

ANAMNESIS, CLINICAL AND PARACLINICAL CHARACTERISTIC OF CHILDREN WITH AUTOIMMUNE THYROIDITIS*

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Autoimmune thyroiditis is a genetically determined chronic autoimmune disease of the thyroid gland, marked by the production of antibodies to peroxidase, thyroglobulin and characterized by enlargement of the thyroid gland and impaired production of peripheral thyroid hormones [1, 2].

The development of this disease is promoted by various factors, in particular, by genetic predisposition in combination with environmental risk factors [3].

To date, autoimmune thyroiditis is the most common inflammatory disease of the thyroid gland in children. The prevalence of autoimmune thyroiditis has been found to vary from 0.3 to 3.3% and is highest in adolescents. At the same time, 31.6% of children have a burdened familial history [4]. Autoimmune thyroiditis is characterized by increased autoantibodies to the thyroid gland with clinical or subclinical manifestations of hypothyroidism, hyperthyroidism or is marked by euthyroidism

[1, 5–7]. The literature suggests that the incidence of overt or asymptomatic hypothyroidism in children is 41.4%, while hyperthyroidism is reported in only 6.5%, since hyperthyroidism is relatively rare in children [3, 6]. While the annual incidence of hyperthyroidism is relatively low, for example, with only 8 cases per 1,000,000 children under the age of 15 and 1 case per 1,000,000 children under the age of 4, autoimmune thyroiditis is still the cause of hyperthyroidism in 80% of cases [3, 8].

The clinical symptoms of autoimmune thyroiditis reported to the physician are highly varied. Thus, to date, patients suffering from autoimmune thyroiditis have a variety of complaints and symptoms, as well as comorbid conditions [5, 9]. The disease may also be diagnosed incidentally during medical examinations and screening of children [3, 10].

Due to the fact that the current stage of early autoimmune thyroiditis detection in children is important in order to timely pre-

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vent the negative impact of thyroid diseases on the functional state and development of the child's body, this article is relevant and topical for addressing this problem. **The aim:** to conduct a comparative characterization of medi-

cal history and clinical and paraclinical data of children suffering from autoimmune thyroiditis and those with no thyroid pathology in order to optimize early diagnosis of the disease.

MATERIALS AND METHODS

The study was conducted according to the ethical and moral requirements of the Ukrainian Association for Bioethics and the Standards of GCP (1992), GLP (2002), the principles of the Declaration of Helsinki on Human Rights, the Council of Europe Convention on Human Rights and Biomedicine. The medical history and clinical and paraclinical data were examined in an observation group of 127 children diagnosed with autoimmune thyroiditis (53 boys and 74 girls), aged 11.66 ± 0.37 , and in a control group of 577 children with no thyroid pathology (268 boys and 309 girls), aged 11.49 ± 0.17 . The semantic method of study was used to analyze the literature data. The criteria for inclusion in the study were: diagnosis «Autoimmune thyroiditis»; age up to 17 years 11 months 29 days; parental consent

for research and/or patient older 14 years consent for research. The exclusion criteria were: age older 18; oncological diseases; psychiatric pathology; parental refusal and/or patient take part in the research. Statistical study techniques were applied using the licensed software package Statistica, serial number AXR712D833214SAN5. When distributing the data according to Gaussian law, parametric methods of statistical analysis with determination of mean values (M), standard error (m), relative values with calculation of their differences were used. Nonparametric statistical methods: «table 2×2 », chi-square ($df = 1$) was used if the distribution was abnormal. The differences of $p < 0.05$ were considered statistically significant [11].

RESULTS AND THEIR DISCUSSION

An analysis of complaints in the children under study was performed at the beginning of the study (Table 1).

