



Reference values for thyroid volume established by ultrasound in Polish schoolchildren

Polskie ultrasonograficzne normy objętości tarczycy dla dzieci szkolnych

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Abstract

Introduction: A frequency in excess of 5% of goitre in children is an approved WHO marker of iodine deficiency. As thyroid ultrasound remains the main method of thyroid volume (TV) assessment, the choice of adequate normative values is important for the proper interpretation of epidemiologic data. There is disagreement as to whether local or international normative values should be used. The aim of this study was to establish Polish local TV normative values in children aged 6–12 years.

Material and methods: The study was carried out in a group of 642 children aged 6–12 years (312 girls and 330 boys) living in the Polish seaside area with a proven history of best iodine supply. Inclusion criteria were: iodine concentration in casual morning urine samples above 100 µg/L, no goitre on palpation, no pathological findings on thyroid US, no history of thyroid disorders, no treatment affecting thyroid function, and written informed consent from the child's parents. TV was measured ultrasonographically with a 7.5 MHz linear transducer. Urinary iodine concentration (UIC) was measured in urine spot samples using the Sandell-Kolthoff method.

Results: Median UIC ranged according to age from 126.6 to 155.1 µg/L in girls, and from 132.23 to 157.62 µg/L in boys. TVs at P97 were: 3.96, 4.23, 4.33, 5.44, 6.07, 9.5, and 10.9 for girls and 3.99, 4.2, 4.79, 6.61, 7.38, 7.89, and 9.35 for boys. They were lower than the 1997 WHO normative values but higher than the 2004 reference currently adopted by the WHO.

Conclusions: The obtained results may be adopted as normative TV values for Polish children. (*Pol J Endocrinol* 2012; 63 (2): 104–109)

Key words: iodine prophylaxis, iodine deficiency, thyroid volume, normative values

Streszczenie

Wstęp: Częstość wola u dzieci szkolnych powyżej 5% jest zaakceptowanym przez WHO wskaźnikiem niedoboru jodu. Ponieważ ultrasonograficzne badanie stanowi podstawę oceny objętości tarczycy, wybór odpowiednich norm, międzynarodowych lub lokalnych, jest podstawą właściwej interpretacji danych epidemiologicznych. Celem badania było ustalenie prawidłowej wielkości tarczycy u 6–12-latków mieszkających w Polsce.

Materiał i metody: Badanie przeprowadzono w grupie 642 dzieci szkolnych w wieku 6–12 lat (312 dziewcząt i 330 chłopców) zamieszkujących tereny nadmorskie o najlepszym zaopatrzeniu w jod. Kryteria włączenia obejmowały: stężenie jodu w moczu > 100 µg/l, brak wola w badaniu palpacyjnym, prawidłowy wynik USG tarczycy, ujemny wywiad w kierunku chorób tarczycy, niestosowanie leczenia wpływającego na czynność tarczycy, pisemną zgodę rodziców dziecka na badania. Objętość tarczycy oceniano ultrasonograficznie, wykorzystując głowicę liniową 7,5 MHz. Stężenie jodu w moczu (UIC) mierzono metodą Sandell-Kolthoffa.

Wyniki: Mediana UIC wahała się w zależności od wieku od 126,6 do 155,1 µg/l u dziewczynek oraz od 132,23 do 157,62 µg/l u chłopców. Dziewięćdziesiąty siódmy percentyl objętości tarczycy wyniósł: 3,96, 4,23, 4,33, 5,44, 6,07, 9,5, 10,9 oraz 3,99, 4,2, 4,79, 6,61, 7,38, 7,89, 9,35 dla 6–12 letnich dziewcząt i chłopców, odpowiednio. Uzyskane wartości były niższe niż normy WHO z 1997 roku i wyższe niż zaproponowane w 2004 roku i obecnie zaakceptowane przez WHO.

