Original Article

Thyroid Autoimmunity Role in the Evolution of Endemic Goiter in Rural Area, Fars, Iran

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Abstract

Background: WHO reports indicate no iodine insufficiency in Iran, however, goiter is still endemic in Fars Province. This study evaluates the role of thyroid autoimmunity in the evolution of endemic goiter.

Methods: A total of 516 permanent residents of Akbarabad County of the Kavar area in Fars Province, Iran were selected by simple random sampling. Patients with thyroid malignancy and dysfunction, and those who consumed drugs affecting thyroid function were excluded. After signing a written consent form and undergoing a thyroid examination, 5 cc of blood were drawn to measure free T_3 and T_4 (RIA), TSH (IRMA), and anti-thyroid peroxidase (competitive RIA) levels. Moreover, samples of 50 cc morning urine were collected for the measurement of urinary iodine excretion (UIE; chloridric acid digestion). Data were analyzed by SPSS (version 13). $P<0.05$ was significant.

Results: The prevalence of goiter was 38.4% by WHO classification. The prevalence of children with UIE 2 – 4.9 µg/dL was 5.8%, which indicated sufficient iodine intake. Goiter was more prevalent in females, as well as in patients with positive anti-TPO or higher TSH titers ($P<0.01$). The prevalence of positive anti-TPO was higher in goiterous patients than healthy persons ($P=0.002$), which increased with an increase in age, grade of thyromegaly or TSH ($P<0.02$). Regression analysis showed the odds ratio for diagnosing goiter in females was 2.4 ($P<0.001$), in those with positive anti-TPO it was 1.87 ($P=0.03$) and in those with TSH>5.2 mIU/mL the odds ratio was 2.74 ($P=0.01$). In adolescents compared to children the odds ratio was 0.36 ($P=0.01$) and the odds ratio in adults to children was 0.33 ($P=0.001$).

Conclusion: This study indicates that despite normal UIE, goiter is endemic in Akbarabad County. Some degree of goiter endemicity may be due to thyroid autoimmunity.

Keywords: endemic goiter, urinary iodine excretion, thyroid autoimmunity.

Introduction

Goiter is still endemic in Fars Province, Iran ten years after mandatory salt iodinization.[1] Therefore other causes of endemic goiter should be determined. Genetic and environmental factors such as thyroid autoimmunity, malnutrition and the presence of goiterogenous agents in soil and water should be considered.[2–8] The major criteria of autoimmune disease[9] such as the presence of thyroid autoantibodies and lymphocytic infiltration in thyroid tissue have been seen in endemic goiters. Braverman[10] has shown that the most common cause of goiters in adolescents in an iodine sufficient area is autoimmune thyroid disease. Kretowski et al.[6] and Hashemipour et al.[11] have found that positive anti-thyroglobulin (anti-Tg) is several times more prevalent in goiterous than non-goiterous school children and anti-Tg titer[6] is higher in goiterous than non-goiterous children. However, Doufas et al.[7] have shown that the prevalence of positive anti-TPO and its titer is higher in goiterous than non-goiterous patients in areas with a history of endemic and non-endemic goiter, and autoimmunity evidence in thyroid tissues increased from 5.94% to 13.9% during the ten years after iodine supplementation. Therefore, we evaluated goiter prevalence, iodine status and thyroid autoimmune disease to determine the role of autoimmunity in goiter evaluation.

