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Abstract: This study was conducted in an endemic goitre area to determine thyroid profiles TSH, freeT4 (fT4), T4, fT3 and T3, as well as the degree of the severity of hypothyroidism and the prevalence of the disease. Tonbak is a small village in Kahramanmaraş. The iodine content of the water is < 1 mg/L. A randomly selected group of 121 subjects aged 16-55 were included in the study.

The percentage of goitre was 71.1% upon physical examination. Subjects with primary hypothyroidism were 16.5%. Mean scores of fT4 were 8.9±2.6 pmol/l (range: 2.7-12.9) and mean scores of TSH were 18.1±26.1 mU/ml (range: 4.33-100<). Subjects with subclinical hypothyroidism were 7.5%, having mean scores of fT4 16.5±3.2 pmol/l, (13.3-23.3) and TSH of 6.2±1.7 mIU/ml (4.6-9.4). Cases having low fT4 with normal TSH were 38%. These cases should be further investigated and followed up. In conclusion, the measurement of TSH and fT4 is sufficient in thyroid hormone screening for endemic goitre areas. Just a simple iodine prophylaxis would be more cost effective than having mentally retarded individuals or providing for the treatment of advanced hypothyroid cases. In addition, attention should be paid to regions where the mineral Baryte is found leading to the disease of goitre.

Key Words: Goitre, TSH, fT4, Iodine deficiency, Kahramanmaraş (Turkey)

Introduction

Iodine deficiency is a major health problem in developing as well as in developed countries. Delange (1) has noted that at least one billion people were at risk of iodine deficiency disorders (IDD). Hetzel (2) defined IDD as disorders of severe iodine deficiency resulting in functional and developmental abnormalities including thyroid function causing endemic goitre, cretinism, mental retardation, decreased fertility rate and increased perinatal death and infant mortality. Greenspan and Rapoport (3) documented that iodine is vital in feotal development, especially in neural and skeletal systems, and is important for metabolism in all tissues concerned throughout life. Iodine deficiency in infants and children results in a marked slowing of growth, development and the onset of mental retardation. One of the causes of hypothyroidism is iodine deficiency. Though the main areas where goitre is prevalent have been identified, the degree of severity, the percentage of the population affected and the precautions for treatment and preventive measures have not been evaluated. Urgancioglu et al. (4) drew attention to 13 perspective endemic goitre areas in Turkey (Rize, Giresun, Gümüşhane, Bolu, Bursa, Çanakkale, Eskişehir, Konya, İzmir, Antalya, İçel, Diyarbakır, Muş) where the iodine content of waters was < 10 mg/L. The objectives of this study are to determine the thyroid profile in an endemic goitre area, correlate clinical findings with the thyroid profile and assess the prevalence of thyroid dysfunction. Finally, this study sought to assess whether analyses of one or two parameters were sufficient laboratory tests for screening surveys and to emphasize the cost effectiveness of screening surveys.

Materials and Methods

Region investigated: Tonbak village is a rural community (population 2117) in Kahramanmaraş, a province in Southeast Turkey.

Survey: The sample size was determined with 95% confidence by the Epi Info 6.0 computer program. A randomly selected group of 121 subjects aged 16-55 years were taken into the study. Of these, 81 were female, mean ages 29.6±10.4 years, and 40 were male, mean ages 31.3±9.7.

Sampling: A questionnaire was filled out for each subject by a nurse and the medical examination was done by a general surgeon. Physical examination results were classified by WHO criteria (5). Blood samples were taken into EDTA and the samples were transported in cold chain to the laboratory. Water samples were taken from water sources for iodine analysis.

Methods: Haematological tests were performed the next day using an electronic cell counter, Cell Dyne 1700 (Abbott diagnostics, USA). After haematological analysis, the plasma were separated and the samples were kept frozen at -20ºC awaiting analysis.

The thyroid profile T3, fT3, T4, fT4 and TSH was done in an Elecsys 1010 by Chemiluminescence (Roche diagnostics, Germany). Iodine analysis was done by Pesavento's spectrophotometric titration methods (6).

Statistics: The data were analysed by Epi Info 6.0 statistical software.

