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Pediatric Thyroid-Associated Orbitopathy: Clinical Spectrum, Systemic Implications, and Outcomes Over a 26-Year Single-Center Experience

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Abstract

Background:

Thyroid-associated orbitopathy (TAO) is an uncommon extrathyroidal manifestation of Graves' disease in children and adolescents. Compared with adults, pediatric TAO usually presents with a milder clinical course, although its systemic and psychosocial impact may be underestimated.

Methods:

A retrospective case series was conducted including patients younger than 18 years diagnosed with TAO between 1999 and 2025 at a tertiary ophthalmology referral center in Mexico. Demographic characteristics, clinical manifestations, diagnostic studies, treatment modalities, and outcomes were analyzed. A narrative review of the literature was also performed.

Results:

Seventeen patients were included (70.6% female), with a mean age at diagnosis of 12 years. The most frequent clinical manifestations were eyelid retraction (100%) and proptosis (88.2%). No cases of dysthyroid optic neuropathy or irreversible visual loss were identified. Most patients were successfully managed with conservative medical treatment and endocrinologic control. Orbital decompression surgery was required in two patients (11.7%). Clinical outcomes were favorable in all cases.

Conclusions:

Pediatric TAO is an infrequent condition with a generally mild ocular course. Conservative management is effective in most patients, reserving surgery for selected cases. Pediatric TAO should be regarded as part of a systemic autoimmune disorder with ocular, behavioral, and psychosocial implications distinct from adult disease.

Introduction

Thyroid-associated orbitopathy (TAO), also known as thyroid eye disease, is an uncommon extrathyroidal manifestation of Graves' disease in children and adolescents [1–3]. Compared with adults, pediatric patients typically exhibit a milder clinical phenotype, characterized by eyelid retraction, mild proptosis, and limited inflammatory activity. Severe complications such as dysthyroid optic neuropathy or orbital apex syndrome are rare in this population but have been reported [4, 5].

The immunopathogenesis of TAO is largely shared across age groups and involves autoimmune activation of orbital fibroblasts mediated by the thyroid-stimulating hormone receptor, leading to downstream inflammatory and remodeling pathways [6, 7]. Nevertheless, the clinical expression, disease course, and response to treatment in pediatric patients differ from those observed in adults, likely reflecting age-related immunologic and hormonal factors [2, 3, 8].

Evidence guiding management in pediatric TAO remains limited and is derived mainly from small case series, multicenter cohorts, and narrative reviews [3, 5, 9]. Current recommendations favor a conservative approach in most children, reserving systemic immunosuppression or surgical intervention for progressive or severe cases, in accordance with pediatric endocrine and ophthalmic guidelines [10–12]. Given the rarity of this condition and the paucity of long-term data, institutional experiences remain valuable. This study aims to describe the clinical spectrum, diagnostic evaluation, management strategies, and outcomes of pediatric TAO over a 26-year period, highlighting its distinctive features compared with adult disease.

Methods

A retrospective case series was conducted including patients younger than 18 years diagnosed with thyroid-associated orbitopathy between 1999 and 2025 at a tertiary ophthalmology referral center in Mexico. Demographic variables, clinical manifestations, diagnostic studies, treatment modalities, and outcomes were collected from medical records. A narrative review of the literature was also performed to contextualize the findings. This study adhered to institutional ethical standards and the principles of the Declaration of Helsinki.

This retrospective observational study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the institutional ethics committee of the Asociación para Evitar la Ceguera en México (APEC). Due to the retrospective nature of the study and the use of anonymized clinical data, the requirement for informed consent was waived.

Results

Demographic characteristics of the study population are summarized in Table 1.

Table 1
Demographic characteristics of pediatric TAO cases (1999–2025)

Variable	n	%
Total patients	17	100
Female	12	70.6
Male	5	29.4
Mean age (years)	12	—
Most frequent age (years)	17	—

Seventeen patients were included, of whom 12 (70.6%) were female and five (29.4%) were male. Age at diagnosis ranged from 8 to 17 years, with a mean age of 12 years. The most common clinical manifestations were eyelid retraction (100%) and proptosis (88.2%). Typical orbital features similar to

those observed in adult disease are shown in Fig. 1. Diplopia and dysthyroid optic neuropathy were not observed. Five patients received exclusively medical treatment, while two patients (11.7%) required orbital decompression surgery. All patients showed favorable clinical evolution following achievement of euthyroid status, and no cases of irreversible visual loss were documented. The frequency of the main clinical manifestations is shown in Table 2. Treatment modalities and clinical outcomes are summarized in Table 3.

