

# Thiocyanate status does not play a role in the etiology of residual goiter in school children of Isfahan, Iran

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Isfahan, Iran

**Background:** Despite long standing iodine supplementation in Iran the prevalence of goiter remains high in some areas. In the present study we investigated the possible role of thiocyanate as a goitrogen in the etiology of goiter in Isfahan, Iran.

**Methods:** A total of 2331 (6-13 year old) school children were selected by multistage random sampling. Thyroid size was estimated in each child by inspection and palpation. Urinary iodine concentration (UIC) and urinary thiocyanate (USCN) were measured.

**Results:** Overall, 32.9% of the 2331 students had goiter. The median UIC was 195.5 µg/L. The mean±SD of USCN in goitrous and nongoitrous subjects was 0.42±0.28 mg/dL and 0.41±0.32 mg/dL, respectively ( $P=0.86$ ). USCN level in goitrous and nongoitrous boys was 0.41±0.32 mg/dL and 0.43±0.37 mg/dL, respectively ( $P=0.67$ ). USCN level in goitrous and nongoitrous girls was 0.43±0.26 mg/dL and 0.40±0.28 mg/dL, respectively ( $P=0.43$ ).

**Conclusions:** Thiocyanate overload does not play a role in high prevalence of goiter in the studied population. We suggest the role of other goitrogenic factors should be investigated in this region.

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**Key words:** goiter;  
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## Introduction

Iodine deficiency (ID) is recognized as the major preventable public health problem worldwide.<sup>[1]</sup> Iodine deficiency disorders (IDD) present with a wide variety of clinical manifestations ranging from congenital anomalies, cretinism, deaf mutism, psychomotor defects, severe hypothyroidism to goiter.<sup>[2]</sup>

The relationship between goiter and iodine deficiency is well established, but there are a number of genetic and environmental factors contributing to the risk of goiter.<sup>[3]</sup> Natural goitrogens are environmental factors causing goiter.<sup>[4-6]</sup> Thiocyanate, one of the best known and widely studied goitrogens responsible for causation or aggravation of endemic goiter especially in a relative or severely iodine deficient region,<sup>[7]</sup> affects thyroid function by its concentration. At a low concentration, thyroid function was found to be stimulated,<sup>[8]</sup> whereas at a pathologically elevated concentration, thiocyanate acts as a competitive inhibitor of the I-transport in the thyrocytes.<sup>[9]</sup> Besides absorption through nutrients, thiocyanate is also generated in the organism as a product of the cyanide-thiosulfate-mercaptopyruvate-sulfurtransferase (Rhodanase) system.<sup>[10]</sup>

Endemic goiter is present in most regions of Iran,<sup>[11]</sup> and iodine deficiency was considered a contributing factor for endemic goiter for several years in this country.<sup>[12]</sup> The National Committee for Control of IDD in Iran was initiated in 1989. The production and distribution of iodized salt (40 mg of potassium iodide per kg of sodium chloride) and the education program of policymakers, health personnel and the public were initiated in 1990. However, a rapid survey of iodized salt consumption showed that less than 50% of the population consumed iodized salt in 1993, with a mean urinary iodine of 50 to 82 µg/L. Therefore, the first law for the mandatory iodination of all salts for household use was proclaimed in 1994.<sup>[13]</sup> The prevalence of goiter in Isfahan was 92% in girls and 85% in boys in 1989.<sup>[14]</sup> According to another study conducted in 1997, the prevalence of goiter among 6-18 year old children in Isfahan was 62%.<sup>[15]</sup>

The present study aimed to estimate the goiter prevalence, iodine status and the possible role of thiocyanate as a goitrogen in Isfahan school children.

## Methods

A cross sectional study was performed among school children of Isfahan with an approximate population of 1 700 000 in 2005. Multistage cluster random sampling was used for enrolling the students. The calculation of sample size was based on assumed goiter prevalence of 50% ( $\alpha=0.05$ ), and desired confidence interval of 3%, resulting in a minimum sample size of 1607 children. We excluded those children with a history of exposure to radioactive iodine, thyroid surgery, or significant underlying diseases such as cardiopulmonary diseases, liver or renal diseases by means of medical records and interview with parents and teachers. Written consent was obtained from the parents of children who were informed about the study. The study was approved by the Ethics Committee of Isfahan Endocrine and Metabolism Research Center of Isfahan University of Medical Sciences.

