DOI: 10.7860/JCDR/2026/85879.24003

Review Article

Ophthalmology Section

Long-term Outcomes of Corneal Involvement in Thyroid Eye Disease: A Narrative Review

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ABSTRACT

Thyroid Eye Disease (TED), an autoimmune inflammatory condition of the orbit, can result in a variety of ocular surface issues, including corneal breakdown. Although corneal involvement is less common than other manifestations such as proptosis or diplopia, it can result in significant morbidity and visual impairment if not promptly managed. The present narrative review explores the long-term clinical outcomes associated with corneal involvement in TED. Literature reporting ocular conditions, including exposure keratopathy, epithelial defects, and corneal ulceration in patients with TED, was considered. Although relatively rare, corneal complications in TED carry a risk of serious visual sequelae. Long-term prognosis depends largely on the severity at presentation and timeliness of intervention. Routine corneal monitoring and a proactive management approach are essential for preserving ocular integrity and vision in affected individuals. Therefore, the aim of the present review was to evaluate the long-term visual and corneal outcomes in patients with TED presenting with corneal involvement, and to assess the extent of residual ocular surface morbidity over time.

Keywords: Autoimmune condition, Corneal ulceration, Exposure keratopathy, Ocular surface, Orbit inflammation

INTRODUCTION

The TED is a type of autoimmune illness that begins with increased inflammation, which is referred to as 'active' or 'acute' TED. Inflammation and/or enlargement of the orbital as well as retro-orbital tissues can cause eye pain, proptosis, diplopia, exposure keratopathy, and optic neuropathy [1,2]. After one to three years, Proptosis and diplopia are among the chronic, less active long-term consequences that TED causes in varying degrees [3]. Only around 2% of people with moderate-to-severe TED may improve with more recent, focused treatments and be considered as Graves' Orbitopathy (GO) free [4].

Graves' disease affects 90% of all TED patients, with just around 6% of TED patients having normal thyroid function. Thyroid-Stimulating Immunoglobulins (TSI) is frequently used to detect and diagnose TED [5]. It occurs in two distinct clinical phases: inflammatory/active and fibrotic/inactive. The "active" period (6-24 months) has a higher level of inflammatory cytokines compared to the inactive phase. Cytokines are considered indications of active TED and one of the causes of ocular surface abnormalities in TED [6,7]. Inflammatory cytokines stimulate keratocytes, which produce matrix metalloproteinases and cause corneal stromal deterioration [8]. The density of functional keratocytes increases during the phase of inflammation when compared to the dormant period [9]. Patients having TED may have variable ocular biomechanical features depending on stage and activity. Increase extraocular muscle, adipose, and connective tissue volume in TED leads to an elevation of intra-orbital tension orbital congestion, in addition to an increase within episcleral venous pressure. Due to these orbital alterations, 8.5% of the total of TED sufferers develop Ocular Hypertension (OHT), whereas 2.5% develop glaucoma. The prevalence of OHT in TED patients is greater than in the normal population [10], while OHT is not a preventable, frequent eye exams and the identification of these persons during the active phase of TED may help prevent the condition from advancing to glaucoma [11,12]. Glaucomatous eyes have reduced Corneal Hysteresis (CH), which has been established as a risk factor for glaucoma development [13]. The most common symptoms in adolescents and children include pain, foreign body sensation, intolerance towards brightness, excessive tearing, as well as less frequently, diplopia. The most prevalent findings in paediatric patients are Graefe sign (lid lag), eyelids retraction (typically upper eyelid), proptosis, and soft-tissue involvement. However, in rare situations, children and adolescents with Graves' illness may develop myopathy and Dysthyroid Optic Neuropathy (DON) [14]. Puberty was associated with an increased risk of significant consequences such as restricted strabismus and exposure keratopathy [15].

