Original Article

Corneal breakdown in thyroid eye disease: Presentation and outcomes over a decade

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Purpose: Corneal breakdown in thyroid eye disease (TED) is an ocular emergency. This study aimed to assess the outcome of multimodal management for corneal breakdown in TED. **Methods:** This retrospective audit included all consecutive corneal breakdowns in TED patients between November 2011 and May 2023. The primary outcome measure was the best corrected visual acuity (BCVA), and secondary outcome measures included proptosis, clinical activity score (CAS), and proportion of globe salvage. **Results:** In all, 35 TED patients (50 eyes; 15 bilateral) were included in this study. The mean age was 50.6 + 16 years (range 17–83), and 23 were male. Median TED duration was 5 months (range 1–108). Seven patients (nine eyes) developed corneal breakdown ≥2 years after disease onset. Corneal breakdown was graded as superficial punctate keratopathy in 18, microbial keratitis in 14, and microbial keratitis with thinning and/or perforation in 18 eyes. At median follow-up of 17 months (range 2–72), in the orbital decompression group, overall mean BCVA before and after orbital decompression showed improvement from 1.2 to 0.7, mean proptosis from 25.4 ± 3.5 to 20.7 ± 2.1 mm, and median CAS from 4.2 ± 1.3 to 0.3 ± 0.6. In the medical management group, the mean BCVA changed from 1.7 to 1.5, mean proptosis from 22.5 ± 2.5 to 22.3 ± 2.4 mm, and CAS from 3.0 ± 1.4 to 1.1 ± 1.4 before and after treatment, respectively. At the final follow-up, 44 eyes (88%) achieved globe salvage, while six eyes were eviscerated. **Conclusion:** Corneal breakdown necessitates expeditious and intensive multimodal management – topical medications, systemic medications, eyelid surgery, and orbital decompression surgery. In severe corneal breakdown with microbial keratitis with thinning and perforation, multimodal management helps achieve a high percentage of vision and globe salvage.

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The corneal breakdown is a sight-threatening type of thyroid eye disease (TED) and is relatively rare with ≤2% prevalence.[1] The progression from superficial punctate keratitis to full-fledged microbial keratitis may be insidious over weeks, or rapid in days, causing a precipitous decrease in visual function. Tissue remodeling arising from the expansion and differentiation of orbital fibroblasts in TED causes proptosis and alteration in eyelid position. There is exposure of the ocular surface.[2] Concurrently, there is an alteration in the cytokine expression in the tear film.[2] The underlying mechanism behind corneal breakdown in TED is complex, involving various factors.[3] Selter *et al*.[3] estimated that 65–95% of patients with TED have ocular surface disease (OSD). A population-based study in 2019 investigating co-morbidities in patients with dry eye disease found that 24.7% of those with chronic dry eye also had systemic thyroid disease.[4] Dry eye in TED is complex with multiple contributing factors – reduced aqueous production, increase in tear evaporation, meibomian gland dysfunction, and mechanical friction between the ocular surface and eyelid due to an increased eyelid pressure.[3,5-7]

The management of corneal breakdown necessitates a tailored approach depending on the severity of the disease. Therapeutic strategies range from temporary and permanent tarsorrhaphy, botulinum toxin chemo-denervation, amniotic membrane graft, eyelid surgery involving the Muller's and levator muscle or full-thickness blepharotomy, orbital decompression – endoscopic, transcutaneous or transconjunctival, and orbital radiotherapy. Corneal breakdown is rare, and there is a dearth of literature on its spectrum of presentation and outcomes in TED. The present study is an attempt to document the phenotypic spectrum of corneal breakdown in TED and its outcome after expeditious and multimodal surgical and medical therapy from single tertiary eye care center over a decade.

Methods

This was a retrospective study done at a tertiary eye care center. Institutional ethics committee approval (2023-179-BHR-4) was obtained, and the study adhered to the tenets of the Declaration

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of Helsinki. The study cohort included all consecutive patients of TED who presented with or developed corneal breakdown throughout treatment between November 2013 and June 2024. Cases were identified by searching the electronic medical record (EMR) database with the diagnoses – thyroid eye disease (TED), microbial keratitis, and exposure keratopathy. Patients who had a minimum follow-up of 6 weeks from the date of presentation were included. Patients where the requisite clinical details were not available – primary management was performed elsewhere, were excluded. The demographic data and history were recorded from the medical records: age (years), gender, duration of TED onset (months), thyroid metabolic status, corneal status, systemic co-morbidities if any were present, and a history of smoking. History of prior thyroid surgery if available was documented.

