

## The severity of ophthalmic manifestations in children and young adults with thyroid diseases

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**Introduction.** Graves' disease (GD) is an organ specific autoimmune disorder which affects the thyroid gland, orbital and periorbital tissues and pretibial skin [1]. In majority of cases (80%) Graves' ophthalmopathy (GO) is associated with hyperthyroidism. In 5 to 10% of cases, ophthalmopathy may occur in euthyroid status, primary hypothyroidism, Hashimoto's thyroiditis [2]. Studies by investigators showed many factors contributing to the development of ocular symptoms in GO [3] There have been a few series of paediatric cases of Graves' disease in the literature describing the eye manifestations [4]. Ocular signs of ophthalmopathy were documented in 62.7% of children [5]. The severity of GO was defined according to the degree of ocular involvement by EUGOGO Multi-center study on the characteristics and treatment strategies of patients with Graves' orbitopathy: There was made consensus on how to assess the severity of the various symptoms and signs caused by the orbitopathy [6]. Severe forms of GO can lead to sight-threatening complications. Evaluation of the severity of GO can help to make better decision for treatment of patients with GO [7]. There are many articles about eye signs in adults with thyroid diseases; however, few have examined the clinical features of the disorder in children and adolescents. Due to this lack of data, we aimed to investigate the prevalence and severity of ophthalmopathy in patients with thyroid diseases in our Clinic.

**Materials and methods.** There were investigated 95 patients with thyroid diseases who attended to the Eye and Endocrine clinics of the Lithuanian University of Health Sciences. The group under 18 years included 34 patients, and the group from 18 to 34 years - 61. The diagnosis of thyroid diseases was based on clinical and laboratory findings of diffuse enlargement of thyroid gland, free triiodothyronine (T3) and thyroxine (T4) levels, raised free T4 or T3 levels, suppressed TSH levels. A comprehensive ophthalmic examination was performed in a standardized way for all patients. Best corrected visual acuity was documented by Snellen chart. Retraction of either upper or lower eyelid was defined by any exposed superior or inferior sclera beyond the limbus in the primary gaze. The degree of proptosis was measured by digital image processing system consisting of Hertel exophthalmometer, video camera, and personal computer. Slit lamp examination was performed in order to detect conjunctival injection, chemosis. Corneal involvement was assessed with fluorescein staining under slit lamp biomicroscopy. Fundus examination was done for evaluation of optic disc and retina.

Assessment of disease severity was derived from L. Bartalena et al. (2008) [6]. For this study, according to the most recent EUGOGO definition mild GO was characterized by one or more of the following features: mild soft tissue swelling, minor lid retraction ( $< 2$  mm), exophthalmos  $< 3$  mm above normal data, no or only intermittent diplopia, no corneal or optic nerve involvement.

Moderate disease was when patient has any one or more of the following features: marked soft tissue swelling, lid retraction  $\geq 2$  mm, and/or proptosis exophthalmos  $\geq 3$  mm above normal records, and/or inconstant diplopia, and/or punctate staining of the cornea, but no optic nerve involvement.

Severe eye disease was defined as constant diplopia and/or optic nerve involvement - dysthyroid optic neuropathy (DON) (optic disc swelling or pallor, a visual field defect, or if visual acuity less than 0.63 in the absence of other reasons for sight loss) or corneal breakdown.

Statistical analysis was conducted using statistical SPSS software package (Version 16.0). The studied characteristics were expressed as mean value and standard deviation (SD). The statistical difference between patient and control groups was performed using Mann-Whitney and Student's t- tests.

**Results.** The mean age of children with thyroid diseases was  $13.7 \pm 3.5$  years, ranged from 4 to 18 years, 29 girls and 5 boys. The mean age of young adults was  $25.3 \pm 2.6$  years, ranged from 18 to 34 years, 54 females and 6 males.

Most children with thyroid diseases 14 (41.2%) had milder forms of ophthalmopathy, whereas 4 (11.8%) had moderate and no patients had severe eye disease.

Young adult patients 35 (57.38%) had mild forms of ophthalmopathy, 11 (18.0%) had moderate and 4 (6.6%) had severe eye disease.

