Original Article

Dysthyroid optic neuropathy: Demographics, risk factors, investigations, and management outcomes

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Purpose: To analyze the clinical presentations, risk factors, and management outcomes in patients presenting with dysthyroid optic neuropathy (DON). **Methods:** This is a retrospective, single-center study carried out on consecutive patients presenting with DON over a period of 4 years (2013–2016). The VISA classification was used at the first visit and subsequent follow-ups. The diagnosis was based on optic nerve function tests and imaging features. Demographic profiles, clinical features, risk factors, and management outcomes were analyzed. **Results:** Thirty-seven eyes of 26 patients diagnosed with DON were included in the study. A significant male preponderance was noted (20, 76.92%). Twenty patients (76.9%, $P = 0.011$) had hyperthyroidism, and 15 (57.69%, $P = 0.02$) were smokers. Decreased visual acuity was noted in 28 eyes (75.6%). Abnormal color vision and relative afferent pupillary defects were seen in 24 (64.86%) eyes, and visual field defects were seen in 30 (81.01%) eyes. The visual evoked potential (VEP) showed a reduced amplitude in 30 (96.77%, $P = 0.001$) of 31 eyes and delayed latency in 20 (64.51%, $P = 0.0289$) eyes. Twenty-six (70.27%) patients were treated with intravenous methyl prednisolone (IVMP) alone, whereas 11 (29.72%) needed surgical decompression. The overall best-corrected visual acuity improved by 0.2 l logMARunits. There was no statistically significant difference in outcome between medically and surgically treated groups. Four patients developed recurrent DON, and all of them were diabetics. **Conclusion:** Male gender, hyperthyroid state, and smoking are risk factors for developing DON. VEP, apical crowding, and optic nerve compression are sensitive indicators for diagnosing DON. Diabetics may have a more defiant course and are prone to develop recurrent DON.

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Dysthyroid optic neuropathy (DON) is a serious vision-threatening complication and has been reported to occur in 5–8.6% of patients with TED.[1] An Indian study stated the incidence of visual morbidity in TED to be as high as 19% with DON showing a prevalence of 14.3%.[2] DON may occur as a result of compressive or ischemic optic neuropathy. The stretching of the optic nerve may also result in stretch optic neuropathy, but this remains debatable.[3-7]

The diagnosis of DON is essentially based upon deranged optic nerve function tests. However, these patients can present with normal visual acuity, color vision, and pupillary reactions, making the diagnosis challenging. Apical crowding documented on computed tomography (CT) or magnetic resonance imaging (MRI) has been described as a good predictor of DON.[3,8] Co-existing ocular morbidities such as cataract, glaucoma, exposure keratopathy, and retinal pathologies may lead to both a delay and over-diagnosis of DON. Visual evoked potential (VEP) has been described as a sensitive indicator of DON, and it helps in early detection of sub-clinical cases.[3,6] Early diagnosis and prompt management can prevent further deterioration of optic nerve functions and improve the visual prognosis.

Algorithms for management of thyroid eye disease have been described in the literature; however, the treatment is still widely subjective based on the clinician and geographical variation.[9] Pulse intravenous methylprednisolone (IVMP) has been the mainstay of treatment.[2,3,5,6,9] Surgical decompression of the orbit, radiotherapy, and immuno-suppressants along with biologic agents have been reported to be beneficial with variable results.[8,9]

The literature on DON and its outcomes from the Indian sub-continent is limited. The present study aims to analyze the demographic profile, clinical characteristics, and risk factors of DON in TED patients presenting to a tertiary eye care center in the Indian subcontinent. To the best of authors' knowledge, this is the first study to compare the management outcomes among

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the group treated with IVMP alone with that undergoing orbital decompression, risk factors, and the sensitive indicators of DON in the Indian subset.

Methods

We performed a retrospective analysis of 214 consecutive patients diagnosed with thyroid eye disease seen at a tertiary eye care center in South India over a 3-year period. Records of 26 patients diagnosed with DON were analyzed in detail and included in the study. The study was approved by the institutional review board, and it strictly adhered to the tenets of the Declaration of Helsinki. All the patients provided written informed consent.

