

Research paper

Increased goiter prevalence in schoolchildren of Isfahan despite long-term iodine sufficiency

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ABSTRACT

OBJECTIVE: Iodine Deficiency (ID) was for years considered a contributing factor for endemic goiter in Iran. The present study was conducted to assess the goiter prevalence and iodine status in schoolchildren of Isfahan 16 years after the initiation of salt iodization in Iran. **DESIGN:** 2331 schoolchildren, aged 6-13 years were selected by multistage random sampling. Thyroid size was estimated in each child by inspection and palpation and was graded according to the criteria recommended by WHO. Urinary Iodine Concentration (UIC) was also measured. **RESULTS:** Overall, 32.9% of the 2331 students had goiter. 4.6% of them were classified as goitrous grade 2. The median UIC was 195.5µg/l (Range: 10-580µg/l). 15.8% of total samples had iodine excretion level below 100µg/l and 3.7% had iodine level below 50µg/l. UIC in nongoitrous and goitrous children was (mean±SD) 220.91±119.44 µg/l and 220.16±114.64µg/l, respectively (p= 0.949). **CONCLUSION:** According to the present study there is no biochemical ID and the iodine intake of the total population is adequate. Goiter prevalence has decreased significantly after the new legislation, nevertheless it is still a public health problem in this region. The data suggest that other goitrogens, micronutrient deficiencies and thyroid autoimmunity may be operative and must be investigated in Isfahan schoolchildren.

Key words: Goiter, Iodine, Iran, Schoolchildren

INTRODUCTION

Iodine Deficiency (ID) is recognized as a major preventable public health problem worldwide. It is

estimated that 750 million people worldwide are at risk of Iodine Deficiency Disorders (IDD).¹ IDD can be presented with a wide variety of clinical manifestations, which induce congenital anomalies, cretinism, deaf mutism, psychomotor defects and severe goiter.²

Endemic goiter had been present in most parts of Iran³ and for several years ID was considered a contributing factor for endemic goiter in this country.⁴ Iran's National Committee for Control of IDD was initiated in 1989 by the Ministry of Health and

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Medical Education. The production and distribution of iodized salt, with 40 mg of potassium iodide per kg of sodium chloride, was then started and the education of policymakers, health personnel and the public was initiated in 1990. However, a rapid survey in 1993 of iodized salt consumption showed that less than 50% of the population consumed iodized salt with mean urinary iodine ranging from 5.0 to 8.2 µg/dl. As a result, the first law requiring the mandatory iodization of all salts for household use was proclaimed in 1994.⁵

Isfahan is a city in the central part of Iran with an approximate population of 2,000,000. The prevalence of goiter in Isfahan had been estimated in 1989 to be 92% in girls and 85% in boys.⁶ According to another study conducted in 1997 the prevalence of goiter among Isfahan 6-18-year-old children was estimated to be 62%.⁷

The present study was conducted to estimate goiter prevalence and urinary iodine concentration in Isfahan schoolchildren 16 years after the initiation of salt iodization in this city.

METHODOLOGY

This was a cross-sectional study performed on schoolchildren of Isfahan in 2005. Subjects were enrolled with a multistage cluster random sampling. We excluded subjects with a history of exposure to radioactive iodine, thyroid surgery or significant underlying disease such as cardiopulmonary, liver or renal problems based on available medical records and interviews with parents and teachers.

Goiter grading was performed by two endocrinologists according to WHO/UNICEF/ICCIDD classification:¹

Grade 0: No palpable or visible goiter;

Grade 1: A goiter that is palpable but not visible when the neck is in the normal position (i.e. the thyroid is not visibly enlarged);

Grade 2: A swelling in the neck that is clearly visible when the neck is in a normal position and is consistent with an enlarged thyroid when the neck is palpated.

Weight and standing height were measured. Height was recorded to the nearest 0.1 cm and weight was

recorded to the nearest 100 g. Body Mass Index (BMI) was calculated using the following formula: $BMI = \text{weight (Kg)} / \text{height (m)}^2$. Body surface area (BSA) was calculated by the formula: $\text{weight (Kg)}^{0.425} \times \text{height (cm)}^{0.725} \times 71.84 \times 10^{-4}$.

The blood samples were transferred on dry ice to the reference laboratory of the "Isfahan Endocrine and Metabolic Research Center". The samples were stored at -70°C until analysis. All urine and blood assays were performed within a median of 26h of sampling. The same person performed each assay using the same method.

Urine Iodine Concentration (UIC) was determined by the digestion method based on a modification of Sandell-Kolthoff reaction^{1,8} (intra-assay CV 1.2% and inter-assay CV 2.2%).

Serum T4 concentration was measured by radioimmunoassay (Iran Kavoshyar Co., Tehran, Iran) (Intra-assay CV 4.7% and inter-assay CV 4.9%). Normal range for T4 level was 4.5-12 µg/dl. Serum TSH concentration was determined with immunoradiometric assay (Iran Kavoshyar Co., Tehran, Iran) (Intra-assay CV 1.5% and inter-assay CV 1.9%). Normal range for TSH level was 0.3-3.9 mIU/l. Overt hypothyroidism was defined as elevated TSH and low T4, subclinical hypothyroidism as elevated TSH and normal T4 and subclinical hyperthyroidism as low TSH and normal T4.

