Brief communication

Thyroid eye disease in patients at the Salvadoran Social Security Institute

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Abstract

Introduction. Thyroid eye disease is an autoimmune inflammatory disease more common in women and negatively influenced by factors such as smoking and age. It affects orbital structures such as the extraocular muscles and periocular fat. Clinical activity and severity determine its treatment and prognosis. **Objective.** The epidemiological and clinical characteristics of thyroid eye disease were determined in the population that consulted in Ophthalmology at Salvadoran Social Security Institute Specialty Hospital between January 2021 and December 2022. **Methodology.** A descriptive, cross-sectional study was conducted. Occurrence, clinical activity, thyroid status, and treatment were determined through a review of clinical records. **Results.** The disease occurred in 14.28 %, with a female predominance and a mean age of 46.21 years. A total of 61.42 % had best-corrected visual acuity was < 0.18), and 6 % reported smoking. The most frequent signs were eyelid edema and conjunctival hyperemia. Hypothyroidism occurred in 45.71 % of patients. The most common treatment was topical ocular lubricants in patients with mild thyroid disease. **Conclusion.** Thyroid eye disease is more common in women, with a higher presence in the sixth decade of life and controlled thyroid disease. Clinically inactive disease with good best-corrected visual acuity predominated. Patients with moderate to severe clinical activity due to thyroid disease received treatment with systemic steroids and surgical intervention.

Keywords
Graves Ophthalmopathy, Hyperthyroidism, Hypothyroidism, Glucocorticoids.

Resumen

Introducción. La orbitopatía tiroidea es una enfermedad inflamatoria autoinmune, más frecuente en mujeres, cuya evolución se ve influenciada por factores como el tabaquismo y la edad. Compromete estructuras orbitarias, en particular los músculos extraoculares y el tejido adiposo periocular. La actividad inflamatoria clínica y la severidad constituyen determinantes clave para orientar el tratamiento y establecer el pronóstico. **Objetivo.** Caracterizar el perfil clínico y epidemiológico de la orbitopatía tiroidea en la población que consultó en Oftalmología del Consultorio de Especialidades del Instituto Salvadoreño del Seguro Social entre enero 2021 y diciembre 2022. **Metodología.** Estudio transversal descriptivo. Se determinó la distribución de la enfermedad, la actividad clínica, niveles de hormonas tiroideas y tratamiento a través de la revisión de expedientes clínicos. **Resultados.** La enfermedad se presentó en el 14,28 %, con predominio en el sexo femenino y una edad media de 46,21 años. El 61,42 % presentó una agudeza visual mejor corregida < 0,18, mientras que el 6 % refirió consumo de tabaco. Los signos clínicos más frecuentes fueron el edema palpebral y la hiperemia conjuntival. El 45,71 % de los pacientes se encontraba en estado hipotiroideo. El tratamiento más utilizado consistió en lubricantes oculares tópicos en pacientes con enfermedad tiroidea leve. **Conclusión.** La orbitopatía tiroidea predominó en mujeres de mediana edad, con mayor frecuencia en la sexta década y en contexto de enfermedad tiroidea controlada. Se observó un predominio de formas clínicamente inactivas, con adecuada agudeza visual corregida. En los casos con actividad inflamatoria moderada a severa, se indicó tratamiento con glucocorticoides sistémicos y manejo quirúrgico.

Palabras clave
Oftalmopatía Asociadas a la Tiroides, Hipertiroidismo, Hipotiroidismo, Glucocorticoides.

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Orbitopatía tiroidea en pacientes del Instituto Salvadoreño del Seguro Social

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Introduction

Thyroid orbitopathy[1] is a chronic edematous and inflammatory condition caused by stimulation of thyroid-stimulating hormone receptors (TSH) in fibroblasts and adipocytes of the retroorbital tissue by antibodies against the TSH receptor; this stimulates the growth of extraocular muscles and an increase in orbital fat.[2-5] It is generally bilateral, but may be asymmetric in 4 % to 14 % or unilateral in 9 % to 34 % of cases.[2,6] It is more common in females, with a female-to-male ratio of 2.1:1.[7] It usually manifests between the third and fifth decades of life, eigth to ten with a bimodal incidence in the 40 to 44 and 60 to 64 age groups in women and the 45 to 49 and 65 to 69 age groups in men.[8]