Wnioski: Uzyskane wyniki mogą zostać wykorzystane jako normy objętości tarczycy dla polskich dzieci szkolnych. (*Endokrynol Pol* 2012; 63 (2): 104–109)

Słowa kluczowe: profilaktyka jodowa, niedobór jodu, objętość tarczycy, normy

Introduction

Iodine deficiency remains a serious public health problem in Europe [1]. Although considered the most effective prophylactic measure, mandatory salt iodisa-

tion has been applied only in a minority of European countries [1–2]. Following an epidemiologic survey undertaken in 1992/3, moderate iodine deficiency was recognised across the whole of Poland except for the coastal area, where mild iodine deficiency was noted



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[3]. In further studies carried out in 1994, some of the seaside towns were noted as being iodine sufficient [4]. According to the recommendation of the Polish Council for Control of Iodine Deficiency Disorders (PCCIDD), Poland introduced mandatory iodisation of household salt with 20–40 mg KI/kg in 1997 [5]. Other recommendations were to iodise formulas for bottle-fed infants [6] and to additionally supplement pregnant and lactating women with 150–200 μg of iodine [7]. Since then, the effectiveness of iodine prophylaxis in our country has been controlled by the PCCIDD within the National Programme for Elimination of Iodine Deficiency supported by the Polish Ministry of Health [8]. This model has proved to be effective: the prevalence of goitre has fallen in the group of youngest schoolchildren, aged 6–8 years, from 24.5% to 4.7% (i.e. below the endemic level) [9–10], in pregnant women from 80% to 19% [11], and the frequency of neonatal thyrotropinaemia above 5.0 mIU/L has decreased from 12.68% to 4.1% [12].

A frequency of goitre in children of below 5% has been recognised by the WHO as a marker of iodine sufficiency. As thyroid palpation is considered to have relatively low sensitivity, particularly in detecting slightly enlarged glands, ultrasound (US) has become the preferred method for the evaluation of thyroid size, also for epidemiological purposes [2]. However, normative values of thyroid volume have been disputed. The first international references proposed by Gutekunst et al. [13] were questioned because their use resulted in estimated high goitre prevalence even in iodine-replete countries. They were replaced by the normative values established for four European countries in 1997 [14–15], which were soon criticised as too liberal, as the result of supposed marginal iodine deficiency and measurement bias [16]. The WHO finally adopted a new reference for thyroid volume assessment, developed based on the research conducted in countries with confirmed long-standing iodine sufficiency [2, 16]. However, the feasibility of an international reference is still being disputed, as some authors have suggested that the use of a local reference is more appropriate [17–19].

The aim of this paper was to establish new local normative values for thyroid volume assessed by US for the population of Polish 6–12 year-old children.

Material and methods

Subjects

The study included 6–12 year-old children living in the iodine-sufficient Polish coastal area. The study — called ‘Thyromobil action’ was performed in six primary schools in seaside towns in 2006, i.e. 10 years after the introduction of mandatory iodine prophylaxis in

Poland. A group of 642 children was selected for the final evaluation, based on the following criteria: iodine concentration in casual morning urine samples above 100 $\mu\text{g/L}$, no goitre on palpation, no pathological findings on thyroid US, no history of thyroid disorders or surgery, no current or previous treatment with medications affecting thyroid function, and written informed consent from the child’s parents. The ethnicity of the investigated population was homogenous, with nearly all children being of Caucasian origin.

Methods

In each child, basic anthropological measurements as well as thyroid palpation, were performed. The children were measured and weighed in light clothing according to standard protocols. The body surface area (BSA) was calculated according to the equation:

$$\text{BSA [m}^2\text{]} = \text{weight [kg]}^{0.425} \times \text{height [cm]}^{0.725} \times 71.84 \times 10^{-4}.$$

A Siemens Sonoline Prima ultrasonograph equipped with a 6-cm 7.5 MHz linear transducer installed within the ‘Thyromobil’ van (provided by Merck KGaA, Darmstadt, Germany) was used for thyroid volume assessment. The measurements were performed in supine subjects with their neck extended. The width and depth of each lobe were assessed on the transverse images, and the length on the longitudinal images. Neither isthmus nor thyroid capsule were included in the measurement. The thyroid volume (TV) was calculated according to Brunn et al. as the sum of both lobes’ volumes (mL), counted as lobe width (cm) \times depth (cm) \times length (cm) \times 0.479 [2].