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Subjects and Methods

This cross-sectional study was conducted from October 2007 to September 2008 and included 516 permanent residents (264 females, 252 males; ages 6 – 81 years; mean age: 33.42±16.69 years) of Akbarabad County, Kavar area, Fars Province who were selected by simple random sampling. Patients with a positive history of thyroid malignancy or dysfunction and those who consumed drugs that affected thyroid function (e.g., thyroid hormones, thionamides, oral contraceptive pills, or radioactive iodine) were excluded. This study was approved by the Ethics Committee of Shiraz University of Medical Science. The participants were invited to the county health center by health coordinators. After an explanation of the study, participants were asked to sign an approved written consent form. Then, a questionnaire that contained questions about demographic data, history of thyroid disease and current medications was taken by the study coordinators. Afterwards, a thyroid exam was performed on the participants by an endocrinologist. Samples of blood (5 cc) were drawn for the measurements of free T_3 and T_4 (RIA, Immunotech, Czech), TSH (IRMA, Immunotech, Czech) and anti-TPO (Competitive RIA, Immunotech, Czech). Moreover, 50 cc samples of morning urine were collected for the measurement of urinary iodine excretion (UIE) by the chloridric acid digestion method. Serum blood was separated and kept frozen at -20°C along with urine samples until analysis.

We measured only anti-TPO levels, which is more prevalent and has a higher titer than anti-Tg,[12] to determine the role of thyroid autoimmunity in goiter endemicity. Goiters were graded according to the WHO classification.[13] The ranges of UIE were determined as follows: ≥30 µg/dL (excessive iodine levels), 20 – 29.9 µg/dL

Table 1. The prevalence of various UIE categories by goiter.

Total	Non-goiterous	Goiterous	Goiter
			UIE (µg/dL)
129 (25%)	77 (24.2%)	52 (26.3%)	≥30
111 (21.5%)	70 (22%)	41 (20.7%)	20 – 29.9
188 (36.4%)	122 (38.4%)	66 (33.3%)	10 – 19.9
61 (11.8%)	36 (11.3%)	25 (12.6%)	5 – 9.9
27 (5.2%)	13 (4.1%)	14 (7.1%)	2 – 4.9
516 (100%)	318 (100%)	198 (100%)	Total
(*P*=0.49)			

Table 2. The prevalence of positive anti-TPO by goiter grade.

Total	II	I	0	Goiter grade
				Anti-TPO
62 (12%)	12 (21.4%)	24 (16.8%)	26 (8.2%)	Positive
453 (88%)	44 (78.6%)	119 (83.2%)	291 (91.8%)	Negative
516 (100%)	56 (100%)	143 (100%)	317 (100%)	Total
(*P* = 0.02)				

Table 3. Logistic regression model for locating goiter.

95% CI for Exp (β)	Exp (β) Odds ratio	*P*-value	Variable
1.59 –3.60	2.4	<0.001	Sex[1]
0.16–0.80	0.36	0.012	Adolescents[2]
0.17–0.62	0.33	0.001	Adults[3]
1.03–3.38	1.87	0.03	Anti-TPO[4]
1.198–6.31	2.74	0.017	TSH <5.2[5]

[1]Females to males; [2]Adolescents to children; [3]Adults to children; [4]Positive anti-TPO to negative anti-TPO; [5]TSH<5.2 to TSH≤5.2 mU/mL

(excess of iodine) and 10 – 19.9 µg/dL (adequate iodine levels). UIE levels of 5 – 9.9 µg/dL, 2 – 4.9 µg/dL and <2 µg/dL were considered as mild, moderate, or severe iodine deficiencies.[14] A prevalence of <20% for moderate iodine deficiency (UIE 2 – 4.9 µg/dL) in children was considered as an evidence for adequate iodine supplementation.[15] Free T_3, free T_4, and TSH levels of 2.5 – 5.8 pmol/L, 11.5 – 23 pmol/L and 0.17 – 4.05 mIU/mL were taken as normal values, respectively. A TSH level of >5.2 mIU/mL was considered as hypothyroidism. Anti-TPO levels >50 IU/mL were considered positive.

Data were analyzed by *t*-test, Chi square and one-way ANOVA. Non-parametric tests (for data which do not have normal distribution) such as the Kruskal Wallis and Mann Whitney, and logistic regression by SPSS software (version 13, Chicago, IL) were also performed. *P* value <0.05 was significant.

