Protein-energy Malnutrition in Goitrous Schoolchildren of Isfahan, Iran

Samaneh Khanpour Ardestani[1,2], Mahin Hashemipour[1], Noushin Khalili[3], Arash Zahed[1], Ammar Hassanzadeh Keshteli[4]

[1]Department of Pediatrics, Child Growth and Development Research Center, Isfahan University of Medical Sciences, Isfahan, Iran, [2]Department of Pediatrics, CARE Program, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Canada, [3]Isfahan Endocrine and Metabolism Research Center, Isfahan University of Medical Sciences, Isfahan, Iran, [4]Department of Medicine, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Canada

Correspondence to:
Dr. Noushin Khalili,
Isfahan Endocrine and Metabolism Research Center, Seddigheh Tahereh Research Complex, Khorram Street, Isfahan, Iran.
E-mail: n_khalili@med.mui.ac.ir

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Original Article

ABSTRACT

Background: Some studies have shown the possible role of protein-energy malnutrition (PEM) in persistence of endemic goiter in iodine replenished areas. The present study was conducted to assess the association between PEM and goiter in schoolchildren of Isfahan, Iran.

Methods: In a cross-sectional study using multistage cluster random-sampling, 2331 schoolchildren with age ranged from 6-13 years old with a female to male ratio of 1.60 were enrolled. Thyroid size was examined by two endocrinologists for goiter detection. Children were considered goitrous if they had palpable or visible goiters according to World Health Organization (WHO)/United Nations children's Fund/International Council for the Control of Iodine Deficiency criteria. Weight and standing height were measured using the standard tools and anthropometric indices were calculated using the WHO AnthroPlus software developed by the World Health Organization. Height-for-age Z-scores (HAZ), weight-for-age Z-scores (WAZ) and body mass index (BMI) for age were calculated for each child. Children with a HAZ, WAZ or BMI-for-age of Z-score < –2.0 were classified as stunted, underweight or thin, respectively. Blood samples were drowned to measure serum thyroid hormones.

Results: Overall, 32.9% of subjects were classified as goitrous. Weight, height, BMI, WAZ and BMI-for-age Z-score were significantly lower in children with goiter than in children who did not have goiter ($P < 0.05$). The prevalence of goiter in thin children was higher than that in non-thin ones (48.4 vs. 31.6%, odds ratio [OR]: 2.02, 95% confidence interval [CI]: 1.52-2.69, $P < 0.001$). Although 33.4% of non-stunted children were goitrous, 31% of stunted ones had goiter ($P = 0.5$). According to the logistic regression model taking sex and age as covariates, the only significant parameter affecting palpable goiter detection was thinness (OR = 2.13, 95% CI: 1.22-3.69, $P < 0.001$).

Conclusions: In the present study, we found a high prevalence of goiter in children who were malnourished. It seems that PEM may play a role in the still high prevalence of goiter in this region.

Keywords: Body mass index-for-age Z-score, goiter, height-for-age Z-score, Iran, protein-energy malnutrition, weight-for-age Z-score

INTRODUCTION

Two billion individuals have insufficient iodine intake around the world, particularly those in south Asia and sub-Saharan Africa.[1] Globally, 246 millions of school-aged children are estimated to have insufficient iodine intakes.[2] Currently, 111 countries have adequate iodine nutrition. 30 countries remain iodine-deficient, 9 are moderately deficient, 21 are mildly deficient and none are currently considered severely iodine-deficient.[3] Furthermore, 10 countries have excessive iodine intake. Although substantial progress has been made over the last several decades, iodine deficiency (ID) remains a significant public health problem worldwide, including in developed nations.[3] Inadequate intake of iodine impairs thyroid function and results in a wide variety of clinical manifestations, including goiter, impaired cognitive development and congenital abnormalities, collectively referred to as iodine-deficiency disorders.[4] ID is the most common cause of preventable mental impairment worldwide.[1] Deficiencies of micronutrients such as iron, selenium, vitamin A and possibly zinc may interact with iodine nutrition and thyroid function, as well.[4]

Endemic goiter had been presented in most provinces of Iran and for several years ID was considered a contributing factor for endemic goiter in this country. Since 1994, production of uniodized house salt has been forbidden by legislation, and thereafter, frequent regular evaluations of salt and urine iodine by provincial organization and local officials of health have confirmed adequate iodine intake.[5]

