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Hair Trace Elements are Associated with Increased Thyroid Volume in Schoolchildren with Goiter

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Abstract The objective of the study was analysis of hair trace elements content in children with goiter living in Aktubinsk region. Children with goiter and age- and sex-adjusted controls were involved in the current study. Hair trace elements content was assessed using inductively coupled plasma mass spectrometry. Thyroid volume was measured using an ultrasound scanner and compared to the previously calculated normal values. The obtained data indicate that children with goiter were characterized by 20 and 15 % lower values of hair Cr and Zn, and 66, 42, 16, and 42 % higher hair levels of I, Mn, Si, and V as compared to the control values, respectively. Moreover, children with goiter were characterized by a twofold higher hair B levels than the control ones. Correlation analysis demonstrated a significant direct association only between thyroid volume and hair B ($r = 0.482$; $p = 0.004$), I ($r = 0.393$; $p = 0.021$), Mn ($r = 0.364$; $p = 0.034$), and Si ($r = 0.446$; $p = 0.008$) levels. It is also notable that hair I content was interrelated only with Si ($r = 0.346$; $p = 0.045$). No significant correlation was detected between I and B ($r = 0.250$; $p = 0.155$) and Mn ($r = 0.076$; $p = 0.669$) in hair of children. It is hypothesized that an increase in thyroid volume in children is associated with a complex interplay of iodine with other trace elements rather than with altered iodine status itself.

Keywords Iodine · Boron · Silicon · Thyroid · Goiter · Schoolchildren

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Introduction

Thyroid hormones are involved in regulation of multiple metabolic processes including growth, energy metabolism, nervous system development and functioning, etc. [1]. Therefore, alteration of thyroid functions is associated with neuropsychiatric disorders in adults [2] and altered brain development in children [3], infertility [4], cardiovascular diseases [5], and other diseases. It is also notable that thyroid disorders are especially harmful in children leading to irreversible dysfunction [6].

Thyroid diseases are rather common in population. In particular, in India, nearly 42 million of people suffer from thyroid diseases [7], whereas in the UK, thyroid diseases are observed in 0.2 % of men and 2 % of women [8]. In iodine-deficient areas, the most incident pathology is goiter, while in iodine-repleted regions, autoimmune thyroid diseases are the most common [9]. Therefore, iodine intake is the main determinant of thyroid disorders [10]. At the same time, other environmental factors are also involved in thyroid health [11]. In particular, Se deficiency may also result in altered thyroid function [12]. Oppositely, a number of toxic trace elements like mercury [13], lead, and cadmium [14] and other metals [15] affect thyroid metabolism. However, data on trace element status in patients with goiter are single [16–21].

Therefore, the primary objective of the current study was analysis of hair trace elements content in children with goiter living in Aktubinsk region.

Materials and Methods

The protocol of the current survey was approved by the Local Ethics Committee (protocol No. 4, 08.10.2013). The analysis was performed in accordance with the principles of the Declaration of Helsinki and later amendments. Informed consent was obtained from children and their parents.

The following exclusion criteria were used in the current study: (i) acute infectious, surgical and traumatic diseases; (ii) endocrine disorders (instead of thyroid pathology); (iii) metallic implants (including dental amalgam fillings); (iv) vegetarian diet; and (v) consumption of vitamin-mineral supplements.

The current study involved 14 schoolchildren with goiter and 20 sex- and age-matched controls in order to diminish the influence of age and sex on hair trace elements content [22]. Moreover, only children with similar body mass index (BMI) values participated in the current investigation. Earlier studies demonstrated that obesity and overweight may significantly affect trace element status [23–25]. Body surface area was also calculated according to the existing formula [26]. The obtained data were used for calculation of normal thyroid volume for the schoolchildren. Thyroid volume was assessed using Aloka SSD-500 v ultrasound scanner with a 7.5-MHz transducer (Aloka Ltd., Tokyo, Japan).

All children washed their hair at the day of sampling using their shampoos. It has been demonstrated that the use of different commercially available shampoos does not significantly alter hair trace elements content [27]. Hair samples (0.1 g) were collected from the occipital region using precleaned stainless steel scissors.

Proximal hair strands were washed with acetone and rinsed thrice with deionized water with subsequent drying on air at 60 °C. The samples were digested with concentrated HNO_3 at 180 °C for 20 min in Berghof Speedwave 4 system (Berghof Products & Instruments, Germany).