The diagnosis of DON was based on deranged optic nerve function tests.[3,9-11] The diagnostic criteria for DON in the present study were the presence of any one deranged optic nerve function test in a diagnosed case of thyroid eye disease, reduced visual acuity (in the absence of other co-existing intra-ocular conditions, amblyopia, exposure keratopathy), abnormal color vision (without pre-existing color blindness), presence of RAPD, optic disc changes (disc edema, non-glaucomatous disc pallor), visual field defects, and abnormal VEP, supported by imaging features (the presence of apical crowding with or without optic nerve compression). Vision was recorded with Snellen's chart and converted to logMAR units. Color vision was recorded with standard isochromatic Ishihara's chart. Humphrey's visual field 30-2 (HVF) test was deferred in eyes where visual acuity was too less to perform the test. The clinical features of the patients were graded according to the VISA (Vision, Inflammation, Strabismus, and Appearance) scoring system introduced by ITEDS (International Thyroid Eye Disease Society) at each visit. Imaging in the form of computerized tomogram or, preferably, MRI was performed in all patients. Apical crowding, optic nerve compression, and extra-ocular muscle thickness at the mid-orbit level were measured by a single experienced radiologist as described in the literature.[10,11]

All patients diagnosed with DON were initially treated with intravenous methylprednisolone (IVMP) 1 gm daily in 500 ml normal saline slowly injected over 2 hours for 3 consecutive days. The patients who showed improvement with IVMP were started on a weekly tapering course of oral steroids (1 mg/kg/body weight) to reduce inflammation and orbital congestion and to prevent a relapse. This treatment protocol was devised based on the literature available at the beginning of the study.[12,13] Patients who failed to respond to medical management or wherein steroids were contraindicated or patients who had reached the maximum dose limit for IVMP (8 gms) were taken up for surgical orbital decompression. The outcome was measured based on the improvement in the optic nerve function and resolution of DON. Patients with a follow-up of less than 6 months were excluded from the study.

Statistical analysis was performed using the Chi-square test, t-paired test, and Wilcoxon signed rank test. Data were analyzed using SPSS version 14.0.

Results

A total of 26 out of 214 (12.1%) TED patients developed DON. Thirty-seven eyes of these 26 patients were included in the study. A strong male preponderance (20, 76.92%; P = 0.003) was noted. Twenty-one (80.76%) patients had known thyroid disorder at presentation, whereas the remaining five (19.24%) were subsequently diagnosed to have thyroid dysfunction. Seventeen patients (65.38%, P = 0.02) were addicted to tobacco (15 smokers and two tobacco chewers, 3.84%). Five patients (19.23%) had associated diabetes mellitus. The most common presenting complaint was prominence of the eye, with diminution of vision (21 patients, 80.76%, P = 0.01). Bilateral DON was seen in 11 (42.30%) patients with a mean VISA inflammatory score of 3.9 (2-9). The mean best-corrected visual acuity (BCVA) at presentation was 0.74 ± 0.926 logMAR units. Exposure keratopathy was seen in five eyes of four patients. The mean intra-ocular pressure (IOP) in the primary gaze was 20.88 ± 5.35 mm of Hg (range 14–40 mm Hg). Ten (38.46%) patients were already on anti-glaucoma medications (AGMs) at presentation. The demographic details have been summarized in Table 1. The mean exophthalmos documented on a Hertel's exophthalmometer was 24.14 mm ± 4.39. (15–29 mm). VEP was recorded in 31 of 37 eyes and showed reduced amplitude in 30 eyes (96.77%; P = 0.001) and delayed latency in 20 eyes (64.51%; P = 0.0289).

Out of 37 eyes, the most common deranged optic nerve function was VEP (30, 96.77%; P = 0.001) and abnormal HVF (30, 81.08%; P = 0.001), followed by decreased BCVA (27, 75.67%), abnormal color vision (24, 64.86%), and relative afferent pupillary defects (24, 64.86%). The most common visual field abnormalities were central (7) and para-central (6) defects and enlarged blind spot (5), followed by inferior altitudinal defects (2). Generalized field depression was seen in ten eyes (33.33%). Disc edema was seen in 13 (35.13%) eyes, and four eyes (10.81%) had disc pallor at presentation [Table 2].

Table 1: Demographic profile and common clinical features of patients with DON

Variables		*P* value
Age	47.96 yrs±10.98 yrs (27-68 yrs)	
Sex (*n*=26)	Male: Female: 3.3:1	*P*=0.003
Laterality (*n*=26)		
Right eye	5, 19.23%	*P*=0.117
Left eye	10, 38.46%	*P*=0.113
Bilateral	11, 42.30%	*P*=0.079
Smoker (*n*=26)	15, 57.69%	*P*=0.02
Thyroid status (*n*=26)		
Hyperthyroid	20, 76.92%	*P*=0.011
Hypothyroid	6, 23.07%	*P*=0.25
EOM (*n*=37 eyes)		
Elevation <30°	16, 43.2%	*P*=0.411
Depression <30°	10, 27.03%	*P*=0.28
Abduction <30°	11, 29.7%	*P*=0.5064
Adduction <30°	7, 18.9%	*P*=0.393
Proptosis (*n*=26)	24.14±4.39 (15-29)	
IOP (*n*=26)	20.88±5.35 mmHg (range 14-40 mmHg)	
Mean inflammatory score (VISA)	3.84 (0-10)	
Follow-up	21.57 months±3.42 months (6-84 months)	

EOM: Extra-ocular motility, IOP: Intra-ocular pressure, VISA: Vision inflammation strabismus appearance.

