original article

Urine iodine excretion ın patients with euthyroid noduler disease

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Ann Saudi Med 2011; 31(2): 167-170

PMID: **** DOI: 10.4103/0256-4947.78204

BACKGROUND AND OBJECTIVES: Different nutritional and environmental factors are responsible for the pathogenesis of goiter, but iodine deficiency is the most important factor. However, little is known about the natural course of benign thyroid nodules in euthyroid patients over time. Few studies have used ultrasonographic evaluation to address this issue, especially in iodine-deficient areas. In this study, we present the long-term follow-up of benign thyroid nodules in a iodine-deficient area.

DESIGN AND SETTING: Cross-sectional study at a tertiary referral center.

PATIENTS AND METHODS: This study included 62 randomly selected patients with benign euthyroid nodule. Thyroid volume and nodules were measured with sonography. Iodine intake was estimated by patient diet history and by measuring iodine excretion in spot urine samples. Patients were followed one year.

RESULTS: Patients were divided into three groups according to level of urine iodine excretion: Group 1: <50 µg/L (severe iodine deficiency group), Group 2: 50-100 µg/L (mild iodine deficiency group), Group 3: >100 µg/L (iodine sufficient group). The presence of additional disease (hypertension, diabetes mellitus, coronary heart disease, chronic renal failure and a history of any medication for chronic disorder) and smoking rates were significantly higher in first group compared to the second and third group. Among groups, no significant difference was observed in either right or left thyroid lobe volume after one year. A clinically significant increase in nodule volume was observed in the first group, while there was a significant decrease in the second and third group.

CONCLUSION: In this study, iodine deficiency was associated with an increase in thyroid nodule volumes. Smoking rates were higher in iodine deficient groups. It is thought that smoking impairs iodine intake or absorption consistent with a previous report.

Thyroid nodules are common clinical findings.[1] 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.[2] Different nutritional and environmental factors are responsible for the pathogenesis of goiter but iodine deficiency is the most important factor. Iodine is an essential component of thyroid hormones.[3-6] A minimum of approximately 70 µg of iodine is therefore needed to produce thyroid hormones in the thyroid gland each day.[7]

The prediction of iodine intake is difficult.[8,9] The standard measure of iodine nutrition in a community or country is the median urinary iodine excretion, expressed in micrograms per liter. The values correspond to 70 to 80 percent of the daily iodine intake, which often varies widely among people in the same community or country.[7] According to the WHO, a median urinary iodine excretion of 100 to 199 µg/L indicates that the iodine intake is adequate.[10]

Gutekunst et al found a higher prevalence of thyroid nodules in an iodine-deficient area compared with an iodine-sufficient area.[11] However, little is known about the natural course of benign thyroid nodules in euthyroid patients over time. Therefore, the purpose of the current study was to evaluate the association between iodine intake, smoking, urine iodine excretion and euthyroid noduler disease.

PATIENTS AND METHODS

Sixty-two patients were recruited from the outpatient clinics of Ankara Numune Education and Research Hospital. All patients had thyroid nodules determined

Table 1. Patient characteristics in by level of urine iodine excretion.

	Group 1 18 (29%)	Group 2 18 (29%)	Group 3 26 (41.9%)	Total 62 (100%)
Mean age (years)	49.5 (7)	41.8 (13)	45.3 (12)	45.5 (11)
Presence of additional disease	12 (66.7%)	7 (38.9%)	6 (23.1%)	25 (40.3%)
Iodine rich diet	4 (22.2%)	12 (66.7%)	19 (73.1%)	35 (56.5%)
Smoking	9 (50%)	2 (11.1%)	8 (30.8%)	19 (30.6%)