Quantitative variables are presented as mean \pm SD. Normality of data distribution was assessed with the Kolmogorov-Smirnov test. Independent sample t-test and one-way ANOVA were used to compare normally distributed measurements in different groups. Parameters not normally distributed were compared by the Mann-Whitney U or Kruskal-Wallis H tests. Prevalence of goiter in boys and girls was compared by the chi-square test. Correlation between quantitative variables was calculated by Pearson correlation coefficient. P value less than 0.05 was considered statistically significant. All analysis was performed using SPSS version 15 (SPSS Corp, Chicago, IL, USA).

Written consent was obtained from all children's parents who were informed about the study. The study was approved by the Ethics Committee of the

Isfahan Endocrine and Metabolism Research Center of Isfahan University of Medical Sciences.

RESULTS

Two thousand three hundred and thirty-one schoolchildren were enrolled in this study with female to male ratio of 1.60. Their age ranged from 6 to 13 years. The mean age \pm SD was 9.39 ± 1.18 years for girls and 9.47 ± 1.12 years for boys. Overall, 32.9% of subjects were classified as goitrous (Table 1). Goiter prevalence among girls was 32.4% while 33.7% of boys were goitrous ($P=0.518$).

UIC was measured in 454 schoolchildren. The mean \pm SD and median UIC was 220.66 ± 17.33 and $195.50 \mu\text{g/l}$, respectively. Table 2 shows the mean, values, the range, as well as the 10th, 25th, 50th, 75th and 90th percentiles of UIC by goiter status. 15.8% of total samples had iodine excretion level below $100 \mu\text{g/l}$ and 3.7% had iodine level below $50 \mu\text{g/l}$. 25.6% of subjects had UIC between 200 and $300 \mu\text{g/l}$ and 23.8% had UIC more than $300 \mu\text{g/l}$. UIC in nongoitrous and goitrous children was 220.91 ± 119.44 and $220.16 \pm 114.64 \mu\text{g/l}$, respectively ($P=0.949$). There

was also no significant difference in UIC levels between nongoitrous subjects and children with grade 1 or grade 2 goiter. UIC did not differ significantly in boys and girls (221.25 ± 123.99 vs. $220.16 \pm 112.53 \mu\text{g/dl}$, $P=0.922$). The mean \pm SD of UIC in goitrous and nongoitrous boys was $215.70 \pm 118.02 \mu\text{g/l}$ and $223.93 \pm 127.09 \mu\text{g/l}$, respectively ($P=0.657$). UIC in goitrous and nongoitrous girls was 223.68 ± 112.49 and $218.33 \pm 112.85 \mu\text{g/l}$, respectively ($P=0.723$). No significant relationship was found between UIC and different goiter grades.

Serum T4 and TSH were measured in 485 children. All children had T4 levels within normal range. There were 6 (1.2%) children with subclinical hyperthyroidism and 82 (16.9%) children with subclinical hypothyroidism. Goitrous children had significantly lower T4 levels than nongoitrous ones (8.46 ± 1.47 vs. $8.84 \pm 1.48 \mu\text{g/dl}$, $P=0.008$) (Table 3). There was no significant difference between TSH levels in goitrous and nongoitrous children (3.18 ± 3.96 vs. $2.65 \pm 1.36 \text{ mIU/l}$, $P=0.098$). However, comparing TSH levels

Table 1. Thyroid size determined by inspection and palpation in schoolchildren of Isfahan, Iran

	Number	Thyroid size		
		Nongoitrous	Grade 1 goiter	Grade 2 goiter
Boys	898	66.3%	27.3%	6.4%
Girls	1433	67.6%	29%	3.4%
All	2331	67.1%	28.3%	4.6%

Table 3. TSH and T4 levels in schoolchildren of Isfahan according to goiter status

	Number	TSH (mIU/l)	T4 ($\mu\text{g/dl}$) ^a
Nongoitrous	323	2.65 ± 1.36^a	8.84 ± 1.48^b
Goiter	Total	3.18 ± 3.96	8.46 ± 1.47^c
	Grade 1	2.66 ± 1.10	8.81 ± 1.10
	Grade 2	3.56 ± 5.09	8.20 ± 1.65

^aTo convert to SI units multiply by 12.87

^bSignificant difference vs. goiter grade 2

^cSignificant difference vs. nongoitrous

Table 2. The mean \pm SD, range and the 10th, 25th, 50th, 75th and 90th percentiles of values of Urinary Iodine Concentration (UIC) in $\mu\text{g/L}$ in Isfahan schoolchildren by goiter status

	Number	Mean \pm SD	Range	UIC ($\mu\text{g/l}$)				
				10 th Percentile	25 th Percentile	50 th Percentile	75 th Percentile	90 th Percentile
Nongoitrous	302	220.91 ± 119.44	10-530	85.60	126.75	198.50	300.00	420.00
Goiter	Total	220.16 ± 114.64	30-580	89.00	134.00	192.00	286.00	410.00
	Grade 1	240.45 ± 121.66	57-490	97.90	136.00	209.50	352.50	420.00
	Grade 2	206.19 ± 108.03	30-580	83.10	130.00	188.50	264.25	355.70
Overall	454	220.66 ± 17.33	10-580	87.50	130.00	195.50	296.25	410.00

in children according to the grades of goiter showed that children with grade 2 of goiter had significantly higher TSH levels than nongoitrous ones (Table 3).