The progression from Superficial Punctate Keratitis (SPK) to fullblown Microbial Keratitis (MK) may be slow over weeks or abrupt in days, resulting in a severe decrease in visual function. In TED, tissue remodelling mediated by the proliferation and differentiation of orbital fibroblasts results in proptosis and alterations in eyelid position. The surface of the ocular lens is exposed. Similarly, there is a change within cytokine expression from the tear film [16]. The underlying mechanism of corneal degeneration in TED is complex, with multiple components. Selter JH et al., estimated that 65-95% of TED patients exhibit Ocular Surface Disease (OSD) [17]. A 2019 population based study of co-morbid conditions in dry eye disease patients revealed that 24.7% of those suffering from dry eye also had systemic thyroid dysfunction [18]. The presence of dry eye in TED can be triggered by a variety of factors, including reduced aqueous production, increase in the tears evaporation, the meibomian gland dysfunction, and mechanical friction among the ocular surface and the eyelid due to high pressure [19,20].

The treatment of corneal breakdown requires a personalised strategy based on the degree of the condition. Treatment options include temporary and permanent tarsorrhaphy, botulinum toxin chemodenervation, amniotic membrane graft, eyelid surgery using the Muller's as well as levator muscles or as full-thickness blepharotomy, orbital decompression (endoscopic, transcutaneous and transconjunctival), along with orbital radiotherapy [1]. Corneal breakdown is unusual, and there is little knowledge on its appearance and effects at TED. Therefore, to address the concerns related to the TED, the present review article will provide a comprehensive detail on the outcomes and management of the TED involving the cornea.

Since Grave's first definition, it has become obvious that TED comprises a broader set of traits than exophthalmos. Multiple

studies in the scientific literature have shown the existence of OSD in TED patients [17,18,20]. A significant portion of the published research on sight-threatening sickness in TED focusses on DON, encompassing classifications, diagnostic criteria, risk factors, treatment, and results [21]. There is a lack of publicly accessible data about corneal damage at TED. Therefore, the aim of the review was focused on understanding the visual and corneal outcomes in the TED.

Grading of Corneal Breakdown in TED

Various categorisation approaches for assessing corneal deterioration have been investigated [22,23]. Werner's NOSPECS (No physical signs or symptoms, Only signs, Soft tissue involvement , Proptosis, Extraocular muscle involvement, Corneal involvement, Sight loss) categorisation method evaluates corneal involvement based on growing severity categories such as soft-tissue involvement, proptosis, extraocular muscle involvement, corneal involvement, loss of vision [Table/Fig-1] [24].

Class	Grade	Symptoms and signs
0		No symptoms or signs
1		Only signs (upper lid retraction, without lid lag or proptosis)
2		Soft-tissue involvement with symptoms (excess lacrimation, sandy sensation, retrobulbar discomfort, and photophobia, but not diplopia); objective signs as follows:
	0	Absent
	a	Minimal (oedema of conjunctivae and lids, conjunctival injection, and fullness of lids, often with orbital fat extrusion, palpable lacrimal glands, or swollen extraocular muscles beneath lower lids)
	b	Moderate (above plus chemosis, lagophthalmos lid fullness)
	c	Marked
3		Proptosis associated with classes 2 to 6 only (specify if inequality of 3 mm or more between eyes, or if progression of 3 mm or more under observation)
	0	Absent (20 mm or less)
	a	Minimal (21-23 mm)
	b	Moderate (24-27 mm)
	c	Marked (28 mm or more)
4		Extraocular muscle involvement (usually with diplopia)
	0	Absent
	a	Minimal (limitation of motion, evident at extremes of gaze in one or more directions)
	b	Moderate (evident restriction of motion without fixation of position)
	c	marked (fixation of position of a globe or globes)
5		Corneal involvement (primarily due to lagophthalmos)
	0	Absent
	a	Minimal (stippling of cornea)
	b	Moderate (ulceration)
	c	Marked (clouding, necrosis, perforation)
6		Sight loss (due to optic nerve involvement)
	0	Absent
	a	Minimal (disc pallor or choking, or visual field defect, vision 20/20 to 20/60)
	b	Moderate (disc pallor or choking, or visual field defect, vision 20/70 to 20/200)
	c	Marked (blindness, i.e., failure to perceive light; vision less than 20/200)

[Table/Fig-1]: Clinical features of Werner's NOSPECS classification [24].

