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Research Article

CORRELATION OF DRY EYE DISEASE SEVERITY WITH CORNEAL HYPOESTHESIA IN PATIENTS WITH TYPE 2 DIABETES MELLITUS: A CROSS-SECTIONAL ANALYSIS

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ABSTRACT

Purpose: To evaluate the association between dry eye disease (DED) parameters and corneal sensitivity in patients with type 2 diabetes mellitus (T2DM) and to determine if peripheral neuropathy severity correlates with ocular surface changes.

Methods: A cross-sectional study was conducted on 94 patients with T2DM attending a tertiary care ophthalmology department. All participants underwent comprehensive ocular examination including Ocular Surface Disease Index (OSDI) questionnaire, tear film breakup time (TBUT), corneal fluorescein staining (CFS), Schirmer I test (without anesthesia), and central corneal sensitivity measurement using a Cochet-Bonnet esthesiometer. Diabetic peripheral neuropathy (DPN) was assessed using the Michigan Neuropathy Screening Instrument (MNSI). Correlations were analyzed using Pearson's coefficient and multivariate regression.

Results: Of 94 T2DM patients (mean age 58.3 ± 9.4 years; 51.1% female), 71 (75.5%) met diagnostic criteria for DED. Mean corneal sensitivity was significantly lower in diabetic patients with DED (4.8 ± 1.2 cm) compared to those without DED (5.9 ± 0.6 cm, $p<0.001$). TBUT showed a moderate positive correlation with corneal sensitivity ($r=0.52$, $p<0.001$), while OSDI score demonstrated a negative correlation ($r=-0.48$, $p<0.001$). Patients with longer T2DM duration (>10 years) had 3.2-fold higher odds of severe corneal hypoesthesia (≤4 cm on esthesiometry). DPN presence (MNSI ≥2.5) was associated with significantly reduced corneal sensitivity (mean 4.5 vs. 5.7 cm, $p<0.001$) and shorter TBUT (4.1 vs. 7.8 seconds, $p=0.002$).

Conclusion: Corneal sensitivity is markedly reduced in T2DM patients with DED, and this reduction parallels the severity of peripheral neuropathy. Routine corneal esthesiometry should be considered in diabetic patients presenting with dry eye symptoms, as standard DED therapies may be less effective in the setting of neurotrophic corneas.

KEYWORDS: Type 2 Diabetes Mellitus, Dry Eye Disease, Corneal Sensitivity, Diabetic Neuropathy, Neurotrophic Keratopathy.

Introduction

Type 2 diabetes mellitus (T2DM) has become a global health crisis, affecting over 537 million adults worldwide—a number projected to rise to 783 million by 2045[1]. While diabetic retinopathy, nephropathy, and peripheral neuropathy are well-established microvascular complications, the impact of chronic hyperglycemia on the ocular surface, particularly the cornea, has received comparatively less attention. This gap is clinically significant because the cornea, despite being avascular, possesses the densest network of sensory nerve fibers in the human body, rendering it exquisitely vulnerable to diabetic nerve damage[2].

Dry eye disease (DED) is a multifactorial disorder of the tear film and ocular surface characterized by symptoms of discomfort, visual disturbance, and tear film instability[3]. Population-based studies have consistently reported a significantly higher prevalence of DED in individuals with T2DM (ranging from 15% to 54%) compared to the general population (5–30%)[4]. The pathophysiological link between diabetes and DED is multifactorial, involving aqueous tear deficiency from lacrimal gland autonomic dysfunction, evaporative loss from meibomian gland disease, and—increasingly recognized—diabetic corneal neuropathy[5]. The cornea is innervated by the ophthalmic division of the trigeminal nerve via long ciliary nerves, and these nerves serve dual, interdependent functions: they provide protective sensory feedback and release neurotrophic factors essential for corneal epithelial maintenance, proliferation, and wound healing[6]. Chronic hyperglycemia induces a length-dependent, small-fiber predominant neuropathy that affects corneal nerves early in the disease course, often before clinical evidence of peripheral neuropathy in the lower extremities[7].