Table 2: Pre- and post-treatment optic nerve functions in IVMP and surgical decompression groups

Variable	IVMP group (*n*=26)			Surgical decompression (*n*=11)			Overall (*n*=37)		
	Pre	Post	*P*	Pre	Post	*P*	Pre	Post	*P*
Visual acuity									
Log MAR units	0.44	0.2	0.13	1.048	0.84	0.42	0.72	0.5	0.3
Color vision									
Normal	11		0.0001	02		0.0006	13	-	<0.001
Improved	-	13		-	08		-	21	
No improvement	-	02		-	01		-	03	
Pupil									
RAPD	16	02	0.0001	08	03	0.033	24	05	<0.001
HVF									
Normal	06		0.0001	0		0.0004	06	-	
Improved	-	14		-	06		-	20	<0.001
No improvement	-	06		-	02		-	08	
VEP									
Normal	01	04	0.134	0	04	0.021	1	08	0.001
Abnormal	23	05		07	04		30	09	

The term "improvement" for different parameters implies that functions got better and not necessarily became normal. Parameters which were normal in the pre-treatment period remained normal in the post-treatment period also, and hence, the post-treatment column has been left blank to avoid confusion.
HVF: Humphery's visual field, VEP: visual evoked potential, IVMP: intravenous methyl prednisolone

Table 3: Sensitivity, specificity, positive predictive, and negative predictive factors for optic nerve function tests

Parameters	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Visual acuity	80%	52.94%	66.67% (CI: 53.58-77.61%)	69.23% (CI: 45.57-85.76%)
Color vision	46.15%	10%	57.14% (CI: 45.61-67.95%)	6.67% (CI: 1.06-32.17%)
Abnormal pupillary reaction	80%	76.47%	80% (CI: 62.29-90.64%)	76.47% (CI: 56.55-89.03%)
HVF	75%	56.25%	68.18% (CI: 53.78-79.78%)	64.29% (CI: 42.91-81.44%)

*The PPV and NPV for VEP and apical crowding could not be calculated because of inadequate data post treatment

None of the patients with diabetes had any retinopathy at presentation.

MRI was performed in 22 patients (84.61%), whereas four (15.38%) patients had a pre-existing CT scan. Imaging showed apical crowding in all (37 eyes, 100%, $P = 0.0001$) cases and optic nerve compression in 33 of 37 eyes (89.18%, $P = 0.002$) [Fig. 1]. The mean muscle thickness of all four recti measured at the mid-orbit level was 6.957.49 mm ± 2.22 (range 2.3–14.3 mm). The inferior rectus muscle was reported to be the thickest (7.49 ± 2.3 mm, range 3–12.1 mm), followed by superior rectus (7.41 ± 2.9 mm, range 4–14.3 mm), medial rectus (7.37 ± 2.25 mm, range 3–10.9 mm), and finally lateral rectus (5.53 ± 1.445, range 2.3–8.6 mm). Enlargement of all four recti muscles was seen in 19 eyes (51.4%); three muscle enlargements were seen in 12 eyes (32.4%) and two muscle enlargements were seen in 5 eyes (13.5%). A single muscle enlargement was seen in only one eye (2.7%). None of the patients in the present study showed optic nerve stretching or orbital fat prolapse through the superior orbital fissure (SOF) on imaging.

IVMP was administered to all patients at presentation. Twenty-six eyes of 17 patients (65.3%) responded to IVMP alone, whereas 11 eyes (29.72%) of nine patients who failed to respond to IVMP were taken up for surgical decompression after a median duration of 7 days. Eyes which required surgical decompression had poorer visual acuity at presentation, compared to those which required only IVMP (1.082 log MAR units vs 0.44 log MAR units, $P = 0.0295$). The mean dose of IVMP administered was 7 ± 2.6 gm [Fig. 2].

Post IVMP, after an initial improvement, three eyes of two patients showed persistent DON at mean follow-up of 3 weeks (range: 2–4 weeks). Both these patients refused to undergo orbital decompression and received external beam radiation (20 Gray in 10 fractions) with concurrent tapering oral steroids. Complete resolution of DON without any further recurrence was noted in these two patients at the last follow-up.