Werner's NOSPECS classification system, which includes soft-tissue alterations, proptosis, extraocular muscle involvement, corneal involvement, and final visual loss, rates the degree of corneal involvement in thyroid eye illness in a progressive manner [24]. The variety of corneal appearances and how they change over time in TED are both captured by this approach. While secondary MK is an infectious consequence that is superimposed, mild disease usually manifests as sterile corneal epithelial erosions. Corneal thinning and, in rare instances, perforation may develop in more severe patients [22].

Multifactorial Pathogenesis of Corneal Breakdown in TED

Thyroid eye illness causes a complex process of corneal degradation that is brought on by immunological-mediated inflammation, neuromuscular dysfunction, tear film instability, and mechanical exposure. While inflammatory cytokines, irregularities in the tear film, and reduced blinking jeopardise the integrity and repair of the epithelium, lid retraction and proptosis enhance the exposure of the ocular surface. The use of topical or systemic steroids, chronic inflammation, and fibrosis of the extraocular muscles all exacerbate epithelial damage, making the cornea more vulnerable to ulceration, permanent defects, and, in severe circumstances, perforation [Table/Fig-2] [23,25].

S. No.	Factors involved	Pathogenesis
1.	Lid retraction	Early indications of TED include upper lid retraction. It leads to incomplete eyelid closure (lagophthalmos) and increased ocular surface exposure, resulting in exposure keratopathy. This constant exposure predisposes the cornea to dryness and epithelial damage.
2.	Proptosis (Exophthalmos)	Anterior displacement of the globe due to orbital tissue expansion and fat accumulation. Worsens ocular surface exposure, contributing to tear film instability and corneal desiccation.
3.	Orbicularis muscle dysfunction	Orbicularis oculi weakness or mechanical restriction impairs normal blinking. Reduced blinking frequency or completeness exacerbates tear film disruption and epithelial trauma.
4.	Tear film abnormalities	Tear film quality and quantity may be altered due to mechanical lag and inflammation. Tear film instability increases the risk of dry eye disease, leading to epithelial defects and keratopathy.
5.	Inflammatory cytokines	TED involves autoimmune inflammation, with release of cytokines like TNF-α, IL-1, and IFN-γ. These mediators can promote corneal epithelial apoptosis, compromise healing, and worsen damage.
6.	Muscle fibrosis and diplopia	Restricted eye movements from fibrotic extraocular muscles can alter corneal protection dynamics. Misalignment might cause exposure or irregular stress on certain corneal zones.
7.	Impaired corneal healing	Chronic inflammation and mechanical stress delay normal epithelial regeneration. Leads to persistent epithelial defects, stromal thinning, and potentially ulceration or perforation.
8.	Use of topical and systemic Steroids	While often necessary for inflammation control, steroids can suppress corneal healing and increase infection risk, further contributing to corneal breakdown.

[Table/Fig-2]: Etiopathogenesis of corneal involvement in TED [23,25].
TNF-α - Tumor Necrosis Factor-alpha; IL-1 - Interleukin-1; IFN-γ-Interferon-gamma

Unlike DON, the risk factors that predict corneal breakdown are unknown [26]. An earlier study of 201 TED patients revealed older age, smoking, and diabetes as significant risk factors for DON, although none predicted corneal degeneration. A large percentage of TED patients demonstrated or developed corneal breakdown during the disease's initial progressive (active) phase [21]. In a study conducted by Narnoli P et al., seven people had corneal breakdown more than two years after development of TED [22]. This separates corneal disintegration from DON, since the probability of developing the former remains regardless of whether TED is inactive. Selter JH et al., postulated a complicated aetiology for corneal deterioration in TED, which included exposure, inflammation, and ocular surface components. To achieve appropriate visual and globe salvage, a multimodal treatment approach must be implemented, which includes vigorous topical antimicrobial therapy, orbit, eyelid, and ocular surface surgery to improve exposure, profuse lubrication, and systemic immunotherapy where TED is present [17].

