Erciyes Med J 2023; 45(2): 177–81 • DOI: 10.14744/etd.2022.56687
ORIGINAL ARTICLE – OPEN ACCESS

Differences Between Chronological Age and Height Age in Goiter Interpretation

Serkan Bilge Koca[1], Turgut Seber[2], Ahu Paketçi[1], Kürşad Özdemir[3]

ABSTRACT

Objective: Some factors (age, weight, height, body mass index, body surface area, puberty stage, and iodine nutrition status) may affect thyroid volume (TV). We aimed to investigate the differences between chronological age and height age in interpreting goiter.

Materials and Methods: The thyroid ultrasonography records of 420 children aged 1–18 years were evaluated. We searched the difference between the interpretations of goiter by recalculating the TV standard deviation score (SDS) in terms of both chronological ages and corrected for height age. We also evaluated those with negative thyroid autoantibodies and normal thyroid hormone levels by subgroup analysis. The evaluation of TV according to chronological age and height age and the change of goiter interpretation were compared with the McNemar test.

Results: A total of 180 children who had euthyroid and negative thyroid autoantibodies were analyzed. A weak correlation was detected between TV and age (r=0.29, p<0.001), body weight (r=0.35, p<0.001), height (r=0.32, p<0.001), height age (r=0.32, p<0.001), body weight SDS (r=0.20, p=0.008) and height SDS (r=0.21, p=0.005). When the changes of goiter interpretation were compared, a statistically significant difference was determined in the whole group (p=0.029); however, there was no significant difference in children who were both euthyroid and found to have negative thyroid autoantibodies (p=0.375).

Conclusion: We observed that the interpretation of goiter changed according to chronological age and height age if thyroid hormone level and/or thyroid autoantibody positivity were included.

Keywords: Children, Goiter, height age, thyroid ultrasonography, thyroid volume

Cite this article as: Koca SB, Seber T, Paketçi A, Özdemir K. Differences Between Chronological Age and Height Age in Goiter Interpretation. Erciyes Med J 2023; 45(2): 177-81.

[1]Division of Pediatric Endocrinology, Department of Pediatrics, Health Sciences University, Kayseri City Hospital, Kayseri, Türkiye
[2]Division of Pediatric Radiology, Department of Radiology, Health Sciences University, Kayseri City Hospital, Kayseri, Türkiye
[3]Department of Radiology, Health Sciences University, Kayseri City Hospital, Kayseri, Türkiye

Submitted 17.09.2022

Revised 20.10.2022

Accepted 16.12.2022

Available Online 27.02.2023

Correspondence
Serkan Bilge Koca, Health Sciences University, Kayseri City Hospital, Department of Pediatrics, Division of Pediatric Endocrinology, Kayseri, Türkiye
Phone: +90 352 77 00 - 40280
e-mail: kocaserkanbilge@yahoo.com.tr

INTRODUCTION

Thyroid function tests and thyroid ultrasonography are important tools for evaluating thyroid diseases, both in the diagnosis and follow-up of conditions requiring treatment. Thyroid ultrasonography informs the clinician about important parameters such as the anatomical location of the thyroid gland, gland size, echogenicity, and vascularization. In addition, its important advantages are that it does not require radiation, is not invasive, and is easily accessible and cost-effective. Reference cards with age and sex-specific values evaluate thyroid volume (TV). However, it has also been stated by the World Health Organization that the cards created for this evaluation show regional, ethnic, racial, and nutritional differences (1). Many studies have reported that age, body weight, height, body mass index, body surface area, puberty stage, and iodine nutrition status affect TV evaluation with B-mode ultrasonography (2–4). In a study conducted in our country, the most important predictors of TV were stated as body weight, body surface area, and height, respectively (5). Differences in countries or regions of a country, nonhomogeneous age range distribution in the sample group, and differences in pubertal assessments at certain ages were not taken into account while determining TV reference cards (6, 7). So, diagnostic problems may occur when using these reference cards, such as sometimes detecting goiter in individuals without having goiter or performing normal evaluations in individuals with goiter. In our study, we evaluated TV with a reference card designed in our country according to chronological age (8). We aimed to explore the effect of the difference between the evaluations on the diagnosis of goiter by recalculating the TV corrected for height and age with the same reference card. In this way, we investigate the differences in the goiter interpretation by ultrasonography measured TV according to chronological age and height age of children.

