Section A-Research paper

ANTERIOR SEGMENT OPTICAL COHERENCE TOMOGRAPHY (AS-OCT) ASSESSMENT OF CORNEAL EPITHELIAL THICKNESS IN DRY EYES DISEASE

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Abstract:

Aim-To study the corneal epithelial thickness in dry eye disease (DED) eyes versus normal eyes using anterior segment optical coherence tomography along with its correlation with current dry eye diagnostics. ***Methodology-*** It was a cross-sectional study that took place from November 2021 to April 2022, enrolling 52 patients with symptomatic dry eye disease (DED) as cases and 52 healthy people as controls after thorough clinical examination, Schirmer's test, Tear breakup time (TBUT) along with ocular surface disease index (OSDI) questionnaire. 208 eyes of 104 cases were subjected to Anterior segment Optical Coherence Tomography (AS-OCT) based Corneal epithelial thickness analysis. The corneal epithelial thickness in Central zone, Zone 1,2, &3 along with an average of 0 to 9 mm zone was calculated. ***Results-*** Corneal epithelial thickness in each zone was significantly higher compared to normal eyes. Schirmer's test results and TBUT results have significant negative correlation to corneal epithelial thickness and OSDI score showed significant positive correlation to same. ***Conclusion-*** Increased epithelial thickness may be an objective clinical indicator of DED with potential to replace multiple invasive procedure like Schirmer and T-BUT for definitive DED diagnosis. AS-OCT is a simple non-contact approach offering fast, highly reproducible, quantifiable, precise corneal epithelial thickness. Corneal epithelial thickness can be incorporated in AI systems to screen for DED.

Keywords: Corneal epithelial thickness, Dry eye disease, Optical coherence tomography, Ocular surface disease, Artificial intelligence

INTRODUCTION

Dry eye disease (DED), a multifactorial disorder, could impair the conjunctival and corneal epithelium through influencing tears and the ocular surface. The optical properties of cornea are maintained by the corneal epithelium. As a result, changes in the thickness and distribution of the corneal epithelium may be one of the first symptoms of several corneal diseases, such as ectasia, dystrophy, contact lens-associated keratopathy and keratoconus. [1] A study showed that characteristic corneal and its sublayer thickness changes in subclinical keratoconus could be detected with very high accuracy with high-resolution Fourier-domain OCT. [2] Therefore, corneal thickness evaluation can be an early indicator of DED when other parameters are normal.

The clinical ocular symptoms of DED, such as eye pain, photosensitivity, and changing vision, may have been influenced by the damaged corneal epithelium.[3] The thickness of the corneal epithelium can be mapped to determine the morphological signs of epithelial deterioration. Anterior segment optical coherent tomography and in vivo Confocal Microscopy are used to quantify the corneal epithelial thickness (AS-OCT).[4]

Early detection and intervention of DED is crucial to improve the condition using therapeutic regimes. In the search for an objective, repeatable, and quantitative clinical test that may help in the differential diagnosis of DED, the idea of corneal epithelial thickness as a practical tool in DED evaluation can be successfully applied. Epithelial thickness, a significant anatomical factor, has recently been studied in dry-eye patients using epithelial maps created by optical coherence tomography.[5]

MATERIALS AND METHODS

This prospective case control study design was conducted in in a tertiary teaching hospital in North Karnataka between November 2021 to April 2022. It was in accordance with the ethical standards of the institutional research committee and the principles of Helsinki declaration.

The sample size was calculated with anticipated correlation between TBUT and OSDI Score in DED r= -0.720 (ref), at >99% confidence level and >90 power in the study. In this single blinded study, we included 52 patients (104 eyes) with DED using simple random sampling technique. Age and gender matched 52 healthy individuals (104 eyes) were assigned as control. Patients under 18- 40 years of age group with symptoms of DED and having 6/6 BCVA (best corrected visual acuity) were included in study. Patients who had recently received artificial tear drops or who had worn contact lenses in the past and patients with history of foreign body on ocular surface, glaucoma, ocular trauma, or ocular surgeries were excluded from study.

All patients attending mandatory annual institutional health checkup were included in this study. The participation in the survey was totally voluntary. Each patient had a standard proforma filled out for them after being informed about the study and having their history, clinical findings, and

investigations recorded. Additionally noted were prior treatment histories, pre-existing ocular conditions, and relevant local and systemic findings. Participants were made to answer the ocular surface disease index (OSDI) questionnaire. The senior optometrist was in charge of explaining the questions to patients and then recording their responses in order to limit any bias.