Multimodal Management of Corneal Breakdown

A phased, multimodal strategy that is adapted to the underlying aetiology, disease activity, and degree of corneal involvement is necessary for the management of corneal breakdown. The cornerstone of treatment is ocular surface protection, which includes regular lubricants without preservatives, lubricating ointments, moisture chambers, and punctal occlusion to stop tears from evaporating [27]. Medical therapy aims to control infection and inflammation. Topical antibiotics are used to treat MK or epithelial defects, topical or systemic corticosteroids and immunomodulatory agents are used sparingly to treat inflammatory conditions (e.g., active TED), and cycloplegics are used to treat pain. Adjuvant therapy includes autologous serum eye drops, amniotic membrane transplantation, Tissue Adhesive (TA) with Bandage Contact Lenses (BCL), and growth factor-based treatments may be used in situations of delayed epithelial repair [23].

Surgical procedures are recommended to restore corneal integrity and protection when conservative methods are ineffective or exposure is substantial. These include orbital decompression in some situations, eyelid realignment techniques, and temporary or permanent tarsorrhaphy [28]. Lamellar or Penetrating Keratoplasty (PK) may be necessary for advanced corneal injury with thinning or perforation. Optimising thyroid function in TED, managing dry eye disease, regulating diabetes, and avoiding aggravating variables like smoking are all examples of systemic and contributory issues that must be addressed for effective therapy. In order to maintain vision and stop corneal breakdown from developing again, a coordinated, multidisciplinary strategy is necessary [29].

Patients are classified as having active or inactive disease once their TED activity is initially assessed. From SPK and epithelial abnormalities to more serious disorders like MK and MK with corneal thinning or perforation, corneal involvement can vary in both stages. Since inflammation is a major factor in active TED, treatment involves anti-inflammatory and immunomodulatory medication, frequently in the form of systemic or intravenous corticosteroids, along with ocular surface protection (topical lubricants, tarsorrhaphy). Topical antibiotics are necessary for superimposed infections, and severe instances including thinning or perforation may need orbital decompression, TA, BCL, PK, or eyelid surgery. Treatment for inactive TED mostly consists of orbital decompression, eyelid surgery, tarsorrhaphy, and lubricants to mechanically correct exposure; antimicrobials are given if infection is present [22].

Both active and inactive phases of TED may present with overlapping clinical features, as MK and soft-tissue inflammation can independently or concurrently produce similar symptoms such as ocular pain, redness, photophobia, and reduced vision. This clinical overlap makes it challenging to distinguish inflammatory activity of TED from secondary infectious processes based on surface examination alone. In such situations, accurate assessment of underlying disease activity is crucial, as management strategies differ substantially between active inflammatory disease, which may require immunosuppression, and inactive disease complicated by infection, where antimicrobial therapy is paramount [25,30].

Orbital imaging, particularly Magnetic Resonance Imaging (MRI), plays a vital role in resolving this diagnostic dilemma by allowing detailed evaluation of deep orbital structures. MRI can identify features of active TED such as extraocular muscle enlargement with tendon sparing, increased orbital fat volume, and inflammatory oedema [31]. Advanced MRI sequences have shown strong correlations with disease activity: increased signal intensity ratios and prolonged T2 relaxation times reflect tissue oedema and active inflammation; T1-weighted sequences help assess muscle enlargement and fatty infiltration; and Diffusion-Weighted Imaging (DWI) with reduced Apparent Diffusion Coefficient (ADC) values indicates inflammatory cellular infiltration [30]. These imaging biomarkers aid clinicians in differentiating active from inactive TED, guiding appropriate therapeutic decisions, and preventing inappropriate use of immunosuppressive therapy in the presence of infection [31].

Visual Prognosis and Outcomes in Sight-threatening Corneal Involvement in TED

In TED, the degree and kind of corneal involvement at presentation, together with the promptness and vigour of treatment, are all strongly associated with the visual prognosis after corneal breakdown. While severe symptoms like MK, stromal thinning, or perforation pose a significant risk of irreversible vision loss, mild corneal alterations like superficial punctate keratopathy are often linked to favourable long-term visual results. Poor initial visual acuity is the most reliable indicator of adverse outcomes across all trials, highlighting the significance of early detection and management [22,32].

