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Research paper

Thyroid volume, selenium levels and nutritional habits in a rural region in Albania

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ABSTRACT

OBJECTIVE Environmental factors are involved in goiter development. An increased number of goitrous patients were identified among outpatients in Gyrocaster, a mountainous region in Southwestern Albania. We examined possible associations of thyroid enlargement with nutritional factors. DESIGN 112 consecutive patients, 104 females, aged 52.8 ±12.1 (mean±SD), who either were taking thyroxine (n=27) or were suspected to have thyroid disease were examined. Thyroid parameters and nutritional habits were recorded and serum selenium and urine iodine levels were determined; thyroid ultrasound was performed. RESULTS The median thyroid volume (TV) was 20.4ml (range 4.4-97.6). All consumed food was home-produced. TV correlated negatively with the frequency of lamb-goat meat and vegetables consumption (p=0.05 and p=0.03, respectively). Mean TV was significantly lower in those eating lamb-goat >1 times/week (21.4±13.3 vs 31.9±23 ml, p<0.01). The association of TV with lamb meat consumption was independent of sex, education or occupation (p<0.009). Selenium levels ranged from 30.6-138μg/L (reference range 43-190). There was no association between selenium levels and TV. 43% of the subjects had TSH<0.3 mU/L (those on thyroxine were excluded). Log TSH correlated negatively with TV and fT4 levels (p<0.007), indicating the presence of autonomy (TSHRab positive in two subjects). Mean urinary iodine excretion was 99.8±35.3μg/gr creatinine (normal >100). CONCLUSIONS Nutritional factors may be involved in the development of goiter in Southwestern Albania. No role of selenium was found. The higher consumption of lamb-goat meat and vegetables, all non-industrialized, appeared to be protective. This finding may reflect better socioeconomic status, although this was not identified. Unrecognized subclinical hyperthyroidism, probably due to thyroid autonomy, was quite common.

Key words: Albania, Iodine, Nutrition, Protein diet, Selenium, Thyroid

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INTRODUCTION

Albania is an in-transition country in the Balkan area and among those with the lowest per capita income in Europe. The Health System of Albania, as the Albanian society itself, is now taking its first steps in adopting the Western financial model. Globalization in modern Western society, even at the level of dietary practices, either in the form of food or at the level of dietary habits, tends to eradicate the effect of local dietary factors over various diseases mostly in urban areas.[1] In rural areas where the socioeconomic status is based on agriculture and farming, local dietary patterns tend to be unchanged.[2] Albania which has not yet completely entered the modern Western way of life may still provide the opportunity to study the effects of traditional local diet on thyroid disease.

It is also known that Albania is a country with iodine deficiency, mainly due to the mountainous morphology of its terrain. Meanwhile, iodine deficiency has been reported to be the main cause of the high incidence of goiter in this country.[3] Moreover, the type of diet seems to play a role in the manifestation of goiter.[4,5]

There are several reports in the literature which examine the role of nutritional factors in the aetiology of goiter. Such nutritional factors include iodine, selenium, vitamin A and iron as well as foods containing thiocyanates and proteins.[6-10]

The purpose of this paper was to study thyroid status in inhabitants of the region of Gyrocaster in Southwestern Albania, who were attending the outpatients' clinic for routine examination, in relation to their dietary habits and their socioeconomic level.

MATERIALS AND METHODS

All patients attending the internal medicine outpatients' clinic of the General Military Hospital of Gyrocaster, a mountainous region in Southwestern Albania, were examined for the presence of clinical goiter during a period of six months. We included in the study 112 consecutive patients (mean age 52.8±12.1yrs, 104 females) who had known or suspected thyroid disease.

The nutritional factors that were recorded included the type and frequency (portions per week) of food consumption such as lamb-goat, chicken, beef, pork, fish, vegetables, carbohydrates, dairy products. The manner of food preparation, as boiled, fried, baked, was also recorded. In all cases the ingredients as well as the consumed food were home-produced. With regard to fish only sea-fish consumption was reported. All eggs consumed were locally obtained from free-fed chickens and hens kept by the family. No industrial food or mineral supplements were given to the chickens. Dairy products (yogurt, cheese) mainly came from sheep and goat milk. Most families in Southwestern Albania obtain their everyday milk from animals that are free-fed in the fields and raised in small family units. No industrialised food supplementation was used to feed these animals.