Trace elements content in the obtained samples was assessed using inductively coupled plasma mass spectrometry at NexION 300D (PerkinElmer Inc., USA) equipped with an ESI SC-2 DX4 autosampler (Elemental Scientific Inc., USA). The system was calibrated using the Universal Data Acquisition Standards Kit (PerkinElmer Inc., USA). Internal online standardization was performed using Yttrium-89 isotope solution prepared from Yttrium (Y) Pure Single-Element Standard (PerkinElmer Inc., USA). Laboratory quality control was performed using the certified reference materials of human hair GBW09101 (Shanghai Institute of Nuclear Research, PR China). Recovery rates for all studied elements exceeded 80 %.

The obtained data were processed using Statistica 10 software (StatSoft Inc., USA). Data distribution was assessed using the Shapiro-Wilk test. The latter has demonstrated that data on hair trace elements content in hair were not distributed normally. Therefore, median and the respective 25 and 75 percentile boundaries were used for descriptive statistics (Median (25–75)). The Mann-Whitney U test was used for group comparisons. Correlation analysis was performed using Spearman's coefficient of rank correlation. The level of significance was set as $p < 0.05$ for all analyses. Variables correlating with the thyroid volume with $p < 0.05$ were included in a multiple linear regression model.

Results

The obtained data indicate that there were no significant differences in anthropometric values in children with goiter and the control ones (Table 1). The values of normal thyroid volume calculated using data on body surface area were also similar between the studied groups. At the same time, children with goiter were characterized by more than twofold values of thyroid volume as compared to the healthy children.

It has been demonstrated that hair essential trace elements content is significantly different between the groups (Table 2). In particular, children with goiter were characterized by 20 and 15 % lower values of hair Cr and Zn content than the control ones, respectively. At the same time, hair content of I, Mn, Si, and V in these children exceeded the control levels by 66, 42, 16, and 42 %, respectively. No significant group difference in hair Co, Cu, Fe, Li, and Se was detected.

Surprisingly, hair toxic element content was characterized by a lower variability (Table 3). Significant difference between the studied groups was detected only in the case of hair B content, being more than twofold higher in children with

Table 1 Anthropometric parameters and thyroid volume in children from Aktubinsk region (Kazakhstan)

Group	Control	Goiter	*P* value
Boys, %/girls, %	55/45	57/43	–
Age, years	8.5 ± 0.6	8.5 ± 0.7	0.766
Height, cm	129.3 ± 5.5	128.9 ± 7.9	0.847
Weight, kg	26.0 ± 3.2	26.7 ± 5.9	0.624
Body mass index	15.5 ± 1.4	15.9 ± 2.1	0.363
Body surface area, m^2	1.0 ± 0.1	1.0 ± ±0.1	0.726
Normal thyroid volume, ml[a]	3.7 ± 0.4	3.7 ± 0.6	0.411
Thyroid volume, ml	2.5 ± 0.6	6.7 ± 2.3	<0.001*

Data presented as mean ± SD

*Significant difference in comparison to the control group values ($p < 0.05$)

[a] Normal thyroid volume as predicted using body surface area in children

Table 2 Hair essential and potentially essential trace elements content (μg/g) in children

Group	Control	Goiter	*P* value
Co	0.018 (0.013–0.021)	0.016 (0.012–0.022)	0.637
Cr	0.595 (0.401–0.841)	0.476 (0.243–0.585)	0.034*
Cu	8.478 (7.898–9.094)	8.685 (7.723–9.813)	0.930
Fe	32.086 (26.505–40.329)	33.074 (22.139–46.134)	0.930
I	1.191 (0.884–1.673)	1.980 (1.044–2.764)	0.041*
Li	0.033 (0.023–0.048)	0.036 (0.022–0.068)	0.903
Mn	0.835 (0.601–1.101)	1.184 (0.999–1.287)	0.044*
Se	0.315 (0.286–0.329)	0.317 (0.287–0.329)	0.958
Si	24.222 (19.202–30.033)	28.098 (26.359–44.108)	0.048*
V	0.059 (0.045–0.085)	0.084 (0.064–0.105)	0.041*
Zn	127.579 (94.768–146.208)	108.284 (96.498–137.684)	0.431

Data presented as median (25–75)

*Significant difference in comparison to the control values ($p < 0.05$)

goiter than in the control ones. No marked difference in hair Al, As, Be, Cd, Hg, Ni, Pb, and Sn content was observed between the studied groups of children.

