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Hypothyroidism in Pediatric Population – Bosnian and Herzegovinian Situation

Edo Hasanbegovic¹, Snijezana Hasanbegovic², Edin Begic³

¹Pediatric Clinic, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina

²Faculty of Medicine, Sarajevo School of Science and Technology, Sarajevo, Bosnia and Herzegovina

³Pediatric Clinic, UCC Sarajevo, Sarajevo, Bosnia and Herzegovina

Corresponding Author: Edo Hasanbegovic, MD, PhD, Pediatric Clinic, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina. ORCID ID: <http://www.orcid.org/0000-0001-7960-6707>. E-mail: edo.hasanbegovic@gmail.com

ABSTRACT

Introduction: Thyroid gland diseases in children are in second place by frequency among all endocrine disorders. When interpreting the results of the thyroid function assessment it should be taken into account the significant differences in the concentrations of TSH, thyroid hormones, thyroid binding proteins and calcitonin among children of different ages. **Goal:** To present the age and sex structure of the patients diagnosed with hypothyroidism, evaluate diagnostic methods for making diagnosis, evaluation of etiology of hypothyroidism, with special review of the therapeutic modality. **Patients and methods:** The study have retrospective character and includes all patients who have the diagnosis of hypothyroidism, but at the moment of data collection were aged 0-18 years. **Results:** Distribution of patients on the basis of gender, revealed more significant representation of female (65.93%), and without significant difference in the presence of the disease in relation to age ($p>0.05$). Physical examination of the struma was not verified in the majority of cases (74; 81.32%, $p<0.05$) suffering from hypothyroidism. Ultrasound review in 22 (50%) cases confirmed the struma. Ultrasound findings in most cases 14 (31.81%) demonstrated diffuse struma and Hashimoto thyroiditis together. In relation to the etiology of hypothyroidism most patients belong to a group where hypothyroidism is associated with other diseases and conditions (27; 29.67%), but the least with congenital hypothyroidism with 18 (19.78%) cases. The average dose of L-thyroxine in the age of 0-1 months was 50 mg, 1 month-10 years 37.5 mcg, and the group of patients over 10 years 65 mcg. **Conclusion:** Congenital hypothyroidism has about one-fifth of patients. Physical examination revealed in about one fifth of patients the struma of the thyroid gland; TSH levels is critical for the diagnosis and correction of therapy in pediatric patients with hypothyroidism. Congenital hypothyroidism is diagnosed on average at the age of 12 days, which is optimal for period for therapeutic response; Substitution treatment is carried out with L-thyroxine which is relatively reduced in doses from neonatal age onwards.

Keywords: Hypothyroidism, pediatric population.

1. INTRODUCTION

Thyroid gland disease in children are in second place by frequency among all endocrine disorders (1). When interpreting the results of the assessment of thyroid function should be taken into account the significant differences in the concentrations of TSH, thyroid hormones, thyroid a binding protein and calcitonin between children of different ages. Also, different content of iodine in the diet has an impact on the results of hormone tests and the results of radio-nucleotide tests of the thyroid

gland. Measurement of Serum TSH is the most sensitive test for the detection of primary hypothyroidism. Significantly better indicator of thyroid function are the concentrations of free T_4 and T_3 in relation to their total concentration in the blood. In cases of suspected thyrotoxicosis, measuring serum T_3 is the most sensitive test for hypersecretion (or exogenous input) of thyroid hormone. Exceptions are conditions associated with a syndrome of so called "euthyroid" disease. Confirmation of primary hyperthyroidism today is based

on the determination of very low (previously “undetectable”) concentration of TSH levels (<0.1 mJ/l). In differentiating false (thyrotoxicosis factitia) from organic hyperthyroidism is used the ¹²³J–fixation. Within the false hyperthyroidism, caused by exogenous intake of thyroid hormones, iodine fixation is reduced or absent entirely. Congenital hypothyroidism (CH) includes all conditions in which exist insufficient function of the thyroid gland, regardless of etiology, and is clinically or laboratory detected at birth. The incidence of CH of 1:1,500 is comparable to reports in other jurisdictions (1,2). The disease is twice as common in female children. Hypothyroidism in the newborn period is almost always overlooked and delayed diagnosis leads to the most severe outcome, mental retardation (emphasizing the importance of neonatal screening) (3). The development of the central nervous system during the first trimester of pregnancy up to age of 18-24 months depends on the presence of normal amounts of thyroid hormones. Given the fact that the early introduction of substitution therapy is essential for the achievement of normal psycho motor development, it needs to start immediately after confirming the diagnosis, or finding high levels of TSH in a repeated sample of blood.

