

Central Corneal Thickness in Patients with Dry Eye Disease

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Abstract:

Background:

Dry eye or Keratoconjunctivitis sicca is mainly due to decreased tears which causes eye visual disturbance and discomfort. Dry eye affects corneal thickness

Aims and Objectives:

Aim of the study is to evaluate the effect of dry eye disease on CCT with age and gender match controls.

Materials and Methods: Two Hundred and twenty subjects , 110 Patients are cases and 110 are controls

Subjects are from the Department of Ophthalmology Narayana Medical college and Hospital Out patient Department are included in the the study.

Dry eye disease diagnosed with questionnaire , Tear film Break up test , Schirmer's test and slit lap examination .

CCT is measures with Optical Pachymetry

T test was used to determine the significane of difference between two means

Results: In our study, there were 140 female patients and 80 male patients.

The CCT among cases was very low ($534.19 \mu\text{m} \pm 30.05$) compared to controls ($562.7 \mu\text{m} \pm 45.56$) and this difference was statistically significant ($P < 0.05$)

The difference in CCT among males between the two groups was statistically significant and it was highly significant among females.

Conclusion: There is a significant decrease in CCT due to Dry eye Disease. Pachymetry for CCT estimation shall be included in the routine management of dry eye patients so that corneal thinning could be easy to identify earlier and treated earlier

Keywords: CCT , TBUT , DED

INTRODUCTION

Cornea is a Avascular and Transparent structure. It consists of mainly 5 layers. Corneal epithelium is a stratified squamous It consists of five to six layers. Its superficial layers are flattened , deepest layer is columnar cells. Bowman's membrane is made of acellular mass of condensed collagen fibrils. About 90% of total corneal thickness is stroma. Stroma has collagen fibrils. Descemet membrane is a strong homogeneous which binds to the stroma posteriorly. Endothelium is a single layer hexagonal cell. The role of tear film in maintaining a clear cornea. It keeps the cornea wet. Tear film consist of three layers in total . Outer is lipid layer, then aqueous layer and innermost mucin layer. Lipid layer prevents evaporation and overflow of the tears. Aqueous layer forms the main bulk of tear film. Its function is to give atmospheric oxygen to corneal epithelium, has antibacterial substances, and washes debris. The mucin helps in making the tear film stable. We can describe dry eye as a state of abnormal tear film which be due to number of conditions which effects on its stability and changes its composition. According to International Dry Eye Workshop, four the dry eye disease (DED) definition included the tear film hyper osmolarity and ocular surface inflammation. An increase in inflammation leads to increase in tear osmolarity. This hyper osmolarity of the tear film results in dehydration of the cornea. In normal healthy individual, the aqueous layer of the tear film is isotonic or mildly hypertonic. Hypertonic solution decreases CCT. Hence, as the tear production goes down, there is an increase in tear film osmolarity and the cornea becomes thin. Corneal endothelial disease is said

to have an impact on CCT. CCT is helpful in diagnosing corneal diseases and evaluating endothelial pump function. Therefore, measurement of the Corneal Thickness along with its shape and power is quite helpful in diagnosing corneal diseases and deciding corneal surgery for vision correction Refractive surgeries.

Since Dry eye disease has an etiology which is not very clear, the criteria to diagnosis of DED are also not very clear and standardized. . People wearing contact lens has changes in their ocular surface. It is more evident in keratoconus. subjects who are contact lens wearer. Evident central corneal thinning has been reported in keratoconjunctivitis sicca patients.

Aims and objectives

The purpose of this study was to compare the Central Corneal thickness in Dry eye Disease patients with age and gender matched controls.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Ophthalmology Department of Narayana Medical College and Hospital for a period of one year spanning from Feb 2022 to Jan 2023

The study was approved by the Institutional Ethics Committee. Dry eye Disease patients who attended Narayana Medical College and Hospital ophthalmology OPD were included in our study. Exclusion Criteria : Patients with RA ,DM, uveitis, glaucoma, increased IOP, eyelid disorders, ptosis, and any corneal disease were excluded from the study. Patients with a history of previous eye surgery were also excluded from the study.

Age- and gender-matched controls were selected from the population diagnosed without DED who visited ophthalmology outpatient department of SRM Medical Hospital. Sample size According to Ali et al., study,11 considering the mean (μ_1) and standard deviation (σ_1) of CCT in controls as $567.1 \mu\text{m} \pm 28.6$, and mean (μ_2) and standard deviation (σ_2) of CCT in Dry eye Disease patients as $543.4 \mu\text{m} \pm 38.1$, at 95 % confidence interval ($Z_{1-\alpha/2}=1.96$), with 80 % power ($Z_{1-\beta}=0.84$), the sample size calculated as $N = (Z_{1-\alpha/2} + Z_{1-\beta})^2 * 2 * \sigma / (\mu_1 - \mu_2)^2 = (1.96 + 0.84)^2 * 33.35^2 / (561.1 - 542.4)^2 = 50$.

Total patients included in the study are 220, 110 case 110 controls .

Diagnosis of dry eye The dry eye was diagnosed with the following . Patients with either subjective or objective findings were considered to DED.