The clinical evaluation included the best corrected visual acuity (BCVA; expressed in the logarithm of the minimum angle of resolution; LOG MAR), proptosis measured by Hertel's exophthalmometer, and the clinical activity score (CAS) described by the European Group on Graves's Orbitopathy (EUGOGO).[8] TED was considered active if the CAS ≥ 3 or there was an increased signal intensity ratio of extraocular muscles compared to the temporalis muscle on T2 weighted sequence of magnetic resonance imaging (MRI).[8,9]

Corneal breakdown was defined in the presence of persistent exposure-related changes on the corneal surface that failed to resolve with topical lubrication alone within a period of 4 weeks.[10] We graded corneal breakdown into three distinct groups drawing from NOSPECS (Werner 1969) and VISA (Dolman 2006) classification systems: (a) superficial punctate keratopathy (SPK; Fig. 1a), (b) microbial keratitis, and (c) microbial keratitis with thinning [Fig. 1b and c] or perforation.[11,12] Associated dysthyroid optic neuropathy (DON) when present was diagnosed based on criteria published earlier.[10] In cases where corneal clouding or media haze precluded visualization of pupil and fundus details, DON was diagnosed based on apical crowding on an orbital CT scan or MRI.[10] A cornea specialist (SD, SMR) evaluated all cases, and a corneal scraping was performed followed by a direct microscopic examination and culture. Appropriate antimicrobials were initiated based on the culture and sensitivity. Select cases underwent minor surgical interventions, such as tarsorrhaphy and tissue adhesive with bandage contact lens as and when indicated.

Both endoscopic and conventional orbital decompression techniques were performed by trained oculoplastic surgeons (SR, DT, SM) experienced in TED management. All the patients underwent thorough evaluation with the endocrinologist and physician before planning surgery under general anesthesia. All patients received medications to attain euthyroid status before surgery was scheduled and high-risk consent was taken where applicable. Degree of proptosis, activity, bone anatomy as observed on CT scan, and presence of associated DON were considered before deciding on the choice of incision and bony walls versus fat in orbital decompression. Orbital decompression was tailored to address corneal breakdown with meticulous planning before and during surgery to avoid and manage the risk of an impending perforation. First, intensive antimicrobial treatments based on sensitivity patterns were continued in the perioperative period, before and after orbital decompression, to control infection and promote healing. Second, in cases of severe corneal breakdown, endoscopic orbital decompression was preferred over conventional methods due to its minimally invasive nature with regard to globe manipulation and improved morbidity after surgery. Third, interventions to provide tectonic support to the thinned or perforated cornea were prioritized before orbital decompression. Finally, corneal protectors were utilized during the surgery to minimize the risk of corneal perforation and eyelid tarsorrhaphy, if not done prior, was performed at the conclusion of orbital decompression.

The primary outcome measure was BCVA and secondary outcome measures included proportion of globe salvage, proptosis, and CAS score at final follow-up visit.

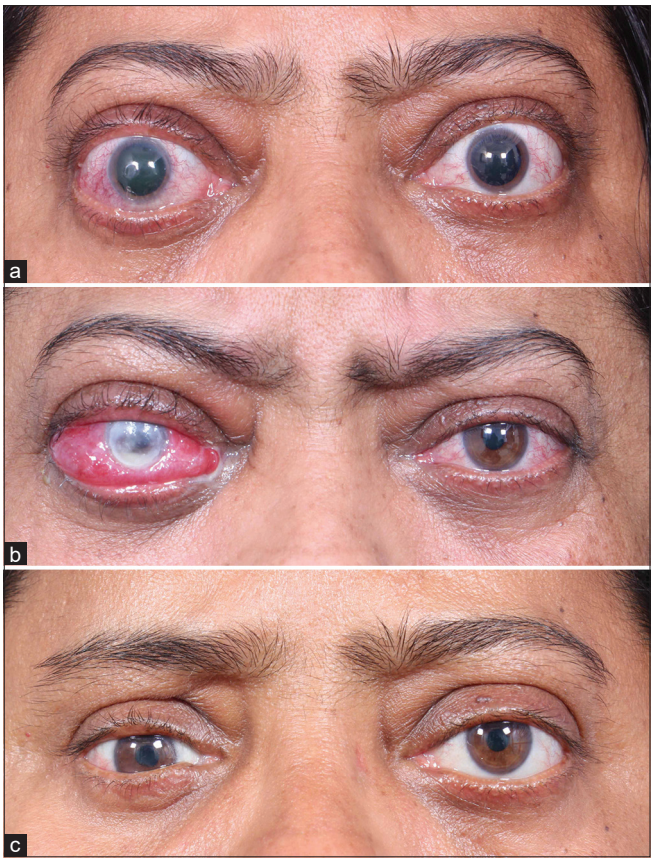

Figure 1: (a-c) Clinical photograph 38-year-old hyperthyroid female who presented 4 months after onset of thyroid eye disease with a – proptosis and eyelid retraction of both eyes. The right eye showed corneal breakdown with inferior corneal erosion and diffuse coalescent superficial punctate keratopathy necessitating intervention. The right eye was managed with a bandage contact lens which is seen in the clinical picture. b- She progressed over the next 3 weeks and frank microbial keratitis with inferior infiltrate, endoexudate, thinning, and hypopyon of 3 mm. The right eye also shows diffuse conjunctival congestion, chemosis, and caruncular edema. The left eye showed mild conjunctival congestion. c-The same individual as shown in Fig. a, b after complete resolution of the corneal infection with residual scar. She underwent right eye orbital decompression and medical management of microbial keratitis. She declined any further eyelid surgery to correct the overriding lower eyelid after inferomedial bony decompression and mild residual lower eyelid retraction in the left eye