Clinical series data show that in cases with sight-threatening corneal illness, medical treatment alone is frequently insufficient. According to Tramunt B et al., despite rigorous topical therapy, around two-thirds of eyes with severe TED-related corneal involvement particularly MK-required subsequent surgical intervention. This finding highlights the limited effectiveness of conservative therapies in advanced cases [33]. Similarly, Naik MN et al., reported that many eyes came with severe infection, thinning, or perforation and poor baseline vision in a 10-year cohort analysis of 1,000 TED patients. They also reported that MK was present in 1.3% of cases, primarily during the active phase of TED. The severe prognosis linked to advanced illness was highlighted by the fact that, despite rigorous multimodal care in certain instances, visual recovery was restricted and some eyes needed to be eviscerated [34].

Even in cases of severe corneal disease, multimodal and prompt surgical intervention appears to enhance globe survival, according to longitudinal investigations. Even though one-third of patients had thinning or perforation, Narnoli P et al., showed that timely orbital decompression, ocular surface protection, antimicrobial medication, and targeted eyelid or corneal surgery led to effective globe preservation in 88% of instances. However, postoperative problems including new-onset diplopia were common and frequently required follow-up strabismus surgery, and their retrospective nature hampered the ability to follow a regular treatment sequence [22]. Thakar A et al., reported similar results, noting that diplopia after decompression was frequently temporary but seemed to be more likely to remain in individuals with extensive corneal involvement or active TED [35].

These findings are supported by more recent longitudinal investigations, which demonstrate that long-term visual stability is much enhanced by early management of orbital inflammation, exposure reduction, and ocular surface protection. According to prospective data, patients who receive combined immunosuppression and prompt decompression treatment early in the active phase of TED have better long-term best-corrected visual acuity, fewer vision threatening complications, and lower rates of corneal ulceration than those who receive delayed or stepwise treatment [32,36]. The best way to improve long-term results in TED-associated corneal breakdown is to adopt a proactive, customised, and interdisciplinary approach, according to these studies taken together.

DISCUSSION

Corneal involvement in TED is a vision-threatening condition in which results are heavily influenced by the severity, chronicity, and aetiology of corneal breakdown. Mild exposure-related keratopathy often responds well to conservative measures like lubrication and eyelid taping, whereas advanced disease, particularly MK as well as corneal thinning or perforation is associated with a worse long-term visual prognosis and frequently necessitates surgical intervention [22]. The chronic inflammatory environment, associated with lagophthalmos, proptosis, decreased blink rate, and tear film

instability, contributes the cornea to permanent epithelial defects and secondary infections [37].

Several studies have highlighted that medical therapy alone is often insufficient in severe cases. Tramunt B et al., reported that approximately two-thirds of patients with sight-threatening TED and MK required additional surgical procedures despite intensive medical treatment, underscoring the aggressive nature of corneal disease in this subgroup [33]. Similarly, Naik MN et al., demonstrated that MK in TED, though relatively uncommon, predominantly occurs during the active phase and is associated with significant eyelid retraction, restricted motility, and poor presenting visual acuity; multimodal management combining antimicrobial therapy with eyelid, orbital, and corneal surgery was crucial for infection control and visual rehabilitation [30].

Corneal-specific grading techniques, in addition to Werner's NOSPECS method, offer a more targeted evaluation of ocular surface degradation and are helpful in directing prognosis and treatment in TED. These methods classify corneal involvement according to perforation risk, stromal involvement, and epithelial integrity [38,39]. Surface punctate keratopathy and sterile epithelial erosions associated with exposure and tear-film instability are examples of mild illness; these alterations are typically curable with conservative treatment and have a good prognosis. Moderate grades, which frequently need for more intensive medical treatment and careful observation, include early stromal infiltration or chronic epithelial abnormalities. Severe grades, which are linked to poor visual results and sometimes require immediate surgical intervention such as tarsorrhaphy, amniotic membrane transplantation, or keratoplasty, include MK, stromal thinning, descemetocele development, or open perforation [40].