Thyroid hormone levels change markedly during childhood, and that adult reference intervals are not universally applicable to children (4). The treatment of choice is oral administration of L-thyroxine. For infant’s dose is 10-15 µg/kg – or at least 37.5 µg/day, but the recommended dose is 50 µg/day. The levels of T₄ and TSH levels should be regularly monitored and maintained in the upper half of the normal range for the chronological age of the patient. The only known side effects of sodium-L-thyroxine are determined by an overdose of the drug. Monitoring the rate of growth and bone maturation in older children is an excellent indicator of the therapy adequacy.

2. GOAL

To present the age and sex structure of the patients diagnosed with hypothyroidism, evaluate diagnostic methods for making diagnosis, evaluation of etiology of hypothyroidism, with special review of the therapeutic modality.

3. PATIENTS AND METHODS

The study has a retrospective character, and includes all patients who have the diagnosis of hypothyroidism treated at the Endocrinology Counseling Center of the Pediatric Clinic, University Medical Centre in Sarajevo, and at the moment of data collection were aged 0-18 years. Patients were in relation to age divided into three groups (0-1 months, 1 month to 10 years, and over 10 years of age). The diagnosis of patients was based on physical findings, hormonal findings of the thyroid gland (RIA method), with ultrasound findings (linear probe of 7.5 MHz). All patients received as therapy L-thyroxin.

4. RESULTS

Distribution of patients on the basis of gender, revealed more significant representation of female patients (65.93%) (Figure 1). there were no significant differences in the appearance of the disease in relation to patient’s age (p>0.05).

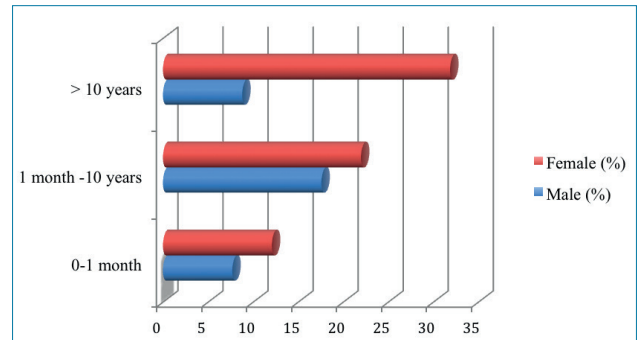


Figure 1. Gender and age distribution of patients

Physical examination of the struma was not detected in the majority of cases (74; 81.32%, p<0.05) among patient suffering from hypothyroidism (Figure 2).

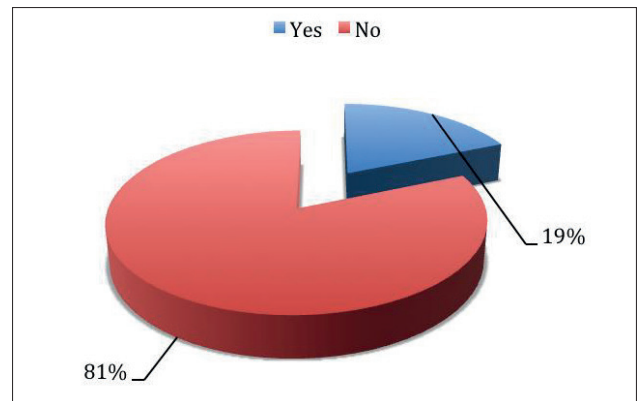


Figure 2. Thireomegaly confirmation by physical examination

The maximum deviation from the average baseline hormone levels shows TSH level, while T₃ is within the reference values, and T₄ values are slightly lower.

	Average value of hormones in time when is diagnosis confirmed	Reference Value
T ₃	2.32 nmol/l	1.3 – 4.86 nmol/l
T ₄	82.29 nmol/l	96.33 – 224.33 nmol/l
TSH	31.66 mIU/l	0.86 – 6.5mIU/l

Table 1. Average value of hormones in time when is diagnosis confirmed

The average TSH value at the time of diagnosis was significantly higher compared to the reference value for all age groups except that the largest deviation was noticed in the age group of 0-1 months.