Results

A total of 835 TED patients presented during the study period. TED was associated with microbial keratitis in 24 patients, exposure keratopathy in 24 patients, and perforated corneal ulcer in two patients. After excluding for duplicate entries, patients where sufficient clinical details were not available and with a follow-up period of <6 weeks, 35 patients (4.1%) with corneal breakdown were included in this study. The mean age was 50.6 + 16 years (range 17–83) of which 23 were male (66%). Table 1 outlines the demography, status of thyroid function, and co-morbidities in all patients. A history of smoking was present in 7 (20%), and 13 patients (37%) had both corneal breakdown and DON. Co-morbidities associated with TED in this cohort included diabetes mellitus (n = 8), hypertension (n = 3), two patients with prior thyroidectomy, one for papillary carcinoma of the thyroid, and another with multinodular goiter. One TED patient had pulmonary tuberculosis and another presented in the first trimester of pregnancy.

The median duration between TED onset and corneal breakdown was 5 months (range 1–108). Seven patients (two with bilateral corneal breakdown) developed corneal breakdown ≥2 years after TED onset and gave a history, suggesting that they had inactive disease when corneal symptoms commenced. Table 2 documents the demographic details, type of sight-threatening disease with the grade of corneal breakdown, primary ocular management with adjuvant surgical, and systemic medical therapy in TED patients with orbital decompression along medical management and adjuvant surgical interventions. In the orbital decompression group, those who had microbial keratitis received topical antimicrobial therapy based on microbiology report for a mean duration of 11 days (range 5–30 days) before orbital decompression. In the orbital decompression group, several adjuvant surgical procedures were performed – tarsorrhaphy, tissue adhesive with bandage contact lens, eyelid retraction correction, cataract, and even full-thickness penetrating keratoplasty. Five patients needed extraocular muscle surgery for new-onset strabismus after orbital decompression. Four patients needed a second orbital decompression in an eye for large residual proptosis after the first. Several patients who underwent orbital decompression in the active phase needed systemic immunomodulation. Another group had TED patients [Table 3] where the corneal breakdown was managed by intensive medical therapy and orbital decompression was not done because they either declined surgery or had systemic co-morbidities with poor control. In the latter group, several adjuvant surgical procedures were performed – tarsorrhaphy, tissue adhesive, and bandage contact lens along with systemic immunomodulation when TED was active.

On a univariate analysis [Table 4] that was done to find factors predictive of worsening of the best corrected visual acuity (BCVA) ≥2 Snellen lines between presentation and final follow-up, female gender, higher grade of corneal breakdown, and visual acuity at presentation were found to be statistically significant. On a multivariate logistic regression, only visual acuity at presentation emerged as the statistically significant (P = 0.037) risk factor. Orbital decompression group did not improve the chances of better final visual acuity [Table 4] when compared with the medical management group. Factors found to be associated with the risk of globe perforation included grade of corneal breakdown, visual acuity at presentation, and Hertel's exophthalmometry measurement, but none of these were significant on a multivariate analysis. In the orbital decompression group, the mean BCVA before decompression was 1.2 ± 0.9, while the mean proptosis and CAS were 25.3 ± 3.5 mm and 4.2 ± 1.3, respectively. At the final follow-up, the mean BCVA had improved to 0.7 + 0.9, proptosis measured 21.0 + 2.1 mm, and CAS 0.3 + 0.6 at a median follow-up of 17 months (range 2–72). In the group who received only medical management, the mean BCVA before treatment was 1.72 ± 0.9, mean proptosis was 22.5 ± 2.5 mm, and CAS was 3.08 ± 1.4. At a median follow-up of 14 months, the BCVA improved slightly to 1.52 ± 0.9, proptosis was 22.30 ± 2.45 mm, and CAS had reduced to 1.16 ± 1.40. At the final follow-up, 20 patients (27 eyes) with a follow-up of ≥ 12 months had stable or improved BCVA when compared to that at presentation and 44 eyes (88%) achieved globe salvage while six eyes were eviscerated.