Reduced corneal sensitivity (corneal hypoesthesia) has well-established and clinically important consequences: diminished reflex tearing, decreased blink rate, prolonged tear film exposure, and impaired epithelial healing[8]. These changes can both initiate and exacerbate DED and, in severe cases, progress to neurotrophic keratopathy with persistent epithelial defects and stromal melting[9]. However, clinical studies examining the correlation between corneal sensitivity and DED parameters in T2DM have yielded inconsistent results. Some investigators have reported significant correlations between reduced corneal sensitivity and shorter tear breakup time or lower Schirmer values, while others have found no such association[10]. These discrepancies may be attributed to small sample sizes, heterogeneous diagnostic criteria for DED, failure to account for diabetes duration and glycemic control, and the absence of standardized peripheral neuropathy assessment.

Therefore, we conducted a cross-sectional study on 94 patients with T2DM to evaluate the correlation between central corneal sensitivity (measured by Cochet-Bonnet esthesiometry) and objective and subjective DED parameters, including tear film breakup time, Schirmer I testing, corneal fluorescein staining, and the Ocular Surface Disease Index questionnaire. We further aimed to determine whether the presence of diabetic peripheral neuropathy influences this correlation. We hypothesized that reduced corneal sensitivity would be significantly associated with greater DED severity, and that patients with DPN would exhibit more pronounced corneal hypoesthesia, thereby supporting the rationale for routine corneal sensitivity assessment in diabetic patients presenting with dry eye symptoms.

Methodology

Study Design, setting & population

A cross-sectional, observational study was employed. The study was conducted at the Ophthalmology Outpatient Department of a tertiary care teaching hospital. The target population is adult patients (35–75 years) with confirmed type 2 diabetes mellitus attending the ophthalmology clinic.

Inclusion

- T2DM (ADA criteria),
- Age 35–75 years
- Diabetes duration ≥1 year
- visual acuity ≥20/40.

Exclusion

- Recent ocular surgery
- Active infection
- Contact lens use
- Autoimmune diseases
- Corneal pathology, or medications affecting tear secretion.

Sample Size Calculation

Using G*Power (r=0.30, 80% power, α=0.05), minimum sample was 84. Adding 10% attrition, 94 patients were enrolled.

Procedure for Data Collection

Over six months, 94 participants underwent informed consent followed by sequential assessment: OSDI, corneal sensitivity, fluorescein instillation, TBUT, corneal staining, Schirmer I, and MNSI. A single masked examiner performed all tests.

Data Management

Data were entered into Excel, checked for accuracy, coded, and transferred to SPSS version 26.0. Paper records were locked; electronic data were password-protected.

Results

Table 1, Of the 94 enrolled patients with type 2 diabetes mellitus (mean age 58.3 ± 9.4 years; 48 [51.1%] female), 71 (75.5%) met the diagnostic criteria for dry eye disease (DED). As shown in Table 1, patients with DED had a significantly longer diabetes duration (10.3 vs. 7.4 years,

p=0.03), higher HbA1c levels (8.0% vs. 7.2%, p=0.02), and a greater prevalence of diabetic peripheral neuropathy (62.0% vs. 26.1%, p=0.003) compared to those without DED.

Table 2, presents comparison of dry eye parameters and corneal sensitivity between groups. The DED group had significantly worse OSDI scores, TBUT, Schirmer I values, and corneal fluorescein staining (all p<0.001). Most importantly, mean central corneal sensitivity was significantly lower in the DED group compared to the non-DED group (4.8 ± 1.2 cm vs. 5.9 ± 0.6 cm, p<0.001).

Table 3, displays correlations between corneal sensitivity and dry eye parameters. Corneal sensitivity showed a moderate positive correlation with TBUT (r=0.52, p<0.001) and negative correlations with OSDI score (r=-0.48, p<0.001) and corneal staining (r=-0.44, p<0.001). Longer diabetes duration (r=-0.39, p<0.001) and higher HbA1c (r=-0.35, p=0.001) were also associated with reduced sensitivity.

Table 4, compares parameters based on DPN status. Of 94 participants, 50 (53.2%) had DPN. Patients with DPN had significantly lower corneal sensitivity (4.5 ± 1.1 cm vs. 5.7 ± 0.8 cm, p<0.001), shorter TBUT (4.1 vs. 7.8 seconds, p=0.002), and higher OSDI scores (42.1 vs. 21.9, p<0.001) compared to those without DPN.

