



# High prevalence of goiter in schoolchildren in Isfahan; zinc deficiency does not play a role

Częste występowanie wola u dzieci w wieku szkolnym w Isfahanie niezależne od niedoboru cynku

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## Abstract

**Introduction:** There are controversial data about the role of zinc deficiency in the aetiology of endemic goiter. The aim of the present study was to determine the association between zinc status and goiter in schoolchildren of Isfahan.

**Material and methods:** This study was performed in 2005. Two thousand three hundred and thirty-one schoolchildren were enrolled, and thyroid size was determined by inspection and palpation. Urinary iodine concentration (UIC) and serum zinc level were measured in a group of those children.

**Results:** The prevalence of goiter was 32.9%. The median UIC was 195.5 µg/L. Serum zinc was measured in 94 goitrous and 326 non-goitrous children. The mean ± standard deviation of serum zinc in goitrous and non-goitrous children was 100.81 ± 22.33 and 96.00 ± 25.79 µg/dL, respectively (P = 0.08). The prevalence of zinc deficiency (serum zinc ≤ 65 µg/dL) in goitrous and non-goitrous children did not differ significantly (6.4% v. 8.0%, P = 0.61).

**Conclusions:** The prevalence of goiter is still high in Isfahan schoolchildren. It seems that zinc status is not involved in the high prevalence of goiter in this region. The role of other possible goitrogens should be investigated in Isfahan.

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**Key words:** Goiter, zinc deficiency, iodine deficiency, Iran

## Streszczenie

**Wstęp:** Dane dotyczące znaczenia niedoboru cynku w etiologii wola endemicznego są niejednoznaczne. Celem niniejszego badania było ustalenie związku między stężeniem cynku w surowicy a występowaniem wola u dzieci w wieku szkolnym w Isfahanie.

**Materiał i metody:** Badanie przeprowadzono w 2005 roku. Włączono do niego 2331 dzieci, u których oceniono palpacyjnie wielkość tarczycy. U części dzieci oznaczono stężenie jodu w moczu (UIC, *urinary iodine concentration*) i stężenie cynku w surowicy.

**Wyniki:** Obecność wola stwierdzono u 32,9% dzieci. Średnie UIC wynosiło 195,5 µg/l. Stężenie cynku w osoczu oznaczono u 94 dzieci z wolem i 326 dzieci, u których nie stwierdzono wola. Średnie stężenie cynku w osoczu ± odchylenie standardowe wynosiło 100,81 ± 22,33 µg/dl u dzieci z wolem i 96,00 ± 25,79 µg/dl u dzieci bez wola (p = 0,08). Częstość niedoboru cynku (stężenie cynku w surowicy ≤ 65 µg/dl) nie różniła się istotnie w grupie dzieci z wolem i bez wola (6,4% v. 8,0%, p = 0,61).

**Wnioski:** Częstość występowania wola u dzieci w wieku szkolnym w Isfahanie jest nadal duża. Wydaje się, że niedobór cynku nie ma wpływu na znaczną liczebność przypadków wola w tym regionie. Wskazane są dalsze badania mające na celu identyfikację czynników zwiększających częstość występowania wola w Isfahanie. (Endokrymol Pol 2010; 61 (3): 287–290)

**Słowa kluczowe:** wole, niedobór cynku, niedobór jodu, Iran

## Introduction

Endemic goiter has been present in most parts of Iran, and for several years iodine deficiency (ID) was considered a contributing factor for endemic goiter in this country [1]. Iran's National Committee for Control of iodine deficiency disorders (IDD) was established in 1989 by the Ministry of Health and Medical Education.

The first law requiring the mandatory iodization of all salts for household use was proclaimed in 1994 [2]. Although the program was successful in reducing the goiter prevalence in most areas, the prevalence of goiter still remains high in some regions.