It is more severe in men over 50.[7-10] It has a prevalence of up to 27 %.[11] It is seven times more common in smokers than in nonsmokers,[12] and is associated with a poorer therapeutic response.[13]

This orbitopathy presents with a spectrum of signs and symptoms that are evaluated to determine its clinical activity and treatment.[2,14] The most common signs are eyelid retraction (Dalrymple), delayed upper eyelid closure (Von Graefe), eyelid edema, exophthalmos, lagophthalmos, exposure keratitis, chemosis, and conjunctival hyperemia.[15,16] Bone and soft tissue characteristics are assessed for the surgical planning of orbital decompression, using complementary imaging studies such as magnetic resonance imaging, computed tomography, ultrasound, and Doppler imaging.[16-19]

There are also several systems for classifying clinical activity, such as the Clinical Activity Score (CAS). This system initially assesses spontaneous retrobulbar pain and pain associated with eye movements, as well as eyelid erythema and edema, caruncle edema, conjunctival injection, and chemosis. In subsequent visits, an increase in proptosis of ≥ 2 mm, a decrease in eye movements of ≥ 8°, and a reduction in visual acuity of ≥ 1 line on the Snellen chart are considered. Additionally, the Vision, Inflammation, Strabismus, and Appearance (VISA) classification system, one of the most widely used, is employed.[13,15,20-22]

However, in El Salvador, there are currently no studies providing epidemiological, clinical, and therapeutic data characterizing this condition or its ophthalmological complications. In this study, we conducted an epidemiological and clinical characterization of orbital disease in patients with thyroid disease who consulted the Ophthalmology Service at the Specialty Clinic of the Salvadoran Social Security Institute between January 2021 and December 2022.

Methodology

The study design was a descriptive cross-sectional study based on a review of clinical records. The study population consisted of all patients evaluated at the Ophthalmology Clinic of a health center in San Salvador, El Salvador, from January 2021 to December 2022 with thyroid-associated orbitopathy.

A total of 490 clinical records of patients with thyroid disease were reviewed using a structured data collection form that included the variables of interest. Patients aged 18 years or older were included, referred from the Endocrinology Service of the National Institute of Health, with a diagnosis of thyroid-associated orbitopathy for ophthalmological evaluation. Incomplete clinical records were excluded, as were patients with thyroid disease without orbital involvement and those with proptosis secondary to neoplasms, vascular malformations, or unrelated orbital inflammatory processes.

The following variables were analyzed: presence of thyroid-associated orbitopathy and clinical activity at the initial consultation, assessed using the CAS, which includes spontaneous retrobulbar pain, pain on eye movements, eyelid erythema and edema, as well as caruncle edema, conjunctival injection, and chemosis.[15]

In addition, epidemiological variables (age, sex, and smoking status) were collected, as well as thyroid hormone levels: total triiodothyronine (T3T), free thyroxine (T4L), and serum thyroid- stimulating hormone. Thyroid function status (hyperthyroidism, euthyroidism, or hypothyroidism) and the type of therapeutic approach were determined. The latter was classified as medical management (including topical, systemic, oral, or intravenous steroids, biological response modulators, and topical ocular antihypertensives) and surgical management, represented by orbital decompression.

Thyroid status was determined by the Endocrinology Service through clinical evaluation and laboratory values of the thyroid hormones TSH, T3T, and T4L. It was classified as hypothyroidism (serum TSH levels greater than 4.4 mU/L, T3T normal or less than 60 ng/dL, and T4L < 0.8 ng/dL), euthyroid (TSH 0.4-4.4 mU/L, T3T 60-180 ng/dL, and T4L 0.8-1.6 ng/dL) or hyperthyroidism (suppressed TSH < 0.1 mU/L, T3T > 180 ng/dL, and T4L > 1.6 ng/dL). Visual acuity was classified according to visual category and degree of impairment using a standardized logMAR acuity scale measured at a distance of six meters, with normal vision defined as 0.00-0.18; mild visual impairment as 0.30-0.48; moderate visual impairment as 0.54-1.00; severe visual impairment as 1.00-1.30; and blindness as greater than 1.30. Moderate and severe visual impairment were considered low vision, and visual impairment was defined as moderate or severe visual impairment or blindness.