MATERIALS and METHODS

Our study was conducted in accordance with the Declaration of Helsinki and approved by the Kayseri City Hospital clinical research ethics committee with its decision dated 18.05.2022 and numbered 631.

Table 1. Anthropometric examinations, baseline characteristics, and thyroid volume data of the study group

	Mean±SD	Median (Q1–Q3)	Minimum	Maximum
Age	12.8±3.8	13.5 (10.3–15.8)	1.1	17.9
Weight	49.7±19.4	49.9 (35–61)	14.1	105
Height	150.3±19.1	156 (139.1–163)	93.6	186
Height age	13±4.5	12.7 (10.1–15.1)	2.8	20
Weight SDS	0.34±1.14	0.33 (-0.40–1.2)	-2.85	3.56
Height SDS	-0.06±1.03	-0.06 (-0.73–0.61)	-2.47	2.51
BMI SDS	0.41±1.17	0.45 (-0.35–1.27)	-3.52	3.85
TV (ml)	10.4±8.2	8.2 (4.8–13.3)	0.55	60.8
TV SDS adjusted for chronological age	2.8±4	1.65 (0.12–4.12)	-2.71	26.4
TV SDS adjusted for height age	3.2±4.6	1.8 (0.24–4.75)	-2.71	35.6

SDS: Standard deviation score; BMI: Body mass index; TV: Thyroid volume. Anthropometric examinations, baseline characteristics, and thyroid volume data of the study group (n=420)

Subjects

A total of 635 pediatric patients who underwent thyroid ultrasonography between January 2020 and 2022 were included in this retrospective cross-sectional study. Ultrasonography with adequate radiological image quality and with both thyroid lobes reported as 3-dimensional (3D) volumes was analyzed. Those whose thyroid gland dimensions had been determined as 3-dimensional volume by ultrasonography were included in this study. In addition, ultrasonography records of children with a concomitant systemic disease were not included. Inclusion criteria were being between 1–18 years of age, having appropriate radiological ultrasonography (homogeneous parenchyma without the presence of nodule), and dwelling in the Kayseri region. Exclusion criteria of the study were determined to have congenital thyroid anomalies (dysgenesis, ectopia; N: 18), nodular thyroid diseases (cyst or nodule larger than 5 mm) affecting thyroid dimensions (N: 52), being treated for congenital hypothyroidism (N: 76), and insufficient data on ultrasonography (N: 69). Of these patients, 420 children who had met the criteria for the study group were analyzed. Our study group consisted of patients who applied to our tertiary healthcare institution's pediatric endocrinology outpatient clinics. Those with non-thyroid systemic diseases (genetic or syndromic short stature, growth hormone deficiency, puberty disorders, etc.) that could affect height and age were excluded from the study. Eighteen children in our sample group were of Syrian and Iraqi origin, and the remaining 402 children were of Turkish origin.

Anthropometric Examinations

Weight, height, body mass index (BMI), and age and sex-specific standard deviation scores (SDSs) of these values were analyzed with an online calculation program (9) (www.childmetrics.org). Centers for Disease Control and Prevention (CDC) reference cards were used for the evaluation of anthropometric data. Since the children of families of Syrian and Iraqi origin (18 children) living in our region were also included in our patient group, it was preferred to use CDC-specific reference cards.

