

# Dynamics of the Frequency of Thyroid Nodules in Adolescents Kashkadarya Region by Districts

Kholikova Adliya Omanullaevna<sup>1</sup>, Saidova Gulchekhra Sobirjonovna<sup>2</sup>

<sup>1</sup>Doctor of Medical Sciences, Head of the Department of Neuroendocrinology Republican Specialized Scientific and Practical Medical Center of Endocrinology of the Ministry of Health of the Republic of Uzbekistan named after academician E.Kh. Turakulov, Medical Association of Kitab District, Kashkadarya Region, Tashkent, Republic of Uzbekistan

<sup>2</sup>Endocrinologist of the Endocrinology Department of the Medical Association of the Kitab District of the Kashkadarya Region, Kashkadarya Region, Kitab District, Tashkent, Republic of Uzbekistan

**Abstract** To study dynamics of the frequency of thyroid nodules in adolescents Kashkadarya region by districts. At the polyclinic of the Kashkadarya branch of the Republican Specialized Scientific and Practical Medical Center of Endocrinology of the Ministry of Health of the Republic of Uzbekistan named after academician E.Kh. Turakulov, from 2020 to 2024, 568 adolescents with nodular diseases of the thyroid gland aged 11 to 15 years were examined. Of these, there were 461 girls and 107 boys. Over the period from 2020 to 2024, there was a tendency towards a slight decrease in the number of adolescents with nodular thyroid diseases in the Kashkadarya region. Thyroid problems in adolescents may present as a goiter, a nodule, or a general set of abnormal symptoms and physical findings. The unique challenge for adolescents is that thyroid problems can adversely affect growth and development during puberty, a critical period of hormonal interaction.

**Keywords** Nodular goiter, Adolescents, Complications

## 1. Introduction

Although the incidence of differentiated thyroid cancer (DTC) in children and adolescents (DTC) is low, it has been steadily increasing in recent years [1-3]. Compared with thyroid cancer in adults, DTC has clear differences in terms of pathophysiological characteristics, clinical features and long-term prognosis. [4-7]. Therefore, treatment guidelines and strategies developed for adult patients with thyroid cancer are not fully applicable to children and adolescents. The American thyroidological the Association of Thyroid Cancer (ATA) published its first guidelines for the diagnosis and management of childhood thyroid nodules and DTC in 2015, with the aim of standardizing the management of patients with DTC. [8].

The 2022 European Thyroid Association Guidelines for the management of thyroid nodules and differentiated thyroid cancer in children were prepared by an expert group. The expert group formulated this guideline specifically for children under 18 years of age with a thyroid nodule or differentiated thyroid carcinoma (DTC). Specific recommendations for the management of DTC in this age group are needed because of the differences in the presentation and genetics of DTC and the importance of treatment-related late effects of DTC in young people. [9].

Treatment of thyroid nodules in children is challenging because the obvious goal is to identify children with a malignant nodule, as a benign nodule does not always require treatment. Thyroid cancer is very rare in childhood with a reported prevalence of 1:1,000,000 in children under 10 years of age and up to 1:75,000 in children aged 15–19 years when diagnosed based on clinical signs and symptoms. [10]. In population screening, ultrasound may detect small, clinically undetectable DTCs at higher rates, without evidence that treatment of such nodules will reduce mortality rates or improve patient outcomes. [11].

The prevalence of benign thyroid nodules in childhood has been described to be approximately 0.5–2% depending on the screening or palpation method [12]. or ultrasound [13], and from the definition of the size that is documented (>5 mm or >10 mm). When proposing thyroidectomy for benign disease, one should keep in mind the possible lifelong adverse effects of the surgery, beginning with the lifelong need for levothyroxine (LT4) replacement therapy after thyroidectomy and, in a small but significant percentage of cases, permanent hypoparathyroidism, which will also require lifelong calcium and vitamin D replacement therapy. [14].

In adults, asymptomatic small thyroid nodules are very common (increasing with age) and are often discovered incidentally [15]. Most of them remain asymptomatic for the rest of their lives.

The expert group questioned the prevalence of non-clinically

significant thyroid nodules in childhood (Appendix A, [Q9]). A literature search was conducted (Appendix B). The largest source of data was found from surveillance programs in Fukushima and other parts of Japan that were not contaminated (Aomori, Yamanashi, and Nagasaki). These data showed that the prevalence of ultrasound-detected thyroid nodules >5 mm or cysts >20 mm in Japanese children was about 1.0% (20). The prevalence of non-clinically significant thyroid nodules in childhood has been found to range from 0.6 to 2% (Appendix C) [16,17]. Based on these findings, the expert group suggests that prospective studies be conducted to improve the level of evidence to provide greater certainty in determining the prevalence of non-clinically significant thyroid nodules in childhood in different populations.