The study was conducted in accordance with the ethical principles established by the World Medical Association, as per the Declaration of Helsinki (2013 version) for medical research involving human subjects. It was also approved by the Research Ethics Committee of the Salvadoran Social Security Institute, under methodological code 708O212AO22 and sequential registration number 2023-16.

Data normality was assessed using the Kolmogorov-Smirnov test. In the descriptive statistics, quantitative variables were expressed as measures of central tendency and dispersion (mean and standard deviation), while qualitative variables were presented as absolute and relative frequencies. The statistical data were entered into the Statistical Package for the Social Sciences (SPSS, version 31.0; Chicago, IL, United States).

Results

Thyroid-associated orbital disease was diagnosed in 70 patients (14.28 %) out of the 490 cases with a diagnosis of thyroid disease who were referred for an ophthalmological consultation. The distribution by sex showed a predominance of females, with 55 patients (79 %) compared to 15 (21 %) males. The mean age was 46.21 years (SD: 13.3), with the highest frequency in the 50-59 age group (20 patients), followed by the 30-39 age group (14 patients).

Forty-three patients (61.42 %) had best-corrected visual acuity between 0.0 and 0.18. Seven point fourteen percent had low vision, and 11.43 % had visual impairment. (Table 1). Seventeen patients (24 %) were identified as non-smokers, while four (6 %) reported smoking, without providing data on the amount consumed. The rest did not provide data on smoking in their medical records.

When characterizing clinical activity using the CAS, 64 patients (91.43 %) had a CAS of three points or less. Twenty-four patients (34.29 %) did not present signs or symptoms associated with thyroid-related eye disease. However, the most common sign was eyelid edema, followed by conjunctival hyperemia (Figure 1).

Upon assessment of thyroid status based on clinical evaluation and thyroid test results (total T3, free T4, and TSH) by the Endocrinology department, 32 (45.71 %) of the patients were found to be hypothyroid, 27 (38.57 %) hyperthyroid, and the remainder euthyroid.

The most frequently administered treatment was topical eye lubricant in 67 patients (95.71 %). Topical steroids were administered via the eye in five patients (7.14 %), orally in one (1.43 %), and intravenously in six (8.57 %). One patient received treatment with a biologic response modifier (tocilizumab). Surgical intervention was performed in eleven patients, with orbital decompression being the most common procedure (Table 2).

Discussion

An epidemiological and clinical characterization of thyroid-associated orbitopathy was performed in the population treated at an ophthalmology clinic. A predominance in females was observed, consistent with what has been described in the literature,[7] as well as a higher prevalence in men over 50, an age group associated with a less favorable prognosis.[7-10]

More than half of the patients had best-corrected visual acuity within normal parameters. However, it was not possible to determine whether cases of visual impairment were directly related to optic neuropathy secondary to thyroid-r thyroid-r to concomitant ocular comorbidities, such as media opacities (corneal, lens, or vitreous) or retinopathies, which constitutes a limitation for the proper interpretation of this finding.

Clinical activity was determined using the CAS, revealing inactive thyroid-associated orbitopathy in most patients; this contrasts with other studies that reported active disease in up to 44 % of patients.[7-10,14,15]

The most common signs and symptoms were eyelid edema and conjunctival hyperemia, in contrast to what has been reported in other studies, where ocular pain and a burning sensation predominate.[15]

The patients in this study were under follow-up by the Endocrinology Department and were receiving treatment for their underlying thyroid disease. Treatment for this condition includes management of the underlying thyroid disease[2,3,9,23-25], management of risk factors such as smoking[2,3,9,15,18,26-28] and

Table 1. Visual Acuity

Visual Acuity (logMAR)	Visual category	N° of patients
0.00 – 0.18	Normal	43
0.30 – 0.48	Mild visual impairment	19
0.54 – 1.00	Moderate visual impairment	4
1.00 – 1.30	Severe visual impairment	1
> 1.30	Blindness	3
Total		70