Correlation analysis demonstrated a significant direct association between thyroid volume and hair B ($r = 0.482$; $p = 0.004$), I ($r = 0.393$; $p = 0.021$), Mn ($r = 0.364$; $p = 0.034$), and Si ($r = 0.446$; $p = 0.008$) levels. Other trace elements studied were not significantly interrelated with the size of thyroid gland. Correlation analysis was also used for assessment of association between hair I and other trace element levels. It has been noted that hair I content was interrelated only with Si ($r = 0.346$; $p = 0.045$). No significant correlation was detected between I and B ($r = 0.250$; $p = 0.155$) and Mn ($r = 0.076$; $p = 0.669$) in hair of children.

The results of multiple linear regression (Table 4) demonstrated that the model incorporating hair B, I, Mn, Si, and V accounted for 37 % of the observed variance in thyroid volume. At the same time, only hair B and Si were significantly related to thyroid volume, whereas no association of the studied parameter with hair I, Mn, and V was found.

Table 3 Toxic and potentially toxic trace elements (μg/g) in scalp hair of children with goiter and control ones

Group	Control	Goiter	*P* value
Al	18.243 (13.081–24.948)	15.474 (9.877–21.315)	0.286
As	0.057 (0.050–0.083)	0.075 (0.060–0.094)	0.226
B	1.517 (1.169–2.592)	3.460 (2.047–8.739)	0.009*
Be	0.002 (0.002–0.002)	0.002 (0.002–0.002)	0.993
Cd	0.043 (0.028–0.069)	0.060 (0.037–0.087)	0.202
Hg	0.069 (0.047–0.133)	0.101 (0.050–0.148)	0.662
Ni	0.173 (0.137–0.285)	0.165 (0.130–0.198)	0.319
Pb	1.027 (0.698–1.622)	1.337 (0.987–2.160)	0.241
Sn	0.139 (0.109–0.263)	0.112 (0.096–0.145)	0.156

Data presented as median (25–75)

*Significant difference in comparison to the control values ($p < 0.05$)

Table 4 Multiple linear regression analysis for the association of hair trace elements content and thyroid volume as a dependent variable

Element	β	Partial correlation	*P* value
B	0.367	0.422	0.007
I	0.005	0.006	0.971
Mn	0.128	0.157	0.334
Si	0.416	0.467	0.002

Standardized coefficients (β), partial correlations and the respective p values are presented for each variable. Multiple $R = 0.658$; $R^2 = 0.434$; adjusted $R^2 = 0.374$; $p < 0.001$

Discussion

The obtained data indicate that the volume of thyroid gland as well as hair trace elements content is significantly altered in children with goiter. The major cause of this pathology is low iodine intake especially in persons living in regions with endemic iodine deficiency [28]. Kazakhstan is the region with endemic iodine deficiency and low iodine intake [29]. However, according to the governmental program, all citizens were supplied with iodized salt that is able to prevent the development of iodine deficiency [30]. Moreover, increased hair I content in persons with goiter indicates that these children are characterized by I excess as hair is the valuable indicator of long-term iodine status [31, 32]. At the same time, our data were at least partially in agreement with the earlier studies indicating increased thyroid volume in persons with high iodine status [33]. The mechanism of such association may include iodine-induced increase in costimulatory molecules expression [34].

The sources of increased hair trace elements are not estimated. It is supposed that it may be related to oil and gas industry in the region. It is known that oil and gas industry significantly contribute to environmental trace elements levels [35]. Aktubinsk region (Kazakhstan) is characterized by large hydrocarbon sources [36] and developed gas and oil industry [37]. Therefore, people living in industrial areas are exposed to metals and other trace elements. In particular, B is a serious environmental concern that may be associated with oil industry [38]. Despite a rather low concentration in surface waters, I concentration in oil field brines and especially pore waters associated with gas hydrates is high [39]. Correspondingly, persons living in Medan (Indonesia), a large industrial center that includes oil field, are characterized by significantly higher hair B and Mn content as compared to the ones living in Harbin (China) and Tokushima (Japan) being in agreement with our observation [40]. However, in contrast to these observations we failed to detect a significant increase in hair Al, As, Cd, Cu, Cr, Fe, Ni, and Pb levels.