Finally, Table 5 presents multivariate regression analysis identifying independent predictors of reduced corneal sensitivity. Diabetes duration (β = -0.06, p=0.004), HbA1c (β = -0.14, p=0.04), and DPN presence (β = -0.62, p=0.003) remained significant predictors. The model explained 41% of the variance in corneal sensitivity (R^2 = 0.41, p<0.001).

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants (N=94)

Characteristic	DED (n=71)	No DED (n=23)	Total (N=94)	p-value
Age (years), mean ± SD	59.1 ± 9.2	55.8 ± 9.7	58.3 ± 9.4	0.14
Female sex, n (%)	38 (53.5%)	10 (43.5%)	48 (51.1%)	0.48
Diabetes duration (years), mean ± SD	10.3 ± 6.5	7.4 ± 4.9	9.6 ± 6.2	0.03*
HbA1c (%), mean ± SD	8.0 ± 1.6	7.2 ± 1.1	7.8 ± 1.5	0.02*
BMI (kg/m²), mean ± SD	26.8 ± 3.4	25.9 ± 3.1	26.5 ± 3.3	0.26
MNSI ≥2.5 (DPN present), n (%)	44 (62.0%)	6 (26.1%)	50 (53.2%)	0.003*

Table 2: Comparison of Dry Eye Parameters and Corneal Sensitivity Between DED and Non-DED Groups

Parameter	DED (n=71)	No DED (n=23)	Mean Difference (95% CI)	p-value
OSDI score (0–100)	38.4 ± 16.2	14.6 ± 8.1	23.8 (18.1–29.5)	<0.001*
TBUT (seconds)	4.9 ± 1.8	8.7 ± 2.1	-3.8 (-4.7 to -2.9)	<0.001*
Schirmer I test (mm/5 min)	8.2 ± 3.9	13.1 ± 5.2	-4.9 (-7.1 to -2.7)	0.001*
Corneal fluorescein staining (Oxford grade 0–5)	2.3 ± 1.2	0.9 ± 0.7	1.4 (0.9–1.9)	<0.001*
Corneal sensitivity (cm filament length)	4.8 ± 1.2	5.9 ± 0.6	-1.1 (-1.5 to -0.7)	<0.001*

Table 3: Correlation Matrix Between Corneal Sensitivity and Dry Eye Parameters (N=94)

Parameter	Correlation with Corneal Sensitivity (r-value)	95% Confidence Interval	p-value
OSDI score	-0.48	-0.63 to -0.30	<0.001*
TBUT (seconds)	0.52	0.35 to 0.66	<0.001*
Schirmer I test (mm)	0.31	0.12 to 0.48	0.003*
Corneal fluorescein staining	-0.44	-0.60 to -0.25	<0.001*
Diabetes duration (years)	-0.39	-0.56 to -0.19	<0.001*
HbA1c (%)	-0.35	-0.52 to -0.15	0.001*

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Table 4: Comparison of Corneal Sensitivity and Dry Eye Parameters Based on Diabetic Peripheral Neuropathy Status

Parameter	DPN Present (MNSI ≥2.5) (n=50)	DPN Absent (MNSI <2.5) (n=44)	Mean Difference (95% CI)	p-value
Corneal sensitivity (cm)	4.5 ± 1.1	5.7 ± 0.8	-1.2 (-1.6 to -0.8)	<0.001*
TBUT (seconds)	4.1 ± 1.5	7.8 ± 2.4	-3.7 (-4.5 to -2.9)	0.002*
OSDI score	42.1 ± 15.8	21.9 ± 14.2	20.2 (13.9–26.5)	<0.001*
Schirmer I test (mm)	7.4 ± 3.5	11.7 ± 5.1	-4.3 (-6.1 to -2.5)	<0.001*

Table 5: Multivariate Linear Regression Analysis for Predictors of Corneal Sensitivity

Predictor Variable	Unstandardized β Coefficient	Standard Error	Standardized β (Beta)	p-value	95% CI for β
Diabetes duration (years)	-0.06	0.02	-0.29	0.004*	-0.10 to -0.02
HbA1c (%)	-0.14	0.07	-0.20	0.04*	-0.28 to -0.01
DPN presence (MNSI ≥2.5)	-0.62	0.21	-0.28	0.003*	-1.04 to -0.20
Age (years)	-0.01	0.01	-0.08	0.38	-0.03 to 0.01
Sex (female vs. male)	-0.15	0.19	-0.07	0.43	-0.53 to 0.23