Goiters were graded by two endocrinologists according to WHO/UNICEF/ICCIDD classification.<sup>[1]</sup> Blood samples were transported on dry ice to the reference laboratory of the Isfahan Endocrine and Metabolism Research Center. The samples were stored at  $-70^{\circ}\text{C}$  until analysis. Urine and blood assays were performed within a median of 26 hours of sampling. Urine iodine concentration (UIC) was determined by the digestion method based on a modification of Sandell-Kolthoff reaction.<sup>[1,16]</sup> Urinary thiocyanate (USCN) was determined by the modified method.<sup>[17]</sup> High USCN was defined above 0.9 mg/dL.<sup>[7]</sup> Serum T4 concentrations (reference range: 4.5-12  $\mu\text{g/dL}$ ) were measured with radioimmunoassay (RIA) by Iran Kavoshyar kits. Serum thyroid stimulating hormone (TSH) concentration (reference range: 0.3-3.9 mU/L) was determined with immunoradiometric assay (IRMA) using Iran Kavoshyar kits.

Quantitative variables were presented as means  $\pm$  SD. Independent sample *t* test was used to compare normally distributed data in different groups. The prevalence of high USCN between goitrous and nongoitrous children was compared by the Chi-square test. *P* value less than 0.05 was considered statistically significant. The data were analyzed using SPSS version 15 for Windows.

## Results

A total of 2331 school children were enrolled in this study with a female to male ratio of 1.6:1. Their age ranged from 6 to 13 years. Of the children, 32.9% were classified as goitrous (Table 1). The goiter prevalence was 32.4% for girls and 33.7% for boys ( $P=0.51$ ).

UIC was measured in 454 school children. The mean $\pm$ SD and median UIC were 220.6 $\pm$ 17.3 and 195.5  $\mu\text{g/L}$ , respectively. About 16% of these children had an

**Table 1.** Thyroid size determined by inspection and palpation in school children of Isfahan, Iran

	<i>n</i>	Thyroid size		
		Grade 0 (%)	Grade 1 (%)	Grade 2 (%)
Boys	898	66.3	27.3	6.4
Girls	1433	67.6	29.0	3.4
All	2331	67.1	28.3	4.6

**Table 2.** Serum levels of TSH, T4, and UIC in children with and without high USCN in Isfahan, Iran

	TSH (mU/L)	T4 ( $\mu\text{g/dL}$ )	UIC ( $\mu\text{g/L}$ )
High USCN	3.60 $\pm$ 2.35	8.78 $\pm$ 1.43	187.9 $\pm$ 122.3
Normal USCN	2.79 $\pm$ 2.64	8.67 $\pm$ 1.50	225.1 $\pm$ 116.6
<i>P</i>	ns	ns	ns

TSH: thyroid stimulating hormone; UIC: urine iodine concentration; USCN: urinary thiocyanate; ns: not significant.

iodine excretion level below 100  $\mu\text{g/L}$  and 3.7% had iodine level below 50  $\mu\text{g/L}$ ; 25.6% of the children had a UIC between 200 and 300  $\mu\text{g/L}$  and 23.8% had UIC more than 300  $\mu\text{g/L}$ . UIC in goitrous and nongoitrous children was 220.9 $\pm$ 119.4  $\mu\text{g/L}$  and 220.2 $\pm$ 114.6  $\mu\text{g/L}$  respectively ( $P=0.57$ ). The mean $\pm$ SD of UIC in goitrous and nongoitrous boys was 215.7 $\pm$ 118.0  $\mu\text{g/L}$  and 223.9 $\pm$ 127.0  $\mu\text{g/L}$ , respectively ( $P=0.66$ ). The UIC in goitrous and nongoitrous girls was 223.7 $\pm$ 112.5  $\mu\text{g/L}$  and 218.3 $\pm$ 112.8  $\mu\text{g/L}$ , respectively ( $P=0.72$ ).

USCN was measured in 150 goitrous children (67 boys and 83 girls) and 297 nongoitrous children (137 boys and 160 girls) as a control group. The USCN (mean $\pm$ SD) in goitrous children and control group was not statistically significant (0.42 $\pm$ 0.28 mg/dL vs. 0.41 $\pm$ 0.32 mg/dL,  $P=0.86$ ). The USCN in goitrous and nongoitrous boys was 0.41 $\pm$ 0.32 mg/dL and 0.43 $\pm$ 0.37 mg/dL, respectively ( $P=0.67$ ). The USCN in goitrous and nongoitrous girls was 0.43 $\pm$ 0.26 mg/dL and 0.40 $\pm$ 0.28 mg/dL, respectively ( $P=0.43$ ). The prevalence of high USCN in goitrous and nongoitrous children was 6.0% and 5.4%, respectively ( $P=0.79$ ). The goitrous boys had a higher prevalence of USCN than the nongoitrous boys (9.0% vs. 6.6%,  $P=0.54$ ). The prevalence of high USCN in the goitrous girls was comparable to the nongoitrous ones (3.6% vs. 4.4%,  $P=0.78$ ).