Urinary iodine concentration (UIC) in casual morning urine samples supplied by the investigated children was measured using the colorimetric Sandell-Kolthoff method. The samples were stored at -20°C prior to analysis.

Statistics

Statistical analysis was performed using Statistica 7.0 software. The assessed parameters were expressed as mean, standard deviation, median, range, 50th and 97th percentile (P50 and P97).

Results

The characteristics of the investigated group of children are set out in Table I.

The median UIC varied depending on age from 126.6 to 155.1 $\mu\text{g/L}$ for girls, and from 132.23 to 157.62 $\mu\text{g/L}$ for boys (Table II).

The age- and sex-specific P97 values were considered the upper normal range of TV (Table III). They varied from 3.96 mL to 10.9 mL for girls and from 3.99 mL to

Table I. Study group characteristics

Tabela I. Charakterystyka badanej grupy

Age (years)	Girls (n = 312)				Boys (n = 330)			
	n	BW [kg]	H [cm]	BSA [m ²]	n	BW [kg]	H [cm]	BSA [m ²]
		$\bar{X} \pm SD$	$\bar{X} \pm SD$	$\bar{X} \pm SD$		$\bar{X} \pm SD$	$\bar{X} \pm SD$	$\bar{X} \pm SD$
6	40	25.28 ± 5.23	122.25 ± 5.40	0.92 ± 0.11	59	24.97 ± 5.13	121.44 ± 6.13	0.91 ± 0.11
7	97	25.90 ± 4.15	126.39 ± 4.90	0.95 ± 0.08	73	27.91 ± 6.31	127.73 ± 4.64	0.99 ± 0.12
8	17	30.16 ± 5.75	130.88 ± 5.63	1.04 ± 0.11	41	30.87 ± 6.19	132.08 ± 6.11	1.07 ± 0.10
9	24	33.04 ± 5.45	138.17 ± 5.31	1.13 ± 0.10	26	34.74 ± 6.86	139.08 ± 6.11	1.16 ± 0.13
10	25	37.41 ± 8.11	144.72 ± 5.71	1.23 ± 0.13	18	37.51 ± 6.71	143.61 ± 6.53	1.23 ± 0.12
11	22	40.97 ± 9.56	149.68 ± 8.78	1.31 ± 0.17	31	43.11 ± 9.52	148.68 ± 6.53	1.33 ± 0.16
12	90	46.24 ± 9.32	155.78 ± 7.38	1.42 ± 0.16	82	48.20 ± 12.33	154.77 ± 9.92	1.44 ± 0.21

BW — body weight; H — height; BSA — body surface area; \bar{X} — mean; SD — standard deviation

Table II. Urinary iodine concentration (UIC $\mu\text{g/L}$) in investigated childrenTabela II. Stężenie jodu w moczu (UIC $\mu\text{g/L}$) u badanych dzieci

Age (years)	Girls (n = 312)				Boys (n = 330)			
	n	UIC			n	UIC		
		\bar{X}	SD	Median (P50)		\bar{X}	SD	Median (P50)
6	40	157.99	56.14	143.51	59	178.33	69.68	157.62
7	97	163.74	60.34	145.77	73	165.79	53.69	156.79
8	17	146.82	36.31	135.79	41	164.37	71.29	132.23
9	24	157.96	54.09	140.17	26	162.39	50.91	147.88
10	25	143.92	49.81	126.60	18	159.45	34.80	156.95
11	22	157.36	56.22	148.52	31	152.78	38.18	147.31
12	90	163.30	51.90	155.10	82	162.26	57.26	140.36

\bar{X} — mean; SD — standard deviation

Table III. Thyroid volume (TV) in children according to age and sex

Tabela III. Objętość tarczycy (TV) u dzieci szkolnych w zależności od wieku i płci

Age (years)	Girls (n = 312)					Boys (n = 330)				
	n	TV [mL]				n	TV [mL]			
		\bar{X}	SD	Me	P97		\bar{X}	SD	Me	P97
6	40	2.53	0.75	2.34	3.96	59	2.46	0.75	2.44	3.99
7	97	3.12	0.73	3.21	4.23	73	3.06	0.77	3.55	4.20
8	17	3.29	0.70	3.31	4.33	41	3.39	0.93	3.47	4.79
9	24	3.59	0.86	3.57	5.44	26	3.78	1.12	3.48	6.61
10	25	4.05	1.13	4.20	6.07	18	4.14	1.20	3.92	7.38
11	22	4.71	1.58	4.47	9.50	31	4.10	1.23	3.89	7.89
12	90	6.91	2.08	6.71	10.90	82	6.07	1.78	6.02	9.35