OSDI is standardized questionnaire containing 12 questions divided into three groups: symptoms of the eye (five questions), vision-related functions (four questions), and environmental factors (three questions). On a scale from 0 to 4, the OSDI questionnaire is graded, with 0 denoting never, 1, some of the time, 2, half of the time, 3, most of the time, and 4, always. The threshold for DED symptoms was set at an OSDI score of 20 or above.[6]

All participants got a thorough evaluation of the ocular surface after completing the OSDI questionnaire, which was followed by the best-corrected visual acuity test, OCT scanning, TBUT, and Schirmer 1 test. If there are DED symptoms (OSDI score of 20) and there is a qualitative or quantitative tear film abnormality (TBUT 5 seconds, or S1t 5 mm/5 min), the diagnosis of DED was confirmed. In total of 1560 cases screened, 52 cases (104 eyes) diagnosed as DED were included in our study as cases. 52 age and gender matched controls were selected by simple random sampling in same screened population. (Fig 1)

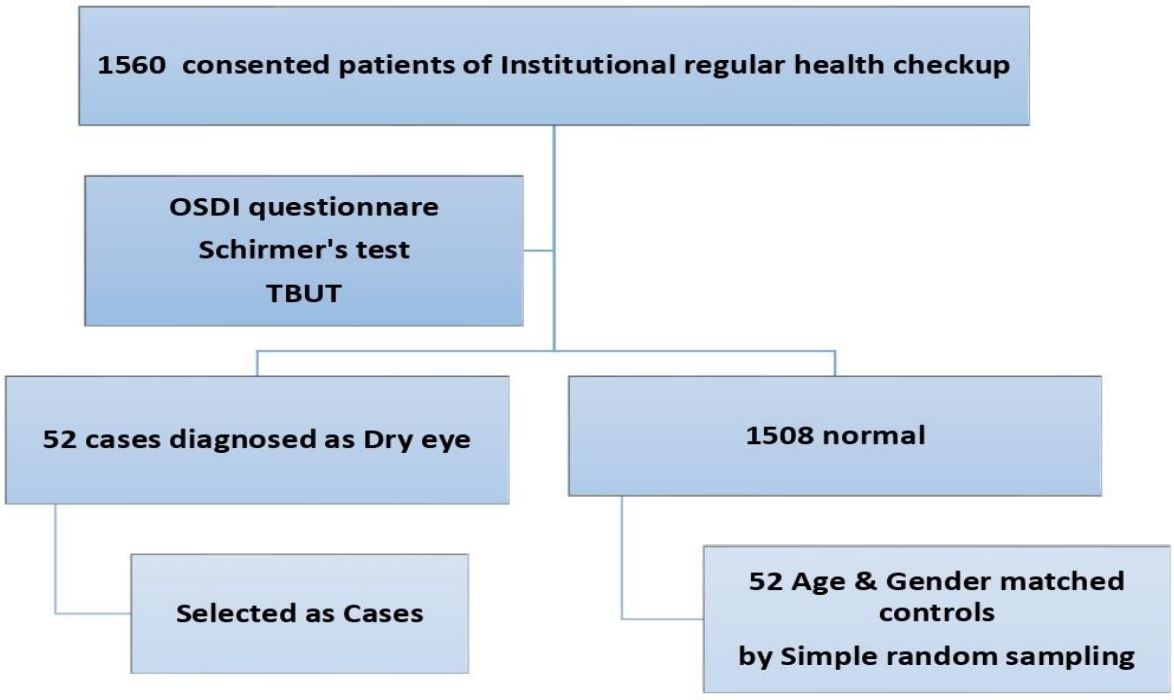

Figure 1: Flow chart showing selection of cases and controls

Using anterior segment optical coherence tomography (AS-OCT), the corneal epithelium was mapped for both groups. Topographic epithelial thickness variations as well as average, center, and periphery epithelial thicknesses were measured. We measured, statistically analyzed, and classified into zones the corneal thickness for each eye, ranging from 0 to 9 millimeters. The thickness of the epithelium in the 2 mm central zone of the cornea—2–5 mm in zone 1, 5-7 mm in zone 2, and 7-9 mm in zone 3—was referred to as the corneal epithelial thickness (CET). For each case, within the 0 to 9 mm zone, the average epithelial thickness (AET) was calculated.[7] Spearman's rank correlation test was performed to analyze the correlation of OSDI scores with other parameters.