Seven eyes underwent two wall decompressions [inferior and medial wall decompressions, 6 patients (54.54%); medial and lateral wall decompressions, 1 patient]. Four eyes of three patients (36.36%) underwent three wall decompressions (inferior, medial, and lateral).

Recurrent DON was seen in six (16.21%) eyes of four patients, and all four (100%) patients had associated diabetes mellitus. Two patients (three eyes) with recurrent DON were successfully treated with a repeat course of IVMP (1 gm for 3 days), followed by tapering oral steroids.

A total of 29 (78.37%) eyes of 21 patients showed improvement. The mean BCVA improved from 0.44 logMAR units to 0.2 logMAR units in the group which received IVMP alone, whereas

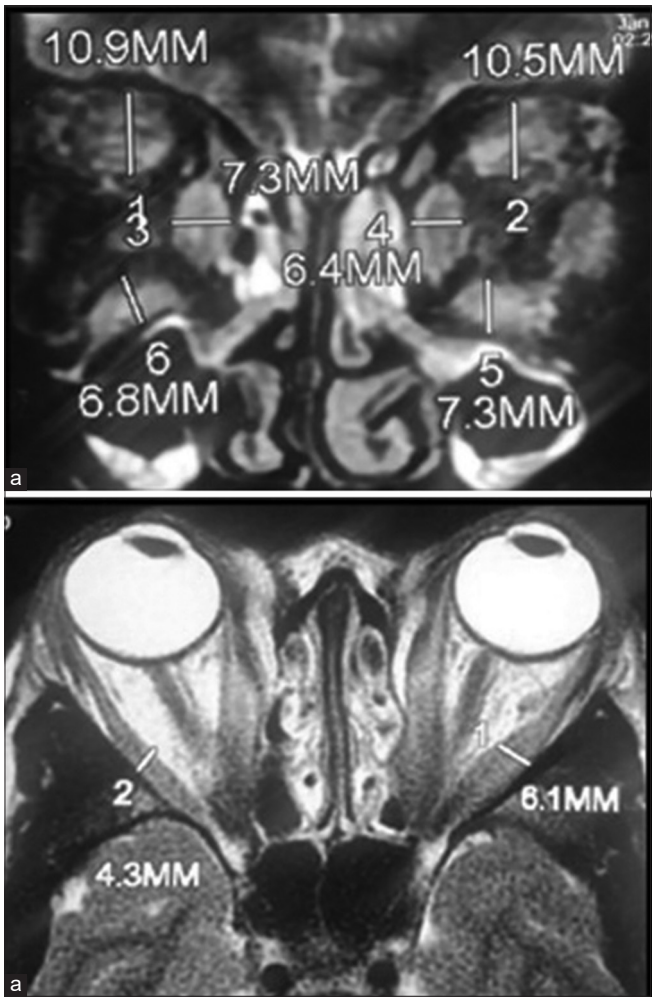

Figure 1: (a and b) MRI T2-weighted images and coronal and axial scans showing gross enlargement of bilateral extra-ocular muscles with a hyper-intense T2 signal and causing apical crowding with optic nerve compression

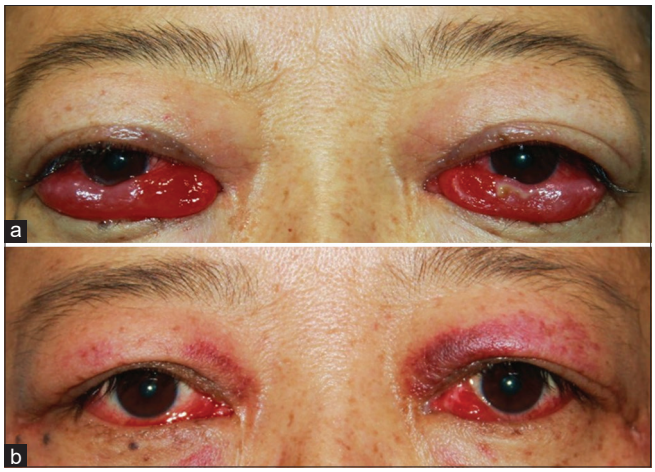

Figure 2: (a) External clinical photograph portraying clinically active bilateral thyroid eye disease with dysthyroid optic neuropathy. (b) External clinical photograph Immediately after bilateral two wall orbital decompression with adjuvant IVMP. Note the reduction in conjunctival chemosis and proptosis

Table 4: Risk Factors for DON

Variable	Odds Ratio	95% Confidence Interval	
		Lower Limit	Upper Limit
Age	1.016	0.981	1.052
Sex: Male	2.842	0.949	8.514
Hyperthyroid	3.071	1.087	8.676
Smokers	6.5	2.351	17.971
Diabetes Mellitus	2.417	0.665	8.789

in the group which underwent orbital decompression, the mean BCVA improved from 1.048 logMAR units to 0.84 logMAR units post surgery. HVF was deferred in three eyes owing to the poor vision [Fig. 3]. The results of the other optic nerve function tests before and after treatment are listed in Table 2.