Ultrasound examination was used in 44 (48.35%) cases, and among patients examined with ultrasound in 22 (50%) cases the struma was confirmed. Ultrasound findings in most cases 14 (31.81%) demonstrated diffuse struma and Hashimoto thyroiditis together, followed by normal results in 11 (25%) cases, hypoplastic thyroid gland in 7 (15.90%) cases, the very diffuse struma in 6

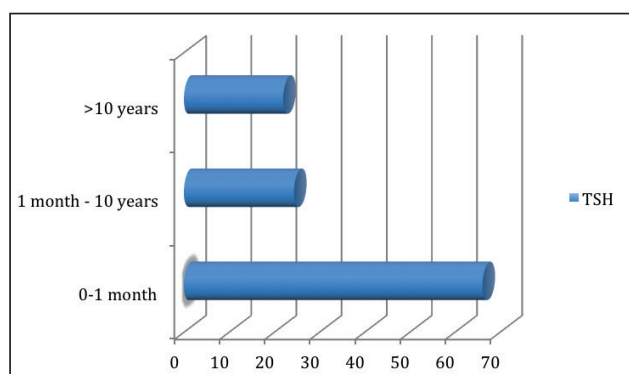


Figure 3. TSH value according to age of patients

(13.63%) of cases, while the nod-like and cystic glands and the Hashimoto thyroiditis is registered in 2 (4.54%) cases, the parenchyma was not visualized in 2 (4.54%) cases, of which one ectopia glands and the second state after total thyroidectomy due to Ca of the gland. In relation to the etiology of hypothyroidism most patients belong to a group where hypothyroidism is associated with other diseases and conditions (27; 29.67%), and the least with the congenital hypothyroidism with 18 (19.78%) of cases. Most patients with congenital hypothyroidism was female (11; 61.11%), while the overall average age at diagnosis was 12 days. Most patients with Hashimoto thyroiditis are female (19; 90.47%), while the overall average age at diagnosis was 11.33 years. Most patients with ordinary hypothyroidism was female (16; 64.00%), while the overall average age at diagnosis was 7.32 years. Distribution of hypothyroidism in relation to sex is approximately equal what is to be expected given that this is a hypothyroidism related with other diseases and conditions, and the average age at diagnosis was 7.21 years. The average dose of L-thyroxine in the age of 0-1 months was 50 μg , 1 month–10 years and 37.5 μg , and the group of patients over 10 years, 65 μg .

5. DISCUSSION

In our sample girls had the hypothyroidism twice more often than boys. Epidemiological studies suggest a higher incidence of thyroid disease and hypothyroidism especially in female population up to six times. Our data correlate with the general conclusion on the higher incidence of hypothyroidism in girls. Nearly 20% of patients have congenital hypothyroidism also with predominance of females. Congenital hypothyroidism (CH) occurs in approximately 1:2,000 to 1:4,000 newborns (6). Prior to the onset of newborn screening programs, the incidence was in the range of 1:7,000 to 1:10,000 (6,7). Before the diagnostic process is necessary to take high-quality medical history of the patient (from perinatal age, including gestational and prenatal history). At the time of diagnosis nearly 40% of patients were aged up to 10 years and the same number at age over 10 years. The incidence of hypothyroidism in our community is twice as high in the pre-teen and children aged over 10 years compared to congenital hypothyroidism. Struma of thyroid gland occurs in one-fifth of our patients. The assessment of the existence of struma was performed by physical examina-

tion which reliably according to the literature is around 60% even for an experienced doctor–examiners. Thus, the real incidence of struma detected by physical examination is 32%. Data on the incidence of struma testifies to the fact that hypothyroidism in most of the patients did not last long and the struma has not developed. All patients with hypothyroidism have a tendency to develop a struma. The existence of struma without hormone deficiency may be the expression of the status of iodine deficiency in the region. Also interesting are the average values of thyroid hormones at the time of diagnosis.