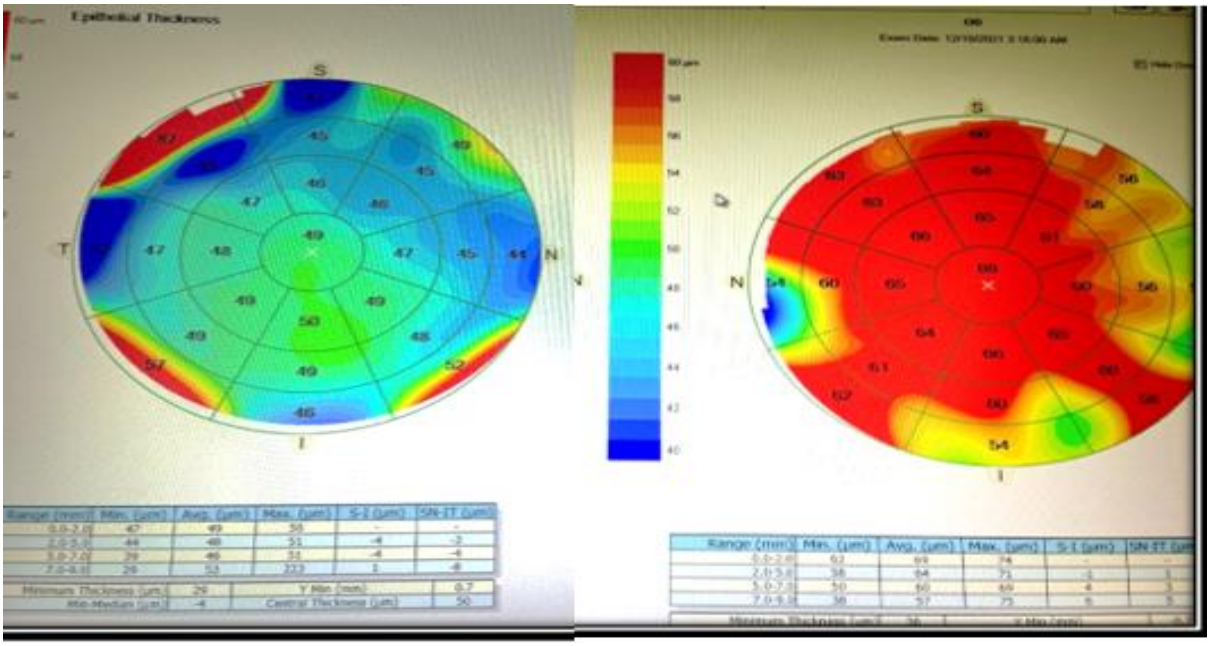

Fig 2- Corneal Epithelial thickness in control group and DED group using AS-OCT

RESULT

208 eyes of 104 adult patients of age 18-40 years were included in current study. The number of male patients enrolled in the study were more than females. (Table 1)

	Male	Female	Total
Cases	30	22	52
Controls	30	22	52
Total	60	44	104

Table 1: Gender Distribution of Cases and Controls

Schirmer test value & TBUT values were significantly lower in DED group (Table 2). In comparison to the control group, the mean OSDI score for the DED group was significantly higher (Table 2). DED group had significantly more corneal epithelium in all three zones as well as a thicker central corneal epithelium than normal eyes. (Table 3)

TEST	DED group (N=104 eyes of 52 cases) Mean ±SD	Controls (104 eyes of 52 controls) **Mean ±SD**	P value (Mann Whitney U test)
SCHIRMER'S TEST in mm	**4.038±1.309**	**12.067±1.325**	**p<0.001**
TBUT in seconds	**4.058±0.662**	**16.673±3.082**	**p<0.001**
OSDI	**29.596±6.2**	**12.519±3.791**	**p<0.001**

Table 2: Clinical test results in each group

Zone	DED group (N=104 eyes of 52 cases) Mean ±SD in microns	Controls (104 eyes of 52 controls) **Mean ±SD** in microns	P value (Mann Whitney U test)
Central Zone	**56.077±4.044**	**48.625±1.63**	**p<0.001**
Zone 1 average	**55.644±3.361**	**48.288±2.175**	**p<0.001**
Zone 2 average	**52.481±3.32**	**48.346±1.638**	**p<0.001**
Zone 3 average	**58.442±3.922**	**48.413±1.927**	**p<0.001**

Table 2: AS-OCT Epithelial thickness in different zones.