Isfahan, the second largest city in Iran, is located in the central part of the country with an approximate population of two million. The prevalence of goiter in Isfa-



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han had been estimated to be 92% in girls and 85% in boys in 1989 [3]. According to another study conducted in 1997, the prevalence of goiter among Isfahan's 6–18-year-old children was estimated to be 62% [4].

Zinc is a trace element with numerous functions in the human organism. It plays a key role in the thyroid function. It is very important in thyrotropin releasing hormone (TRH) synthesis [5], is essential for thyroxine ( $T_4$ )-to-triiodothyronine ( $T_3$ ) conversion [6], and is required for the biological functioning of the thyroid hormone and related receptors [7]. Zinc deficiency has a suppressing effect on thyroid hormones, whereas zinc supplementation has the opposite effect [8, 9].

The present article describes goiter prevalence, iodine status, and the role of zinc deficiency in the aetiology of goiter among Isfahan schoolchildren, eleven years after the mandatory salt iodization in Iran.

## Material and methods

This cross-sectional study was performed 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 [10]:

- 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.

The blood samples were transported on dry ice to the reference laboratory of the Isfahan Endocrine and Metabolic Research Centre. The samples were stored at  $-70^{\circ}\text{C}$  until analysis. The same person performed each assay using the same method.

Urine iodine concentration (UIC) was measured by the digestion method based on a modification of the Sandell-Kolthoff reaction [10, 11]. Serum  $T_4$  and TSH were measured with radioimmunoassay and immunoradiometric assay, respectively. The normal range of  $T_4$  was 4.5–12  $\mu\text{g/dL}$  and for TSH was 0.3–3.9 mIU/L. Serum zinc concentrations were measured with atomic absorption spectrometry. Zinc deficiency was defined as serum zinc  $\leq 65 \mu\text{g/dL}$  [12].

Quantitative variables are presented as mean  $\pm$  SD. Independent sample t-test and one-way ANOVA were used to compare normally distributed measurements. Param-

**Table I.** Thyroid size determined by inspection and palpation in schoolchildren in Isfahan, Iran

**Tabela I.** Wielkość tarczycy określona na podstawie badania palpacyjnego u dzieci w wieku szkolnym w Isfahanie, Iran

	Number	Thyroid size		
		Non-goitrous	Goiter of grade 1	Goiter of grade 2
Boys	898	66.3%	27.3%	6.4%
Girls	1433	67.6%	29%	3.4%
All	2331	67.1%	28.3%	4.6%

eters not normally distributed were compared by Mann-Whitney U or Kruskal-Wallis H tests. Prevalence of zinc deficiency between goitrous and non-goitrous children was compared by Chi-square test. Pearson correlation was used to find the correlation between serum zinc and different quantitative variables. P value less than 0.05 was considered statistically significant. All analysis was performed by 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 Centre.

## Results

Two thousand three hundred and thirty-one schoolchildren were enrolled in this study, with a female to male ratio of 1.60. Their ages ranged from 6 to 13 years. The mean age  $\pm$  SD was  $9.39 \pm 1.18$  for girls and  $9.47 \pm 1.12$  for boys. Overall, 32.9% of subjects were classified as goitrous (Table I). The goiter prevalence among girls was 32.4%, and among boys was 33.7% ( $P = 0.51$ ).

Urine iodine concentration was measured in 454 randomly selected children. The mean  $\pm$  SD and median UIC was  $220.66 \pm 17.33$  and 195.50  $\mu\text{g/L}$ , respectively. Of the total samples, 15.8% had iodine excretion level below 100  $\mu\text{g/L}$  and 3.7% had iodine level below 50  $\mu\text{g/L}$ . Among the subjects, 25.6% had UIC between 200 and 300  $\mu\text{g/L}$  and 23.8% had UIC more than 300  $\mu\text{g/L}$ . Urine iodine concentration in goitrous and non-goitrous children was  $220.91 \pm 119.44$  and  $220.16 \pm 114.64 \mu\text{g/L}$ , respectively ( $P = 0.57$ ).