Thyroid nodules in children are reported to have a two- to three-fold higher risk of malignancy compared to thyroid nodules in adults. Depending on the background iodine status of the country (due to the fact that thyroid nodules are more common in iodine-deficient countries), the risk that a clinically significant thyroid nodule (>1 cm) will become malignant is 20–25% in children compared to 5–10% for a thyroid nodule in adults, respectively. [18-20]. The above was the reason for the present study.

## 2. Material and Methods

At the polyclinic of the Kashkadarya branch of the Republican Specialized Scientific and Practical Medical Center of Endocrinology of the Ministry of Health of the Republic of Uzbekistan named after academician E.Kh.

Turakulov, from 2020 to 2024, 568 adolescents with nodular diseases of the thyroid gland aged 11 to 15 years were examined. Of these, there were 461 girls and 107 boys.

Inclusion criteria: children and adolescents with thyroid diseases, aged 0 to 18 years.

Exclusion criteria: adults, over 18 years of age.

Research methods—general clinical, biochemical (bilirubin, direct, indirect, ALT, AST, PTI, coagulogram, CRP), hormonal (TSH, free thyroxine, antibodies to TPO, to thyroglobulin and thyrocyte receptors, prolactin in the blood) and instrumental: ECG, ultrasound of the thyroid gland, internal organs, chest X-ray, etc.

The analysis included American recommendations for thyroid nodules according to the ACR-TIRADS (American College of Radiology-Thyroid Image Reporting and Data System) classification.

Statistical software Microsoft Excel and STATISTICA\_6 was used for statistical analysis, and  $p < 0.05$  was considered a significant difference. Quantitative data with normal distribution were expressed as mean and standard deviation ( $M \pm SD$ ).

## 3. Results and Discussion

Table 1 shows a list of adolescents with primary nodular goiter and registered for dispensary care in the Kashkadarya region. This table shows that over the period from 2020 to 2024, there was a tendency for a slight decrease in the number of adolescents with nodular thyroid diseases in the Kashkadarya region.

**Table 1.** List of adolescents with primary nodular goiter and registered with the dispensary in the Kashkadarya region

№.	Name of district/ name of city	List of adolescents with primary incidence of nodular goiter in the region										List of adolescents under medical observation with nodular goiter in the region									
		2020		2021		2022		2023		2024 (6 mo)		2020		2021		2022		2023		2024	
		total	Girls	total	Girls	total	Girls	total	Girls	total	Girls	total	Girls	total	Girls	total	Girls	total	Girls	total	Girls
1	City of Karshi	29	23	0	0	5	4	0	0	0	0	29	23	29	23	34	27	31	25	28	22
2	City of Shahrisabz	8	7	26	26	10	10	5	5	6	6	16	15	41	40	51	50	46	45	45	44
3	Guzor district	20	12	34	24	9	4	19	13	25	12	37	23	46	29	47	27	41	25	63	41
4	Dobogonobod district	2	2	5	5	5	5	9	8	3	3	42	41	42	41	41	40	43	42	44	41
5	Karshi district	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6	Kanon District	36	33	0	0	38	24	19	10	11	6	48	45	26	25	59	49	67	50	75	55
7	Kamashi district	2	2	2	2	0	0	3	3	1	1	24	21	23	21	20	18	23	21	22	20
8	Kashir area	0	0	0	0	0	0	0	0	2	2	0	0	0	0	0	0	0	0	2	2
9	Kinob District	10	10	7	7	14	12	11	11	21	21	11	11	15	15	22	20	33	31	46	45
10	Kukobulo district	0	0	0	0	3	3	1	1	3	2	0	0	0	0	3	3	4	4	7	6
11	Nisbon District	0	0	9	5	0	0	12	12	3	3	0	0	9	5	0	0	24	22	27	25
12	Nisborak District	0	0	3	3	1	1	3	3	2	2	10	9	13	12	14	13	32	12	14	14
13	Nirishkor district	5	5	6	5	4	4	11	11	1	1	16	16	22	21	26	25	37	36	38	37
14	Chirchik district	0	0	0	0	9	9	2	2	0	0	9	9	9	9	17	17	19	19	17	17
15	Shahrisabz region	7	7	31	10	6	6	18	16	6	2	21	21	29	29	35	35	41	39	39	38
16	Yakkabog District	6	5	16	11	3	7	11	9	4	3	30	26	40	32	42	33	47	36	45	33
	Total	125	106	119	96	112	89	124	104	88	64	293	260	344	302	411	387	468	407	512	442

Thyroid diseases are known to cause abnormal puberty, suggesting interactions between the hypothalamic-pituitary-thyroid (HPT) and hypothalamic-pituitary-gonadal (HPG) axes, which are important for sexual development. Hypothalamic gonadotropin-inhibitory hormone (GnIH) has been shown to be decreased in the early prepubertal stage, suggesting a role for GnIH in the onset of puberty [21].