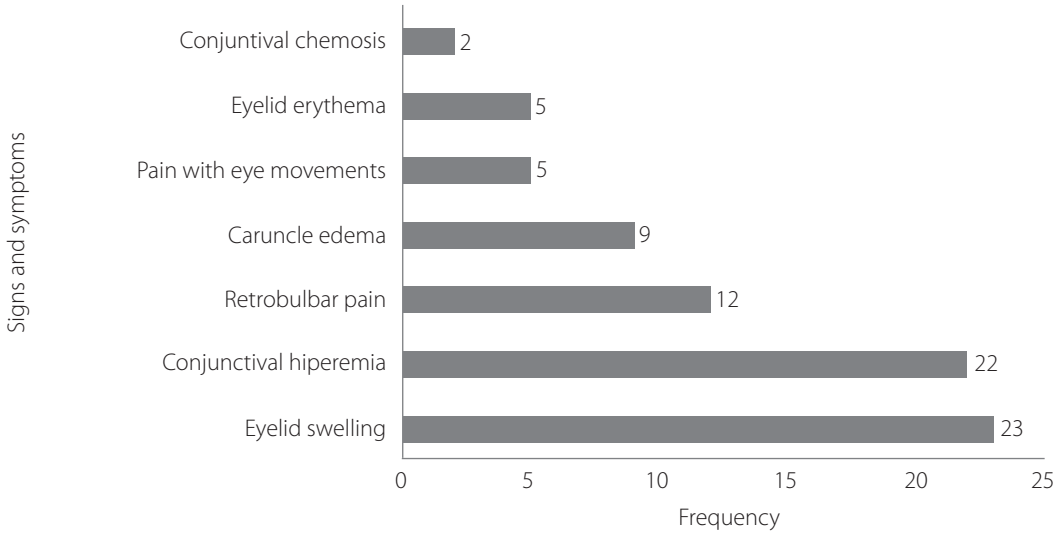

Figure 1. Signs and symptoms associated with thyroid-related eye disease.

Table 2. Treatment of patients

Visual acuity (logMAR)		No. of patients	Percentage
Topical	Lubricant	67	95.71 %
	Steroid	5	7.14 %
	Antihypertensive	9	12.86 %
Oral steroid		1	1.43 %
Intravenous steroid		6	8.57 %
Biological response modifiers		1	1.43 %
Surgical	Orbital decompression	10	14.29 %
	Transpalpebral biopsy	1	1.43 %

treatment of the ocular surface.[9,15] Most were euthyroid or hypothyroid, with TSH, T3, and T4 (total and free) levels within the reference ranges. This finding differs from that reported in other studies, where thyroid-associated orbitopathy was more common in patients with hyperthyroidism.[2,7,8] These findings suggest a timely and appropriate interdisciplinary approach among the involved specialties, which may have contributed to the adequate control of the underlying thyroid disease in the studied population.

The predominant clinical manifestation was inactive orbital disease; consequently, the most indicated treatment consisted of topical eye lubricants in patients with mild forms, in accordance with current recommendations.[9,15] However, oral selenium supplementation has been reported to improve outcomes in cases of mild disease.[9,15] Intravenous steroids such as methylprednisolone are considered the first-line treatment for patients with moderate to severe disease.[9,3,9,15,24] Teprotumumab is the first monoclonal antibody approved by the U.S. Food and Drug Administration (FDA) in 2020 for the treatment of moderate-to-severe disease.[15,23-25,27,29,30] Other medications have been studied for the management of forms resistant to conventional treatment, such as tocilizumab[15,17,24,2531] and rituximab.[15,24,25,32] In this study, systemic steroid treatment was not needed in most patients. Tocilizumab was administered in cases of orbital disease refractory to glucocorticoids.

Surgical treatment involving orbital decompression is reserved for emergency procedures in cases of optic neuropathy, subluxation of the eyeball, or corneal thinning or perforation due to exposure keratitis.[9,24] It is also considered an option following the active phase of orbital disease, provided that clinical signs of stability have been present for at least six to nine months prior.[9,15,24,33]

Among the study's limitations is the inability to determine the interval between the endocrinology referral and the ophthalmological evaluation in patients with thyroid-associated orbitopathy, due to the lack of documentation in the medical records. Likewise, it was not possible to analyze the association between tobacco use and thyroid-associated orbitopathy, as this variable was not documented in approximately one-quarter of the cases; however, nearly three-quarters of the patients reported not using tobacco.

Conclusion

Thyroid-associated orbitopathy was more common in women, with a ratio of 3.7:1, and was most prevalent in men over 50 among patients with well-controlled thyroid disease. The predominant presentation was non-clinically active disease with good best-corrected visual acuity. Patients with clinical activity associated with moderate and severe disease received treatment with systemic steroids and surgical intervention, in accordance with current recommendations.

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