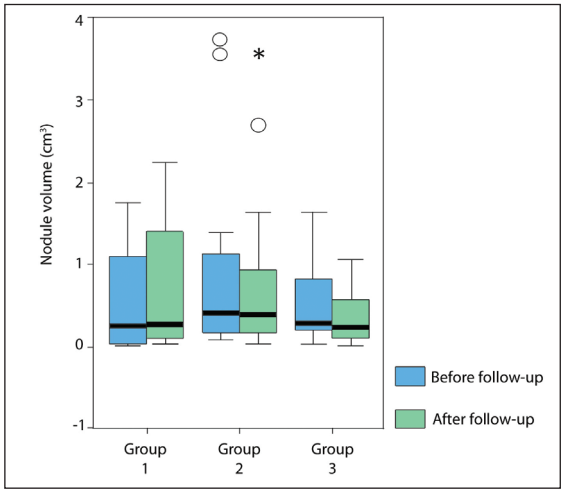

Figure 1. Nodule volume changes between groups before and after follow up by urine iodine level. (Group 1: <50 µg/L [severe iodine deficiency group], Group 2: 50-100 µg/L [mild iodine deficiency], Group 3: >100 µg/L [iodine sufficiency]). The nodule volume increase in first group patients was statistically significant when compared to the nodule volume decrease in second and third group patients (*P*=.002, *P*<.001, respectively). The horizontal lines in the middle of each box indicate the median, the top and bottom borders of the box mark the 25th and 75th percentiles. The whiskers above and below the box mark the maximum and minimum levels. Open circles indicate outliers. Asterisks represents extreme cases.

by ultrasonography. Cytology by fine-needle aspiration showed tumors to be benign. Patients with nodules greater than 2 centimeters, cystic nodules, or neoplastic lesion were excluded from the study. All patients were clinically euthyroid with normal levels of serum free T4 and thyroid stimulating hormone (TSH).

All patients were asked about the presence of chronic disease like diabetes mellitus, hypertension, coronary heart disease, and others, and patients with serious cardiovascular disease, liver disease, renal disease were excluded. Chronic diseases under control were considered an of additional disease and were included in the study.

A semi-quantitative food frequency method was used to investigate the usual iodine intake of the subjects. The questionnaire contained questions regarding the average food consumption frequency. The food items included those with a relatively high iodine content. All patients were divided into three groups according to level of urine iodine excretion analyzed at first visit. Group 1: <50 µg/L (severe iodine deficiency group, n=18), Group 2: 50-100 µg/L (mild iodine deficiency group, n=18), Group 3: >100 µg/L (iodine sufficient group, n=26). Serum free T4 and TSH were checked, and differences in thyroid ultrasono graphic findings before and after follow up were noted. The measurements of nodule diameter were performed by the same person using high-resolution sonography (General Electric LOQIC 400, USA). Nodule volumes were calculated from the ultrasound measurements by multiplication of three diameters and the constant value 0.52. Serum TSH and free T4 concentrations were measured by an Abbott Architect 2000 device (Illinois, USA) with chemiluminesence microparticule immunassey methods. Normal ranges were 0.9-1.7 ng/mL for freeT4 and 0.2-4.2 mIU/L for TSH. In the early morning first voided urine samples were analyzed by Sandell-Kolthoff reaction with spectrophotometry for iodine concentration.

Statistical evaluations were performed with Shapiro Wilk test, the t or Mann Whitney U test, one-way ANOVA, the Kruskal Wallis test, and the Pearson chi-square test. Initial thyroid volumes, nodule volumes and thyroid functions were compared with the values after one year follow up by the dependent *t* test and Wilcoxon test. Significance was defined as *P*<.05.

RESULTS

Between groups mean age (*P*=.14) and disease duration (*P*=.97) were similar (**Table 1**). The presence of additional disease (*P*=.004) and smoking rates (*P*=.011) were significantly high in the first group compared to the third group. In the first group the percentage of iodine-rich fed patients was 22% while it was 73.1% in third group (*P*<.001) (**Table 1**).

There was no significant differences among groups in the number of thyroid nodules larger than one centimeter (*P*=.787). No statistically significant change was observed in right, left lobe nor nodule volume before and after one year follow up period (*P* values for changes were .79, .96, .318 respectively, **Table 2**). Thyroid lobe and nodule volume changes after one-year follow up were shown in **Tables 1 and 2**.

In first group, the mean nodule volume was 0.468 cm^3 at the initial visit and increased to 0.672 cm^3 after one year follow up. This volume increase was 45.6%. Fifteen of 18 patients showed an increase, but two showed a decrease in nodule volume and one patient had no change. Although a decrease in mean nodule volume was observed in two patients, the difference was not found to be statistically significant. In third group mean nodule volume decreased from 0.47 cm^3 to 0.33 cm^3. This volume decrease was 29.7% (**Figure 1**). Sixteen of 26 patients showed a decrease, but six showed an increase in nodule volume and four patients had no change. The nodule volume increase in first group patients was found to be statistically significant when compared to the nodule volume decrease in second and third group patients (*P* values; *P*=.002; *P*<.001 respectively).

Table 2. Right lobe volume, left lobe volume and nodule volume at first visit and at one-year follow-up visit.