The results presented showed that children diagnosed with autoimmune thyroiditis sought medical assistance with complaints of psychoemotional disorders considerably more often than those in the control group, (37% vs. 4.7%, $p < 0.001$), boys with autoimmune thyroiditis complained of emotional and neurological disorders, such as increased anxiety, emotional disturbance or apathy, tearfulness, headaches, and were registered three times more often than girls. Boys diagnosed with autoimmune thyroiditis also complained of cardiac arrhythmias more frequently than boys without thyroid pathology (15.1% vs. 3.7%, $p < 0.01$). Complaints of prolonged low-grade fever predominated in girls diagnosed with autoimmune thyroiditis (6.8%), whereas children in the control group had no such complaints, regardless of their gender. Such complaints as dry skin and fatigue were registered in both observation groups with varying incidence, however,

there were no significant differences between the indicators. Also, children with complaints of aphonia or hoarseness had no autoimmune thyroiditis. In contrast, complaints of elevated blood pressure were found significantly more often in children without thyroid pathology (12.3%) than in those with autoimmune thyroiditis (1.6%), $p < 0.001$.

The medical history of the children examined is presented in Table 2. Thus, the medical history study showed that patients diagnosed with autoimmune thyroiditis had a significantly more predominant burdened familial history of thyroid disease. Thus, mothers of 14.96% of the children examined were observed and treated by an endocrinologist and obstetrician-gynecologist with thyroid pathology during pregnancy. Thus, there were 11 (8.7%) examined patients from the observation group who had 11 (an unfavorable perinatal period versus 3 (0.52%) children from the control group ($p < 0.01$). Despite the fact that children diagnosed with autoimmune thyroiditis had higher weight at birth (more than 4,000 g) in their

Table 1

Complaints of the children examined (abs/%)

Parameter	Children diagnosed with autoimmune thyroiditis			Children without thyroid pathology		
	B n = 53	G n = 74	All n = 127	B n = 268	G n = 309	All n = 577
Emotional and neurological disorders	32 / 60.4#	15 / 20.3#	47 / 37#	11 / 4.1	16 / 5.2	27 / 4.7
Cardiac rhythm abnormalities	8 / 15.1*	9 / 12.2	17 / 13.4°	10 / 3.7	24 / 7.8	34 / 5.9
Prolonged low-grade fever	2 / 3.8	5 / 6.8°	7 / 5.5°	0	0	0
Dry skin	0	1 / 1.4	1 / 0.8	5 / 1.9	2 / 0.7	7 / 1.2
Fatigue	7 / 13.2	9 / 12.2	16 / 12.6	17 / 6.3	25 / 8.1	42 / 7.3
Hoarseness, aphonia	0	0	0	3 / 1.1	0	3 / 0.5
Increased arterial pressure	1 / 1.9#	1 / 1.4#	2 / 1.6#	30 / 11.2	41 / 13.3	71 / 12.3

Notes:

B — boys; G — girls; All — all the examined children in the primary group with autoimmune thyroiditis and in the control group without thyroid pathology;

° — $p < 0.05$, * — $p < 0.01$, # — $p < 0.001$ — significance of differences between the groups of children with autoimmune thyroiditis and those without thyroid pathology.

Table 2

Anamnesis of the children examined (abs/%)

Parameter	Children diagnosed with autoimmune thyroiditis			Children without thyroid pathology		
	B n = 53	G n = 74	All n = 127	B n = 268	G n = 309	All n = 577
Burdened familial history of thyroid diseases	11 / 20.75#	8 / 10.8°	19 / 14.96#	3 / 1.12	4 / 1.3	7 / 1.2
Unfavorable perinatal period	4 / 7.5	7 / 9.5*	11 / 8.7*	3 / 1.1	0	3 / 0.52
High weight at birth	4 / 7.5	2 / 2.7	6 / 4.7	1 / 0.37	0	1 / 0.17
Living in an area with increased radioecological control	0	1 / 1.35	1 / 0.79	2 / 0.75	0	2 / 0.35

Notes:

B — boys; G — girls; All — all examined children in the primary group with autoimmune thyroiditis and in the control group without thyroid pathology;

° — $p < 0.05$, * — $p < 0.01$, # — $p < 0.001$ — significance of differences between the groups.

medical history, there were no significant differences when comparing the two observation groups. Also, the incidence of autoimmune thyroiditis had no reliable dependence on the place of residence, including residence in the zone of high radioecological control.