Serum zinc was measured in 94 children with goiter grade 2, and in 326 non-goitrous children who were randomly selected. The mean  $\pm$  SD of serum zinc in goitrous and non-goitrous children was  $100.81 \pm 22.33$  and  $96.00 \pm 25.79 \mu\text{g/dL}$ , respectively ( $P = 0.08$ ). Serum zinc level in goitrous boys was not statistically different from that in non-goitrous boys ( $101.40 \pm 21.40$  v.  $95.41 \pm 30.49 \mu\text{g/dL}$ ,  $P = 0.13$ ). Serum zinc in goitrous

**Table II.** Assessment of thyroid gland function in children with and without zinc deficiency in Isfahan, Iran**Tabela II.** Ocena czynności gruczołu tarczowego u dzieci z niedoborem i bez niedoboru cynku zamieszkałych w Isfahanie, Iran

	TSH [mU/L]	T <sub>4</sub> [μg/dL]	UIC [μg/L]
Zinc deficient	2.74 ± 1.29	8.55 ± 1.59	192.48 ± 116.55
Zinc sufficient	2.87 ± 2.80	8.71 ± 1.54	219.52 ± 116.91
P value	> 0.05	> 0.05	> 0.05

**Table III.** Different variable concentrations based on quartiles of serum zinc in schoolchildren in Isfahan**Tabela III.** Stężenie hormonów tarczycy u dzieci zamieszkałych w Isfahanie w zależności od kwartyła stężenia cynku w surowicy

Serum zinc concentration [μg/L]	TSH [mU/L]	T <sub>4</sub> [μg/dL]	UIC [μg/dL]
Zinc ≤ 81	2.70 ± 1.39	8.65 ± 1.49	215.53 ± 118.86
81 < zinc ≤ 96	3.17 ± 4.54	8.97 ± 1.45	222.45 ± 118.84
96 < zinc ≤ 112	2.80 ± 1.83	8.56 ± 1.55	218.71 ± 122.10
Zinc > 112	2.86 ± 2.71	8.57 ± 1.69	212.51 ± 107.88
P value	> 0.05	> 0.05	> 0.05

and non-goitrous girls was 100.12 ± 23.62 and 96.49 ± 21.10 μg/dL, respectively (P = 0.36).

The prevalence of zinc deficiency in goitrous and non-goitrous children was 6.4 % and 8.0%, respectively (P = 0.61). Zinc deficiency was seen in 5.9% of goitrous boys and 9.4% of non-goitrous boys (P = 0.44). The prevalence of zinc deficiency in goitrous and non-goitrous girls was 7.0% and 6.8%, respectively (P = 0.96).

There was no statistically significant difference between the mean serum TSH, T<sub>4</sub>, and UIC in subjects with and without zinc deficiency (Table II).

There was also no significant difference between these measurements in different quartiles of zinc concentration (Table III). Serum zinc was not correlated with these parameters either.

There were 6 (1.2%) children with subclinical hyperthyroidism and 82 (16.9%) children with subclinical hypothyroidism in the studied group.

## Discussion

As revealed by the present study, goiter prevalence in Isfahan has decreased from about 89% in 1989 [3] and 62%

in 1997 [4] to 32.9% in 2005. This proves that ID has been the most important cause of endemic goiter in Isfahan and shows the effective role of the legislation and salt iodization in treating goiter. However, goiter is still endemic in this area and a severe public health problem according to WHO/UNICEF/ICCIDD recommended criteria [10].

According to WHO/UNICEF/ICCIDD recommended criteria, the indicator of ID elimination is a median value for UIC of 100 μg/L, and UIC should not be below 50 μg/L in more than 20% of samples [10]. In our study the median UIC was 195.50 μg/L, and 3.7% of the population had UIC below 50 μg/L. This means that there is no biochemical ID or inadequacy in iodine intake in the overall population. In the present study, 25.6% of children had more than adequate iodine intake and 23.8% had excessive iodine intake. This indicates the risk of iodine-induced harmful conditions. We strongly suggest performing studies to analyze the iodine content of commercially available salt samples in Isfahan.