When combined with NOSPECS and activity scores [23], these corneal focused grading systems help clinicians distinguish between infectious or inflammatory corneal disease and exposure related keratopathy, identify eyes at high-risk of vision loss, and promptly escalate to surgical and multimodal management, all of which improve long-term visual and globe survival outcomes.

CONCLUSION(S)

Corneal breakdown in TED is a vision-threatening emergency driven by exposure, inflammation, and mechanical factors, requiring prompt multidisciplinary management. Early, aggressive intervention combining ocular surface protection, immunosuppression during active disease, and timely surgical correction is essential for globe and vision preservation. Delayed presentation and poor baseline vision predict worse outcomes, underscoring the importance of early detection and individualised care strategies.

REFERENCES

[1] Bartley GB, Fatourechi V, Kadrmas EF, Jacobsen SJ, Ilstrup DM, Garrity JA, et al. Clinical features of Graves' ophthalmopathy in an incidence cohort. Am J Ophthalmol. 1996;121:284-90. Doi: 10.1016/S0002-9394(14)70276-4.

[2] Dickinson AJ, Hintschich C. Clinical manifestations. In: Wiersinga WM, Kahaly GJ, editors. Graves' orbitopathy: A multidisciplinary approach-questions and answers. 3rd ed. Basel: Karger; 2017. p. 1-25.

[3] Bartalena L, Tanda ML. Clinical practice. Graves' ophthalmopathy. N Engl J Med. 2009;360:994-1001. Doi: 10.1056/NEJMcp0806317.

[4] Sabini E, Leo M, Mazzi B, Rocchi R, Latrofa F, Nardi M, et al. Does Graves' orbitopathy ever disappear? Answers to an old question. Eur Thyroid J. 2017;6:263-70. Doi: 10.1159/000477803.

[5] Versura P, Campos EC. The ocular surface in thyroid diseases. Curr Opin Allergy Clin Immunol. 2010;10:486-92. Doi: 10.1097/ACI.0b013e32833e1749.

[6] Huang D, Luo Q, Yang H, Mao Y. Changes of lacrimal gland and tear inflammatory cytokines in thyroid-associated ophthalmopathy. Invest Ophthalmol Vis Sci. 2014;55:4935-43. Doi: 10.1167/iovs.13-13704.

[7] Huang D, Xu N, Song Y, Wang P, Yang H. Inflammatory cytokine profiles in the tears of thyroid-associated ophthalmopathy. Graefes Arch Clin Exp Ophthalmol. 2012;250:619-625. doi:10.1007/s00417-011-1863-x.

[8] Sakimoto T, Ohnishi T, Ishimori A. Simultaneous study of matrix metalloproteinases, proinflammatory cytokines, and soluble cytokine receptors in the tears of noninfectious corneal ulcer patients. Graefes Arch Clin Exp Ophthalmol. 2014;252:1451-56. Doi: 10.1007/s00417-014-2708-1.

[9] Villani E, Viola F, Sala R, Salvi M, Mapelli C, Currò N, et al. Corneal involvement in graves' orbitopathy: An in vivo confocal study. Invest Ophthalmol Vis Sci. 2010;51:4574-78. Doi: 10.1167/iovs.10-5380.

[10] Hsia Y, Wei YH, Liao SL. The changes in ocular biomechanical response parameters and intraocular pressure after surgical treatment for thyroid eye disease. Invest Ophthalmol Vis Sci. 2023;64(10):31. Doi: 10.1167/iovs.64.10.31.

[11] Behrouzi Z, Rabei HM, Azizi F, Daftarian N, Mehrabi Y, Ardeshiri M, et al. Prevalence of open-angle glaucoma, glaucoma suspect, and ocular hypertension in thyroid-related immune orbitopathy. J Glaucoma. 2007;16(4):358-62. Doi: 10.1097/IJG.0b013e31802e644b.

[12] Cross JM, Girkin CA, Owsley C, McGwin G., Jr The association between thyroid problems and glaucoma. Br J Ophthalmol. 2008;92:1503-05. Doi: 10.1136/bjo.2008.147165.