The study showed that patients diagnosed with autoimmune thyroiditis had a significantly higher incidence of acute respiratory diseases and history of lymphadenitis than children without thyroid disease (24.4% and 29.13% vs. 2.43% and 0.17%, $p < 0.001$) (Table 3). In contrast, gastrointestinal diseases and diabetes melli-

tus were reported more frequently in children without thyroid pathology than in those with autoimmune thyroiditis. It was also demonstrated that the children examined in both observation groups had mitral valve prolapse (11.8% and 11.09%, $p > 0.05$) and urinary system diseases (9.45% and 6.41%, $p > 0.05$) with almost equal incidence. Moreover, hepato-biliary diseases were only reported in children without thyroid pathology, and leukemia was only reported in those with autoimmune thyroiditis.

Subsequently, the physical development of all children was assessed (Table 4).

Table 3

Comorbid diseases in the children examined (abs/%)

Parameter	Children diagnosed with autoimmune thyroiditis			Children without thyroid pathology		
	B n = 53	G n = 74	All n = 127	B n = 268	G n = 309	All n = 577
Respiratory diseases	15 / 28.3#	16 / 21.6#	31 / 24.4#	6 / 2.24	8 / 2.59	14 / 2.43
Lymphadenitis	12 / 22.64#	25 / 33.78#	37 / 29.13#	0	1 / 0.32	1 / 0.17
Gastrointestinal diseases	2 / 3.77	0#	2 / 1.57*	25 / 9.34	41 / 13.3	66 / 11.44
Diabetes	0*	2 / 2.7	2 / 1.57*	11 / 4.1	15 / 4.85	26 / 4.5
Diseases of the hepato-biliary system	0	0	0	6 / 2.2	3 / 0.97	9 / 1.56
Mitral valve prolapse	4 / 7.55	11 / 14.86	15 / 11.8	26 / 9.7	38 / 12.3	64 / 11.09
Urinary system diseases	5 / 9.43	7 / 9.46	12 / 9.45	22 / 8.2	15 / 4.85	37 / 6.41

Notes:

B — boys; G — girls; All — all examined children in the primary group with autoimmune thyroiditis and in the control group without thyroid pathology;

° — $p < 0.05$, * — $p < 0.01$, # — $p < 0.001$ — significance of differences between the groups.

Table 4

Characteristics of physical development indicators (abs/%)

Parameter	Children diagnosed with autoimmune thyroiditis			Children without thyroid pathology		
	B n = 53	G n = 74	All n = 127	B n = 268	G n = 309	All n = 577
Normal weight	52 / 98.1#	64 / 86.5	116 / 91.34	237 / 88.43	281 / 90.94	518 / 89.77
Overweight	0#	5 / 6.76	5 / 3.94	19 / 7.1	11 / 3.6	30 / 5.2
Underweight	1 / 1.89	5 / 6.76	6 / 4.72	12 / 4.5	17 / 5.5	29 / 5.03
Average height	42 / 79.2	63 / 85.14	105 / 82.68	223 / 83.2	281 / 90.94	504 / 87.35
Tall	10 / 18.87	8 / 10.8	18 / 14.17	41 / 15.3	27 / 8.7	68 / 11.8
Short	1 / 1.89	3 / 4.05	4 / 3.15	4 / 1.5	1 / 0.32	5 / 0.87

Notes:

B — boys; G — girls; All — all examined children in the primary group with autoimmune thyroiditis and in the control group without thyroid pathology;

° — $p < 0.05$, * — $p < 0.01$, # — $p < 0.001$ — significance of differences between the groups.

There were no reliable differences between the height indices of examined children from different observation groups found. When assessing body weight, reliable differences were only registered among the boys. Thus, it was found that excessive body weight was registered only in 19 (7.1%) boys without thyroid pathology ($p < 0.001$). In contrast, normal body weight was registered significantly more often in the group of boys with autoimmune thyroiditis (98.1%).

Upon laboratory examination, children diagnosed with autoimmune thyroiditis showed thyroperoxidase antibody levels ranging from

209.7 to 694.7 IU/mL, thyroid stimulating hormone (TSH) from 0.01 to 5.93 to 89.9 IU/mL, and free thyroxine (free T4) from 1.14 to 28.8 ng/dL. At the same time, 77.95% of the children were of the euthyroid type, 17.32% were hypothyroid, and 4.72% were hyperthyroid. The level of antibodies to thyroperoxidase in children without thyroid pathology was within the age limit (5.8–9.31 IU/mL).