Recorded clinical and epidemiological data were the following: presence of clinical goiter, height, weight, blood pressure, tobacco use, family history of thyroid disease, occupation and education level. The place of residence from birth to 10yrs was also recorded. The study was approved by the local Ethics Committee. Ultrasound imaging (US) was used in all subjects included in the study to determine thyroid volume.

Twenty-seven patients were receiving thyroxine for nodular goitre or hypothyroidism and 85 were suspected to have thyroid disease based on symptoms and/or physical examination (such as presence of goiter, tachycardia and changes in body weight).

Hormone and biochemical measurements

Fasting blood samples were obtained by venipuncture between 08:00-09:00h. The specimens were stored at -20° C until the determination of the levels of thyrotropin (TSH), triiodothyronine (T3), free thyroxine (fT4) and thyroid autoantibodies using the same or consecutive batches of assays.

TSH was measured by chemiluminescence ILMA two-site chemiluminescence immunoassay (DPC Immulite 2000, 5210 Pacific Concourse Drive, Los Angeles, CA 90045-6900, USA). The reference range was 0.3-4.0 mU/L, while the intra- and inter-assay variability were both 5.3% at 0.32 mU/L and 3.8% and 4.6% at 1.3 mU/L, respectively. Total triiodothyronine was measured by chemiluminescence immunoassay (DPC Immulite 2000, Los Angeles, USA). The reference range was 0.8-2.8 nmol/L, while the intra- and inter-assay variability was 7.6% and 8.6%

(at 1.3 nmol/L), respectively. Free thyroxine was measured by chemiluminescence immunoassay (DPC Immulite 2000, Los Angeles, USA). The reference range was 10-25 pmol/L, while the intra- and inter-assay variability were 6.4% and 7.1% (at 18 pmol/L), respectively.

Antibodies to thyroperoxidase (anti-TPO Ab) were measured by chemiluminescence (DPC Immulite 2000, Los Angeles, USA). The intra-assay variability was 4.4% (at 274 IU/mL), while the inter-assay variability was 7.0% (at 349 IU/mL). Reference values of anti-TPO Ab were lower than 30 IU/mL. Antibodies to thyroglobulin (anti-Tg Ab) were measured by chemiluminescence (DPC Immulite 2000, Los Angeles, USA). The intra-assay variability was 3.5% (at 205 U/mL) and the inter-assay variability was 5.0% (at 201 IU/mL). Reference values of anti-Tg Ab were lower than 40 U/mL. TSH-Receptor Ab (TSHRAb) were measured in those patients with TSH <1 mU/L using the BRAHMS human TRAK RIA assay (BRAHMS, Hennigsdorf, Germany).

Serum selenium levels were determined using a spectrophotometric assay. Selenium levels reference range is 43-190 μg/L.[11] Urinary iodine was determined by a spectrophotometric method employing chloric acid as an oxidizing agent[12] and was calculated as the ratio of microgram iodine per gram creatinine (μg I/gr creatinine). Normal urinary iodine excretion is >100 μg/gr creatinine.

Thyroid ultrasound

Thyroid volume was determined by real-time ultrasonography, this test being carried out with each subject lying supine with the neck hyper-extended. The length (l), width (w) and depth (d) of each thyroid lobe (in centimeters) were measured on transverse and longitudinal scans. The volume (V) of each lobe expressed in milliliters was estimated by the modified formula of the rotation ellipsoid V (ml) = 0.479 x d x w x l, as previously described.[13] The thyroid volume was defined as the sum of the volumes of both lobes. The volume of the isthmus was not included; the presence of nodules was also recorded.