Children with goiter were characterized by lower hair Zn and Cr concentration. Hypothetically, these deficiencies may occur due to metabolic antagonism of trace elements. In particular, it has been demonstrated that chronic manganese exposure decreases zinc levels in rats' tissues [41]. Such effect may be at least partially associated with the role of zinc transporters in manganese uptake in mammals [42]. Experimental studies have also demonstrated that V treatment decreases tissue Zn content in Wistar rats [43]. Earlier data also indicate the possibility of inhibition of Cr absorption by V compounds [44]. Moreover, it has been shown that altered thyroid state disrupts Cr(III) retention in rats [45].

Generally, the obtained data on decreased hair Cr and Zn content in the goitrous children are in agreement with the earlier study in Morocco [21]. At the same time, in the present study, we failed to detect a significant decrease in hair Se and I levels. Moreover, the differences in hair trace elements content between the children in Morocco and Kazakhstan are of particular interest. In particular, children from Kazakhstan were characterized by significantly higher hair Zn levels and lower Se values than those earlier reported for Morocco. It is supposed that lower hair Zn content in Moroccan children may be associated with the higher risk of Zn deficiency in Morocco as compared to Kazakhstan [46]. In turn, higher hair Se in Moroccan children also seem to have dietary origin. In particular, Morocco is a coastal state where seafoods, being a significant dietary source of Se [47], are more available in comparison to continental Kazakhstan.

Our results indicate a significant association between thyroid volume and hair B, I, Mn, and Si in children. Moreover, this association was more expressed than that for iodine. Earlier studies proposed that Si metabolism is regulated by steroid and thyroid hormones and decreased thyroid activity may decrease Si absorption [48]. It has been also demonstrated that Si supplementation in thyroidectomized rats fed a high-aluminum low-silicon diet prevented a decrease of brain zinc levels [49]. Our earlier data also indicate that hair silicon tended to increase in children with goiter [50]. Moreover, our further studies demonstrated that excessive hair Si content was characterized by a significant association with thyroid volume in a regression model [51]. Single indications of the interaction between B and thyroid metabolism also exist. In particular, B supplementation in gilts significantly altered serum triiodothyronine concentrations in a negative manner [52]. B supplementation also altered serum thyroxin and triiodothyronine concentrations in peri-menopausal women, but the effect depended on the treatment regimen [53]. Our data on increased hair Mn content in children with goiter are in agreement with the previous works indicating the role of this metal in thyroid pathology [54]. Therefore, it is supposed that B and Si metabolism may be associated with thyroid pathology. However, the causal relationships are still to be estimated.

Despite the absence of significant association between hair zinc and chromium content and thyroid volume, deficiency of these trace elements may have a significant impact on thyroid metabolism. Particularly, it has been demonstrated that Zn supplementation in Zn-deficient subjects improves the level of thyroid hormones [55]. In addition, Zn treatment also possess protective effect against Li-induced alteration of thyroid functions and I kinetics [56]. Earlier data also demonstrate that Cr may interfere with thyroid metabolism [57].

Therefore, it is hypothesized that an increase in thyroid volume in children with goiter is associated with a complex interplay of iodine with other trace elements rather with altered iodine status itself.

The present study has several limitations. Higher number of examinees from various geographical locations is required to prove the influence of Si and B on thyroid volume and the incidence of goiter in general. Moreover, other markers of iodine and thyroid status like urinary I and serum thyroid hormones should be assessed to propose the possible mechanism of influence of B and Si.

Generally, the obtained data indicate that:

i) Children with goiter are characterized by increased hair I, Mn, Si, V, and B content as well as decreased Cr and Zn levels as compared to the control values
ii) Thyroid volume is significantly associated with hair B and Si concentrations and, to a lesser extent, with I and Mn levels in scalp hair
iii) Hair iodine content in children is directly associated with Cd, Fe, Mn, Pb, Si, and V content and inversely correlates with scalp hair Zn concentration.

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Compliance with Ethical Standards The protocol of the current survey was approved by the Local Ethics Committee (protocol No. 4, 08.10.2013). The analysis was performed in accordance with the principles of the Declaration of Helsinki and later amendments. Informed consent was obtained from children and their parents.

Conflict of Interest The authors declare that they have no conflict of interest.

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