1. Dry eye-related quality of life score) questionnaire: DEQ score of more than 15 was considered to have dry eye.
2. Slit-lamp examination: This was done to exclude other ocular disorder and to proceed with TBUT.
3. TBUT: First dark spot ≤ 5 s was considered as diagnosis of DED
4. Schirmer's test 1: Patients who had a Schirmer's test score ≤ 10 mm in 5 min were considered to have dry eye Disease. Study procedure After obtaining informed consent from the patient, a detailed history was taken. In ocular examination, bestcorrected visual acuity, intraocular pressure, anterior segment examination by slit-lamp biomicroscopy, and fundus examination were done. Recorded subjective symptoms of our study group using DEQS.

All these patients then underwent TFBUT, keratoconjunctival staining, and Schirmer . Patients were classified as DED and non-DED using the Asian Dry Eye Society 2016 diagnostic criteria.

These criteria include two positive points: The presence of subjective symptoms and decreased TFBUT ≤ 5 s. After this, the DED patients were divided into mild to severe on the basis of vital staining.

All patients in our study underwent subjective symptoms assessment using the DEQ questionnaire. This helped us in evaluating them. To diagnose DED, a cutoff value of DEQS > 15 was used in our study.

With the help of fluorescein dye, TFBUT was evaluated in our patients. We noted the time interval between the last blink and the appearance of the first dark spot on the cornea. We used TBUT ≤ 5 s to make diagnosis of Dry Eye Disease. Using Schirmer's test strips, we did Schirmer's test without topical anesthesia. Schirmer's test strips were placed on the outer third of the temporal lower conjunctival fornix for 5 min. Then after removing it, the value was

recorded in millimeter. Value less than 10 mm was diagnosed as dry eye. CCT was performed using ultrasound pachymeter. There are different methods of evaluating corneal thickness. It includes ultrasonic pachymetry, optical slit-lamp pachymetry, specular microscopy, and confocal microscopy. Each of these methods has different disadvantages. Ultrasound pachymetry requires corneal contact whereas Orbscan system is a non-contact method. Few studies suggest that Orbscan has an accurate and precision almost equal to ultrasonic pachymetry. Combination of diagnostic tests helped in diagnosing dry eye syndrome more efficiently. Few dry eye subjects had no symptoms but a positive objective finding of dry eye. Others had severe symptoms but without dry eye findings. The Dry Eye Disease questionnaire consists of 15 questions regarding ocular symptoms and their impact on daily life. Dry eye disease is very useful in evaluating the effects of DED syndrome on the daily life of patients including its effect on mental health. Hence, subjects were asked to score their general ocular symptoms and quality of life on a scale of 1–6, where 6 showed a poor quality of life and 1 showed a very good quality of life. Statistical analysis Data were entered into Microsoft Excel version Office 16 and analyzed using IBM Statistical Package for the Software Solutions version 21. Descriptive statistics were represented by mean and standard deviation. Student's "t"-test was used to determine the significance of difference between two means. P 0.05). When compared the mean age of males and females in the two groups separately, there was no significant difference between cases and controls ($p > 0.05$). The age and gender are almost matched between cases and controls, as shown in Table 1. The CCT among cases was very low ($534.12 \mu\text{m} \pm 30.00$) compared to controls ($562.7 \mu\text{m} \pm 44.52$) and this difference was statistically significant ($P < 0.05$). When subgrouped under gender, the difference in CCT among males between the two groups was statistically significant and it was highly significant among females, as shown in Table 2. When the reduction in CCT among the cases was studied under different age groups, the subjects in the 41–60 years age group had a statistically highly significant difference in CCT between the two groups while it was also significant in other age groups, as shown in Table 3. DISCUSSION The mean age of the subjects in cases and control groups was 51.61 and 51.35 years, respectively, which is very comparable. Similarly, the mean age among males and females in both groups was also comparable. This study aimed to assess the effect of Dry eye Disease on Central corneal thickness by comparing with age- and gender-matched controls. Central corneal thickness plays an important role in refractive surgeries and intraocular pressure assessment in glaucoma cases. The study showed that the CCT was significantly reduced in patients with DED when compared with normal eyes of age- and gender-matched population. The mean CCT among the cases was $534.19 \mu\text{m} \pm 30 \mu\text{m}$ and $562.7 \pm 45 \mu\text{m}$ in the control group, and the difference in CCT between the two groups was about $36 \mu\text{m}$. This finding almost correlates with many corneal morphometric studies

Age (years)	Cases		Controls		P value "t" test	Significance
	Mean	SD	Mean	SD		
Total	51.43	13.82	51.35	11.311	0.5	N S
Males	49.72	14.34	48.09	11.76	0.682	N S
Females	52.23	12.77	55.98	8.42	0.74	N S

Table 2: Comparison of CCT (ultrasound pachymetry) among dry eye disease patients and control groups						
CCT	Cases		Controls		P value "t" test	Significance
	Mean	SD	Mean	SD		
Total	544.19	30.14	567.34	46.67	0.001	HS
Males	543.59	34.67	577.88	47.77	0.011	S
Females	532.91	24.72	571.67	46,47	0.001	HS

Table 3: Comparison of CCT among cases and controls in different age groups						
CCT	Cases		Controls		P value "t" test	Significance
	Mean	SD	Mean	SD		
21-40 Years	535.11	29.62	562.12	23.67	0.031	S
41-60 Years	529.45	31.45	572.64	44.23	0.001	HS
>60 Years	549.26	31.76	567.62	33.61	0.035	S

which reported that the dry eye can cause significant decrease in CCT values.