Table 1: Demography, risk factors, and severity of TED patients with a corneal breakdown

Patient characteristics	Patient characteristics	Values
Age	Mean+SD	50.6+16 years
	Range	17–83 years
Gender	Female	12 (34%)
	Male	23 (66%)
Thyroid function	Hyperthyroid	32 (91%)
	Hypothyroid	3 (9%)
Smoking history	Present	7 (20%)
	Absent	28 (80%)
Diabetes mellitus (DM)	DM	8 (23%)
	No DM	27 (77%)
The time between onset of TED and CB diagnosis	Median duration	5 months
	Range of duration	1–108 month
Type of sight-threatening thyroid eye disease (EUGOGO)	Corneal breakdown alone	22 (63%)
	Corneal breakdown and dysthyroid optic neuropathy	13 (37%)
Follow-up	Median	14
	Range	2–60

Table 2: Demography, type, and grade of sight-threatening thyroid eye disease with corneal breakdown managed by orbital decompression and medical management with outcome

Case No	Eye; Right OD; Left OS	Age years/ Gender	Onset of TED months	Type of sight-threatening TED: CB/DON	Primary surgical modality	Adjuvant surgical procedures	Medical treatment	Proptosis (mm)		BCVA LOGMAR		CAS		Globe salvage	Follow-up in months
								Before	After	Before	After	Before	After		
1	OD	37/F	3	SPK	Medial wall, Floor and Fat OD	Tarsorrhaphy	IVCS –- 6.5g m	25	22	0	0.1	6	1	Yes	11
	OS		3	MK	Medial, lateral, floor and fat OD	Tarsorrhaphy, electrolysis	IVCS	27	18	2.3	0.2	6	1	Yes	
2	OD	24/M	24	SPK	Medial wall, floor and fat OD	Levator recession, lateral decompression	Oral CS	28	21	0	0	5	0	Yes	32
3	OD	36/M	7	SPK	Medial wall and floor OD	Tarsorrhaphy	Oral CS	25	–	0	0	4	0	Yes	11
	OS		7	MK	Medial + Floor + Fat OD	Tarsorrhaphy	Oral CS	25	–	2.2	2.4	4	0	Yes	
4	OD	56/F	8	SPK; DON	Medial, floor and fat OD	Full-thickness blepharotomy, cataract surgery	Azathioprine	20	18	0.8	0	4	0	Yes	30
	OS		8	MK with perforation	Medial wall and floor OD	Full-thickness blepharotomy, tarsorrhaphy, cataract	AZT	23	20	2.3	1.7	4	1	Yes	
5	OS	33/M	8	SPK; DON	Endoscopic:Medial wall, Floor and Lateral wall OD	Strabismus surgery	–	31	23	0.1	0.1	1	0	Yes	30
6	OD	71/M	6	SPK; DON	Endoscopic medial wall OD	-	IVCS + MTX	18	–	0.3	0.2	4	0	Yes	28
7	OD	35/M	4	SPK	Medial wall and floor OD	Strabismus surgery	Oral CS	29	24	0	0.1	4	0	Yes	30
	OS		4	SPK	Medial, lateral, and floor OD	Strabismus surgery	Oral CS	29	22	0.2	0	4	0	Yes	
8	OD	33/F	3	SPK; DON	Endoscopic medial wall and floor OD	–	Oral CS + MMF	22	20	0	0	1	0	Yes	28
	OS		3	SPK	Endoscopic Medial wall, Floor and Fat	–	Oral CS + MMF	18	16	0	0	1	0	Yes	
9	OD	47/M	6	SPK	Endoscopic medial wall and floor OD	Tarsorrhaphy; penetrating keratoplasty	Oral CS	–	23	0.6	0.1	6	1	Yes	11

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Table 2: Contd...

Case No	Eye; Right OD; Left OS	Age years/ Gender	Onset of TED months	Type of sight-threatening TED: CB/DON	Primary surgical modality	Adjuvant surgical procedures	Medical treatment	Proptosis (mm)		BCVA LOGMAR		CAS		Globe salvage	Follow-up in months
								Before	After	Before	After	Before	After		
10	OS	71/M	3	MK	Medial wall and floor OD	Tarsorrhaphy	–	25	–	2.3	–	5	–	Yes	5
	OD		3	MK	Medial wall and Floor OD	Tarsorrhaphy	–	30	–	2.3	–	5	–	No	
11	OD	67/M	36	SPK	Medial wall, floor and fat OD	Tarsorrhaphy; cataract surgery	Oral CS	25	23	0.3	0.4	5	0	Yes	30
12	OD	34/M	2	MK with thinning	Endoscopic medial wall + Floor + Fat OD	Tarsorrhaphy, TA + BCL	IVCS + oral CS	29	22	0.8	0	4	0	Yes	24
	OS		30	MK with thinning	Endoscopic medial wall + Floor + Fat OD	Glue + BCL, Conjunctival resection	IVCS + oral CS + TA+BCL	28	22	0.1	0.2	2	0	Yes	
13	OS	42/M	24	MK	Tarsorrhaphy	Deep lateral, medial wall and fat	–	25	22	1.6	0.1	5	0	Yes	24
14	OD	33/M	48	MK	Endoscopic medial wall + floor OD	Levator recession	–	–	-	2.3	2.4	4	0	Yes	5
	OS		48	MK	Endoscopic medial wall + floor OD	Tarsorrhaphy, spacer graft	–	–	-	2.2	2.2	6	1	Yes	
15	OD	72/M	2.5	MK; DON	Endoscopic medial wall + floor + fat OD	Tarsorrhaphy, glue +BCL	Oral CS + Mycophenolate	-	-	2.2	2.2	4	0	Yes	11
16	OD	41/M	1	MK	Endoscopic medial wall OD	Tarsorrhaphy; Add-on orbital decompression	Oral CS	25	–	0.3	–	4	–	No	7
17	OD	58/F	2	MK	Endoscopic medial wall OD	Full-thickness blepharotomy	IVCS	22	19	1.7	2.1	5	0	Yes	5
	OS		2	MK	Endoscopic medial wall OD	Full-thickness blepharotomy	IVCS	22	19	1.2	1.3	5	0	Yes	
18	OD	46/M	4	MK with thinning	Endoscopic medial wall and fat	Tarsorrhaphy	IVCS	23	22	0.5	0.1	4	1	Yes	32

