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Ophthalomology

ASSESSMENT FOR DRY EYE DISEASE IN OCULARLY ASYMPTOMATIC PATIENTS OF HANSEN'S DISEASE

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INTRODUCTION

By bringing down the prevalence rate to less than 1/10,000 at the national level in 2005 itself, India had officially reached the leprosy elimination goal, as a public health issue (Prevalence rate <1 per 10,000 population as defined by the WHO). However, with over 1.14 lakh new leprosy cases detected in 2020, India has more than 55 per cent of the total cases reported globally. This is however restricted to areas of hyperendemicity. **[1, 2]**

An important morbidity in general ophthalmic practice is dry eye disease (DED). It is also a fact that the incidence of this entity is increasing by the day. In USA, from 2003–2015, the most common ocular conditions in decreasing order of prevalence were errors of refraction (25.84%), cataracts (17.14%), glaucoma (7.27%), diseases of the conjunctiva (6.76%), retinal disorders (5.94%), and DED (5.28%). DED was the fifth most prevalent ocular condition in women (7.78%) and ninth most prevalent in men (2.96%) and has been increasing every year **[3]**

The lacrimal secretory system consists of the basal secretors which are the accessory lacrimal glands of Wolfring and Krause, coupled with the sebaceous glands of Meibomian, Zeiss and Moll. The Main lacrimal gland is a reflex secretor of tear fluid [4].

Over a13-year period, in a population study in Taiwan, age-adjusted prevalence of DED for men and women were 6.81% and 16.16%, respectively **[5]** The "Dry Eye World Study" (DEWS II) defines that the diseases of the surface of the eye are multifactorial and characterized by the tear film instability, inflammation, tear hyperosmolarity, damage to the surface of the eye, and neurosensory abnormalities of the cornea **[6].** The same maybe one of the principal factors among patients with HD**.**

Watering from the eyes is a common complaint in patients with (HD). The anterior segment manifestations of Hansen's which include loss of eyelashes associated with infiltrative and nodular skin lesions, beading and opacification of corneal nerves, punctuate sub-epithelial opacities associated with interstitial keratitis and corneal anaesthesia, vascularisation of the cornea, upper eyelid entropion, blepharochalasis, trachiasis, nodular episcleritis, miliary lepromas on the iris, iris pearls and nodular iritis and its complications due to the lepromatous form of the disease and lagophthalmos, exposure keratitis with attendant corneal complications, poor blink response and ectropion of the lower lid due to the tuberculoid form of the disease are all causes of watering. This is caused by injuries to the fibres of the intermediate nerve that follows the facial nerve which gives parasympathetic innervation to the lacrimal gland, causing reduced tear production, and potentiating the signs and symptoms of tear film abnormality **[7].**

Yet, there are many patients who attend an ophthalmologist's office with clinically normal ocular examination but with persistent complaints of watering. The most common clinical tests done in an OPD are ST and Tear Break-Up Time (TBUT) **[6].** ST provides a measure of tear production per unit time. It is the most common technique for assessing tear secretion. TBUT helps in assessing the stability of preocular tear film using a fluorescein dye and cobalt blue filter. A combination of these two tests have been used to assess DED.

Dry eye as a cause un-associated with any anterior segment abnormality in Hansen's patients without reactions has not been investigated frequently. There is a paucity in literature on the study done in patients with HD with these tests in cases with no obvious anterior segment abnormalities. A study had been done but only with ST and only in males **[8]**. A study was, therefore conducted to assess the dry eye situation in patients with HD with no abnormal anterior segment pathology and to correlate the altered tear production with the various clinical sub-types of Hansen's disease

MATERIALS AND METHODS

The study was conducted in the Ophthalmology Department after clearance of institute ethical and research committee. Diagnosed patients of HD were evaluated for this study. These patients were then subjected to complete ophthalmic examination as follows:

1. Ocular alignment at 06 m and at 33 cm
2. Amount of convergence
3. Best corrected visual acuity
4. Anterior segment and detailed fundus evaluation.
5. Measurement of intraocular pressure by Goldman's applanation tonometry

After this ocular examination, the following cases were recruited in the study after subjecting the following inclusion and exclusion criteria.