Statistical analysis

Statistical analysis was done using the SPSS statistical package. All descriptive data are presented as mean ± SD. Correlations between continuous variables were calculated using Pearson's correlation coefficient or Spearman's correlation coefficient. Multivariate analysis (step multiple regression) was performed including as possible confounders all the variables for which there was some correlation which was statistically significant or tending to be significant in the univariate analysis. Where the distribution was normal, the t-test was used for comparing the means, otherwise the Mann-Whitney rank-test was used.

RESULTS

Four patients were current and four were ex-smokers. Twenty percent of them reported a family history of thyroid disease, 23.8% of them had positive anti-TPO ab and 25.7% had positive anti-TG ab.

Food consumption according to the type and frequency is shown in Figure 1. The most popular food types consumed by the patients were milk products followed by vegetables in second place. The type of meat consumed consisted almost exclusively of roasted lamb and goat. Fish consumption was rare and was never reported more than twice a week.

According to the ultrasound data the median thyroid volume was 20.4 ml (range 4.4-97.6). Assuming an upper normal limit of 20 ml for non-iodine deficient areas, roughly 50% of our patients had increased thyroid volume. Thyroid volume was negatively correlated with the frequency of lamb and goat meat, as well as vegetable consumption ($r=-0.200$, $p=0.05$ and $r=-0.218$ $p=0.03$, Spearman's correlation coefficient). Mean thyroid volume was significantly lower in those subjects who ate lamb more than once a week (21.4±13.3ml vs 31.9±23.0ml, $p<0.01$, t-test). Similarly, when subjects with known hypothyroidism and/or with positive TRab were excluded from the analysis, thyroid volume was negatively associated with the frequency of lamb and goat consumption ($r=-0.483$, $p=0.01$ Spearman's correlation coefficient). In the same subgroup mean thyroid volume was significantly lower in those who ate lamb more than once a week (21.72±13.5 vs 42.13±27.0, $p=0.02$, t-test).

Stepwise multivariate analysis showed that the association of thyroid volume with the frequency of lamb and goat consumption was independent of sex, of vegetable consumption, educational status or occupation ($p<0.009$, Table 1).