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Table 2: Contd...

Case No	Eye; Right OD; Left OS	Age years/ Gender	Onset of TED months	Type of sight-threatening TED: CB/DON	Primary surgical modality	Adjuvant surgical procedures	Medical treatment	Proptosis (mm)		BCVA LOGMAR		CAS		Globe salvage	Follow-up in months
								Before	After	Before	After	Before	After		
19	OS	46/M	5	MK with perforation	Medial wall + Floor OD	TA + BCL, Full-thickness blepharotomy, Strabismus surgery	Oral CS	23	21	1.8	0	5	0	Yes	17
	OD		5	MK with perforation	Medial wall + Floor OD	TA + BCL, full-thickness blepharotomy, Strabismus surgery	Oral CS	23	21	1.8	0.3	5	0	Yes	
20	OD	17/F	108	MK with thinning	Lateral wall OD	Penetrating keratoplasty, cataract	Oral CS	29	–	2.3	0.8	4	0	Yes	72
	OS		108	MK with thinning	Lateral wall and floor OD	Eyelid surgery	Oral CS	30	–	2.3	-	4	1	Yes	
21	OD	46/F	48	MK with perforation	Medial wall and floor OD	Levator recession; evisceration	IVCS + Oral CS	30	–	2.3	NA	4	NA	No	12
22	OD	83/M	1.5	MK with perforation with DON	Endoscopic medial wall OD	Tarsorrhaphy, TA + BCL, Lateral wall + Floor add-on decompression; Eyelid surgery	IVCS	ND		1.3	1.8	5	2	Yes	2
	OS		1.5	MK with thinning with DON	Endoscopic medial wall OD	Eyelid surgery, tarsorrhaphy, TA + BCL, lateral and Floor decompression	IVCS	ND		1.8	1.8	5	2	Yes	
23	OD	38/F	4	MK with thinning	Medial and lateral wall OD	Tarsorrhaphy	IVCS	26	17	2.2	0.6	3	0	Yes	14

Male-M; female-F; Corneal breakdown-CB; Dysthyroid optic neuropathy-DON; Superficial punctate keratopathy-SPK; Microbial keratitis-MK; orbital decompression-OD; tissue adhesive and bandage contact lens-TA+BCL; corticosteroid-CS, Mycophenolate-MMF

Table 3: Demography, type and grade of sight-threatening thyroid eye disease with corneal breakdown primarily managed by medical management with outcome

Case No	Eye; Right OD; Left OS	Age in years/ Gender	Onset of TED mths	Type of sight-threatening TED: CB/DON	Primary treatment modality	Adjuvant surgical procedures	Medical treatment	Proptosis (mm)		BCVA LOGMAR		CAS		Globe salvage	Follow-up in months
								Before	After	Before	After	Before	After		
1	OD	60/M	6	MK with thinning	Medical management	Tarsorraphy	Oral CS + IVCS	–	–	3	–	–	–	No	11
	OS		6	SPK	Medical management	Tarsorraphy	Oral CS + IVCS	–	–	1	0.5	5	5	Yes	
2	OS	43/M	12	SPK	Medical management	Tarsorraphy	Oral CS	24	22	0.7	0.4	1	0	Yes	60
3	OD	52/F	12	MK with thinning	Medical management			–	–	2.7	–	–	–	No	3
	OS		12	MK with thinning	Medical management			–	–	2.7	–	–	–	No	
4	OD	49/F	4	SPK with DON	Medical management		Oral CS + IVCS + AZT	23	23	0	0	2	1	Yes	24
	OS		4	MK with DON	Medical management		Oral CS + IVCS + AZT	23	23	0	0	2	1	Yes	
5	OS	61/F	6	MK with thinning	Medical management	TA-BCL		22	22	2.1	2.4	4	0	Yes	18
6	OD	57/M	9	SPK	Medical management	–		28	28	2.1	2.1	3	1	Yes	7
7	OD	56/F	18	MK with DON	Medical management	Tarsorrhaphy	Oral CS	21	21	2.1	2.1	2	2	Yes	60
8	OS	60/M	6	MK with thinning	Medical management	Tarsorrhaphy	Oral CS	–	–	2.1	2.1	4	2	yes	3
9	OD	50/F	6	MK with DON	Medical management	Tarsorrhaphy	IVCS	22	22	0.8	0.2	4	1	yes	60
10	OS	74/M	1	SPK with DON	Medical management		IVCS + AZT	22	22	0.4	0	4	1	yes	6
11	OD	77/M	1	MK with thinning	Medical management	TA + BCL	Oral CS	18	18	2.4	2.4	1	0	yes	5
12	OS	67/M	4	SPK with DON	Medical management			22	22	0.3	0	5	0	yes	28