Table 2
Main clinical manifestations

Clinical manifestation	n	%
Eyelid retraction	17	100
Proptosis	15	88.2
Diplopia	0	0
Dysthyroid optic neuropathy	0	0
Caruncular hyperemia	3	17.6

Table 3
Treatment modalities and outcomes

Treatment	n	%
Medical treatment only	5	29.4
Medical treatment with follow-up	10	58.9
Orbital decompression surgery	2	11.7
Favorable outcome	17	100

Discussion

In our series, pediatric thyroid-associated orbitopathy represented a very small proportion of cases managed over a 26-year period. The observed female predominance and adolescent age distribution are consistent with previously published international data, including the multicenter study by Ionescu et al. Clinical presentation was predominantly mild, characterized by eyelid retraction and proptosis, with complete absence of dysthyroid optic neuropathy, supporting previous reports that severe disease is uncommon in the pediatric population. Mild clinical findings in a younger pediatric patient are shown in Fig. 2.

Beyond ocular findings, the clinical course of pediatric thyroid-associated orbitopathy in our cohort appeared to be closely linked to the systemic activity of Graves' disease. Achievement of euthyroidism was associated not only with stabilization or improvement of orbital manifestations, but also with a general clinical improvement observed by caregivers and clinicians. This systemic–ocular relationship

underscores that pediatric thyroid-associated orbitopathy should be understood as part of a multisystem autoimmune disorder rather than an isolated orbital condition.

Importantly, several patients in our series exhibited non-ocular manifestations related to thyroid dysfunction, including behavioral changes such as irritability, mood fluctuations, decreased attention span, and difficulties in academic performance during periods of active disease. An example of clinically active thyroid-associated orbitopathy in an adolescent patient is illustrated in Fig. 3. The systemic and behavioral manifestations associated with pediatric thyroid-associated orbitopathy observed in our cohort are summarized in Table 4. Although these aspects were not formally quantified using validated behavioral or quality-of-life instruments, they were consistently reported by parents and caregivers and improved following adequate endocrinologic control. These observations are consistent with prior pediatric endocrine literature describing the neuropsychological and behavioral impact of thyroid hormone imbalance in children and adolescents.

Table 4
Systemic and behavioral manifestations associated with pediatric thyroid-associated orbitopathy

System involved	Manifestations	Clinical relevance in children
General / Metabolic	Weight loss, heat intolerance, increased appetite, fatigue	Often precede ocular findings; related to hyperthyroid state
Cardiovascular	Palpitations, tachycardia	May be subtle; important for systemic assessment
Neuromuscular	Fine tremor, muscle weakness	Frequently reported during active disease
Sleep regulation	Insomnia, restless sleep	Common and often under-recognized
Neuropsychological / Behavioral	Irritability, anxiety, mood swings, emotional lability	Frequently reported by parents; improves after achieving euthyroidism
Cognitive / Academic performance	Decreased attention span, impaired concentration, poor school performance	Particularly relevant in school-aged children and adolescents
Autonomic	Excessive sweating, heat intolerance	Reflects increased sympathetic activity
Growth and development	Accelerated bone age, growth disturbances (rare)	Related to prolonged thyroid hormone imbalance
Psychosocial	Reduced self-esteem, social withdrawal	May be influenced by ocular appearance and systemic symptoms

Footnote: Systemic manifestations are primarily related to thyroid dysfunction but frequently coexist with ocular disease activity in pediatric patients.

Regarding management, the majority of patients were successfully treated with conservative medical strategies focused on systemic disease control, with surgical intervention reserved for selected cases with significant functional or cosmetic impairment. The low rate of orbital decompression in our cohort compared with other series may reflect early diagnosis, close interdisciplinary follow-up, and an emphasis on medical stabilization prior to considering surgical options.

Conclusions

Pediatric thyroid-associated orbitopathy is an infrequent condition with a predominantly mild ocular course; however, its clinical impact extends beyond orbital manifestations. In our 26-year single-center experience, ocular findings generally evolved in parallel with systemic thyroid dysfunction, and clinical improvement was closely associated with achieving and maintaining euthyroidism. Importantly, several patients exhibited systemic and behavioral manifestations related to thyroid disease activity, including changes in mood, irritability, decreased attention, and reduced academic performance, underscoring the broader impact of Graves' disease in the pediatric population.

Surgical intervention was required only in a small subset of patients with significant functional or cosmetic involvement. These findings highlight that pediatric thyroid-associated orbitopathy should be approached as part of a systemic autoimmune disorder with potential ocular, systemic, and psychosocial consequences. Early recognition, interdisciplinary collaboration between ophthalmology and endocrinology, and timely control of thyroid dysfunction are essential not only to optimize ocular outcomes but also to improve overall well-being, behavior, and quality of life in affected children and adolescents.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the institutional ethics committee of the Asociación para Evitar la Ceguera en México (APEC). Due to the retrospective nature of the study and the use of anonymized clinical data, the requirement for informed consent was waived.

