
Subjects without goiter	131	5.9±5.5	5.2	0.0-25
Total	250	4.5±4.6	2.9	0.0-25

UIC*: Urinary iodine concentration.

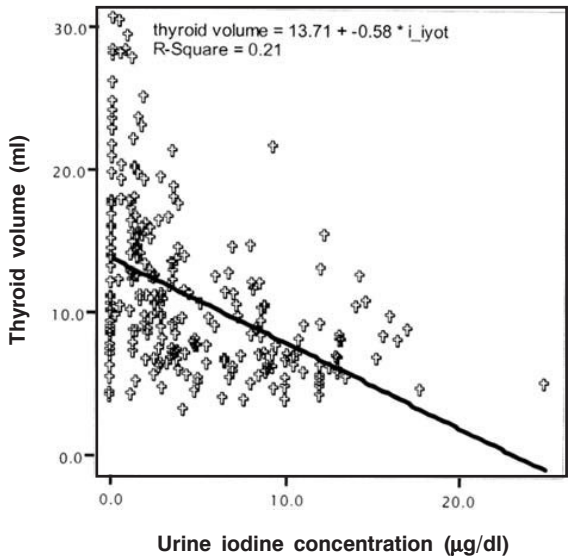

Fig. 1. Correlation between urine iodine concentration and thyroid volume (r=0.45, p<0.01).

hyper-or hypothyroidism. The differences in the mean values of thyroid hormones and TSH levels between subjects with and without goiter were not significant (p>0.05). No correlation was found between urinary iodine concentrations and thyroid hormone levels (p>0.05). A weak negative correlation was found between urine iodine concentration and TSH levels (r=0.12, p=0.05). Isolated TSH elevation was diagnosed in 15 (12.6%) subjects with goiter. Mean TSH values of the subjects having isolated TSH elevation was 7.32±1.1 (5.9-10.6) mIU/ml. Of 119 subjects with goiter, 16 (13.0%) had elevation of total T_3 and/or FT_3 levels when compared with the reference thyroid hormone values in the literature. Mean T_3/T_4 ratio between the subjects with and without goiter did not show statistical difference (p>0.05), although it was slightly higher in subjects with goiter (Table III).

Individuals with goiter were investigated etiologically: biochemical hypothyroidism was detected in 2% (3/119), autoimmune thyroiditis in 2% (3/119), nodular goiter in 3% (4/119, and isolated high TSH level with autoimmune thyroiditis in 0.08% (1/119).

Discussion

According to the World Health Organization (WHO), if more than 5% of school-age children are suffering from goiter, the area should be classified as endemic for iodine deficiency. Earlier studies concerning iodine deficiency which have been conducted in different regions of the country have indicated that Turkey is a moderately iodine deficient country. In a large survey performed by Urgancıoğlu and Hatemi[1], overall goiter prevalence by palpation was found as 30.5% nation-wide. They also reported that goiter prevalence may increase up to 50% in some regions. In 1995, a nation-wide salt iodization program implemented by the Ministry of Health was initiated to control iodine deficiency. However, Yordam et al[2]. recently reported that goiter prevalence was 92% in a remote area, which points to severe iodine deficiency. The present study was conducted in a mountain region suspected to be moderately or severely iodine deficient. Overall goiter prevalence by ultrasound was found to be 47.6%, suggesting severe iodine deficiency. Goiter prevalence tended to be higher in boys (24.8%) than in girls (22.8%), but this did not reach statistical significance. For the field studies in remote areas where no other methods are available, goiter staging by physical examination set by WHO has been used to detect goiter prevalence. Although the sensitivity of clinical examination in establishing presence of goiter increases with better training

Table III. Mean Thyroid Hormone Levels and T_3/T_4 Ratio in Subjects with and without Goiter

	Subjects with goiter		Subjects without goiter		
	Mean±SD	Range	Mean±SD	Range	P
TSH (mIU/Ml)	2.28±1.48	0.49±10.6	2.41±1.33	0.50-4.08	>0.05
TT_3 (ng/ml)	1.61±0.26	1.09-2.40	1.59±0.26	1.08-2.33	>0.05
FT_3 (pg/ml)	3.84±0.38	2.97-5.27	3.79-0.37	3.04-4.28	>0.05
TT_4 (µg/dl)	8.02±2.05	1.00-14.0	8.70±1.46	4.30-13.60	>0.05
FT_4 (ng/ml)	1.13±0.18	0.59-1.65	1.11±0.19	0.47-1.63	>0.05
TT_3/TT_4	0.20±0.05	0.15-0.45	0.18±0.02	0.10-0.29	>0.05