When comparing the results of the study with the published literature, it was noted that the common complaints were fatigue, headaches, heart rhythm disturbance, dry skin. However, the complaints of hair loss, obe-

sity, weight gain, short stature, delayed puberty, presented in the studies of Admoni O. et al. (2020); Brown Rosalind S. (2013); Marco Cappa (2011), were not observed in our study [3, 5, 7]. In addition, our study observed gender features. Thus, girls diagnosed with autoimmune thyroiditis complained of prolonged low-grade fever, while Marco Cappa (2011), on the contrary, reported complaints of hypothermia [3].

Notwithstanding the fact that the burdened familial history was also registered in our examined children diagnosed with autoimmune thyroiditis, the incidence was nevertheless 2.5 times lower than the data presented in the literature for a long-term follow-up of 8.1 years [5]. Moreover, in contrast to the data of other authors, in which the established causes of autoimmune thyroiditis included an interaction between environmental and genetic factors, no such pattern was observed in our study [3].

The results of examinations by Filippo De Luca et al. (2013) showed that euthyroidism was registered in 52.1%, subclinical hypothyroidism in 41.1%, subclinical hyperthyroidism in 6.5% of patients; in the study by Giorgio Radetti et al. (2019) euthyroidism was reported in 77.10% of patients, subclinical hypothyroidism in 6.42%, hypothyroidism in 15.93%, hyperthyroidism was reported only in 0.55% of cases, while our study reported euthyroidism in 77.95% of patients, hypothyroidism in 17.32%, hyperthyroidism in 4.72% of cases [6, 12]. However, the levels of thyroid stimulating hormone (TSH) and free thyroxine (free T4) found

in our study differed from those presented in other works [7, 12].

When studying comorbid conditions, the literature suggested that autoimmune thyroiditis was diagnosed in children with such chromosomal diseases as the Down and Turner syndromes and such diseases as celiac disease, morbus Addison, pernicious anemia, vitiligo, alopecia, but there were no such diseases found in our study [3, 5]. Moreover, Marco Cappa et al. (2011) noted the presence of comorbid type 1 diabetes mellitus in the patients examined, and in our study, this disease was registered only in 2 of all 132 patients (1.52%), and yet the incidence was significantly higher in the control group and occurred in 26 of 577 children from the control group (4.5%). However, like our study, Giorgio Radetti et al. (2019), found that children diagnosed with autoimmune thyroiditis had concomitant lymphadenopathy in 24.6% of cases (which was almost the same as in our study, 29.13%) [12]. Furthermore, our study reported mitral valve prolapse in 15 patients, and gastrointestinal diseases in only 2 children, while other studies showed that patients also had cases of acute rheumatic fever and functional gastrointestinal diseases accompanied by constipation and bloating [5, 9]. When comparing physical development parameters, it can be stated that whereas our study reported excessive body weight and short stature in isolated cases, other studies, on the contrary, reported increased body weight and stunted growth as typical for patients with autoimmune thyroiditis [3, 7].

CONCLUSIONS

1. Children diagnosed with autoimmune thyroiditis were found to be euthyroidism in 77.95% of cases, hypothyroid in 17.32%, and hyperthyroid in 4.72%. At the same time, burdened familial history of thyroid diseases was noted in 14.96% of those examined.
2. The most common complaints registered in children suffering from autoimmune thyroiditis were psychoemotional, neurological disturbances (37%) and cardiac arrhythmias (13.4%), predominantly in boys (60.4% and 15.09). Also, 5.5% of patients complained of prolonged low-grade fever, predominantly girls (6.8%).
3. Among comorbid conditions, respiratory diseases (24.4%) and lymphadenitis (29.13%) were the most common.
4. The data presented should be considered as criteria for early diagnosis of autoimmune thyroiditis in children.

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АНАМНЕСТИЧНА ТА КЛІНІКО-ПАРАКЛІНІЧНА ХАРАКТЕРИСТИКА ДІТЕЙ З АУТОІМУННИМ ТИРЕОЇДИТОМ

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Сьогодні аутоімунний тиреоїдит є розповсюдженим захворюванням щитоподібної залози у дітей. **Мета дослідження.** Провести порівняльну характеристику анамнестичних та клініко-параклінічних даних у дітей з аутоімунним тиреоїдитом і без патології щитоподібної залози.