Thyroid nodules in children present a significant diagnostic challenge. Although thyroid nodules are relatively rare in children compared to adults, they require careful evaluation due to the increased risk of malignancy [22].

Next, we divided the patients by age into 5 groups according to 5 Tanner stages (Table 2).

**Table 2.** Distribution of patients by age (according to 5 Tanner stages)

Tanner's stages of puberty	Age, years, by stages of puberty according to Tanner	n=568
I	prepuberty	-
II	11.7 ± 1.3 years	95 (16.6%)
III	13.2 ± 0.8 years	199 (35.0%)
IV	14.7 ± 1.1 years	144 (25.3%)
V	15.5 ± 0.7 years	130 (22.8%)
	Total: n = 568	568

The next step of our research was to study the frequency delays and various developmental disorders in adolescents in combination with nodular diseases of the thyroid gland (Table 3).

**Table 3.** Frequency of developmental delays and various disorders in adolescents in combination with nodular diseases of the thyroid gland

No.	Type of violation development	Number of patients, N=102
1	Delayed puberty	49 (8.6% of 568)
2	Growth retardation	24 (4.2% of 568)
3	Delayed growth and puberty	26 (4.6% of 568)
5	Delayed speech development.	3 (0.5% of 568)
<b>Total</b>		<b>102</b>

From Table 3 it follows that among 568 adolescents 49 were identified cases of delayed puberty, 24 cases of growth retardation, 26 cases of delayed growth and puberty and 3 cases of speech delay. Thyroid nodules in children are less common than in adults, but they exhibit a higher rate of malignancy. Accordingly, the treatment of thyroid nodules in children is more complex the younger the patient is and requires careful evaluation by physicians. In adult patients, certain ultrasound (US) features are associated with an increased risk of malignancy (RM) in thyroid nodules. Moreover, several ultrasound risk stratification systems (URS) have been developed to determine RM, combining the ultrasound features of the nodule.

## 4. Conclusions

Thyroid problems in adolescents may present as a goiter, a nodule, or a general set of abnormal symptoms and physical findings. The unique challenge for adolescents is that thyroid problems can adversely affect growth and development during puberty, a critical period of hormonal interaction.

## REFERENCES

- [1] Miller KD, Fidler-Benaoudia M, Keegan TH, Hipp HS, Jemal A, Siegel RL. Cancer statistics for adolescents and young adults, 2020. // *CA Cancer J Clin.* (2020) 70: 443–59. doi: 10.3322/caac.21637.
- [2] Vergamini LB, Frazier AL, Abrantes FL, Ribeiro KB, Rodriguez-Galindo C. Increase in the incidence of differentiated thyroid carcinoma in children, adolescents, and young adults: a population-based study. // *J Pediatr.* (2014) 164: 1481–5. doi: 10.1016/j.jpeds.2014.01.059.
- [3] Bernier MO, Withrow DR, Berrington de Gonzalez A, Lam CJK, Linet MS, Kitahara CM, et al. Trends in pediatric thyroid cancer incidence in the United States, 1998–2013. // *Cancer.* (2019) 125: 2497–505. doi: 10.1002/cncr.32125.
- [4] Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 American thyroid association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American thyroid association guidelines task force on thyroid nodes and differentiated thyroid cancer. // *Thyroid.* (2016) 26: 1–133. doi: 10.1089/thy.2015.0020.
- [5] Cistaro A, Quartuccio N, Garganese MC, Villani MF, Altini C, Pizzoferrero M, et al. Prognostic factors in children and adolescents with differentiated thyroid carcinoma treated with total thyroidectomy and RAI: a real-life multicentric study. // *Eur J Nucl Med Mol Imaging.* (2022) 49: 1374–85. doi: 10.1007/s00259-021-05586-8.
- [6] Durante C, Haddy N, Baudin E, Leboulleux S, Hartl D, Travagli JP, et al. Long-term outcome of 444 patients with distant metastases from papillary and follicular thyroid carcinoma: benefits and limits of radioiodine therapy. // *J Clin Endocrinol Metab.* (2006) 91: 2892–9. doi: 10.1210/jc.2005-2838.
- [7] Lebink CA, Links TP, Czarniecka A, Dias RP, Elisei R, Izatt L, et al. 2022 European Thyroid Association Guidelines for the management of pediatric thyroid nodules and differentiated thyroid carcinoma. // *Eur Thyroid J.* (2022) 11(6): e220146. doi: 10.1530/ETJ-22-0146.
- [8] Francis GL, Waguespack SG, Bauer AJ, Angelos P, Benvenega S, Cerutti JM, et al. Management guidelines for children with thyroid nodules and differentiated thyroid cancer. // *Thyroid.* (2015) 25: 716–59. doi: 10.1089/thy.2014.0460.
- [9] Lebink CA, Links TP, Czarniecka A, Dias RP, Elisei R, Izatt L, Krude H, Lorenz K, Luster M, Newbold K, Piccardo A, Sobrinho-Simões M, Takano T, Paul van Trotsenburg AS, Verburg FA, van Santen H.M. 2022 European Thyroid Association Guidelines for the management of pediatric thyroid nodules and differentiated thyroid carcinoma. // *Eur*