Results

Some 99.5% of the people taken into the study were of indigenous origin. Following physical examination the prevalence of goitre was found to be 71.1%. Among our subject group, 31.4% had had goitre since birth, 20.7%, 8.3% and 18.2% had had it since the age of 5, 10 and 20 years, respectively. A total of 81.8% of the subjects reported the presence of goitre in their relatives, mothers, children and/or siblings. Only 9.1% subjects had undergone a thyroid operation previously and 28.1% of the subjects were receiving treatment for goitre. Some 99.2% of villagers were consuming water from the wells and from the village fountain. The content of iodine in these sources was less than 1 mg/L. Only 5% of the village population were using iodized salt.

Table 1 shows the thyroid profile and haematological parameters and reference values (7,8) in primary (PH), subclinical hypothyroidism (SCH) and euthyroid cases. In

Table 1. The thyroid profile and haematological parameters in Tonbak village.

	Primary hypothyroidism TSH high fT4 low	Subclinical hypothyroidism TSH high fT4 Normal	Euthyroidism TSH Normal fT4 Normal	Reference values
n (%)	20 (16.5)	9 (7.5)	92 (76.0)	
TSH (mIU/ml)	18.10±26.10	6.20±1.70	1.89±0.95	0.27-4.20
(Range)	(4.33- <100.00)	(4.60-9.40)	(0.31-4.17)	
FT4 (pmol/L)	8.90±2.60	16.50±3.20	14.41±4.51	13.00-23.00
(Range)	(2.7-12.9)	(13.3-23.3)	5.53-28.7	
T4 (nmol/L)	80.44±32.95	130.87±2.50	115.83±39.90	66.00-181.00
(Range)	(29.22-165.51)	(93.57-195.88)	(50.54-218.92)	
FT3 (pmol/L)	5.28±1.38	6.27±1.08	5.40±1.10	2.80-7.10
(Range)	(1.94-8.52)	(6.27-7.91)	(3.10-7.50)	
T3 (nmol/L)	2.60±0.66	2.75±0.32	2.63±0.54	1.30-3.10
(Range)	(1.08-3.03)	(2.81-3.10)	(1.75-4.98)	
Hb (g/dl)	13.36±1.96	14.21±1.40	13.66±2.47	< 12.00
(Range)	(6.70-15.50)	(13.40-15.70)	(10.40-16.70)	
Hct (%)	38.33±4.43	40.45±3.46	39.09±6.38	< 37.00
(Range)	(23.60-43.80)	(38.60-44.20)	(31.60-47.00)	
MCV (fL)	81.87±8.45	83.26±6.06	80.75±8.36	< 80.00
(Range)	(51.30-88.10)	(82.00-83.90)	(67.20-89.10)	

n: subject number, Hb: haemoglobin, Hct: haematocrit, MCV: mean corpuscular volume, Means, standard deviations and ranges were calculated for all thyroid hormones and haematological parameters. Reference values of thyroid function tests were taken from Heil W, Koberstein R, Zawta B (7), Haematological parameters were evaluated according to Wintrobe's clinical haematology (8).

primary hypothyroidism, TSH is high and fT4 is low, whereas subclinical hypothyroidism is characterised by normal fT4 and high TSH levels without clinical symptoms (9). The percentages for PH and SCH were 16.5% and 7.5%, respectively. Cases with normal TSH but low fT4 were 38.0%.

Analyses of haematological data showed only 4 cases (13.3%) of PH and SCH having low values of mean corpuscular volume (MCV) and haemoglobin (Hb) that would be attributed to iron deficiency.

Table 2 shows a comparison of the laboratory results of the subjects and all physical examination findings.

Table 3 shows the correlation between fT4 and TSH as well as clinical findings.

Discussion

It is known that there are a lot of areas endemic in goitre in Turkey. Iodine deficiency areas shown by Urgancıoğlu (4) correlate well with the mineral Baryte map of Turkey. Thus, it is suggested that thyroid dysfunction should be investigated in areas where the baryte mineral exists (10).

Table 2. shows comparison of the laboratory results of the subjects and physical examination findings.