Male - M; Female-F; Corneal breakdown-CB; Dysthyroid Optic neuropathy -DON; Superficial punctate keratopathy-SPK; Microbial keratitis-MK; orbital decompression-OD; tissue adhesive and bandage contact lens-TA + BCL; corticosteroid-CS, IVCS- Intravenous corticosteroid, AZT - Azothioprine

Table 4: Factors associated with a decline in visual acuity in thyroid eye disease patients with a corneal breakdown

Variables	VA stable/better	VA worse	*P*
Age in years (mean±SD)	47.48±16.03	54.20±15.85	0.244
Gender *n* (%)			
Male	29 (67.4)	3 (30.0)	0.039
Female	14 (32.6)	7 (70.0)	
Thyroid disease *n* (%)			
Hyperthyroidism	40 (93.0)	7 (70.0)	0.073
Hypothyroidism	3 (7.0)	3 (30.0)	
Diabetes *n* (%)			
Yes	9 (21.4)	1 (10.0)	0.664
No	33 (78.6)	9 (90.0)	
Smoking *n* (%)			
Yes	9 (21.4)	1 (14.3)	0.998
No	33 (78.6)	6 (85.7)	
CB *n* (%)			
SPK	20 (46.5)	0 (0)	0.025
MK	14 (32.6)	4 (40.0)	
MK with thinning	8 (18.6)	5 (50.0)	
MK with perforation	1 (2.3)	1 (10.0)	
Decompression *n* (%)			
Yes	32 (74.4)	6 (60.0)	0.442
No	11 (25.6)	4 (40.0)	
Side *n* (%)			
Right	19 (61.3)	3 (50.0)	0.670
Left	12 (38.7)	3 (50.0)	
VA DOP (mean±SD)	1.10±0.96	1.94±0.86	0.013
Duration TED in months	10.21±14.19	12.30±13.59	0.365
Pre-op CAS score	3.33±1.81	3.63±1.99	0.594
Pre-op Hertel's score	24.79±3.34	25.86±4.01	0.626
Follow-up in months	18.74±17.90	16.60±19.22	0.657

Discussion

Since Grave's initial description, it has become increasingly evident that TED includes a broader spectrum of manifestations beyond exophthalmos. Multiple reports in the literature have highlighted the coexistence of OSD in patients with TED.[2-7] A significant portion of the existing literature on sight-threatening disease in TED caters to DON elaborating the types, diagnostic criteria, risk factors, treatment, and outcome.[10] There is a paucity of published data on corneal breakdown in TED. Our study provides insights into phenotype, treatment, and outcome of corneal breakdown in TED. We reviewed various classification systems for grading corneal breakdown.[11,12] Werner's NOSPECS classification system grades corneal involvement based on worsening severity grades as stippling, ulceration, and clouding with necrosis and/or perforation.[11] We followed Werner's classification and graded corneal involvement in our study as superficial punctate keratitis, microbial keratitis alone, and finally microbial keratitis with thinning or perforation. This classification system covers the spectrum and longitudinal changes in the cornea in TED. Mild disease [Fig. 1a] presents as a sterile erosion. A super-added infective pathology manifests as microbial keratitis. Among these, a few progress to thinning [Fig. 1b] or perforation.

Unlike DON, risk factors predicting progression in corneal breakdown remain unknown.[10] An earlier study including 201 TED patients showed older age, smoking, and diabetes as major risk factors for DON, but none were predictive for corneal breakdown.[10] A majority of TED patients who presented or developed corneal breakdown in our series were in the early progressive (active) phase of the disease. Seven patients (nine eyes) developed corneal breakdown more than two years after onset when TED was quiescent.