[13] Wells AP, Garway-Heath DF, Poostchi A, Wong T, Chan KC, Sachdev N. Corneal hysteresis but not corneal thickness correlates with optic nerve surface compliance in glaucoma patients. Invest Ophthalmol Vis Sci. 2008;49:3262-68. Doi: 10.1167/iovs.07-1556.

[14] Olayanju JA, Griepentrog GJ, Mohney BG. Incidence and clinical characteristics of pediatric eyelid retraction. J AAPOS. 2019;23(4):213.e1-213.e4. Doi: 10.1016/j.jaapos.2019.03.004.

[15] Szczapa-Jagustyn J, Gotz-Więckowska A, Kocięcki J. An update on thyroid-associated ophthalmopathy in children and adolescents. J Pediatr Endocrinol Metab. 2016;29(10):1115-22. Available from: https://doi.org/10.1515/jpem-2016-0122.

[16] Ismailova DS, Fedorov AA, Grusha YO. Ocular surface changes in thyroid eye disease. Orbit. 2013;32:87-90. Doi: 10.3109/01676830.2013.764440.

[17] Selter JH, Gire AI, Sikder S. The relationship between Graves' ophthalmopathy and dry eye syndrome. Clin Ophthalmol. 2014;9:57-62. Doi: 10.2147/OPTH.S76583.

[18] Dana R, Bradley JL, Gurein A, Pivnea I, Evans AM, Stillman IO. Comorbidities and prescribed medications in patients with or without dry eye disease: A population-based study. Am J Ophthalmol. 2019;98:181-92. Doi: 10.1016/j.ajo.2018.10.001.

[19] Takahashi Y, Ichinose A, Kakizaki H. Topical rebamipide treatment for superior limbic keratoconjunctivitis in patients with thyroid eye disease. Am J Ophthalmol. 2014;157:807-12. Doi: 10.1016/j.ajo.2013.12.027.

[20] Park J, Baek S. Dry eye syndrome in thyroid eye disease patients: The role of increased incomplete blinking and meibomian gland loss. Acta Ophthalmol. 2019;97:800-06. Doi: 10.1111/aos.14000.

[21] Rath S, Pattnaik M, Tripathy D, Mohapatra S, Panigrahy B, Ali MH. Sight-threatening thyroid eye disease: Role of diabetes mellitus and interaction with other risk factors. Ophthalmic Plast Reconstr Surg. 2021;37:352-60. Doi: 10.1097/IOP.0000000000001871.

[22] Narnoli P, Rath S, Tripathy D, Mohapatra S, Priyadarshini SR, Das S, et al. Corneal breakdown in thyroid eye disease: Presentation and outcomes over a decade. Indian J Ophthalmol. 2025;73(4):567-76. Doi: 10.4103/IJO.IJO_1067_24.

[23] Bartalena L, Kahaly GJ, Baldeschi L, Dayan CM, Eckstein A, Marcocci C, et al; EUGOGO. The 2021 European Group on Graves' orbitopathy (EUGOGO) clinical practice guidelines for the medical management of Graves' orbitopathy. Eur J Endocrinol. 2021;185(4):G43-G67. Doi: 10.1530/EJE-21-0479.

[24] Bartalena L. Graves' disease: Complications. In: Feingold KR, Adler RA, Ahmed SF, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000. Available from: https://www.ncbi.nlm.nih.gov/books/NBK285551/table/tyd-graves-complica.classgrade/.

[25] McAlinden C. An overview of thyroid eye disease. Eye Vis (Lond). 2014;1:9. Doi: 10.1186/s40662-014-0009-8.

[26] Wolffsohn JS, Benítez-Del-Castillo JM, Loya-Garcia D, Inomata T, Iyer G, TFOS collaborator group,et al. TFOS DEWS III: Diagnostic Methodology. Am J Ophthalmol. 2025 Nov;279:387-450.