Consent for publication

Written informed consent for publication of clinical images was obtained from the patients' legal guardians.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors’ contributions

AGE contributed to study conception and design, data collection, analysis, and drafting of the manuscript. FOG contributed to clinical supervision, interpretation of data, and critical revision of the manuscript. All authors read and approved the final manuscript.

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Use of Generative Artificial Intelligence

During the preparation of this manuscript, the authors used ChatGPT (OpenAI, GPT-5.2) to assist with language editing, clarification of scientific writing, and improvement of structure and style. The content was reviewed, edited, and validated by the authors to ensure accuracy, originality, and compliance with journal standards. The use of this tool did not replace the authors’ critical thinking, data interpretation, or responsibility for the final content of the manuscript.

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Figures

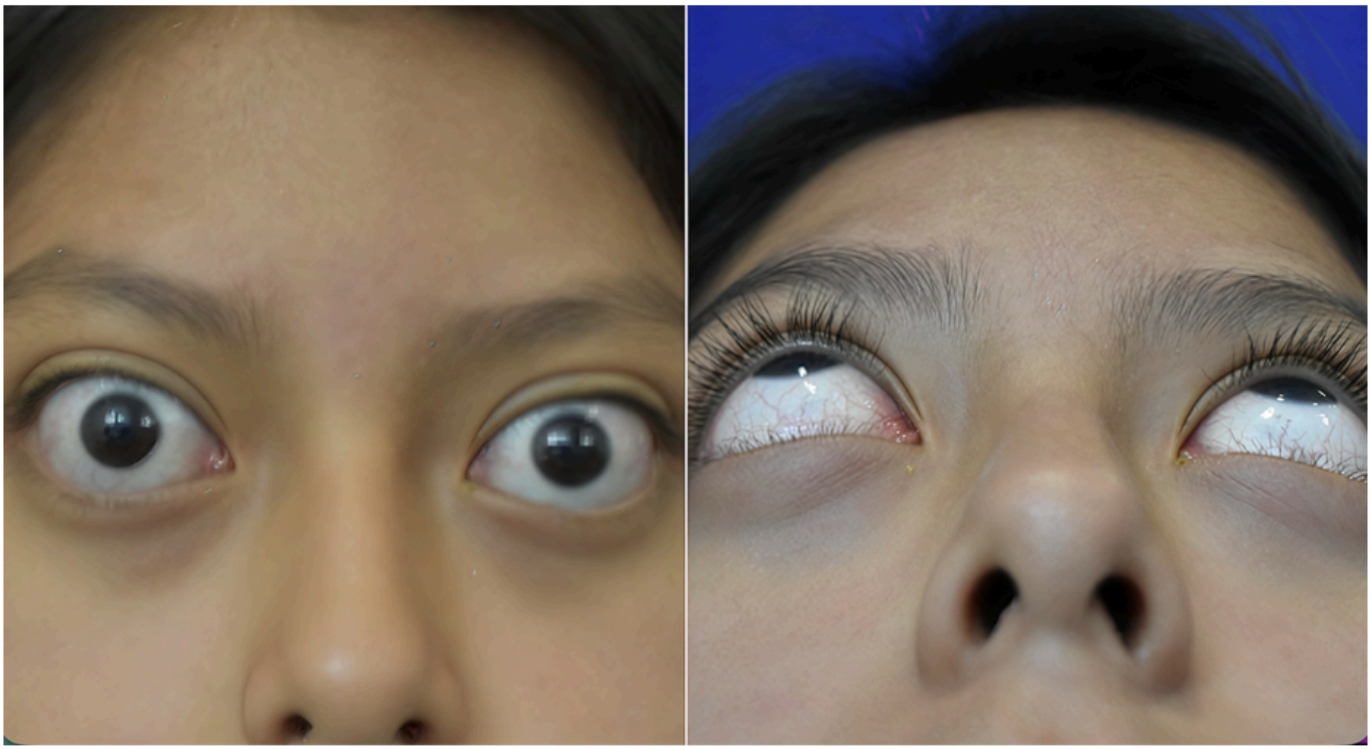


Figure 1

Orbital features similar to those observed in adult disease

(A) Frontal view showing eyelid retraction and mild proptosis in a 13-year-old patient at initial presentation.

(B) Upward gaze view demonstrating inferior scleral show in the same patient.



Figure 2

Mild clinical findings in a younger pediatric patient.

(A) Frontal view of a 10-year-old patient showing mild eyelid retraction.

(B) Upward gaze view demonstrating right-sided proptosis.



Figure 3

Clinically active thyroid-associated orbitopathy

(A) Frontal view at 17 years of age showing eyelid retraction and conjunctival hyperemia at the extraocular muscle insertions

(B) Upward gaze view at 17 years of age showing bilateral proptosis