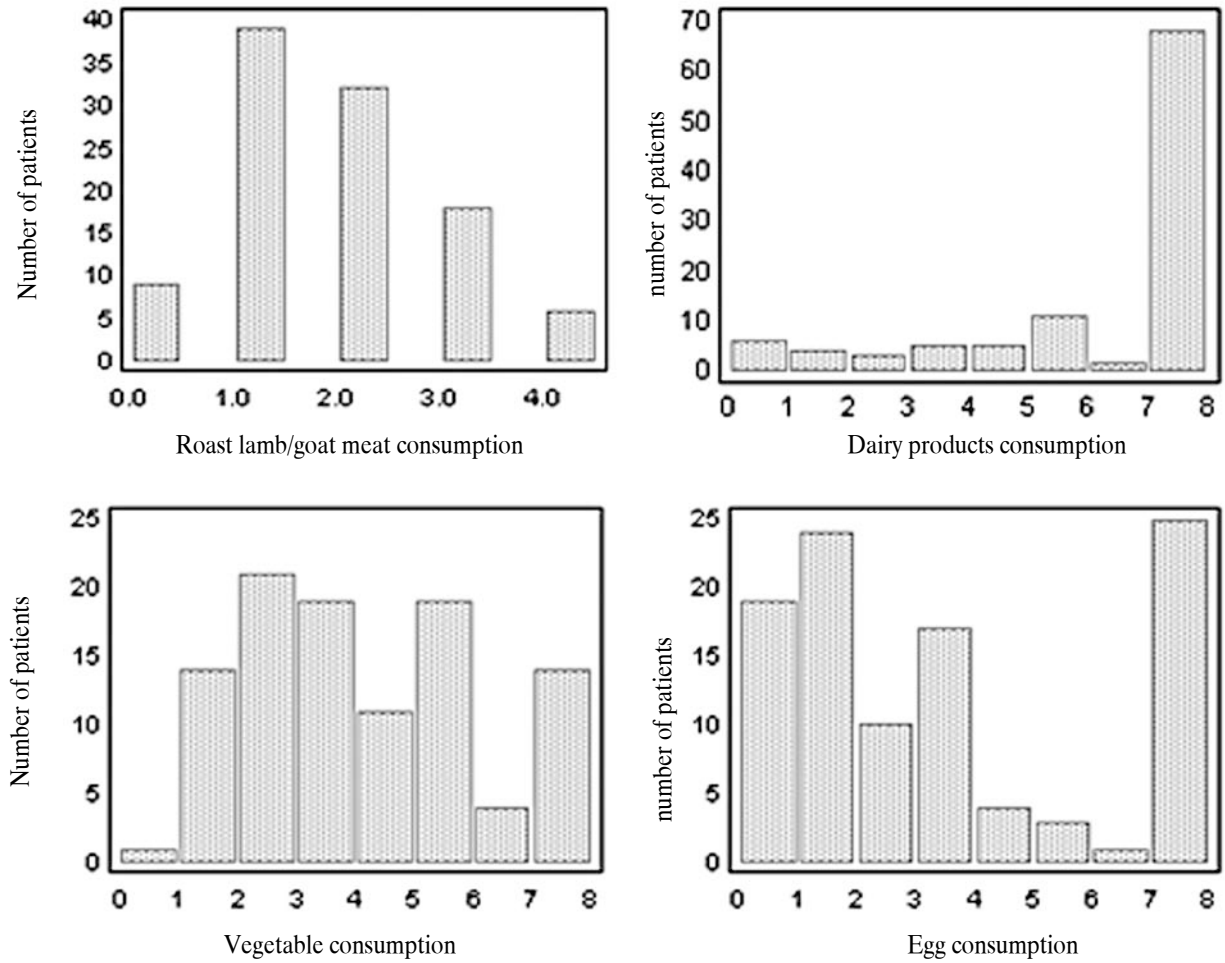

Figure 1. Type and frequency of food consumption (portions/week) in outpatients in Southwestern Albania.

Table 1. Stepwise multiple regression model for predicting thyroid volume in patients of Southwestern Albania

Variable	Predictor	Beta	T	p	R^2 (%)
Thyroid volume	Lamb/goat meat consumption	-0.274	-2.707	0.008	
	Sex	-0.203	-2.019	0.046	0.274
	Vegetable consumption	-0.193	-1.853	0.067	p<0.009
	Educational status or occupation	0.035	0.448	0.727	

As the number of men included in the study was very small, these analyses were repeated in the group of women only. Similar results were obtained in all cases and the associations remained significant at the same statistical level. In this subgroup, multivariate analysis showed again an independent effect of lamb and goat consumption as well as vegetable consumption on thyroid volume ($r=0.249$, $R^2=0.062$, $p<0.05$).

There was no significant association between thyroid volume or TSH levels with other parameters such as family history of thyroid disease (thyroid volume in patients with vs without family history: 27.9±20.9 vs 17.7±11.1 ml, $p<0.08$, t-test), smoking status or socioeconomic parameters such as educational level and daily occupation. Mean thyroid volume was significantly larger in men compared to women (41.3±29.7 vs 24.6±17.9, $p<0.03$, t-test). However, it must be noted that the number of males included in

the study was small (n=8). There was no significant association between thyroid volume or TSH levels with consumption of other kinds of food or with the mode of food preparation. Similarly, no significant associations were found between T3 or fT4 levels with any nutritional parameter.

TSH levels were 1.3±3.8 mU/L. After those on thyroxine treatment were excluded, 43.5% of patients had TSH <0.3 mU/L. In this group, log TSH was negatively correlated with thyroid volume and fT4 levels (r=-0.29, p<0.006 and r=-0.680, p<0.0001, respectively), suggesting the presence of autonomy (Figure 2). TSHRab were found positive in only two subjects.