Laboratory Measurements

Blood samples were obtained early morning after a 10-hour fasting period for hormone measurements. Serum TSH, free T4 (fT4), free T3 (fT3), thyroglobulin (Tg), antithyroid peroxidase (anti-TPO), and antithyroglobulin (anti-Tg) levels were measured by electrochemiluminescence immunological method (ECLIA) on the Cobas 8000 e602 analyzer (Roche Diagnostics, Mannheim, and Germany).

Thyroid Ultrasonography

Ultrasonography of the thyroid gland was performed by two radiologists (TS [pediatric radiologist] and K.Ö., with 12 and 31 years of experience, respectively) with an Aplio 500 ultrasound system (Toshiba Medical Systems, Tokyo, Japan) via 14 MHz linear array transducer. Thyroid gland volume was calculated from the dimensions of each thyroid lobe (length x width x depth x 0.52). The TV is the sum of the volumes of both lobes. Thyroid volumes were evaluated according to age and sex-specific references, and SDSs were calculated (8). Thyroid volume standard deviation score (SDS) according to age and gender below -2 standard deviation (SD) was considered hypoplasia, and above +2 SD was considered goiter (8). The inter-observer variability of ultrasonography findings was assessed using Kappa (K) statistics (poor, <0; slight, 0.01–0.20; fair, 0.21–0.40; moderate, 0.41–0.60; good, 0.61–0.80; almost perfect, 0.81–0.99). Inter-observer agreement of ultrasonography findings was good (K 0.72–0.78).

Statistical Analysis

Data were analyzed by SPSS Version 24.0 (Armonk, NY, USA) software program. The mean, SD, median, 1st, and 3rd quartiles, and minimum and maximum values of the numerical variables were specified. Categorical variables were shown as frequency and percentage (%). The normal distribution of the variables was analyzed with the Shapiro-Wilk test. In addition, it was checked whether the kurtosis and skewness values of the variables ranged between -2 and +2. Chi-Square analysis was used to compare categorical variables. McNemar test was also used to compare the change before and after the process while investigating the effect of chronological age and height age on the interpretation of goiter. The Spearman correlation coefficient analyzed the association between TV and variables, and a p-value less than 0.05 was accepted as statistically significant.

Table 2. Evaluation of thyroid volume according to chronological age, height age, and the change of goiter interpretation

	Thyroid volume SDS adjusted for height age			p
	Goiter (no)	**Goiter (yes)**	**Total**	
Thyroid volume SDS adjusted for chronological age				<**0.029***
Goiter (no)	215	19	234	
Goiter (yes)	7	177	184	
Total	222	196	418	

*: McNemar test; SDS: Standard deviation score

Table 3. Anthropometric examinations, baseline characteristics, and thyroid volume data of the euthyroid and negative thyroid autoantibody group

	Mean±SD	Median (Q1–Q3)	Minimum	Maximum
Age	11.5±4.1	12.5 (8.3–14.7)	1.1	17.9
Weight	44.3±19.7	43.9 (29–55.1)	14.1	96.2
Height	145.1±22.2	150 (130–162)	93.6	186
Height age	11.8±4.8	11.9 (8.3–14.3)	2.8	20
Weight SDS	0.20±1.23	0.22 (-0.52–1.05)	-2.85	3.56
Height SDS	-0.08±1.05	-0.04 (-0.90–0.66)	-2.47	2.25
BMI SDS	0.27±1.27	0.30 (-0.59–1.05)	-3.52	3.85
TV (ml)	6.1±4.4	5 (3.2–8.7)	0.83	32.3
TV SDS adjusted for chronological age	0.7±2.1	0.27 (-0.48–1.37)	-2.3	14.8
TV SDS adjusted for height age	0.9±2.3	0.43 (-0.38–1.6)	-2.3	17.8

SDS: Standard deviation score; BMI: Body mass index; TV: Thyroid volume. Anthropometric examinations, baseline characteristics, and thyroid volume data of the euthyroid and negative thyroid autoantibody group (n=180)