Decreased BCVA and the presence of abnormal pupillary reaction had an 80% sensitivity each and a specificity of 52.94% and 76.47%, respectively, in establishing the diagnosis of DON. The sensitivity, specificity, and positive and negative predictive values for other optic nerve function tests and risk factors for DON were calculated and are summarized in Tables 3 and 4; Fig 4.

Eight eyes (21.62%) of five patients showed no further improvement with either IVMP or after undergoing decompression, of which 50% had disc pallor at presentation.

The mean follow-up period was 21.57 months ± 6.42 months (range, 6–84 months).

Discussion

Optic neuropathy in TED has been attributed to direct nerve compression and impairment of the axonal flow or is because of micro-vascular ischemia secondary to increased peri-neural apical tissue pressure.[3,7,14,15] According to Rose *et al*.,[7] this micro-vascular ischemia can be reversible.

Neigel *et al*.[16] found that older patients were more prone to develop DON and the average age at presentation in their study was 57.7 years. In fact, the risk of developing DON may increase by up to 58% with the increase in the age by every decade.[3] The patients in our study were relatively younger (mean age 47.97 years) as compared to other studies.[17-19] We noticed that four of the five patients who showed no improvement to treatment were comparatively older (mean age 54 years). This finding was in concordance with another study from the Indian sub-continent, which reported a total of 42 sight-threatening TED (mean age 54.4 years). Rath *et al*.[20] concluded that older age (HR 1.05) was a risk factor for DON.

Although the prevalence of TED among females is higher, the severity of TED has been reported higher in males.[3,15,17] Studies among Europeans and Caucasians have reported a female preponderance among the DON study group (68.08% and 80%, respectively), quite contrary to our study wherein we noticed a strong male preponderance (76.92%) similar to that reported by Rath *et al*.[14,18,20] We found males to be at a higher risk of developing DON (odds ratio 2.842). Jeon *et al*.[18] reported that the majority of the patients in their study (80%) were euthyroid. The majority of patients in our study were