Selenium levels were 84.0±22.4, range 30.6-138.0 μg/L. No correlation was found between selenium levels and thyroid volume. Mean selenium levels tended to be higher in those patients consuming vegetables >3 times per week (≤3/w 78.7±22.7 vs >3/w 86.8±21.8 μg/L, p<0.09).

Finally, urinary iodine excretion was measured in a random sample of 35 patients (one sample taken from every third patient). The iodine excretion ranged from 61.5 – 169.0 μg iodine/gr creatinine, mean 99.8±35.3 μg iodine/gr creatinine, consistent with a mild degree of iodine deficiency in this population. There was no significant correlation between the iodine excretion and thyroid volume (r=-0.271, p=0.121, Figure 3), vegetable consumption (r=-0.031, p=0.863) or lamb and goat meat consumption (r=0.024, p=0.894). There was no significant correlation between iodine excretion and TSH levels. Mean iodine excretion did not differ between those consuming goat and lamb meat ≤1 times a week compared to >1 times a week (107.3±29.4 vs 101.2±31.7, n.s.), vegetables ≤3 times a week compared to >3 times a week (104.4±32, vs 103.2±30.5), eggs ≤2 times a week compared to >2 times a week (96.4±25 vs 113.7±35.5, n.s.) and dairy products ≤4 times a week compared to >4 times a week (101.9±28, vs 104.9±33, n.s.). It should be noted however that iodine excretion data were available for only a random 1/3 of the subjects.

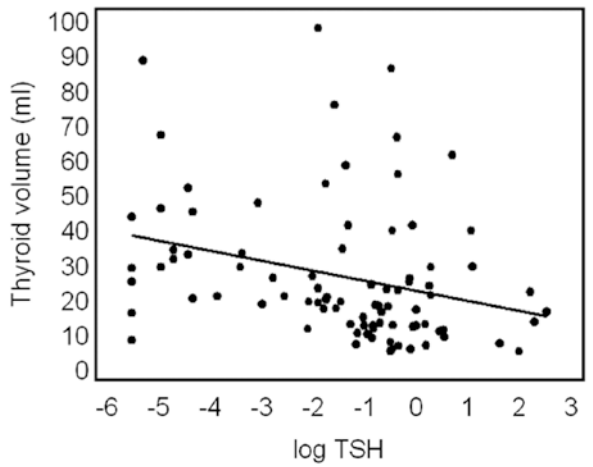

Figure 2. Correlation of log TSH with thyroid volume in outpatients in Southwestern Albania (r= -0.29, p<0.006).

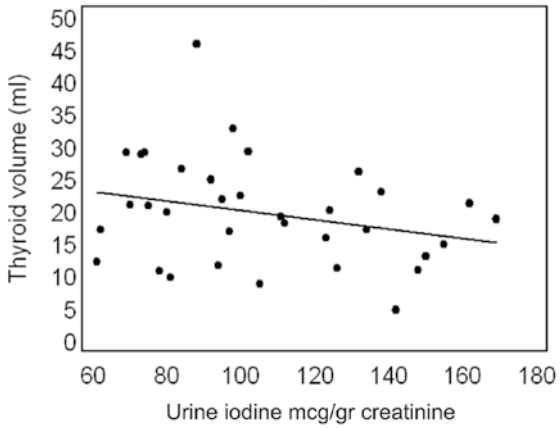

Figure 3. Correlation of thyroid volume with iodine excretion in outpatients in Southwestern Albania (r=-0.271, p=0.121, ns).

DISCUSSION

It is well recognised that dietary habits have a role in the occurrence of goiter. For instance, the consumption of green vegetables, not including vegetables that contain thiocyanate substances, prevents the occurrence of goiter.[14] It is interesting that the consumption of sheep-goat meat has the same if not better effect on the prevention of goiter manifestation. The meat consumed by the patients was from locally bred sheep-goats which graze in fields and have never received iodized food. The preferential consumption of special parts of the sheep and lamb such as the thyroid gland, which might contribute to iodine and selenium intake, cannot be excluded. However, it should be noted that the thyroid gland comprises less than 0.5% of the total mass of a lamb, and side

effects that have been previously described from the consumption of bovine processed meat including large quantities of animal thyroid glands would not be expected.[15] The prevention of goiter in this group is in all probability not related to the iodine content of food, as we were not able to show any differences in iodine excretion in those frequently consuming goat meat and vegetables. Nevertheless, this result should be regarded with the limitation that we only had iodine data in a limited number of subjects and thus the numbers in the subgroups were small.