TV — thyroid volume; \bar{X} — mean; SD — standard deviation; Me — median; P50 — percentile 50; P97 — percentile 97

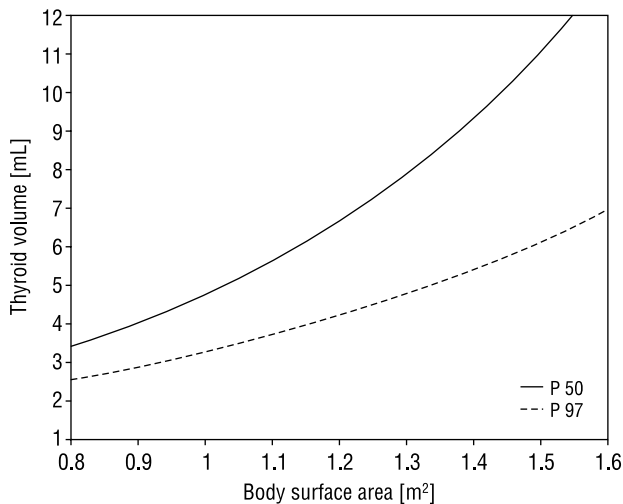


Figure 1. Thyroid volume according to BSA (girls)

Rycina 1. Objętość tarczycy w zależności od BSA (dziewczęta)

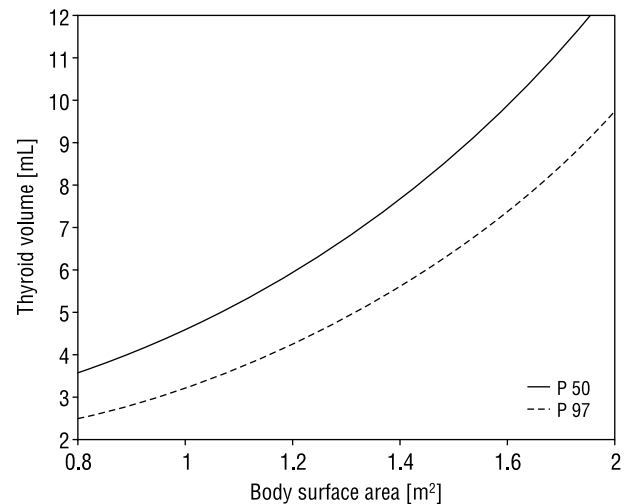


Figure 2. Thyroid volume according to BSA (boys)

Rycina 2. Objętość tarczycy w zależności od BSA (chłopcy)

Table IV. Comparison of the obtained values of thyroid volume (mL) at P97 with normative values obtained by other groups of experts

Tabela IV. Porównanie uzyskanych wartości P-97 objętości tarczycy z normami zaproponowanymi przez inne grupy ekspertów

Age	WHO 1997		Zimmermann 2004, WHO 2007		Local Polish reference	
	Girls	Boys	Girls	Boys	Girls	Boys
6	5.0	5.4	2.84	2.91	3.94	3.96
7	5.9	5.7	3.26	3.29	4.23	4.20
8	6.9	6.1	3.76	3.71	4.33	4.79
9	8.0	6.8	4.12	4.19	5.44	6.61
10	9.2	7.8	4.98	4.73	6.07	7.38
11	10.4	9.0	5.73	5.34	9.49	7.89
12	11.7	10.4	6.59	6.03	10.9	9.35

9.35 mL for boys, depending on age. The P97 and P50 values of TV according to BSA are presented in Figures 1 and 2.

The obtained TV normative values for Polish children were compared to previous and current WHO references (Table IV). The local normative values proposed by our group are lower than those established in 1997, but higher than those recommended today by the WHO.