We have recently indicated the role of selenium deficiency and thyroid autoimmunity in the persistence of goiter in Isfahan schoolchildren [13, 14]. However, the role of vitamin A deficiency was ruled out in these children [15]. Here, we present the results of our investigation on the association between zinc status and endemic goiter in Isfahan schoolchildren.

Zinc is an essential nutrient which serves as a component of more than 300 enzymes including metal-containing enzymes which participate in nucleic acid and carbohydrate metabolism along with protein metabolism [16]. Zinc status was shown to affect thyroid function in different studies. Zinc deficiency significantly reduced serum T<sub>3</sub> concentrations in rats [17]. In a zinc depletion-repletion study conducted in humans, circulating TSH, total T<sub>4</sub>, and free T<sub>4</sub> tended to decrease during the depletion phase, returning to control levels after zinc repletion [18]. Ruz et al. reported decreased T<sub>3</sub> in spite of normal TSH levels in zinc deficient rats [19]. They also showed severe morphological alterations of the thyroid cell caused by zinc deficiency [19]. Baltaci et al. found the lowering effect of zinc deficiency on thyroid hormones secondary to TSH suppression in rats [8]. The nuclear receptor for T<sub>3</sub> is partially zinc dependent. Also, zinc participates in the formation and mechanism of the action of TRH [19].

In the present study we showed that serum zinc levels in goitrous schoolchildren of Isfahan did not differ to those in non-goitrous children. There was also no significant difference in the prevalence of zinc deficiency between goitrous and non-goitrous children. Controversial data exists on the role of zinc status in the development of goiter. Ozata et al. showed that zinc deficiency might contribute to the pathogenesis of endemic goiter in Turkish males [20]. On the other hand, Hampel et al.

showed that zinc deficiency was not involved in the goiter endemic in Germany [21]. There was also no association between zinc status and thyroid volume in 35–60-year-old French adults [22]. Kucharzewski et al. reported higher zinc levels in the whole blood samples of subjects with nodular goiter in comparison to a control group [23]. Similarly to the present study, the previous two studies in Iranian schoolchildren did not find any association between zinc status and endemic goiter [12, 24].

We also showed that zinc deficiency did not affect  $T_4$  and TSH levels. This is in contrast to the findings in a zinc depletion-repletion study in which during the depletion phase thyroid hormones tended to decrease [18]. However, recently published studies in Iranian schoolchildren have reported no difference in  $T_4$  and TSH levels between zinc deficient and zinc sufficient subjects [12, 24].

About 17% of the children in the present study had subclinical hypothyroidism (elevated TSH and normal  $T_4$ ). We suggest that this finding, in the presence of adequate iodine intake in the studied population, can be explained by thyroid autoimmunity [14].

In the present study we used serum zinc levels to determine zinc status. Measurement of zinc in other tissues such as different blood cell types, hair and nails, and a variety of zinc-binding proteins, such as metallothionein and other zinc metalloenzymes, have also been investigated as possible indicators of zinc status. However, these approaches do not seem to provide any greater sensitivity or analytic convenience than using serum zinc concentration [25]. In the present study, dietary intake of zinc was not assessed and we cannot discuss it here.

The classification of children into goitrous and non-goitrous groups by inspection and palpation is the main limitation of our study. The sensitivity and specificity of palpation is poor [26], and it would be more accurate if we used thyroid ultrasonography to determine goiter size.

## Conclusions

Goiter remains endemic in Isfahan eleven years after the initiation of mandatory salt iodization in Iran. We showed that neither iodine deficiency nor zinc status contributes to the residual goiter in Isfahan schoolchildren. The role of other goitrogens should be investigated in this region.

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