UIC was not correlated with BMI, BSA, serum T4 and TSH levels.

DISCUSSION

Approximately 33% of schoolchildren in the present study were classified as goitrous, this implying that goiter is still endemic in this iodine replenished area and a severe public health problem according to WHO/UNICEF/ICCIDD recommended criteria.¹

Iran has been known as a country in which goiter has frequently been seen in the population. The first goiter survey carried out in 1968 showed that goiter was prevalent in many provinces.³ In 1983, 15 years after the original study, with no program for the control of IDD, a series of investigations in Shahriar, Tehran, Kohkiluyeh and Boyerahmad were conducted, the findings of which showed high incidence of goiter in many regions.⁵ In schoolchildren of villages north and north-west of Tehran, manifestations of severe IDD such as defective physical, mental and psychomotor development, neurologic and auditory abnormalities along with frequent occurrence of hypothyroidism was found.^{9,10} The results of these studies prompted the formation of the National Committee for Control of IDD in 1989 and the national survey of goiter.⁶ The results of the survey showed that 20 provinces had a goiter rate of over 40%. Urinary iodine excretion in many regions of the country was below 100µg/l and in some less than 20 µg/l.^{4,5} The salt iodization program began in 1989 and the production, distribution and consumption of iodized salt gradually increased. Qualitative and quantitative monitoring of iodized salt was applied on a regular basis in salt factories, retailers, shoppers and consumers in all provinces. Despite widespread education programs of health personnel and public between 1989 and 1994, the rapid survey of iodized salt consumption in 1994 showed that less than 50% of households consumed iodized salt. Therefore, a law was passed and the production of salt for household use was limited to 1kg yellow bags containing iodized salt. Rapid surveys since 1996 have shown that more than 90% of households consume iodized salt.⁵

The present survey was conducted 16 years after the initiation of iodized salt production and 11 years after the implementation of the new law for mandatory consumption of iodized salt by households.

According to the present study, goiter prevalence in Isfahan decreased from about 89% in 1989⁶ and 62% in 1997⁷ to 32.9% in 2005. This implies that ID has been the most important cause of endemic goiter and also shows the effective role of legislation and salt iodization in treating goiter. Goiter prevalence in the present study was higher than its prevalence in Gorgan (north of Iran)¹¹ and comparable to Semirom (a mountainous city near Isfahan).¹²

The most sensitive method for the monitoring and evaluation of an IDD control program is the determination of urinary iodine excretion.¹³ According to WHO/UNICEF/ICCIDD recommended criteria, the indicator of ID elimination is a median value for UIC of 100µg/l and UIC should not be below 50µg/l in more than 20% of samples.¹ In the studied population, the median UIC was 195.50µg/l and 3.7% of the population had UIC below 50µg/l. This means that there is no biochemical ID or no inadequacy in iodine intake of the overall population. According to WHO/UNICEF/ICCIDD criteria, 25.6% of subjects in our study had more than adequate iodine intake and 23.8% had excessive iodine intake. This indicates a risk of iodine-induced hyperthyroidism within 5 to 10 years after the introduction of iodized salt in susceptible groups.¹ It has been reported that, after prophylaxis with iodized salt in Zaire, 14% of patients had undetectable serum TSH values.²⁹ In the present study, 1.2% of subjects had subclinical hyperthyroidism but there was no case of clinical hyperthyroidism. Although manual goiter palpation technique yields sufficiently precise quantitative results for clinical purposes,¹⁴ it also has some limitations. While goiter rate remains high after iodine supplementation, sonography may reveal significant changes in thyroid volume.¹⁵ Previous studies indicated that measurement of goiters by palpation may not be appropriate in short-term evaluation of iodization programs, though for long-term follow-up it can be reliable.¹⁶ However, even if our assessment of response to iodine replenishment is not adequately sensitive, the high prevalence of goiter in the area studied is undeniable.

There are several studies showing serum TSH in the upper normal range in areas with endemic goiter.¹⁷⁻¹⁹ In the present study we found higher TSH levels in goitrous subjects than in nongoitrous ones.

In conclusion, goiter is still prevalent in Isfahan schoolchildren. ID alone cannot explain the endemic goiter in this region. The role of other possible contributors such as unknown goitrogens,²⁰ autoimmunity¹² or other micronutrient deficiencies such as vitamin A,²¹ iron,²² selenium²³ and zinc deficiencies²⁴ must be considered and should be investigated in Isfahan schoolchildren.

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