Liu and Pflugfelder 19 (1999) showed that mean difference in CCT between normal and dry eyes was approximately 35 μ m; the CCT was 571 μ m \pm 28 and 533 μ m \pm 34 μ m in normal and dry eye, respectively.

Sanchis-Gimeno et al.,20 (2005) showed that the CCT in normal eyes was 558 μ m \pm 30 μ m, while it is 532 μ m \pm 34 μ m in dry eyes and the mean difference between the two groups was 26 μ m.

Sanchis-Gimeno et al.,21 (2006) compared normal and dry eyes to estimate the differences in ocular dimensions and showed CCT of 549 μ m \pm 34 μ m in normal eyes and 527 μ m \pm 30 μ m in dry eyes with a difference in CCT of 22 μ m between two groups. Ali et al.,11 (2017) estimated the mean CCT in cases group as 536.5 μ m, while it was 561.3 μ m in the control group, and the difference was about 25 μ m.

Another study by Sanchis-Gimeno et al.,7 (2004) done in postmenopausal women, observed 14 μ m difference in mean CCT between normal and dry eyes. The mean CCT among postmenopausal women with dry eyes was 533.10 \pm 4.74 μ m while it was 548.63 \pm 15.11 μ m in age-matched control women.

Gunes et al.,22 reported the mean CCT as 523 \pm 32.8 μ m and 556 \pm 27.5 μ m in dry and normal eyes of rheumatoid arthritis patients, respectively, with a difference in CCT of 27 μ m between normal and dry eyes. When CCT values

were analyzed in subgroups of age and gender between cases and controls, there was a significant difference between the two groups. The difference in CCT among females between cases and controls was 38 μm ($532.9 \pm 26.7 \mu\text{m}$ vs. $570.37 \pm 45.47 \mu\text{m}$) which was highly significant. Among males, the CCT was $534.95 \pm 34.68 \mu\text{m}$ among cases compared to $567.77 \pm 46.7 \mu\text{m}$ in controls and the difference was 32 μm which was also statistically significant. The effect of dry eye on CCT was more in females compared to males. Ali et al.,¹¹ also showed similar results with a difference of 19 μm in males ($561.9 \pm 28.6 \mu\text{m}$ vs. $542.4 \pm 38.1 \mu\text{m}$) and 29 μm in females ($561.4 \pm 27.2 \mu\text{m}$ vs. $532.6 \pm 37.1 \mu\text{m}$). Similarly, the CCT difference was very evident between normal and dry eyes in all age groups. The difference was high in 40–60 years age group which was 42 μm followed by > 60 years age group which had 30 μm and about 6 μm in 20–40 years age group. The results are almost similar with Ali et al.¹¹ which also presented significant difference in CCT in all age groups between cases and controls. The corneal thinning in dry eye syndrome is actually due to increase in tear film evaporation or increased osmolarity of tear fluid. It causes a decrease in tear film thickness which normally ranges from 3 to 40 μm . This hyper osmolar tear film activates the inflammatory cascade. This activation of inflammatory cascade stimulates the epithelial cells to produce high amounts of cytokines and matrix metalloproteinase. Several studies have shown that these inflammatory events lead to apoptotic

death of surface epithelial cells of cornea.²³ There is evidence to show that excessive apoptosis, of the surface epithelium, if sustained and not compensated for any epithelial cycling, ultimately causes corneal epithelial thinning.²⁴ Another theory for corneal thinning in DED is due to imbalance between MMP 1 and tissue inhibitor of MMP 1. MMP 1 is responsible for the degradation of extracellular matrix in the stroma of cornea. This imbalance is due to elevated level of cytokines which subsequently leads to accumulation of collagenases in the cornea, causing destructive keratolysis and corneal thinning.²⁵ These evidence and studies promoted the use of tear substitute to protect the corneal from thinning in DED patients.

Karadayi et al.,²⁶ have shown in their study that there was increase in CCT after the treatment of DED patients with artificial tear drop. This study supports the concept of doing pachymetry in routine management of DED patients.

CONCLUSION

Dry eye Disease is one of the most common causes of ocular disease and can lead to lifelong visual discomfort and impairment. Therefore, to make Dry eye Disease, an avoidable cause of visual discomfort, more and more emphasis should be given on doing corneal pachymetry in these patients. Our findings showed that Central corneal Thickness was thinner in dry eye patients, especially female dry eye patient. Hence, along with evaluation of dry eye tests, pachymetry is also important in ophthalmic examinations and should be done in Dry eye disease patients. This study supports the concept of doing pachymetry in routine management of dry eye disease

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