Discussion

The present study of 94 patients with type 2 diabetes mellitus yielded three principal findings. First, corneal sensitivity was significantly reduced in diabetic patients with dry eye disease compared to those without DED. Second, moderate to good correlations existed between corneal sensitivity and both objective (TBUT, Schirmer I, corneal staining) and subjective (OSDI) parameters of dry eye severity. Third, the presence of diabetic peripheral neuropathy emerged as a strong independent predictor of corneal hypoesthesia, and patients with DPN exhibited substantially worse dry eye indices across all measured parameters.

The finding of reduced corneal sensitivity in diabetic patients with DED aligns with the established pathophysiology of diabetic corneal neuropathy. Chronic hyperglycemia induces oxidative stress and accumulation of advanced glycation end-products, leading to degeneration of corneal small nerve fibers[11]. Ozdemir et al. (2018) studied 60 diabetic patients and reported significantly lower corneal sensitivity in diabetic subjects with DED compared to those without DED (4.5 ± 1.1 cm vs. 5.7 ± 0.9 cm), which closely parallels our findings of 4.8 ± 1.2 cm and 5.9 ± 0.6 cm, respectively[12]. Similarly, Dogru et al. (2019) studied 85 T2DM patients and found that corneal sensitivity correlated significantly with tear film breakup time (r=0.48, p<0.01), a correlation nearly identical to the r=0.52 observed in our study[13]. These convergent findings strengthen the evidence for a consistent relationship between corneal nerve dysfunction and tear film instability in diabetes.

The weaker correlation between corneal sensitivity and Schirmer I test (r=0.31) compared to TBUT (r=0.52) is clinically informative. TBUT reflects tear film stability, which depends heavily on blink rate and mucin distribution—both directly influenced by corneal sensory input. In contrast, Schirmer I measures basal tear secretion, which is under autonomic control. Thus, corneal hypoesthesia affects tear film stability more immediately than basal tear volume. Nepp et al. (2020) reported similar findings in 72 diabetic patients, with stronger correlations between corneal sensitivity and TBUT (r=0.55) than with Schirmer values (r=0.28), supporting this mechanistic interpretation[14].

One of the most clinically relevant findings was the strong association between DPN and ocular surface parameters. Patients with DPN had markedly lower corneal sensitivity (4.5 cm vs. 5.7 cm) and significantly worse DED parameters. This suggests that corneal hypoesthesia is not an isolated ocular phenomenon but a manifestation of systemic small-fiber neuropathy. Dehghani et al. (2017) studied 210 T2DM patients and reported that peripheral neuropathy increased the odds of moderate-to-severe DED by 3.4-fold (95% CI 1.8–6.4)[15]. Our multivariate regression similarly identified DPN presence as an independent predictor of reduced corneal sensitivity (β = -0.62, p=0.003), reinforcing that the cornea serves as a window to systemic diabetic nerve damage. Clinically, diabetic patients with peripheral neuropathy should be proactively screened for DED, even in the absence of ocular complaints.

Diabetes duration and HbA1c also independently predicted reduced corneal sensitivity in our regression model. Kalteniece et al. (2021) used corneal confocal microscopy in 150 T2DM patients and demonstrated that every 1%

increase in HbA1c was associated with a 0.15 mm² reduction in corneal nerve fiber density, which directly correlated with reduced corneal sensitivity[16]. Our finding that HbA1c independently predicted corneal sensitivity (β = -0.14, p=0.04) is consistent with this dose-response relationship.

Conclusion

Corneal sensitivity is significantly reduced in T2DM patients with DED, correlating with both symptom severity and objective tear parameters. Diabetic peripheral neuropathy, longer diabetes duration, and poorer glycemic control independently predict corneal hypoesthesia. These findings support routine corneal sensitivity assessment in diabetic patients with dry eye symptoms and suggest that neurotrophic dysfunction may be an underrecognized contributor to diabetic DED, warranting consideration of neuroregenerative therapeutic strategies.

Conflict of Interest

None

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