	Primary hypothyroid	Subclinic hypothyroid	Euthyroid
	n (%)	n (%)	n (%)
Stage OA	5 (25%)	4 (44%)	28 (30%)
Stage OB	5 (25%)	5 (56%)	21 (23%)
Stage 1	3 (15%)	-	28 (30%)
Stage 2	4 (20%)	-	10 (11%)
Stage 3	3 (15%)	-	5 (6%)
Total: n (%)	20 (100%)	9 (100%)	92 (100%)

n: Subject number

Table 3. Correlation between fT4 and TSH and clinical findings.

	fT4	TSH
Clinical findings (+)	- 0.385**	- 0.073

**Correlation is significant at the .01 level (2-tailed)

Previous studies have shown that the most important factor in the aetiopathogenesis of endemic goitre in Turkey was iodine deficiency. In these studies, iodine deficiency was diagnosed by testing urinary iodine (11,12). The most important reason for iodine deficiency goitre is the inadequate dietary intake of iodine.

Kahramanmaraş is an endemic goitre area. In this study, we investigated the components of iodine deficiency in Tonbak village where goitre was endemic.

In a study done in another endemic goitre area in Central Anatolia (Kayseri), Özbakir et al. reported the prevalence of goitre to be 25.8% and the iodine level in the water to be 3 µg/L (13). In our study, the prevalence of goitre was 71.1% and the level of iodine in the water was less than 1 µg/L. We used serum thyroid homone levels to determine the thyroid functions of people living in Tonbak village.

To determine thyroid hormone dysfunction, MacKenzie (14) suggested the measurement of TSH, fT4 and fT3, as the latter can be used to differentiate thyroid disease from non - thyroidal illness (NTI). Thus, for the determination of hypothyroidism, first line tests are serum TSH and fT4. The prevalence of primary hypothyroidism was 16.5% in Tonbak village. The examination of T4 results in PH subjects showed that only 35% (7/20) of the cases had subnormal levels of T4. Thus, fT4 would be a better criterion than T4, as suggested by the above author.

SCH was found to be 7.5%. If we had used only TSH criteria other than T4, as suggested by Rodrigues et al. (15) and Delange (1), we would have missed SCH. Following physical examination, 71.1% of the people studied had goitre. The analysis of our data revealed that the rate of low fT4 values with normal TSH was 38% (46 subjects). These cases should be classified as either prospective primary hypothyroids or primary hypothyroid under the criteria of Zulewski et al (16). The authors have suggested the use of a clinical score which reflects tissue manifestation of primary hypothyroidism along with TSH and fT4. They defined the clinical score as the sum of two simple tests total cholesterol and ankle relaxation time, which have a positive correlation with fT4 and TSH levels in subclinical hypothyroidism. Therefore, a further evaluation is needed.

Anaemia associated with hypothyroidism is not rare as reported by Greenspan and Rapoport (3). In our study,

13.3% (4/30) of our PH and SCH patients were found to be anaemic. However, iron deficiency anaemia is not uncommon in the population of Kahramanmaraş as shown by Kılınç et al. (17)

As seen by the results, thyroidal dysfunction is prominent in Tonbak village. Here the socioeconomic status is low and illiteracy in women is above 15%. In developing countries where socioeconomic status is low, perinatal death and infant mortality tend to be high. The presence of endemic goitre adds to the problem. The main aetiologic factor in endemic goitre is the inadequate dietary intake of iodine. This commonly occurs in communities depending exclusively on local products grown on iodine-poor land. As a result of our examination in Tonbak village, we saw that people were planting their own food and drinking poorly iodized water. Treatment of advanced cases adds more burden to the government than a simple iodine prophylaxis. The prevention of endemic goitre depends mainly on increasing the iodine intake of people in endemic areas. Adding iodine to food staples, such as table salt, is the most widespread and cost-effective method of prevention. In Tonbak village, only 5% of the people were consuming iodized salt.

According to the responses gathered in the questionnaire, 8.3% of the village people had suffered from goitre for 10 years whereas 20.7% had had it for 5 years. These results suggest that the government should take sustainable precautions in endemic goitre areas.

In conclusion, the high prevalence of goitre in Tonbak village was linked to poor dietary iodine intake. Low iodine levels of springs around the village and the consumption of iodine-free salt were found to be the two main causes of poor dietary iodine intake. Detecting urinary iodine is no doubt the most practical and cheapest screening test in areas where iodine deficiency goitre is endemic. However, if no pathology other than hypothyroidism is considered, TSH and fT4 levels in serum are good predictors of iodine deficiency.

It is clear that dietary interventions and informing people about the importance of iodinized salt consumption is crucial for Tonbak village.

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