Isfahan is a city in the central part of Iran with an approximate population of 1,600,000. After the initiation of iodized salt production and implementation of the law for mandatory consumption of iodized salt by households, goiter prevalence in Isfahan decreased from about 89% in 1989 to 62% in 1997.[6] This implies that goiter is still endemic in this area and ID alone cannot explain such high prevalence of goiter. Some studies have shown other possible contributors such as thyroid autoimmunity[7] or other micronutrient deficiencies (vitamin A, iron, selenium, and zinc) that might play a role in increasing prevalence of endemic goiter.[6]

Protein-energy malnutrition (PEM) which is characterized by energy deficit due to a reduced intake of all macronutrients and deficits in many micronutrients is considered one of the factors contributing to endemic goiter.[8] In endemic goiter regions of India, Bangladesh, Africa and Turkey, nutritional deficiencies were prevalent in children with goiter.[9] Centanni *et al*. in their study have reported that even mild PEM might have detrimental effects on thyroid homeostasis in iodine-deficient areas.[10] In an Indian study, thyroid size was larger in children who exhibited sever features of PEM.[11] Another study in Turkey showed body mass index (BMI) Z-scores and weight-for-height ratios were significantly lower in children with goiter.[12]

Because Isfahan is an endemic goiter area, we performed this study to investigate if there is any association between PEM and goiter in this region.

METHODS

This was a study based on data from a large cross-sectional study conducted in 2005 on schoolchildren of Isfahan.[6] 2332 schoolchildren in the age range of 6-13 years were enrolled using a multi-stage cluster random sampling method.[13] Clinical examination of goiter was performed by two endocrinologists according to the classification of the World Health Organization/United Nations children's Fund/International Council for the Control of Iodine Deficiency (WHO/UNICEF/ICCIDD).[14] Children were defined as goitrous if their thyroid was palpable but not visible with the head in a normal position (Grade 1) or a swelling in the neck that was clearly visible when the neck was in normal position and was consistent with an enlarged thyroid when the neck was palpated (Grade 2). They were considered non goitrous if their goiter was not visible or palpable (Grade 0).

Weight and standing height were measured. Children wearing no shoes and light clothes were weighed using a scale with 100 g precision. Height was recorded to the nearest 0.1 cm in bare feet with participants standing upright against a mounted stadiometer. BMI was calculated using the following formula: $BMI = weight(kg)/height(m)^2$. Height-for-age Z-scores (HAZ), weight-for-age Z-scores (WAZ), and BMI-for-age were calculated for each child with the use of WHO AnthroPlus software available at the WHO homepage (http://www.who.int/growthref/

tools/en), which applies the 2007 WHO reference values.[15] These are referred to as the WHO Z-scores. Weight-for-age can be calculated only for children aged <10 years. Children with a HAZ, WAZ or BMI-for-age of Z-score < –2.0 were classified as stunted, underweight or thin, respectively.[15] It is worthy to note that the above mentioned indices are in close relationship with indicators of PEM such as stunting and underweight.[16] A low HAZ indicates stunting (stunted growth) and reflects a failure to reach linear growth potential as a result of suboptimal health and/or nutritional conditions. A low WAZ is considered to indicate underweight in the absence of significant wasting. In addition, BMI is an important index for thinness in children over 10 years of age.[12]

Blood samples were collected in a subsample of participants who were selected randomly and 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 26 h of sampling. The same person performed each assay using the same method. Urine samples were collected in a randomly selected group of participants and urine iodine concentration (UIC) was determined by the digestion method based on a modification of Sandell-Kolthoff reaction (1). According to WHO/UNICEF/ICCIDD recommended criteria (14), 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. Serum T4 was measured with radioimmunoassay (Iran Kavoshyar Co., Tehran, Iran). Serum thyroid stimulating hormone (TSH) concentration was measured using immunoradiometric assay (Iran Kavoshyar Co., Tehran, Iran). The normal range of T4 was 4.5-12 μg/dl and for TSH was 0.3-3.9 mU/l.[6]

Quantitative variables are presented as mean ± standard deviation (SD) and Z-score. Normality of data distribution was assessed with the Kolmogorov-Smirnov test. Independent sample *t*-test was used to compare normally distributed anthropometric measurements between goitrous and non-goitrous children. Parameters not normally distributed were compared by the Mann-Whitney U-test. Qualitative variables such as having goiter or not and different categories of clinical and subclinical thyroid dysfunction are presented as a percentage and were compared by the Chi-square test. Correlation between quantitative variables was assessed by Pearson correlation coefficient. Logistic regression was used to evaluate the association between anthropometric indices, sex and age and goiter. $P < 0.05$ was considered to be statistically significant. All analysis was performed using SPSS version 16.0 (SPSS Corp, Chicago, IL, USA).