Table 4. Evaluation of thyroid volume according to chronological age, height age, and the change of goiter interpretation in the euthyroid and negative thyroid autoantibody group

	Thyroid volume SDS adjusted for height age			p
	Goiter (no)	**Goiter (yes)**	**Total**	
Thyroid volume SDS adjusted for chronological age				<0.375*
Goiter (no)	147	4	151	
Goiter (yes)	1	27	28	
Total	148	31	179	

*: McNemar test; SDS: Standard deviation score

RESULTS

In our study, 420 children, 311 (74%) girls, and 109 (26%) boys, with a mean age of 12.8±3.8 years and between 1.1 and 17.9 years, were evaluated. Anthropometric examinations, baseline characteristics, and TV data of the study group are shown in Table 1.

While no nodule or cyst was observed by the thyroid ultrasonography of 384 (91.4%) individuals, cysts or nodules smaller than 5 mm were detected in 36 (8.6%) cases. While hypothyroidism was found in 35 (8.3%) children, hyperthyroidism was found in 19 (4.5%) children. Thyroid function tests of 366 (87.1%) children were found to be normal (euthyroid). Regarding Hashimoto's thyroiditis, at least one of the thyroid autoantibodies (thyroid peroxidase or antithyroglobulin) was positive in 213 (50.7%) cases. Thyroid autoantibodies were negative in 207 (49.3%) cases.

The evaluation of TV according to chronological age, height age, and the change of goiter interpretation are shown in Table 2.

The effect of chronological age and height age in the interpretation of goiter was evaluated, and a statistically significant difference was found (p=0.029).

A total of 180 children with negative thyroid autoantibodies with euthyroid and no cysts or nodules by thyroid ultrasonography were analyzed. This group consisted of 110 (61.1%) girls and

70 (38.9%) boys, with a mean age of 11.5±4.1 years, between the ages of 1.1 and 17.9. While a weak correlation was detected between TV and age (r=0.29, p<0.001), body weight (r=0.35, p<0.001), height (r=0.32, p<0.001), height age (r=0.32, p<0.001), body weight SDS (r=0.20, p=0.008) and height SDS (r=0.21, p=0.005), no significant correlation was detected between BMI SDS (r=0.13, p=0.09).

Anthropometric examinations, baseline characteristics, and TV data of the euthyroid and negative thyroid autoantibody group are shown in Table 3.

The evaluation of TV in the euthyroid and negative thyroid autoantibody group according to chronological age and height age and the change of goiter interpretation are shown in Table 4.

The effect of chronological age and height age in the interpretation of goiter was evaluated, and no statistically significant difference was found in this group (p=0.375).

DISCUSSION

In our study, the differences in the goiter interpretation by ultrasonography measured TV according to chronological age and height age of children were investigated. In a recent study in our country, in which TV for chronological age was used as a reference in the interpretation of goiter in Turkish children, 205 children under 18 were analyzed (8). In our study, analysis was made with 420 children, and the same reference was first used when evaluating according to chronological age and then to height age. In addition, we evaluated the parameters that correlated with TV in a group (180 children) with normal thyroid function test results, negative thyroid autoantibodies, and homogeneous thyroid gland tissue by thyroid ultrasonography. In terms of the relationship with TV, the most significant factor after body weight was found to be height and age. We observed that the goiter interpretation changed according to chronological age and height age if thyroid hormone level and/or thyroid autoantibody positivity were included. We believe this evaluation will benefit individuals with thyroid diseases, hypothyroidism, or hyperthyroidism, especially when making a treatment decision.