Inclusion Criteria:

1. Any diagnosed patient of Hansen's disease

Exclusion Criteria:

1. Cases with loss of eye- lashes
2. Cases associated with infiltrative and nodular skin lesions
3. Cases associated beading and opacification of corneal nerves
4. Cases with punctuate sub-epithelial opacities
5. Cases associated with interstitial keratitis and corneal anesthesia
6. Cases associated with trichiasis
7. Cases associated with nodular episcleritis
8. Cases associated with lagophthalmos
9. Cases associated with exposure keratitis with attendant corneal complications

The age and sex of all the subjects was noted.
The following tests of DED were then performed on each on a different day.

Schirmer's Test

This test was performed without anaesthesia and was done prior to other tests. **Procedure**: It was performed using 5×35 mm sterile strips of Whatman no.41 filter paper. The patient was made to sit in a dim light air-conditioned room of more than 6 m long with fans switched off. The terminal rounded end of the paper was folded at the pre-marked area at the right angle and was inserted in the lower cul de sac at the junction of medial 2/3rd and lateral 1/3rd of the lid, while the patient was asked to look up at 6m Snellen's Chart. Adequate care had to be taken during this procedure to prevent the paper from touching the cornea in order to avoid reflex tearing. The patient was allowed to blink normally. At the end of 5 minutes, the strip was removed. The length of the filter paper moistened was measured in mm starting from the fold.

Interpretation: If wetting<5 mm, it is a severe dry eye, between 5-10mm, is moderate dry eye, 10mm is mild dry eye, and >10mm is standard.

TEAR FILM BREAKUP TIME (TBUT)

Procedure:

The TBUT is the time in seconds between the last blink and the appearance of a dry spot. Procedure: This test was done using a slit lamp bio microscope. After instilling a drop of 2 % fluorescein into the right eye, the patient was asked to blink a few times and place his chin on the chin rest of the slit lamp. Then he/she was instructed to look straight ahead without blinking. The tear film was observed by moving the slit beam using cobalt blue light, from limbus to limbus. An area of tear film rupture manifesting as a black island within the green sea of fluorescein was watched for. The time elapsed between the last blink and appearance of the first black spot was noted in seconds and termed as tear film break uptime. This measurement was taken for three successive blinks, and the mean was noted as the final reading.

Interpretation: Tear film breakup time of ≤ 10 seconds was considered positive, indicating a dry eye. Greater than 10 seconds was considered negative.

The results were tabulated, analysed, and subjected to statistical analysis.

RESULTS

The results of ST and TBUT were similar in both the eyes, hence the values of the right were taken up for analysis and interpretation

1. Age and gender distribution of patients is depicted in Table 01.

Table 1: Age And Gender Distribution Of Patients

	Male		Female		Total	
Age group	**No.**	**%**	**No.**	**%**	**No**	**%**
11 – 20 years	3	7.1%	0	0.0%	3	4.5%
21 – 30 years	6	14.3%	2	8.3%	8	12.1%
31 – 40 years	6	14.3%	4	16.7%	10	15.2%
41 – 50 years	14	33.3%	6	25.0%	20	30.3%
51 – 60 years	4	9.5%	8	33.3%	12	18.2%
61 – 70 years	4	9.5%	4	16.7%	8	12.1%
71 – 80 years	5	11.9%	0	0.0%	5	7.6%
Total	42	100%	24	100%	66	100%
Mean age ± SD = 47.3 ± 15.8 years (Range = 12 – 78 years)						

1. Distribution of the types of Hansen's Disease.

This has been depicted in table 02.