RESULTS

Mean age of all enrolled children into the study was 9.42 ± 1.15 years (range: 6-13 years) with a female to male ratio of 1.60. Overall 32.9% of subjects were classified as goitrous [Table 1]. While goiter prevalence among girls was 32.4%, 33.7% of boys were classified as goitrous ($P = 0.51$). UIC was measured in 454 schoolchildren. The mean ± SD and median UIC was 220.7 ± 17.3 and 195.50 μg/l, respectively. In total, 15.8% and 3.7% of children had UIC level below 100 and 50 μg/l, respectively. Also, 25.6% of subjects had UIC between 200 and 300 μg/l and 23.8% had UIC more than 300 μg/l. UIC in non-goitrous and goitrous children was 220.9 ± 119.4 and 220.2 ± 114.6 μg/l, respectively ($P = 0.949$).

Although goitrous children were shorter than non-goitrous ones (133.44 ± 8.79 vs. 134.37 ± 9.31 cm, $P = 0.04$), HAZ was not significantly different between two groups. Weight, BMI, WAZ and BMI-for-age Z-score were significantly lower in children with goiter [Table 2]. A total of 108 (9.4%) children were underweight, 184 (8.2%) were stunted and 213 (9.5%) were thin. The prevalence of goiter in thin children was higher than that in non-thin ones (48.4 vs. 31.6%, odds ratio [OR]: 2.02, 95% confidence interval [CI]: 1.52-2.69, $P < 0.001$). While 33.4% of non-stunted children were goitrous, 31% of stunted ones had goiter ($P = 0.5$). The prevalence of goiter among underweight schoolchildren did not

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

Subjects	Thyroid size			
	Number	Non-goitrous (%)	Grade 1 goiter (%)	Grade 2 goiter (%)
Boys	898	595 (66.3)	245 (27.3)	58 (6.4)
Girls	1433	968 (67.6)	416 (29.0)	49 (3.4)
All	2331	1563 (67.1)	661 (28.3)	107 (4.6)

Table 2: Anthropometric indices of children with goiter in comparison with nongoitrous ones

Anthropometric indices	Goitrous children	Non-goitrous children	*P* value
Height (cm)	133.44±8.79	134.37±9.31	0.04*
Weight (kg)	28.04±6.54	31.14±9.29	<0.001*
BMI (kg/m^2)	15.59±2.31	16.98±3.35	<0.001*
HAZ	−0.63±1.03	−0.57±1.10	0.24
WAZ	−0.67±1.12	−0.44±1.27	<0.01*
BMI-for-age Z-score	−0.74±1.25	−0.11±1.38	<0.001*

*Mann-Whitney U-test. BMI=Body mass index, HAZ=Height-for-age Z-score, WAZ=Weight-for-age Z-score

differ significantly in comparison to those who were not underweight (37 vs. 34.3%, $P = 0.5$). According to the logistic regression model taking sex and age as covariates, the only significant parameter affecting palpable goiter detection was BMI-for-age Z-score < –2 (OR = 2.13, 95% CI: 1.22-3.69, $P < 0.001$).

Serum TSH and T4 were measured in 485 randomly-selected children. 6 (1.2%) children had subclinical hyperthyroidism, and 82 (16.9%) had subclinical hypothyroidism. Clinical hyper-or hypothyroidism was not detected in any children. Levels of TSH, T4, UIC as well as the prevalence of subclinical hypothyroidism in thin, underweight or stunted children were not significantly different from those who were not thin, underweight or stunted [Table 3].