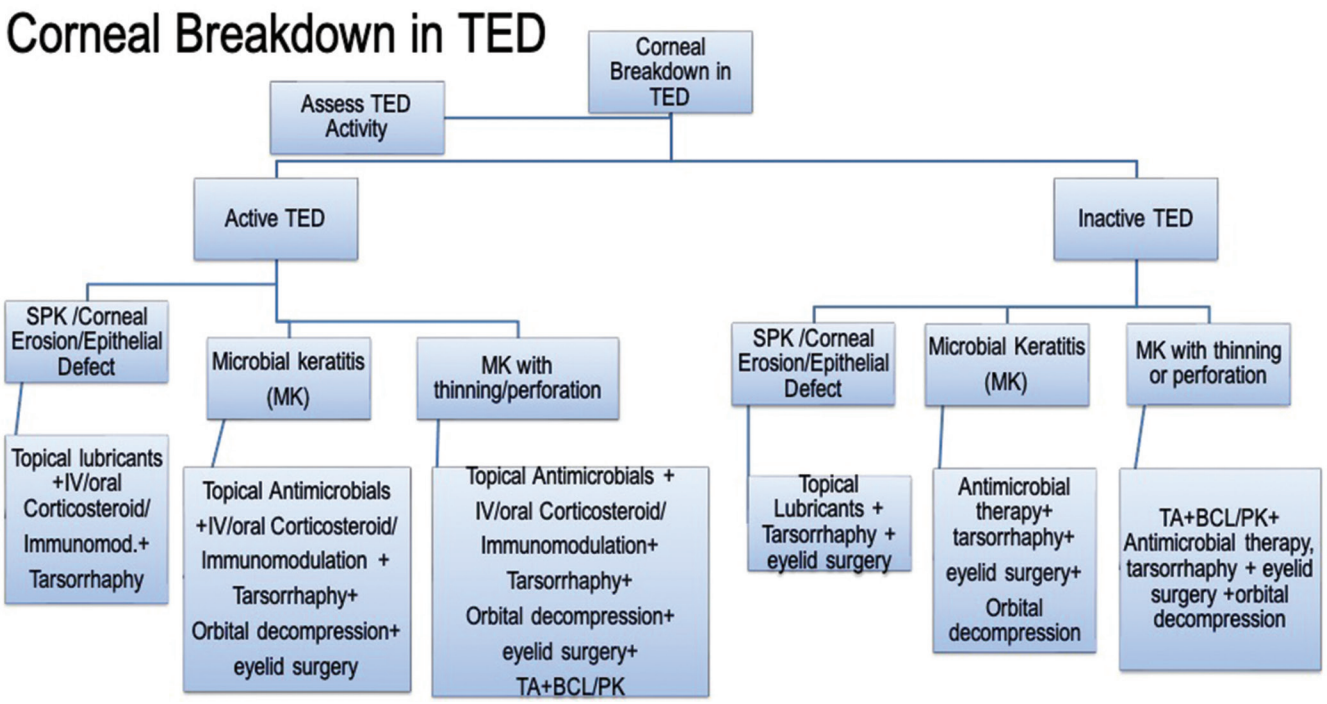

Figure 2: Algorithm to show multimodal management of corneal breakdown in both active and inactive disease

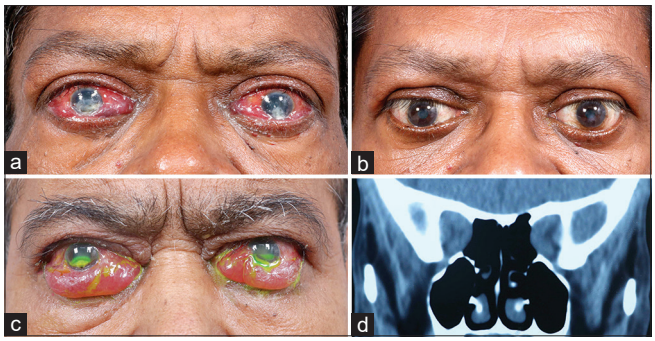

Figure 3: a-d. Clinical photograph of a 46-year-old, hyperthyroid male with active TED showing a - bilateral proptosis, lid retraction, severe inferior chemosis with conjunctival keratinization. Bilateral inferior corneal infiltrates secondary to exposure keratopathy are also seen. b- Complete resolution of the corneal infection in both eyes with consequent corneal scar after orbital decompression, full-thickness blepharotomy. Mild temporal flare of upper eyelids and residual retraction of the lower eyelid in the left eye are also seen. c – Another 83-year-old male who was hyperthyroid and presented 1.5 months after onset of thyroid eye disease. He presented with frank microbial keratitis with inferior corneal infiltration and thinning. Soft-tissue signs – massive conjunctival chemosis, caruncular edema, and eyelid edema – are also seen. d- The same patient's CT scan orbit shows apical crowding suggestive of DON

This makes corneal breakdown unique from DON as the risk of developing the former remains even when TED is inactive. Selter *et al*.[3] hypothesize a multifactorial pathogenesis of corneal breakdown in TED where a combination of exposure, inflammation, and ocular surface factors plays a role. This calls for a multimodal management strategy – intensive topical antimicrobial therapy, surgery of the orbit, eyelid, and ocular surface to improve exposure, copious lubrication, and systemic immunotherapy when TED is active to achieve good visual and globe salvage. We find evidence of this multimodal therapy in our series for both active and inactive disease and depict the same as an algorithm [Fig. 2]. This gives some credence to the multifactorial pathogenesis of corneal breakdown in TED.