Table 02: Distribution Of Types Of Hansen's Disease

Hansen Type	Number	Percentage
TT Hansen's	7	10.6%
BT Hansen's	17	25.8%
BB Hansen's	2	3%
BL Hansen's	18	27.3%
LL Hansen's	22	33.3%
Total	66	100%

2. The distribution of ST results according to the type of HD is given in table 03.

Table 03: Relationship Between ST Results And Type Of Hansen's Disease

SCHIRMER'S right eye	TT (7)	BT(17)	BB(2)	BL (18)	LL (22)	Total (66)
≤ 10 mm	0	0	0	9 (50%)	22 (100%)	31/66 (47%)
> 10 mm	7(100%)	17(100%)	2(100%)	9(50%)	0	35 (53%)
Chi-square = 100.799, d.f = 12, p-value = 0.000 (Sig.)						

3. The distribution of TBUT results according to the type of HD is given in table 04.

Table0 4: Relationship Between TBUT And Type Of Hansen's Disease

TBUT time of right eye	TT (7)	BT(17)	BB(2)	BL (18)	LL (22)	Total (66)
<10 sec	1 (14.3%)	17 (100%)	2 (100%)	18 (100%)	22 (100%)	60 (90.91%)
≥ 10 sec	6 (85.7%)	0	0	0	0	6 (9.09%)
Chi-square = 55.629, d.f = 4, p-value = 0.000 (Sig.)						

DISCUSSION

HD is a chronic disorder. Among the bacteria affecting the eye, M Lepra used to be a leader. Watering from the eyes is a common complaint in patients with HD which may not be due to obvious causes enumerated **[8]**. This study has concentrated on the evaluation of these eyes, which are having no obvious ocular signs.

1. AGE AND GENDER DISTRIBUTION

The range of age in this study group is 12 – 78 years, and the mean age is 47.3 ± 15.8 There were 42 males (63.63%) and 24 female (36.34%) subjects. According to the age and gender distribution more number of males, 14(33.3%) are between the age group of 41 – 50 years and females 8(33.3%) are more in number in between the age group of 51-60 years.

In general population prevalence of leprosy is more common in males than females, and it is most commonly seen above 40 years of age. In this present study, there were 2 children below 15 years of age and 1 case of 18 years of age. No female children were present in this study.

2. DISTRIBUTION OF PATIENTS ACCORDING TO TYPE OF LEPROSY

In this present study, out of 66 patients 24(36.4%) had TT and BT HD while 42(63.6%) patients had BB, BL & LL.

Out of 24 tuberculoid form of HD patients, 7 (10.6%) were TT Hansen's patients and 17 (25.8%) had BT Hansen's disease.

Out of 42 lepromatous type patients, 2 (3%) were BB Hansen's patients, 18(27.3%) were BL Hansen's patients and 22 (33.3%) were LL Hansen's patients.

This predominance of lepromatous type of disease has been in sync with studies of Ebeigbe and Kio **[9],** Hodges et al. **[10]**

3. RELATIONSHIP BETWEEN ST VALUES AND TYPE OF HD

All the 22 type of LL HD and half the cases of BL HD (09) had positive reading by ST. In other words, 31/66 (47%) of the subjects with lepromatous type of HD without any symptom of dry eyes were having DED based on Schirmer positivity.

Based on ST, 35/66 (53%) of the cases were not having DED. These include all types of Tuberculoid Hansen's disease (24), both the cases of BB and half the cases of BL.

There is a sharp difference in the values of ST based on the type of HD, tuberculoid or lepromatous and this difference is statistically highly significant with a 'p' value of 0.000.

4. RELATIONSHIP BETWEEN TBUT TYPE OF HD

It is seen that the entire cohort of HD patients studied only 6/66 (9%) had normal TBUT. With this test it can be seen that 91% (60/66) of the cases were having DED. These included all the types of Hansen's disease except 6/7 subjects (85.7%) of TT.