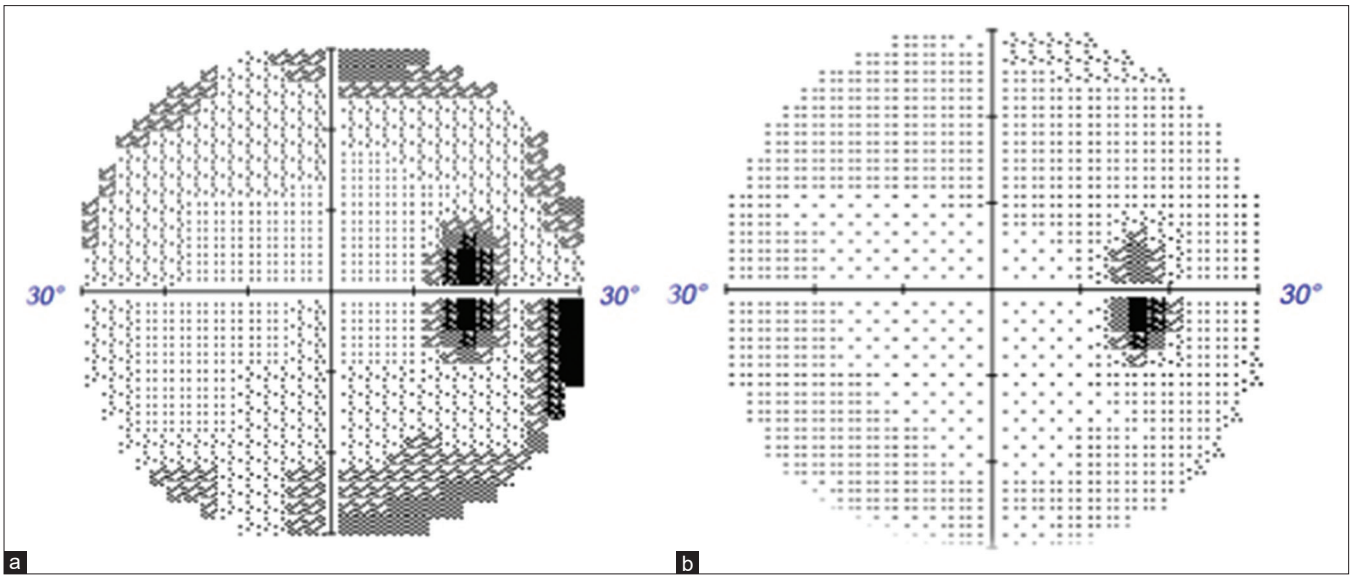

Figure 3: (a) HVF gray scale depicting peripheral defects with enlarged blind spot. (b) HVF gray scale 3 years post treatment shows complete resolution and normal visual fields

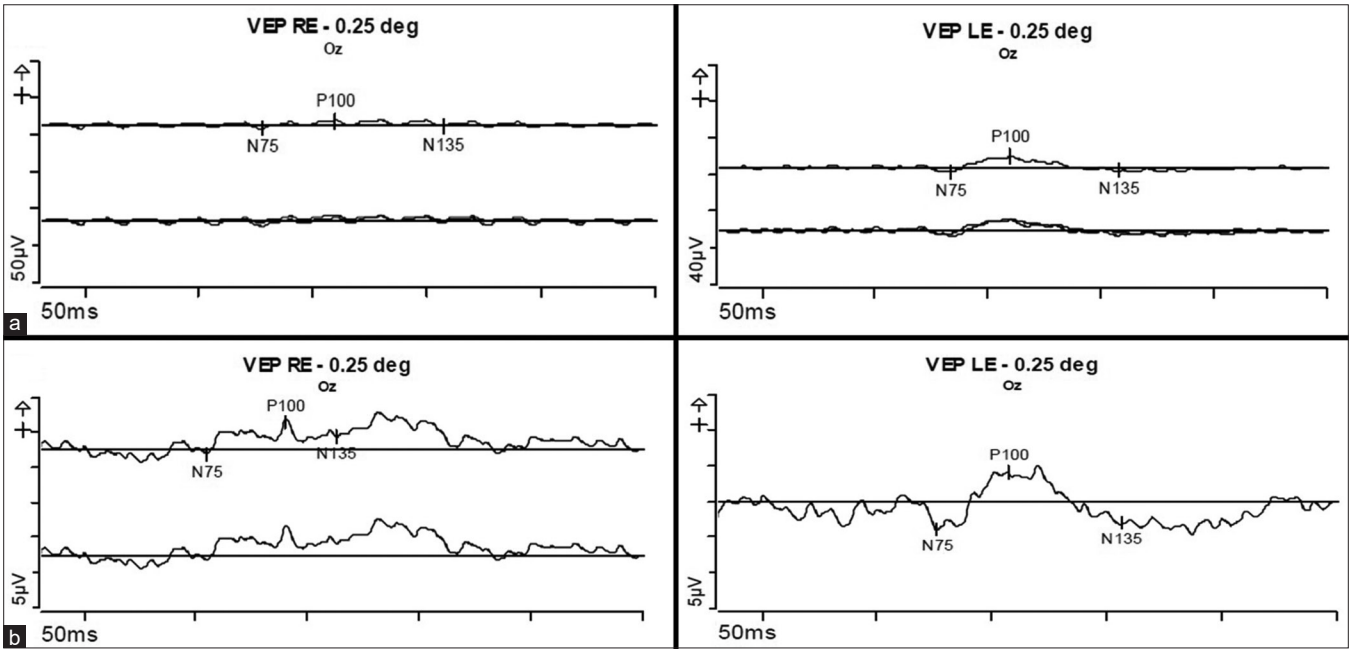

Figure 4: (a) Visual evoked potential (VEP) in a patient with DON. Note the gross reduction in amplitudes as well delay in the P100 latency. (b) VEP post-treatment shows improvement of P100 latency in both eyes with improved amplitudes in the right eye but persistent reduced amplitudes in the left eye

hyperthyroid (76.92%), which is in concordance with the EUGOGO study.[14] The most common presenting complaint was diminution of vision with prominence of the eyes (80.76%) similar to other studies.[18,19]

Jeon *et al.*[18] found that 25% of their patients with DON had associated type 2 diabetes mellitus, similar to our study (19.23%). Four of the five (80%) diabetic patients in our study had recurrent DON, and all patients were on insulin. It has been presumed that diabetics have a more defiant course and are more predisposed to optic neuropathy because of ischemic changes and probably are at a higher risk for developing recurrent DON similar to our study.[3,18] Few studies from the Indian subcontinent have studied the correlation between the severity of TED and diabetes mellitus. They concluded that type 2 diabetes mellitus with thyroid eye disease can be a predictive factor for severity and progression of the disease.[20,21]