TSH mostly deviates from the upper reference value and if we take into account the literature data on desirable variability during therapy of TSH from 0.1 to 5.5 mIU/L, then it is six times more than the upper limit of the reference value. TSH is a long-term indicator of thyroid function or is slow to respond to the change of the target hormone and is of interest to observe the dynamics in the period of 4-6 months. The value of T_3 hormone is within the reference value, despite extremely high TSH and T_4 just below the lower limit value of euthyroid state. It is obvious that young body puts great effort to synthesize in this time the maximum desirable amount of T_3 and T_4 , and markedly elevated TSH indicates hypothyroidism durability. The striking is the average value of TSH with congenital hypothyroidism of 66.12 mIU/l, which undoubtedly confirm this diagnosis and suggest an urgent initiation of therapy. This finding of TSH is three times higher than TSH 20 representing by itself evidence of congenital hypothyroidism, and four times higher than the level of TSH 15 in which the newborn is immediately call for retesting after the screening on congenital hypothyroidism.

Ultrasound examination of the thyroid gland is used in the process of diagnosis in about half of patients. This is a useful diagnostic element to display the volume and morphology of the thyroid gland but because of limited opportunities due to prompt admission and review as part of the initial diagnostic is not always performed. A special benefit for the monitoring of these patients would have a portable (hand held) ultrasound device–and machine that would produce imaging and continuously monitor the evolution of morphology in relation to the functional status of the thyroid gland. The frequency of the ultrasound struma in examined patients of about 50% indicates failure of clinical palpation as thyroid volume estimation method, because of that it is an indication for the administration ultrasound in case of suspected struma or the existence of the node in the thyroid gland.

Interesting is the etiologic classification of hypothyroidism according to ultrasound findings. Most patients were with diffuse struma and morphological substrate that on ultrasound looks like Hashimoto thyroiditis, which is consistent with literature data. Normal ultrasound–and both volumetric and morphological finding is found in as many as 25% of the examined patients. Often children with gracile neck or with protruding thyroid cartilage larynx appears magnified as ultrasound refute findings although clinical and laboratory there is verified

hypothyroidism. Finding hypoplastic thyroid gland is not rare and corresponds to a later stage of Hashimoto thyroiditis or congenital hypoplasia of the thyroid. It is interesting that in two children ultrasound obtained findings did not visualize the thyroid gland and in the case of congenital hypothyroidism and thyroidectomy in children with thyroid cancer. The incidence of nodes and cyst formation in ultrasound examination of the thyroid gland is not large and it is only 4.54% (2 patients), which indirectly speaks about fortunately a small number of potential thyroid cancer, which generally always evolve from a cold thyroid nodule. A quarter of our patients have the so-called ordinary hypothyroidism without elevated antibodies. This form of thyroid insufficiency begins on average in prepubertal age (the average age of diagnosis 7.21 years) and is more common in girls. As a separate entity, we pointed out the occurrence of hypothyroidism with other diseases and conditions existing at the time of diagnosis. It occurs with type 1 diabetes mellitus, slowed growth, Down syndrome, vitamin D-resistant rickets, panhypopituitarism and other chronic diseases and conditions.

The treatment of our patients was with the replacement therapy with L-thyroxine. Patients with congenital hypothyroidism are usually introduced with higher initial dose of the drug in order to minimize the already possibly resulting consequences of reduced thyroid function. Our therapy is completely in accordance with these rules and is in the first month was 50 µg per dose. As child grows the dose of the drug decreases, and an average of 4 mg/kg of body weight, a further increment of body weight dose is relatively smaller calculated on kg of BW. Doses of L-thyroxine are in older children correlated with the therapeutic rules. The American Academy of Pediatrics recommends: at two and four weeks after the initiation of L-thyroxine treatment; every 1-2 months during the first 6 months of life; every 3-4 months between 6 months and three years of age; every 6-12 months thereafter until growth is complete; Four weeks after any change in dose (more frequently if results are abnormal or non-compliance is suspected) (9).

6. CONCLUSION

Hypothyroidism is the second most common endocrine disease in children's age (after TYPE 1 DM), with a predominance of females. Congenital hypothyroidism has about one-fifth of patients. Physical examination revealed in about one fifth of patients the struma of the thyroid gland; TSH levels is critical for the diagnosis and correction of therapy in pediatric patients with hypo-

thyroidism. Congenital hypothyroidism is diagnosed on average at the age of 12 days, which is optimal period for therapeutic response; Substitution treatment is carried out by L-thyroxine which have relatively reduced doses from neonatal age onwards; Future research should be directed to the assessment of iodine deficiency in the region in which our patients lives, as an important etiological factor for the development of struma and thyroid gland pathology.

- Conflict of interest: On behalf of all authors, the corresponding author states that there is no conflict of interest.

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