Results

The prevalence of goiter was 38.4%, which was more prevalent in females than males (46.4% vs 30.6%), and in children (59.1%) when compared with adolescents (31.1%) and adults (37.3%). The prevalence of moderate iodine deficiency was 5.8% in children (6 – less than 12 years). UIE did not differ between goiterous and healthy persons (Table 1). Serum levels of anti-TPO in goiterous and healthy participants was 273.17±725.21 and 137.66±521 IU/mL (*P*<0.001). The prevalence of positive anti-TPO was higher in goiterous patients (*P*=0.02) and increased with goiter size (Table 2). Positive anti-TPO was more prevalent in females (14.8%) than males (9.1%) and in adults (>18 years; 13.9%) than adolescents (8.2%) and children (0%).

Regression analyses of age, sex, anti-TPO, UIE, and TSH showed that the odds ratio for diagnosing goiters is higher in females, those with positive anti-TPO, higher TSH, and adolescents (Table 3).

Discussion

After iodine prophylaxis, the prevalence of goiter has decreased from 68% in 1996 to 38.4% in 2008. Additionally, grade II thyromegaly also declined from 17.6% to 10.8%. Although the prevalence of goiter and thyroid size have decreased, the results are not compatible with expected WHO goals. These results are similar to those seen in Yazd[15] and Marvdasht, Fars Province[1] but are higher than Arak,[16] Markazi Province and lower than villages near Tehran.[17] These differences may be explained by variations in goiter prevalences and thyromegaly grading prior to the iodine replacement program,[7] as well as inconsistencies among examiners when diagnosing grades 0 and I thyromegaly.[15] Moreover, iodine deficiency in the early years of life causes thyroid gland growth; therefore large and visible thyroids may not respond to iodine supplementation and it may take as long as three decades for the goiter to shrink.[15,18–21] After puberty, the enlarged thyroid may gradually become autonomous and unresponsive to adequate dietary iodine intake.[22]

Because the children and adolescents have spent all or most of their lives during the iodine replacement period and this area is an iodine repleted area, therefore other causes of endemic goiter should be determined. Currently, the role of autoimmune thyroid disease in the evolution of goiter is one cause and Braverman has shown that thyroid autoimmunity is the most common cause of goiter in iodine replenished areas.[10] In our study, the anti-TPO titer was higher in goiterous patients and increased with age and goiter grading. The prevalence of a positive anti-TPO was higher in females and in those with goiters or high TSH titers. Other studies have also shown that positive anti-TPO is more prevalent in patients with goiters who also have higher titers of anti-TPO

than non-goiterous individuals.[6–8,11,23] The prevalence of positive anti-TPO in goiterous patients is similar to studies of Tsatsoulis in Greece[23] and Heydarian and Azizi in Tehran[24] but lower than the results of Krewtowski et al. in Poland,[6] Doufas et al. in Greece,[7] Gopalakrishnan et al. in India,[25] Hashemipour et al.,[11] Aminorroaya et al.,[13] and Momenzadeh[26] in Isfahan, Iran.

These may be due to either different populations within the studies, bias in case selection, measurements of anti-Tg or both anti-Tg and anti-TPO, and cross reactivity between these antibodies in some commercial kits. Some of studies evaluated only children,[6,11,23] adults[24] or those who referred to endocrinology clinics,[26] all of which may cause bias in case selection. Although cases who have positive anti-Tg and negative anti-TPO are rare,[24] measurement of both antibodies may increase the prevalence of autoimmunity. Genetic and hormonal factors, infection, anatomical changes, and damage of tissue due to inflammation, ischemia or trauma can also change immune system response and cause autoimmune disease,[27] thus changing the prevalence of these diseases in various populations. Finally, thyroid autoimmunity explains some degree of goiter endemicity but other causes such as malnutrition, micronutrient deficiencies and the presence of goiterous agents[5] in soil or water should be investigated.

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