After a thorough literature search, in combination with accounts concerning specific conditions occurring in developing countries, some explanations for our data may be offered. There are reports which correlate the manifestation of goiter with elements of diet other than iodine, such as low levels of selenium, the consumption of foods rich in thiocyanate, the insufficiency of vitamin A, iron deficiency and low intake of proteins.[7,9,16-18] The countries in which studies were conducted in order to assess the effect of dietary factors in patients with sufficient intake of iodine and which found a correlation with the above-mentioned parameters are mainly developing countries that have serious problems with malnutrition. It is possible that in our study the lower meat intake may have contributed to mild deficiencies in various micronutrients; however, in this population we did not measure iron or vitamin A concentrations. It is interesting that studies concerning Albanian immigrants showed either directly or indirectly low meat consumption or low protein and micronutrients intake.[19,20]

It is likely, even though our study did not definitely show it, that there may be a correlation of the occurrence of goiter with the socio-economic level of the patients. It could for instance be hypothesised that patients who can afford to consume meat more frequently are those who are economically better-off than those that do not have this privilege. Nonetheless, this might not always coincide with better education which was the factor that was recorded in our study. In transition countries like Albania, wealth and welfare are probably not directly associated with the educational level as in the more advanced Western world, i.e. the salary of a social servant such as a teacher may be so low that he/she may not be able to carry through everyday needs.[2]

Selenium is an important trace element and selenium containing enzymes such as glutathione peroxidases may have an anti-oxidative potency.[21,22] No correlation of goiter and selenium levels was found in our study. The absence of a selenium effect was rather expected, as it was shown from our measurements that the intake of selenium was sufficient in the area examined. The consumption of vegetables had a tendency to be associated with higher selenium levels and this might indirectly represent one of the protective factors associated with lower thyroid volume in the frequent vegetable intake group. Vegetables consumption has been implicated in the aetiology of goiter. Vegetables contain micronutrients, such as vitamins and selenium, which play a significant role in the physiological development of the thyroid gland. This is more obvious in areas with a low standard of living where the replenishment of such micronutrients is of importance in the treatment of goiter.[7,8,21-24] On the other hand, thiocyanates contained in vegetables such as cabbage, broccoli and soya are well known goitrogens; thiocyanates also exist as environmental toxins and in cigarette smoke.[10,25] Studies with a larger number of cases are needed in order to clarify with a greater statistical significance any correlation of this or other dietary micro- and macronutrients with the development of goiter.

The high incidence of goiter in women that we found is a classical finding repeatedly reported in all epidemiological studies. The greater thyroid volume in men compared to women is a finding which has been already described in the literature and may be related to parameters such as differences in body weight or lean body mass.[26] The high incidence of goiter and hyperthyroidism with negative antibodies, in other words autonomous goiter, is in accordance with the findings of other researchers.[27,28] The prevalence of autonomous multinodular goiter is directly associated with the existence of iodine deficiency in Albania, which, though more severe in the past, is now becoming borderline.[29] This is likely to be the main reason for the relatively higher incidence of follicular carcinomas compared to papillary carcinomas in Albania that has recently been reported.[30]

In conclusion, nutritional factors may be involved in the development of goiter in Southwestern Albania. Selenium intake seems to be sufficient in this part of Albania, while the presence of goiter in adults is more likely related to iodine deficiency in the past;

this appears now close to elimination. It would be interesting to closely follow up Albania as well as other developing countries in the larger area, as the effect that the Western way of life has on the diet may bring about changes in the incidence, type and severity of some diseases that are related to diet such as thyroid diseases.

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