These 6/66 (9%) cases of TT HD having normal TBUT when compared to all the lepromatous forms of HD were statistically significant with p – value of 0.000

5. DED

In the present study two tests of DED were employed to diagnose DED in asymptomatic cases of HD. Since the cohort was asymptomatic, no questionnaire test was used. By utilising ST, 31/66 (47%) had DED, while with TBUT 60/66 ((90.91%) had DED. It is surprising that 90% of the cohorts with HD without any ocular symptoms were positive for dry eye status when tested with one of the tests. This only implies the widespread affection of HD in the conjunctiva which is neighbouring the skin which is the main seat of pathology. The glands in the conjunctiva are destroyed leading to an alteration in the tear fluid volume and tear fluid constituents leading to dry eye. **[11, 12]**

The work of Koshy et al **[13]** is the nearest to the present study. They had also studied ST and TBUT and found out that the multibacillary had more incidence of dry eye disease than paucibacillary which is similar to the present study.

The second feature of this study is the difference in the affection of dry eye in different types of HD. The differences in the response of conjunctiva of tuberculoid cases and lepromatous cases is a reflection of the underlying histo-pathology. The widespread involvement of the epidermis as it occurs in lepromatous cases, would also be true for the conjunctiva leading to the damage to the conjunctival glands of Wolfring, Krause, Zeiss and Moll and consequently to a decrease in the quantity and quality of tears of patients with HD.

In a similar study done by Gurunadh et al in 1997 **[8]** showed no difference between cases of TT and cases of LL but the borderline cases combined (BT + BL) had ST positivity comprising 78% of all the DED cases in that study.

This wide variation is because of the nature of the test. While ST is a measure of tear production, TBUT is a test for the tear wettability. The prevalence of 91% DED by TBUT test and 47% by ST infers the implication of the tear-producing apparatus of the eye rather than any other factor. Dry eye is a multifactorial disease of the tears and ocular surface **[14].**

This fact also draws attention to the classification systems of HD. The modified Jopling classification has included the histopathological characteristics also. The borderline form contributes the majority of the disease burden due to leprosy. Immunologically, the disease is unstable and may either upgrade to the tuberculoid portion of the spectrum with treatment, or downgrade to the lepromatous portion of the spectrum if untreated. The cell mediated immunity (CMI) in borderline is not stable and ranges between the tuberculoid and lepromatous poles. This immunological instability has resulted in the variability of clinical features seen in this spectrum and translated to a higher chance of developing crippling deformities in the borderline cases.

Majority of work on ocular manifestations of HD has been based on the modified Jopling classification. By utilising this classification, the analysis of the borderline cases would not be missed. In a study like the present one which has been conducted to assess DED among asymptomatic eyes, there might be no great changes whatever classification is used. But when assessment is to be done for fine ophthalmic findings, it would be prudent to use the Jopling classification.

CONCLUSIONS

A cross-sectional study was conducted to assess DED among asymptomatic patients of HD by using ST and TBUT test. In this present study, out of 66 patients 24(36.4%) had TT and BT HD while 42(63.6%) patients had BB, BL & LL. There were more numbers of lepromatous type of HD.

Based on TBUT in this cohort of ocularly asymptomatic cases of HD, 60/66 (91%) subjects had DED. Based on ST 31/66 subjects (47%) had DED. All the cases that had positive ST were LL & BL cases. The sharp difference in the values of ST based on the type of HD whether it is tuberculoid or lepromatous is statistically highly significant with a 'p' value of 0.000. These lepromatous cases were positive with TBUT also. The six cases that had no positivity with TBUT were cases of TT HD cases. These cases had negative ST values also. The 6/66 (9%) of cases of TT HD having normal TBUT when compared to all the lepromatous forms of HD were statistically significant with p value of 0.000.

The first conclusion is that of the two polar ends of Hansen's disease spectrum, LL and TT, LL is more prone for DED as per the present study. Secondly more than half the cohort had ST negativity implying that tear production was not hampered in these cases and in the case of TT Hansen's disease, there appears to be no destruction of the conjunctival glands that are responsible for conjunctival wetting. Cases of HD need periodic ophthalmic evaluation inclusive of evaluation for DED so that timely treatment can be instituted.

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