The frequency of clinical signs is presented in Table 1. The most common apparent ocular sign among children patients with thyroid diseases in this study was eyelid retraction which was noticed in 35.3 % of patients. Lid retraction was bilateral in all of these cases. Eyelid edema appeared in 14.7% of children. Eight patients with thyroid diseases (23.5%) were detected to have mild proptosis. Injection of the conjunctiva was noticed in 14.7% of patients. The frequency of corneal staining and erosions in children with thyroid diseases was very low, only 1 patient (2.9%) stained positive with fluorescein in his cornea and had corneal erosion. No superior limbic keratitis or corneal ulceration was detected. None of the children with thyroid diseases was found to have visual impairment or optic nerve dysfunction.

Most of the young adult patients had eyelid position signs and edema. Eyelid retraction was observed in 57.5% and eyelid edema - in 65.6% of patients. Proptosis was found in 43 (70.5%) of young adult patients. It was bilateral in the majority of cases (88.4%). The differences in most ocular signs were significant between children and young adults groups ( $p < 0.05$ ).

**Table 1.** Frequency of ocular signs in children and young adults with thyroid diseases

Ocular signs	Children	Young adults
Eyelid retraction	12 (35.3%)	35 (57.5%)
Diplopia intermittent	1 (2.9%)	4 (6.6%)
Diplopia constant		2 ((3.3%)
Proptosis	8 (23.5%)	43 (70.5%)
Corneal staining	1 (2.9%)	6 (9.8%)
Eyelid edema	5 (14.7%)	40 (65.6%)
Conjunctival injection	5 (14.7%)	32 (52.5%)
Chemosis	4 (11.8%)	29 (47.5%)
Corneal erosions	1 (2.9%)	6 (9.8%)
Optic neuropathy	0	1(1.6%)

Six young adult patients (9.8%) who had their corneas stained positive with fluorescein. Clinically, all of them had punctate epithelial erosions. One young patient had clinically detectable swollen optic nerve disc and dilated retinal veins.

**Discussion.** In our study, most children with thyroid diseases (44.1%) were assessed as having mild eye disease, 11.8% were with moderate GO.

The prevalence of eyelid retraction in children with thyroid diseases was 35.3 %. Mild proptosis was in 23.5% of children. Conjunctival injection and eyelid edema had 14.7% of children patients. No severe ocular features were noted in children group.

Mild Graves’ of ophthalmopathy in young adults with thyroid diseases was in 57.38% of patients, moderate – in 18.0 % and severe – in 6.6%.

In 57.5% of young adults appeared eyelid retraction. Most young patients had at least signs of soft tissue involvement, eyelid swelling – in 65.6%. Upper eye lid swelling being more frequent than lower eye lid involvement. Mild to moderate proptosis was noted in 70.5% of young adult patients with thyroid diseases. In comparing with children group in young adults there were corneal changes, in 9.8% - corneal staining and epithelial erosions. One (1.6%) of our young patient had optic neuropathy. Visual impairment (visual acuity and visual field changes) was the main symptom.

The prevalence of most of the ocular complications increased with increasing age.

We examined patients with thyroid diseases for the severity of ophthalmopathy. The clinical presentation of our patients was compared with that of previously reported studies. In our study the severity of ocular signs in children with thyroid diseases was less than that seen in young adults. Eyelid retraction and proptosis were the predominant signs in 10/11 of patients under the age of 18 years [8].

Eha et al. (2010) revealed that in children and teens Graves’ ophthalmopathy is less common than in adults [8].

Durairaj VD et al. (2006) findings are in agreement with previous reports [9]. W. Chan et al. (2002) showed that the major symptoms in children were a

sense of irritation in the eyes; excessive tearing, eye or retroorbital discomfort, pain. Sight-threatening corneal ulceration or compressive optic neuropathy are thought to be less frequent or absent in children [5]. Other similar studies show that ocular signs were less severe than in adults GO [9,10].

**Conclusions.** Our investigation confirms that in children ocular signs were less severe than young adults with thyroid diseases. This assessment of ophthalmic manifestations is useful for early diagnostics and appropriate treatment.

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We investigated ocular signs of 95 children and young adults with thyroid diseases in our Clinic. Assessment of the ocular manifestations in patients with thyroid diseases allowed us to determine the severity of ophthalmopathy, which was less well defined for the children than in young adults.