We observed significant differences in interpretation and the diagnosis of goiter in the evaluation of TV according to height, age, and chronological age in all age groups at certain rates. In this study, although thyroid function tests, thyroid autoantibodies, and thyroid ultrasonography were evaluated in the research group, no additional test for iodine deficiency was performed. Our study is considered significant because it was performed in a population with similar characteristics in a region previously shown to be at risk for iodine deficiency in the iodine map of Türkiye (10). We want to emphasize that while age is the parameter that shows the highest correlation with TV in some studies, sometimes it could be one of the other parameters (weight, BMI, height, body surface area, or SDSs of them) (5, 11). Recent studies have used methods such as the correlation between TV and body surface area and TV index corrected for body surface area (6, 12). The main reason for preferring these methods is that it would not be appropriate to diagnose goiter only with chronological age and gender. While thyroid function test results and thyroid ultrasonography were evaluated in terms of treatment decisions, anthropometric changes such as short stature and obesity could be observed in some children, especially children with hypothyroidism. This is noteworthy in a study of children with Turner Syndrome (13). While retardation in bone age is expected in hypothyroidism, progression in bone age is expected in hyperthyroidism, obesity, and precocious puberty. Changes in bone age can affect height growth. While thyroid function tests and thyroid antibodies are used to evaluate goiter, height and age are also parameters that should be used for TV, which can change with physical change (14). Therefore, it would not be appropriate to diagnose goiter only with references specific to chronological age and gender. In one study, TV was associated with lean body mass, but no significant correlation was found with body fat (15). Therefore, it may not be appropriate to evaluate TV by body surface area and BMI while ignoring body fat mass. One of the important features of our study group was carried out on individuals with short and tall stature, malnutrition, and obesity. If we only consider age and gender, we ignore the effect of hormonal changes on an individual's anthropometry. Hypothyroidism or hyperthyroidism may be observed in the patient's admission to the doctor. Therefore, height and weight changes can be observed. This situation can also be long-term. In one study, it was stated that TV was positively correlated with the change in body weight in overweight children. It was emphasized that this relationship was independent of insulin resistance and thyroid function tests and was also reversible with weight loss (16). Height age rather than body surface area is thought to be a more accurate assessment tool in this respect. Recently, reference cards have begun to be created in pediatric endocrinology, which considers height in addition to age and gender in some diseases. For example, it is recommended to use specific references for age, gender, and height in definitions of pediatric metabolic syndrome and hypertension (17, 18). Our study determined that the interpretation of goiter differed significantly according to the evaluation method in individuals.

Limitations

The limitations of our study were that the study group showed a wide range of distribution in terms of weight, height, and BMI and that no additional evaluation was made for iodine deficiency. Although a small group, the 18 children were of different ethnicity.

Our study was conducted in a city, and a single center, where practices to prevent iodine deficiency was carried out. On the other hand, having a wide range of anthropometry can also be considered an advantage.

CONCLUSION

Based on all these points, we wanted to draw attention to the necessity of creating new reference cards that consider height, age, and gender to evaluate pediatric goiter. Chronological age and height age may not always have a correlation, which may lead to different results in the interpretation of goiter by ultrasonography. We think that the clinician should consider these differences in the treatment decision.