Матеріали та методи. Дослідження було проведено у 127 дітей (53 хлопчика і 74 дівчат) з аутоімунним тиреоїдитом у віці $11,66 \pm 0,37$ років. В контрольну групу порівняння було включено 577 дітей (268 хлопчиків і 309 дівчат) без патології щитоподібної залози у віці $11,49 \pm 0,17$ років. Статистичні методи дослідження проводились за допомогою ліцензійного пакета програм Statistica. Статистично значимими вважали відмінності з $p < 0,05$.

Результати. Проведене дослідження дітей з аутоімунним тиреоїдитом та без патології щитоподібної залози продемонструвало, що у пацієнтів основної групи спостереження в 77,95% випадків був діагностований еутиреоз, в 17,32% — гіпотиреоз, в 4,72% — гіпертиреоз. У дітей з аутоімунним тиреоїдитом рівень антитіл до тиреопероксидази був у межах 209,7–694,7 МО/мл, тиреотропний гормон (ТТГ) 0,01 — 5,93–89,9 МО/мл, тироксин вільний (Т4 вільний) 1,14–28,8 нг/дл. У дітей без патології щитоподібної залози рівень антитіл до тиреопероксидази був в межах вікової норми (5,8–9,31 МО/мл). При цьому критеріями ранньої діагностики аутоімунного тиреоїдита були: обтяжений сімейний анамнез (14,96%); скарги на психоемоційні, неврологічні порушення (37%) та порушення серцевого ритму (13,4%), переважно у хлопчиків (60,4% і 15,09% відповідно), тривалий субфебрилитет (5,5%), переважно у дівчаток (6,8%); наявність коморбідної патології: захворювання респіраторного тракту (24,4%) і лімфаденіти (29,13%).

Висновок. Рання діагностика аутоімунного тиреоїдиту у дітей дозволяє своєчасно попередити негативний вплив захворювання на функціональний стан і розвиток дитячого організму.

Ключові слова: аутоімунний тиреоїдит, діти, скарги, анамнез, захворювання.

ANAMNESIS, CLINICAL AND PARACLINICAL CHARACTERISTIC OF CHILDREN WITH AUTOIMMUNE THYROIDITIS

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Purpose. To conduct a comparative characterization of anamnesis and clinical and paraclinical data of children suffering from autoimmune thyroiditis and those with no thyroid pathology in order to optimize early diagnosis of the disease.

Materials and Methods. This examination was carried out on 127 children (53 boys and 74 girls) diagnosed with autoimmune thyroiditis at the age of 11.66 ± 0.37 . For comparison, 577 children (268 boys and 309 girls) without thyroid pathology at the age of 11.49 ± 0.17 were included in the control group. Statistical study techniques were applied using the licensed software package Statistica. The differences of $p < 0.05$ were considered statistically significant.

Results. The comparative study of children diagnosed with autoimmune thyroiditis and those with no thyroid pathology showed that euthyroidism was diagnosed in 77.95% of patients in the primary observation group, hypothyroidism in 17.32%, and hyperthyroidism in 4.72% of patients. Children diagnosed with autoimmune thyroiditis showed thyroperoxidase antibody levels ranging from 209.7 to 694.7 IU/mL, TSH from 0.01 to 5.93 to 89.9 IU/mL, and free T4 from 1.14 to 28.8 ng/dL. The criteria for early diagnosis of autoimmune thyroiditis included: a burdened familial history of thyroid disease (14.96%); complaints of psychoemotional, neurological (37%) and heart rhythm disorders (13.4%), predominantly in boys (60.4% and 15.09%), prolonged low-grade fever (5.5%), predominantly in girls (6.8%); comorbid conditions: respiratory tract diseases (24.4%) and lymphadenitis (29.13%).

Conclusion. At the current stage, early diagnosis of autoimmune thyroiditis in children is important for the timely prevention of the negative impact of the disease on the functional state and development of the child's body.

Key words: autoimmune thyroiditis, children, complaints, anamnesis, diseases.