More than half (51%) of the patients in our study were active smokers. Studies have found smoking to be a strong predictive factor for development of DON (odds ratio = 10.00).[3,20-24] In the current study, the odds ratio calculated was 6.5, and thus, we conclude that smoking is a risk factor for DON similar to that described in the literature.[20]

Table 5: Review of literature (past 2 decades)

Author, Year	Sample size	Study design	Management		Outcome (Visual function)
			MD	SD	
Kazim *et al.*,[7] 2000	8 orbits, 5 patients	R	-	Fat	Improved (100%)
Perry *et al.*,[39] 2003	26 orbits, 16 patients	R	-	Transcaruncular medial, infero-medial wall	Improved or stable. (96% improvement in CV)
Schaefer *et al.*,[43] 2003	41 patients	R	-	Endoscopic, Transconjunctival SD	89.3% Improved
Wakelkamp *et al.*,[25] 2005	15	RCT	9 patients - IVMP pulse + oral steroids	6, SD	MD - 55% improved SD - 18% improved
Liao *et al.*,[33] 2006	22 patients	R, I	-	SD, medial, infero-medial	All parameters improved, 39.8% new onset diplopia
Soni *et al.*,[40] 2010	3 patients	O	-	SD	66.67% Improved
Khanna *et al.*,[41] 2010	4 patients	R	Rituximab	-	Improved (100%)
Choe *et al.*,[29] 2011	28 orbits, 17 patients	R	-	10 - lateral SD 18 - medial SD	Improved (100%)
Jeon *et al.*,[15] 2012	65 orbits, 40 patients	R	6 patients - IVMP 17 patients - IVMP + RT	26 orbits- IVMP + SD -8 IVMP + SD + ORT-8	MD - recurrence 17% SD - recurrence 18.75%
Curro *et al.*,[12] 2014	24 patients, 40 orbits	R	IVMP	-	Improved 42.5%
Baril *et al.*,[37] 2014	34 patients, 59 orbits	R	-	Endoscopic medial + external lateral SD	Improved 100% Total resolution 93.22%
Korkmaz *et al.*,[38] 2016	42 patients, 68 orbits	R	-	41 orbits - 2 wall SD 27 orbits - 3 wall SD	Improved 100%
Singh *et al.*,[35] 2019	17 patients, 17 orbits	R, I	-	Augmented endoscopic SD	Improved 100%
Liang *et al.*,[36] 2019	22 patients, 30 orbits	R	-	SD	Improved 53.33%
Xu J *et al.*,[42] 2020	23 patients, 46 obits (B/L DON)	P	23 patients - IVMP	23 orbits - IVMP + SD	Improved 100% IVMP + SD better outcome
Sears *et al.*,[30] 2020	1 patient	CR	Teprotumumab	-	Improved
Slentz *et al.*,[31] 2020	1 patient	CR	Teprotumumab	-	Improved
Current Study	26 patients, 37 orbits	R, I	17 patients - IVMP	9 patients - SD	Improved 78.37%

B/L - bilateral, R - retrospective, RCT - randomized control trial, I - interventional, O - observational, P - prospective Rx- treatment, MD - medical decompression, IVMP - intravenous methyl prednisolone, ORT - orbital radiation, SD - surgical decompression, CV - color vision

Fifty percent of the patients in our study were unaware of an underlying optic nerve dysfunction, whereas 35% of cases did not show any clinical signs suggestive of DON. Dysthyroid optic neuropathy in these cases was diagnosed based on further investigations (VEP, HVF, and imaging). About 50–70% of established DON cases have been reported to have a good visual acuity (20/40 or better), and optic nerve edema may be seen in only 20–50% cases.[3,14,18] Nine (24.32%) of the 37 eyes in the present study cohort had normal vision, and 13 (35.13%) eyes had normal color vision at presentation. Disc edema was present in only 35.13% eyes in our study. We wish to reiterate that a normal visual acuity or color vision, the absence of an RAPD, or optic nerve swelling does not exclude the diagnosis of DON. This highlights the role of periodic screening and the need to increase awareness among treating physicians, endocrinologists, and general ophthalmologists regarding the possibility of a sub-clinical DON in patients with thyroid dysfunction.