The mean serum levels of TSH, T4, and UIC in children with and without high USCN were not statistically significant (Table 2). There was no significant correlation between the USCN levels and the serum levels of TSH, T4, and UIC.

## Discussion

The present study shows that the goiter prevalence in

Isfahan has decreased from 89% in 1989<sup>[14]</sup> to 62% in 1997<sup>[15]</sup> and to 32.9% in 2005. This indicates that ID is the most important cause of endemic goiter, and the legislation and salt iodization are effective in the treatment of goiter. However, goiter is still endemic in this iodine replenished area and a severe public health problem according to the WHO/UNICEF/ICCIDD recommended criteria.<sup>[1]</sup>

According to the WHO/UNICEF/ICCIDD recommended criteria, the indicator of ID elimination is a median value for UIC of 10 µg/dL, and UIC should not be lower than 5 µg/dL in more than 20% of samples.<sup>[1]</sup> In the studied children, the median UIC was 19.55 µg/dL and 3.7% of the children had UIC below 5 µg/dL. It shows there is no biochemical ID or no inadequate iodine intake of the studied children. According to the WHO/UNICEF/ICCIDD criteria, 25.6% of the children in our study had iodine intake more than adequate and 23.8% had excessive iodine intake, showing the risk of iodine-induced hyperthyroidism after the introduction of iodized salt to susceptible groups.<sup>[1]</sup> It was reported that after prophylaxis with iodine salt in Zaire, 14% of patients had undetectable serum TSH values.<sup>[18]</sup> In the present study, 1.2% of the children had subclinical hyperthyroidism and none of them had clinical hyperthyroidism. We suggest reevaluating the iodine content of salt in this region.

The prevalence of goiter among Iranian school children varies from one region to another. Goiter prevalence was less than 5% in Ahwaz in 2001,<sup>[19]</sup> and about 37% in Semirrom school children in 2003.<sup>[20]</sup> Two recent investigations have reported the goiter prevalence of about 40% and 5% in Marvdasht<sup>[21]</sup> and Arak<sup>[22]</sup> respectively in 2005. The high prevalence of goiter observed in this study and some areas in Iran suggests that other factors such as unknown goitrogens, autoimmunity, or other micronutrient deficiencies could contribute to the persistent goiter prevalence. In this study, we investigated the possible role of thiocyanate as a goitrogen in school children of Isfahan.

Epidemiological observations during the 1950s and 1960s<sup>[23,24]</sup> showing goiter endemics to occur in regions where there was no ID strongly suggested the existence of some goitrogenic factors in the diet or environment other than ID.<sup>[25]</sup> Natural goitrogens were first found in vegetables of the genus *Brassica* (the Cruciferae family). Their anti-thyroid action is related to the presence of thioglucosides, which release thiocyanate after digestion.<sup>[25]</sup> Cassava, maize, bamboo shoots, sweet potatoes, and lima beans are important staples and their glucosides release cyanide after ingestion, which is detoxified by conversion to thiocyanate. Cassava is a basic foodstuff in tropical areas and its role in endemic goiter in association with ID has clearly been

demonstrated.<sup>[25]</sup> The inhibitory action of thiocyanate on iodine uptake is due to a competitive effect of pseudohalide associated with the mechanism of iodide concentration. However, under the experimental conditions, a high plasma concentration of thiocyanate is required to inhibit the iodine uptake by the thyroid gland.<sup>[26]</sup>

In the present study, both goitrous and nongoitrous children had a normal USCN level, indicating that all children were not exposed to the thiocyanate load. Goitrous children had a similar USCN level as did nongoitrous ones. Boys and girls had similar USCN levels in the goitrous and control group.

Environmental thiocyanate exposure through food, industrial waste products and smoking was not investigated in the present study. We categorized participants into the goitrous and nongoitrous group by inspection and palpation. The sensitivity and specificity of palpation are low for mild to moderate IDD.<sup>[27]</sup> Classification of subjects into different goiter groups would be more accurate by thyroid ultrasonography instead of inspection and palpation.

In conclusion, goiter is still endemic in Isfahan. Iodine deficiency or thiocyanate overload is not the contributor to the still high prevalence of goiter in this region. Therefore the possible role of other goitrogens should be further studied in this region.

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**Competing interest:** None declared.

**Contributors:** Hashemipour M suggested the study. Keshteli AH, Hashemipour M, Siavash M and Amini M were involved in designing and performing the study. Keshteli AH, Hashemipour M and Siavash M performed the statistical analysis. Keshteli AH and Hashemipour M prepared the first draft of the article. Keshteli AH, Hashemipour M, Siavash M and Amini M critically reviewed the article and performed any required revision.

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