CAS as described by Mourits *et al*.[13] holds little value in the setting of microbial keratitis in TED. Both etiologies – infection in microbial keratitis and soft-tissue inflammation in TED – can produce similar signs reflected by a high CAS score. When faced with this clinical scenario, clinicians treating TED can resort to orbital imaging preferably MRI to assess disease activity in the deep orbit.[9] Several sequences in MRI orbit – signal intensity ratio, T1 and T2 relaxation time, and diffusion-weighted imaging, have been reported for disease activity in TED.[14] In our series, 13 patients had concurrent DON along with corneal breakdown and two patients had bilateral microbial keratitis with thinning necessitating urgent orbital decompression and intensive medical therapy [Fig 3a-d]. Prevalence of both corneal breakdown and DON in TED occurred on 8/47, 1/24, and none in the series by Tramunt,[1] Naik[15] and Thakar *et al*.,[16] respectively.

Visual outcome after corneal breakdown in TED primarily depends on the type and degree of corneal involvement. Tramunt *et al*.[1] reported on 15 eyes with corneal breakdown in a series of 31 patients with sight-threatening TED. They found that local (medical) therapy alone was usually ineffective in TED patients with microbial keratitis as two-thirds needed additional surgical treatment.[1] Naik *et al*.[15] reported on 13 patients (14 eyes) with microbial keratitis drawn from 1000 TED patients in a decade giving a prevalence of 1.3%.A large majority (92%) of these were active with mean exophthalmometry measuring 24.7 mm. All had severe >2 mm eyelid retraction and motility limitation. One had bilateral disease. The corneal infection was severe in 8/14 eyes (total corneal infiltrate 4; thinning with/without perforation 4; panophthalmitis one), and generally, there was poor visual acuity at presentation.[15] Multimodal aggressive management, including surgery (eyelid, orbit, and cornea) with microbiology-guided antimicrobial therapy helped achieve resolution of corneal infection in 10 and improvement in visual acuity in 2 and 4 eyes, was eviscerated.[15] In our series, the mean LOG MAR visual acuity improved from 1.2 ± 0.9 at presentation to 0.7 ± 0.9 at the final follow-up at a median of 17 months. Globe salvage could be achieved in 44/50 (88%) eyes, and six eyes were eviscerated. The apparent disparity in visual outcome between both studies is due to varied criteria of inclusion with a predominance of florid corneal infections included in the series reported by Naik *et al*.[15] Our series included TED patients with mild corneal breakdown – SPK who were likely to have better BCVA. Poor visual acuity at presentation emerged as the only factor in our series that was associated with a worse final visual outcome. Our results tend to show orbital decompression surgery alone may not be sufficient to manage severe degrees of corneal breakdown. An aggressive multimodal management, encompassing both medical and surgical interventions – orbit, eyelid, and ocular surface along with systemic immunomodulation if TED is active, seems as most effective strategy in vision and globe salvage. Owing to the retrospective design, it is difficult to recommend a desired sequence for optimal outcome. However, for more severe degrees of corneal breakdown, protecting the ocular surface, intensive antimicrobials, and dealing with structural causes for exposure – tarsorrhaphy, orbital decompression, eyelid retraction correction, and anti-inflammatory agents–play an equal and effective role in salvaging the vision and globe.

Several patients in our series developed a new-onset of double vision after orbital decompression surgery necessitating extraocular muscle surgery to correct double vision. Thakar *et al*.[16] reported on a series of 12 patients (24 eyes) who underwent endoscopic decompression for proptosis, corneal exposure/keratitis, and compressive optic neuropathy. They reported early transient diplopia which resolved over 8 weeks. The higher incidence of diplopia in our series can be attributed to the higher proportion of active TED and/or advanced keratitis with thinning or perforation in our series. Thakar *et al*.[16] excluded patients with high CAS scores, and only 2/12 patients in their series had keratitis. An expeditious orbital decompression along with intensive medical therapy and adjuvant surgical procedures of the eyelid and cornea helped us achieve 88% globe salvage. This was significant because a third of the eyes included in our series had severe corneal involvement – microbial keratitis with thinning with or without perforation.

Limitations of our series primarily stem from its retrospective design. Corneal breakdown has a prevalence of <2% of TED patients and is rare. A prospectively designed study is likely

to be challenging for corneal breakdown in TED. Second, the small sample size of this rare complication was a limitation for more statistical tests. Despite these, our retrospective audit of corneal breakdown in TED patients over a decade seems to suggest that an expeditious multimodal management strategy including medical–topical and systemic along with surgery of the orbit, eyelid, and ocular surface for corneal breakdown can help achieve the vision and globe salvage.

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Conclusion

Corneal breakdown is a most severe sight-threatening type of thyroid eye disease necessitating expeditious and intensive multimodal management, topical medications, surgery of the eyelid, orbit, and ocular surface, and systemic immunomodulation, which if done, can salvage the globe and vision.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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