Ethics Committee Approval: The Kayseri City Hospital Clinical Research Ethics Committee granted approval for this study (date: 18.05.2022, number: 631).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – SBK; Design – SBK, AP; Supervision – SBK, TS; Resource – AP, KÖ, TS; Materials – SBK, AP; Data Collection and/or Processing – SBK, TS, KÖ; Analysis and/or Interpretation – SBK, TS; Literature Search – SBK; Writing – SBK; Critical Reviews – SBK.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. González M, González CP, Sanabria A. Ultrasonographic estimation of the normal volume of the thyroid gland in pediatric populations. [Article in Spanish]. Biomedica 2006; 26(1): 95–100. [CrossRef]
2. Kaloumenou I, Alevizaki M, Ladopoulos C, Antoniou A, Duntas LH, Mastorakos G, et al. Thyroid volume and echostructure in schoolchildren living in an iodine-replete area: relation to age, pubertal stage, and body mass index. Thyroid 2007; 17(9): 875–81. [CrossRef]
3. Zou Y, Ding G, Lou X, Zhu W, Mao G, Zhou J, et al. Factors influencing thyroid volume in Chinese children. Eur J Clin Nutr 2013; 67(11): 1138–41. [CrossRef]
4. Xiu L, Zhong G, Ma X. Urinary iodine concentration (UIC) could be a promising biomarker for predicting goiter among school-age children: A systematic review and meta-analysis. PLoS One 2017; 12(3): e0174095. [CrossRef]
5. Çolak E, Özkan B, Genç S, Polat B. Ultrasonographic determination of thyroid volume in infants and children from Aegean region of Turkey and comparison with national and international references. J Pediatr Endocrinol Metab 2021; 34(4): 457–64. [CrossRef]
6. Wang Y, Dong X, Fu C, Su M, Jiang F, Xu D, et al. Associations between thyroid volume and physical growth in pubertal girls: Thyroid volume indexes need to be applied to thyroid volume assessments. Front Endocrinol (Lausanne) 2021; 12: 662543. [CrossRef]
7. Kalantari S, Moghadam MV. Thyroid gland volume of schoolchildren in the North of Iran: Comparison with other studies. J Res Med Sci 2015; 20(11): 1070–6. [CrossRef]
8. Aydıner Ö, Karakoç Aydıner E, Akpınar İ, Turan S, Bereket A. Normative data of thyroid volume-ultrasonographic evaluation of 422 subjects aged 0-55 years. J Clin Res Pediatr Endocrinol 2015; 7(2): 98–101.
9. Demir K, Özen S, Konakçı E, Aydın M, Darendeliler F. A Comprehensive online calculator for pediatric endocrinologists: ÇEDD Çözüm/TPEDS Metrics. J Clin Res Pediatr Endocrinol 2017; 9(2): 182–4.
10. Erdoğan MF, Ağbaht K, Altunsu T, Ozbaş S, Yücesan F, Tezel B, et al. Current iodine status in Turkey. J Endocrinol Invest 2009; 32(7): 617–22.
11. Semiz S, Senol U, Bircan, Gümüşlü S, Bilmen S, Bircan I. Correlation between age, body size and thyroid volume in an endemic area. J Endocrinol Invest 2001; 24(8): 559–63. [CrossRef]
12. Liu Q, Jiang Y, Shen L, Zhu J. Factors affecting thyroid volume in adolescent students attending a rural middle school in East Hangzhou, China. J Pediatr Endocrinol Metab 2020; 34(2): 231–6. [CrossRef]
13. Calcaterra V, Klersy C, Muratori T, Caramagna C, Brizzi V, Albertini R, et al. Thyroid ultrasound in patients with Turner syndrome: influence of clinical and auxological parameters. J Endocrinol Invest 2011; 34(4): 260–4. [CrossRef]
14. Cavallo F, Mohn A, Chiarelli F, Giannini C. Evaluation of bone age in children: A mini-review. Front Pediatr 2021; 9: 580314. [CrossRef]
15. Boyanov MA, Temelkova NL, Popivanov PP. Determinants of thyroid volume in schoolchildren: fat-free mass versus body fat mass--a cross-sectional study. Endocr Pract 2004; 10(5): 409–16. [CrossRef]
16. Lass N, Barth A, Reinehr T. Thyroid volume and thyroid function parameters are independently associated with weight status in overweight children. Horm Res Paediatr 2020; 93(5): 279–86. [CrossRef]
17. Ma C, Lu Q, Wang R, Yin F. Using height-corrected definition of metabolic syndrome in children and adolescents. J Pediatr Endocrinol Metab 2019; 32(5): 429–38. [CrossRef]
18. Spagnolo A, Giussani M, Ambruzzi AM, Bianchetti M, Maringhini S, Matteucci MC, et al. Focus on prevention, diagnosis and treatment of hypertension in children and adolescents. Ital J Pediatr 2013; 39: 20.