	Urine iodine excretion	N	Mean (standard deviation) (cm^3)	Minimum (cm^3)	Maximum (cm^3)
Initial right lobe volume	Group 1	18	12.36 (16)	1.970	73.22
	Group 2	18	8.035 (4)	3.360	21.44
	Group 3	26	11.74 (9)	4.620	44.72
	Total	62	10.83 (10)	1.970	73.22
Last right lobe volume	Group 1	18	12.77 (18)	2.680	85.96
	Group 2	18	8.534 (3)	3.650	14.64
	Group 3	26	11.29 (9)	3.030	38.89
	Total	62	10.91 (11)	2.680	85.96
Initial left lobe volume	Group 1	18	8.639 (118)	0.450	51.11
	Group 2	18	6.528 (3)	1.560	17.05
	Group 3	26	7.901 (3)	2.190	18.52
	Total	62	7.713 (6)	0.450	51.11
Last left lobe Volume	Group 1	18	10.04 (15)	0.960	71.88
	Group 2	18	7.440 (3)	2.730	13.42
	Group 3	26	9.609 (8)	3.040	41.64
	Total	62	9.097 (10)	0.960	71.88
Initial nodule volume	Group 1	18	0.4868 (0.5)	0.014	1.747
	Group 2	18	0.865 (1)	0.072	3.744
	Group 3	26	0.470 (0.4)	0.018	1.638
	Total	62	0.586 (0.7)	0.014	3.744
Last nodule volume	Group 1	17	0.672 (0.8)	0.031	2.246
	Group 2	18	0.783 (0.9)	0.024	3.556
	Group 3	23	0.339 (0.3)	0.014	1.060
	Total	58	0.579 (0.7)	0.014	3.556

DISCUSSION

We divided patients into three groups so as to detect the effect of iodine deficiency at any level. No relationship was found between thyroid volume and urine iodine excretion, even in patients with severe iodine deficiency. A relationship between thyroid nodule volume and urine iodine excretion was observed. Increased iodine excretion, which reflects iodine intake, is inversely related to thyroid nodule volume.

An increased level of iodine intake is associated with a decreased thyroid nodule volume. We have emphasized the importance of a critical level of urine iodine excretion that is related with thyroid nodule enlargement. We think that further studies are needed to determne cut off value of urine iodine excretion. Patients with thyroid nodules can be nourished by an iodine-rich diet, confirmed by urine iodine excretion, to control the thyroid nodule growth.

Iodine deficiency is an important public health problem in Turkey as in other parts of the world. Of the many studies on iodine deficiency, most have not shown a relationship between urine iodine level and prognosis of the thyroid nodule.[12,13] Ultrasonography is the recommended method for evaluating thyroid nodules for volume and consistency. Eighty-five to 90 percent of daily iodine intake is excreted by the urine. Thus, the urine iodine level is an important parameter that reflects the iodine levels of a geographic area and effects chronic iodine deficiency on thyroid gland volumes. In a European study, a relationship was shown between urine iodine level and goiter.[14] However, another study showed no relationship between urine iodine level and goiter.[15] It is known that in a state of iodine deficiency, free T4 levels are low and TSH levels are normal or high as an adaptation mechanism TSH levels increase and thyroid volumes are effected by high TSH levels increase.[2]

The relationship between iodine intake and thyroid nodule formation is not clear. Thyroid size and urinary iodine excretion level are the most widely used measures of iodine status.[16]

Rasmussen et al showed an inverse relationship between 24-hour urine iodine excretion with thyroid volume. For spot urine values, the same relationship was shown but it was not found to be statistically significant. No relationship was found between thyroid nodule formation and iodine level in that study.[17]

In our study, additional disease and smoking rates

were significantly higher in the first group compared to the third group. The percentage of patients with iodine-rich diets was significantly higher in the third group compared to the first and second group. We think that the increased rate of smoking and the presence of additional disease may have caused this much iodine intake variation in same geographic area. In our study, thyroid and nodule volumes were measured by same examiner and ultrasound machine. The fact that patients were evaluated periodically for one year is a major advantage of our study. On the other hand, the small sample size is a disadvantage.

This study has shown the significance of iodine deficiency and detection of this situation by measuring urinary iodine excretion and also the significant effect of iodine deficiency on nodular goiter. In iodine-deficient groups, smoking rates were higher. It is thought that smoking impairs iodine intake or absorption, which is consistent with a previous report by Knudsen et al.[18]

As shown in this study, an increased level of iodine intake is associated with a decreased thyroid nodule volume. Patients with thyroid nodule volumes related to iodine deficiency can be evaluated and if needed, iodine supplementation can be recommended by an iodine-rich diet.

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