Reference values[7-8]: TSH: 04-4.2, TT_3: 0.97-1.95, FT_3: 1.4-4.1, TT_4: 4.4-14, FT_4: 07-2.3.
FT_3: Free triiodothyronine, FT_4: Free thyroxine, TT3: Total triiodothyronine.

of the health personnel, goiter prevalence in the studies based on clinical estimation of thyroid size may result in overestimation of small goiter, especially in children. The distinction between absence of goiter (Stage 0) and presence of small goiter (stage I) is difficult and, consequently, the overall goiter prevalence may be incorrect. Therefore, the frequency of distribution of thyroid volume measured by ultrasound is highly recommended, especially in endemic regions where visible goiter rate is low[4].

In previous studies where the correlation between thyroid volume and variables such as age, sex, weight, height and BSA were analyzed, the strongest correlation was found between the thyroid volume and BSA[9-10]. In the current study, mean thyroid volumes did not differ significantly between sexes ($p>0.05$), and there was significant correlation between thyroid volume and BSA ($r=0.99$, $p<0.05$) and age ($r=0.96$, $p<0.05$). Although thyroid volumes of the students gradually increased with age, there was a striking increase in thyroid volumes after 10 years of age in girls and after 12 years of age in boys, which is consistent with the ages of onset of puberty[4].

In our study, while mean and median urinary iodine measurements of the subjects with goiter were consistent with severe-moderate iodine deficiency, levels in subjects without goiter were consistent with mild-moderate iodine deficiency (Table II). Although some studies failed to show any correlation between the urinary iodine levels and thyroid volume[11], we found negative correlation between thyroid size and the urinary iodine levels ($r=0.45$, $p<0.01$) (Fig. 1). The lowest mean urinary iodine excretion was detected in subjects with the largest thyroid size. As in our study, a negative correlation has also been reported in other studies[1]. However, there may not be a correlation between the thyroid volume and urinary iodine level. Just as reports of normal iodine levels in subjects with goiter are present in the literature, low iodine levels have also been reported in subjects without goiter[11-13]. This situation has been explained by the fact that urinary iodine level is not the unique factor in the forming of goiter, although urinary iodine excretion is an important epidemiological factor. High goiter prevalence in these studies might also be related to environmental factors such as local natural goitrogens, water pollution, dietary minerals, or genetic thyroid hormone biosynthesis disorders[11].

The region in which we performed this study is a plentiful rainy and mountainous area with a partly self contained economy. Most of the families of the students were still consuming uniodized salt, or "rock salt". People living in this area mainly consume agricultural and animal products, which may lead to iodine deficiency. These results show that is region of mountain villages in Yusufeli in which the study was performed, is a highly endemic area due to severe iodine deficiency, comparable to some regions in Latin America, Africa and Asia.

In our study, there was no difference in mean thyroid hormone levels between the subjects with and without goiter (Table III). Mean thyroid hormone levels were comparable to the reference values[7,8]. Also, there was no correlation between the urinary iodine concentration and serum thyroid hormone levels ($p>0.05$). However, a weak negative correlation was found between urine iodine concentration and TSH levels ($p=0.05$). In some studies, significant changes in thyroid hormone levels ranging from isolated high TSH levels to biochemical hypothyroidism in subjects living in endemic regions have been reported[2,4,14,15]. In our study, 15 (12.6%) of the students had isolated high TSH (compensated hypothyroidism), and 3 had biochemical hypothyroidism due to iodine deficiency.

Although some previous studies[8,15] from the Black Sea region, which surrounds the current study area, have indicated moderate-severe iodine deficiency, severe iodine deficiency in this area was not reported before.

In conclusion, although a salt iodization program has been started in Turkey, our study indicates that some regions with severe iodine deficiency still exist. This research suggests that this program should be re-evaluated for remote areas with self-contained economic systems, and should be expanded and more effectively applied nation-wide. As previously suggested by Yordam et al.[2], to prevent the deleterious effects of severe iodine deficiency on populations living in remote areas such as in the mountain villages of Yusufeli, iodized oil and iodine tablets, which are effective in the short-term, should be urgently implemented.

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