Table 3: Thyroid hormone levels and urinary iodine concentration in children with and without indicators of malnutrition

Categories of PEM		*P* value
TSH (mU/l)	**Mean±SD**	
Thin	3.95±7.26	NS*
Non-thin	2.74±1.49	
Stunted	3.07±1.21	
Non-stunted	2.82±2.66	
Underweight	3.01±1.30	
Non-underweight	3.01±3.44	
T4 (µg/dl)	**Mean±SD**	
Thin	8.85±1.42	NS*
Non-thin	8.68±1.48	
Stunted	8.78±1.21	
Non-stunted	8.69±1.50	
Underweight	8.80±1.12	
Non-underweight	8.39±1.45	
UIC (µg/l)	**Mean±SD**	
Thin	208.57	NS*
Non-thin	221.84	
Stunted	221.25	
Non-stunted	221.46	
Underweight	255.04	
Non-underweight	220.12	
Subclinical hypothyroidism	**Percentage**	
Thin	17.1	NS**
Non-thin	17.2	
Stunted	20.0	
Non-stunted	16.9	
Underweight	17.4	
Non-underweight	19.4	

*Independent sample *t* test, **Chi-square test. NS=Not significant, PEM=Protein energy malnutrition, TSH=Thyroid stimulating hormone, T4=Total thyroxine, UIC=Urinary iodine concentration

DISCUSSION

In the present study, we found that 32.9% of children had goiter. This indicates that goiter is still endemic in this area and is a public-health problem according to the WHO/UNICEF/ICCIDD-recommended criteria.[14] Most children had palpable goiter Grade 1 and there were no gender differences in goitrous children. These data are in consistency with the results of previous studies.[8,10,11] However, we could present more accurate data on the prevalence of goiter if we used thyroid ultrasonography to evaluate thyroid size.[17] In the studied population, 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 no inadequacy in iodine intake of the overall population based on WHO/UNICEF/ICCIDD criteria.[14]

The high prevalence of goiter in Isfahan schoolchildren in spite of adequate iodine intake necessitates investigation of possible contributors. We had previously shown that thyroid autoimmunity,[18] and deficiencies of selenium[19] and iron[20] were among the possible contributing factors of goiter persistence in this region. However, the role of thiocyanate overload[13] and deficiencies of zinc[21] and vitamin A[22] were ruled out.

Some studies introduced PEM to be related to endemic goiter.[9,11,12,23] All anthropometric indices in our study were lower in goitrous children than

non-goitrous ones and differences were statistically significant except for HAZ. This implies that children with goiter had worse nutritional status or vice versa. Although the prevalence of goiter in stunted and underweight children was higher, it was not statistically significant while comparing them with children who had not any indicator of malnourishment. In contrary, the rate of goiter among children who were thin according to their BMI-for-age Z-score was significantly higher (48.4 vs. 31.6%). In our study, in the logistic regression model, considering age and sex as covariates and HAZ, WAZ or BMI-for-age Z-score < –2.0 as independent factors, there was still 2 times increased probability of goiter for thin children (defined as BMI-for-age Z-score < –2.0). The mechanism of goiter in the setting of PEM is probably multi-factorial.[11] Firstly, iodine absorption decreases in children with PEM,[10] which leads to decreased iodine concentration in the thyroid gland because of depressed iodide clearance and uptake in PEM.[24,25] Therefore, PEM indirectly results in alterations in iodine metabolism that may cause thyroid hyperplasia and further reduces circulating thyroid hormone levels.[11] Secondly, PEM may contribute to goitrogenesis directly through the lack of substrate availability, in particular the lack of essential amino acids such as tyrosine.[26] In our study, thyroid hormone levels and UIC were not significantly different in thin, underweight or stunted children in comparison with those levels in healthy ones. In addition, there was not any correlation between anthropometric indices and thyroid hormone levels both in goitrous and non-goitrous children (data were not shown). This finding is in agreement with a previous study among Turkish children.[9]

In the present study, the total prevalence of underweight, stunting and thinness in the schoolchildren of Isfahan were 9.4, 8.2 and 9.5%, respectively. In a recently published study of 5570 Iranian children aged 10-19 years, the prevalence of stunting and low BMI were 7 and 8%, respectively.[27]

In a study by Ersoy *et al*.[12] showed that goiter and nutritional deficiencies were more common in children with lower socio-economic status but the frequency of nutritional disorders in children with palpable goiter did not change according to socio-economic status. They indicated that the most important factor in detection of palpable goiter was the socio-economic status. However, in the present study, we did not assess the socio-economic status of the studied population which may influence their nutritional condition.

CONCLUSIONS

In summary, we found that goiter is still highly prevalent in schoolchildren of Isfahan as an iodine replenished area. In addition, we indicated a high prevalence of goiter in children who were malnourished. It seems that PEM may play a role in the still high prevalence of goiter among Isfahan schoolchildren. Therefore, treatment of PEM may improve endemic goiter among children specially in regions with high prevalence of PEM related indicators.

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