Discussion

According to the WHO recommendations, [2] thyroid goitre prevalence in 6–15 year-old children is one of the main indicators of population iodine intake and the effectiveness of the applied model of iodine prophylaxis in a given area. Thyroid US has replaced palpation in the assessment of thyroid size. However, the interpretation

of its results depends on the choice of TV normative values. The WHO recommends the use of international criteria first published in 2004 by Zimmermann et al. [16]. The previously used reference, which was based on results obtained during the evaluation of iodine-replete European countries, was considered too liberal and resulted in underestimation of true goitre prevalence among children. This phenomenon was attributed to the residual effect of iodine insufficiency and observer bias [16, 20].

It should be remembered that the 1997 reference replaced criteria criticised as being too strict, which resulted in unexpectedly high goitre frequency even in areas of long-standing good iodine nutrition [17, 21]. Given the fact that the current normative values are lower than the very first ones [16], it may be feasible to use the local criteria, particularly for clinical decision making. Thyroid volume is influenced by iodine intake,

therefore in establishing the TV reference, factors such as iodine prophylaxis models, their effectiveness, and duration, should be considered. The best group for the creation of TV normative values are children born after effective iodine prophylaxis implementation [16, 22]. In our study, children aged 6 to 8 fulfilled this criterion; however, their P97 values of TV were still higher than the international WHO reference in children of the corresponding age. This may be due to the fact that about half of the children evaluated for the WHO reference were from populations with iodine intake exceeding requirements (median UIC in children above 200 µg/L) [16]. It should be remembered that excessive iodine intake can also lead to goitre formation and higher TV in the general population, as for example in Japan [18].

Additional very important factors influencing TV are the ethnicity of the investigated population and the influence of genetic factors [23–24]. Our investigated children were ethnically homogeneous. Our results are lower compared to the 1997 WHO, and higher than those obtained by the group of experts in 2004, in a study based on a multiethnic group of children. The normative values established for Polish schoolchildren by our group are similar to the data obtained in Malaysia, in an ethnically homogenous group of schoolchildren living in a long-standing iodine replete area [19]. Corresponding data has been obtained in Swedish schoolchildren [25, 26]. This supports the idea of establishing local normative values for thyroid gland volume in schoolchildren in ethnically uniform iodine replete areas.

It should also be noted that the recent Technical Consultation of the WHO [27, 28] recommended limiting the daily intake of sodium, because of its being a risk factor for hypertension and arteriosclerosis. Recommendations on reduction of dietary sodium have also been issued in Poland [29, 30]. As household salt is the main iodine carrier in Poland (salt used in the food industry is not iodised), the effectiveness of iodine prophylaxis should be constantly controlled and new nutritional iodine sources should be promoted [31]. In 2008, the World Health Organisation Collaborating Centre for Nutrition (WHOCC) was established in Krakow. One of the main tasks of WHOCC is the sustainability of iodine prophylaxis effectiveness. This issue was dealt with during the first international conference of similar European WHOCCs for Nutrition in 2010 [32].

Also, the local normative values for TV should be re-evaluated in the future (given that now all Polish children aged 6–12 were born after the implementation of mandatory iodine prophylaxis).

The unanswered question remains as to which criteria (local *vs.* international) should be used for epidemiological purposes. The local reference of TV makes it

difficult to compare the data from different countries in a global assessment of iodine nutrition and progress in the elimination of iodine deficiency. However, the use of international TV normative values may result in overestimation of goitre frequency and disparity between iodine nutrition markers such as goitre prevalence and median UIC in a given population. This underlines the need to search for new iodine nutrition markers.

The presented data, obtained from an iodine-sufficient area in children aged 6–12 years without goitre and with UIC over 100 µg/L, allows us to formulate a local reference for thyroid volume that reflects the influence of geophysical location, and the actual situation of iodine prophylaxis and ethnic homogeneity in Poland.

Conclusions

- The obtained values of TV in children aged 6–12 years were lower than the values introduced by the WHO in 1997, but higher than the values proposed by a group of experts in 2004 and currently adopted by WHO.
- The obtained values of TV may be useful as normative values in controlling the effectiveness of iodine prophylaxis, and in everyday clinical practice in Poland.

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