Correlation of OSDI scores with the clinical parameters of DED in was analyzed with Spearman's rank correlation test to identify contributing factors to subjective dry eye symptoms. Clinical parameters for DED such as T-BUT and Schirmer values were inversely correlated with OSDI score while the corneal epithelial thickness for zone 1, zone 2 and zone 3 were positively correlated with the OSDI scores.

Spearman's rho N=208	**Central zone**	**zone 1 average**	**zone 2 average**	**zone 3 average**	**Sig. (2-tailed)**
OSDI	.733	.687*	.590	.738*	0.000
Schirmer's test	-.719*	-.697	-.629*	-.783	0.000
T BUT	-.710*	-.760*	-.605*	-.734*	0.000

**. Correlation is significant at the 0.01 level (2-tailed).*

Table 4: Correlation between Epithelial thickness and Clinical tests results.

DISCUSSION

The ocular surface deteriorates as a result of DED's interference with tears' protective function. The DED symptom range is the outcome of this, and it may finally result in the loss of eye integrity. [8]. Techniques for diagnosing DED may rely on spotting the aberrant tear film, like in the TBUT or Schirmer's test. Poor correlation between such tests and patients' complaints has been found in studies [9,10].

Several of those tests lack proper standardisation because they are affected by challenging factors including variations in dye concentration and light levels during surface-staining operations and a lack of grading uniformity. Among other approaches, TBUT and fluorescein staining scores have shown poor reproducibility and a significant operator dependence.

Ocular surface staining and the Schirmer's test are intrusive and uncomfortable for the patient. DED is a multifactorial disease that is hard to effectively regulate, standardise, or quantify since it is affected by several characteristics. A strategy that focuses on the injury and its effects may be effective. Recent innovations in imaging technology include confocal microscopy and OCT.

The recently created full-cornea corneal epithelial thickness imaging by AS-OCT may provide a useful clinical tool for quantitative epithelium assessment due to the ease of noncontact application and speed of optical imaging (absolute average, central, and peripheral epithelium thickness measurements).[11]

Previous research has shown that the central corneal epithelial thickness of normal eyes ranges from 48.0 ± 5 to 59.9 ± 5.9 μm. [12,13]

In our study, the epithelium of DED patients was significantly thicker throughout the cornea. On comparision of DED eyes and normal eyes, there was a 7.45microns difference in central epithelial thickness. This result was consistent with the information that Qingfeng et al. and El Sanharawi et al. had previously reported. [14,15]

Fabiani et al. [16] discovered that the average CET thickened substantially more in dry eye mice compared to control animals in a mouse model of dry eye. Our outcomes showed that epithelial development and inflammatory activities had a considerable impact on the average CET during the initial stages of DED. Increased epithelial thickness may be an objective clinical indicator of dry eye, according to studies by Chen et al. [17] and Kanellopoulos and Asimellis.[18]. Epithelial hypertrophy/hyperplasia, swollen cells, and a rise in the number of cellular layers in the epithelium linked to dry eye could be contributing factors to the increased thickness. [19]

The strength of the present study is the AS-OCT screening method, which offers a fast, highly reproducible, quantifiable, precise, non-contact and simple recording approach. Another strength is high sample size and age and gender matched equal number of controls.
Artificial intelligence (AI) is profoundly worked upon to universalize patient access to disease screening and diagnosis, help triage referral and monitor outcomes The most promising Ophthalmic AI tools are currently in the field of the retina – for diabetic retinopathy (DR), age-related macular degeneration (AMD), and retinopathy of prematurity (ROP). There are AI models applicable to glaucoma, keratoconus, cataract, and other anterior segment diseases and oculoplastic surgery [22]. Corneal epithelial thickness can be incorporated in AI systems to screen for DED. The challenge lies in developing an affordable OCT guided system for the same.

CONCLUSION

Increased epithelial thickness may be an objective clinical indicator of DED with potential to replace multiple invasive procedure like Schirmer and T-BUT for definitive dry eye diagnosis. AS-OCT is a simple non-contact approach offering fast, highly reproducible, quantifiable, precise corneal epithelial thickness. Corneal epithelial thickness can be incorporated in AI systems to screen for DED. The challenge lies in developing an affordable OCT guided system for the same.

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