- Thyroid J. 2022 Nov 29; 11(6): e220146. doi: 10.1530/ETJ-22-0146.
- [10] Rivkees SA, Mazzaferri EL, Verburg FA, Reiners C, Luster M, Breuer CK, Dinauer CA, Udelsman R. The treatment of differentiated thyroid cancer in children: emphasis on surgical approach and radioactive iodine therapy. *Endocrine Reviews* 2011;32:798–826. (10.1210/er.2011-0011)
- [11] Lin JS, Aiello Bowles EJA, Williams SB, Morrison CC. Screening for thyroid cancer: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA* 2017;317:1888–1903. (10.1001/jama.2017.0562)
- [12] Rallison ML, Dobyns BM, Keating FR, Rall JE, Tyler FH. Thyroid nodularity in children. *JAMA* 1975;233:1069–1072.
- [13] Suzuki S, Suzuki S, Fukushima T, Midorikawa S, Shimura H, Matsuzuka T, Ishikawa T, Takahashi H, Ohtsuru A, Sakai A et al. Comprehensive Survey Results of Childhood thyroid ultrasound Examinations in Fukushima in the first four years after the Fukushima Daiichi Nuclear Power Plant Accident. *Thyroid* 2016;26:843–851. (10.1089/thy.2015.0564)
- [14] Cléro E, Ostroumova E, Demoury C, Grosche B, Kesminiene A, Liutsko L, Motreff Y, Oughton D, Pirard P, Rogel A et al. Lessons learned from Chernobyl and Fukushima on thyroid cancer screening and recommendations in case of a future nuclear accident. *Environment International* 2021;146:106230. (10.1016/j.envint.2020.106230)
- [15] Guth S, Theune U, Aberle J, Galach A, Bamberger CM. Very high prevalence of thyroid nodules detected by high frequency (13 MHz) ultrasound examination. *European Journal of Clinical Investigation* 2009;39:699–706. (10.1111/j.1365-2362.2009.02162.x)].
- [16] Baez JC, Zurakowski D, Vargas SO, Lee EY. Incidental thyroid nodules detected on thoracic contrast-enhanced CT in the pediatric population: prevalence and outcomes. *American Journal of Roentgenology* 2015;205:W360–W365. (10.2214/AJR.14.13895).
- [17] Calle-Toro JS, Kelly A, Ford EJ, Zemel BS, Schall JJ, Adgent MA, Umbach DM, Rogan WJ, Stallings VA, Darge K et al. Incidental findings during ultrasound of thyroid, breast, testis, uterus and ovary in healthy term neonates. *Journal of Ultrasound* 2019;22:395–400. (10.1007/s40477-019-00365-6).
- [18] Bauer AJ. Thyroid nodules in children and adolescents. *Current Opinion in Endocrinology, Diabetes, and Obesity* 2019;26:266–274. (10.1097/MED.0000000000000495).
- [19] Gupta A, Ly S, Castroneves LA, Frates MC, Benson CB, Feldman HA, Wassner AJ, Smith JR, Marqusee E, Alexander EK et al. A standardized assessment of thyroid nodules in children confirms higher cancer prevalence than in adults. *Journal of Clinical Endocrinology and Metabolism* 2013;93:3238–3245. (10.1210/jc.2013-1796).
- [20] Niedziela M. Pathogenesis, diagnosis and management of thyroid nodules in children. *Endocrine-Related Cancer* 2006;13:427–453. (10.1677/erc.1.00882).
- [21] Kiyohara M, Son YL, Tsutsui K. Involvement of gonadotropin-inhibitory hormone in pubertal disorders induced by thyroid status. *Sci Rep.* 2017 Apr 21; 7(1): 1042. doi: 10.1038/s41598-017-01183-8.
- [22] Bauer AJ. Thyroid nodes in children and adolescents. *Curr Opin Endocrinol Diabetes Obes.* 2019 Oct; 26(5): 266-274. doi: 10.1097/MED.0000000000000495.