[27] Kate A, Deshmukh R, Donthineni PR, Sharma N, Vajpayee RB, Basu S. Management of corneal perforations in dry eye disease: Preferred practice pattern guidelines. Indian J Ophthalmol. 2023;71(4):1373-81. Doi: 10.4103/IJO.IJO_2826_22.

[28] Craig JP, Nichols KK, Akpek EK, Caffery B, Dua HS, Joo CK, et al. TFOS DEWS II definition and classification report. Ocul Surf. 2017;15(3):276-83.

[29] Dua HS, Said DG, Messmer EM, Rolando M, Benitez-Del-Castillo JM, Hossain PN, et al. Neurotrophic keratopathy. Prog Retin Eye Res. 2018;66:107-31.

[30] Rath S. Magnetic resonance imaging in thyroid eye disease: Signal intensity ratio to measure disease activity. Indian J Ophthalmol. 2022;70:1446-47. Doi: 10.4103/ijo.IJO_365_22.

[31] Vaishnav YJ, Mawn LA. Magnetic resonance imaging in the management of thyroid eye disease: A systematic review. Ophthalmic Plast Reconstr Surg. 2023;39(6S):S81-S91. Doi: 10.1097/IOP.0000000000002511.

[32] Kahaly GJ, Douglas RS, Holt RJ, Sile S, Smith TJ. Teprotumumab for patients with active thyroid eye disease: A pooled data analysis, subgroup analyses, and off-treatment follow-up results from two randomised, double-masked, placebo-controlled, multicentre trials. Lancet Diabetes Endocrinol. 2021;9(6):360-372.

[33] Tramunt B, Imbert P, Grunenwald S, Boutault F, Caron P. Sight-threatening graves'orbitopathy: Twenty Years experience of a multidisciplinary thyroid-eye outpatient clinic. Clin Endocrinol. 2018;90:208-13. Doi: 10.1111/cen.13880.

[34] Naik MN, Vasanthapuram VH, Joseph J, Murthy SI. Microbial keratitis in thyroid eye disease: Clinical features, microbiological profile, and treatment outcome. Ophthal Plast Reconstr Surg. 2019;35:543-48. Doi: 10.1097/IOP.0000000000001361.

[35] Thakar A, Tandon N, Lal P. Endoscopic orbital decompression for Graves' orbitopathy. Indian J Endocrinol Metab. 2013;17:26. Doi: 10.4103/2230-8210.109707.
[36] Burch HB, Perros P, Bednarczuk T, Cooper DS, Dolman PJ, Leung AM, et al. Management of thyroid eye disease: A Consensus Statement by the American Thyroid Association and the European Thyroid Association. Thyroid. 2022;32(12):1439-1470. Doi: 10.1530/ETJ-22-0189.
[37] Milner MS, Beckman KA, Luchs JI, Allen QB, Awdeh RM, et al. Dysfunctional tear syndrome: Dry eye disease and associated tear film disorders - new strategies for diagnosis and treatment. Curr Opin Ophthalmol. 2017;27 Suppl 1(Suppl 1):3-47. Doi: 10.1097/01.icu.0000512373.81749.b7.
[38] Werner SC. Classification of the eye changes of Graves' disease. Am J Ophthalmol. 1969;68(4):646-48. Doi: 10.1016/0002-9394(69)91246-x. PMID: 5394450.
[39] Dolman PJ, Rootman J. VISA Classification for Graves orbitopathy. Ophthalmic Plast Reconstr Surg. 2006;22(5):319-24. Doi: 10.1097/01.iop.0000235499.34867.85. PMID: 16985411.
[40] Comert MC, Yilmaz S, Tas AY, Sahin A. The effect of thyroid eye disease on corneal biomechanical properties. Beyoglu Eye J. 2022;7(3):193-98. Doi: 10.14744/bej.2022.08941.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jan 01, 2026
- Manual Googling: Mar 03, 2026
- iThenticate Software: Mar 05, 2026 (8%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? NA
- Was informed consent obtained from the subjects involved in the study? NA
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Dec 14, 2025**
Date of Peer Review: **Jan 02, 2026**
Date of Acceptance: **Mar 07, 2026**
Date of Publishing: **Aug 01, 2026**