Bartalena *et al.*[25,26] observed various abnormal visual field patterns including inferior arcuate defects and inferior altitudinal and infero-lateral defects. We noticed an abnormal visual field in 82.35% eyes with common patterns seen in the form of a central or paracentral scotoma and enlarge blind spots. HVF had a positive predictive value of 68.18% and a negative predictive value of 64.29% in our study.

Electro-physiological abnormality is considered as the most sensitive indicator for detecting early optic neuropathy, and VEP is useful not only for establishing the diagnosis but also to monitor the disease progression and management outcomes.[11,27] Being a retrospective study, the data for VEP were available in only 31 of 37 eyes. We found a decreased amplitude in 96.77% ($P = 0.001$) of the eyes, whereas delayed latency was seen only in 64.51% ($P = 0.0289$) of the eyes. Tsaloumas *et al.*[27] also noticed a reduction in pattern amplitude occurring more frequently than a delay in latency in their study among DON patients.

Apical crowding, when present on imaging, is a sensitive and specific indicator of DON.[3,8-10,18,19] All (100%) cases in the present study showed apical crowding. Optic nerve compression on imaging was seen in 89.18% eyes in our study. In two-third cases with DON, the muscle index (MI) calculated on imaging has been reported greater than 70%.[8,28,29] We did not notice prolapse of orbital fat through the superior orbital fissure in any of our patients, although it has been described as a predictor of DON.[3,14]

Different studies have followed different protocols for the treatment of severe TED with DON.[3,14,16,17,20,21,30] Mega-dose

pulse IVMP has been the mainstay of management and has proved to be more effective with lesser side effects. The mean dose of IVMP administered was 7 ± 2.6 gm. A cumulative dose of over 8 gm has been associated with serious adverse effects, and we kept this as the upper limit for administration.[3,31] Currò *et al*.[15] determined that persistent disc edema and equivocal disease activity at 2 weeks despite treatment are good predictors of unresponsiveness to steroids therapy. If further deterioration in optic nerve function tests is seen after 2 weeks of primary medical management, then surgical decompression is indicated.[3,15] We noticed that eyes which required surgical decompression had a poorer visual acuity at presentation (1.082 log MAR units vs. 0.44 log MAR units, $P = 0.0295$). The improvement in visual acuity among those treated medically as well as those who underwent a surgical decompression was not significant statistically. This is in accordance with the study by Wakelkamp *et al*.[32] Patients with pre-existing disc pallor (11%) at presentation showed a poorer clinical improvement.

A total of 63.63% eyes in our study required a minimum of two wall decompressions, whereas 36.36% underwent three wall decompressions. Choe *et al*.[33] compared medial and lateral wall decompressions in patients with DON and strongly support the efficacy of a single deep lateral wall decompression among patients with DON and significant proptosis.

Recent case reports show encouraging results with the use of teprotumumab for treatment in dysthyroid optic neuropathy.[34,35] Based on the promising safety profile and reliable results from the available multi-centric trials for active TED, teprotumumab may prove useful as an adjuvant or monotherapy for DON in patients refractory or unsuitable for intravenous steroids, although the cost and availability of the drug remain a challenge for developing countries such as India.[36]

Table 5 summarizes studies describing the management outcomes of dysthyroid optic neuropathy over the past 2 decades.

The drawbacks of the current study are its study design being retrospective in nature, a small sample size, and an old treatment protocol which included the use of oral steroids. This study gives us an insight on the clinic-radiological features, risk factor, and outcomes of DON in the Indian sub-continent. We acknowledge these limitations as well as the need for a prospective, multi-centric study with a larger sample size which could shed more light on assessing the prognostic factors, predict outcomes, and help in establishing a standard treatment protocol for DON. Certainly, with the advent of disease-modifying agents such as teprotumumab, we hope to see a decrease in the incidence of this vision threatening condition in the future.[34,35]

Conclusion

Sub-clinical DON is not an infrequent entity and is often missed. Hence, a periodic detailed eye screening of patients diagnosed with thyroid dysfunction must be emphasized upon.

The present study suggests that a male gender, a hyperthyroid state, and smokers have a higher risk for developing DON. VEP, apical crowding, and optic nerve compression seen on imaging are sensitive indicators for establishing a diagnosis. Apical crowding on imaging is a good predictor of DON, and stretching of the optic nerve and fat prolapse through the superior orbital fissure may not be present in all cases of DON. Diabetics are prone to develop recurrent DON and may be refractory to initial medical management. Age may be an important prognostic indicator while assessing outcomes. The current study suggests medical management with mega-dose IVMP to be the first line of management with orbital decompression and/or radiation being reserved for patients refractory to medical management.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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