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Original Article

Regional Tear Film Instability in Dry Eye Disease: A Comparative Analysis of Central and Inferior Tear Breakup Time

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ABSTRACT

Background: Dry eye disease is a multifactorial ocular surface disorder characterized by tear film instability, ocular discomfort, and visual disturbance. Conventional tear breakup time assessment commonly emphasizes the central corneal zone, although regional tear film disruption may occur earlier in more vulnerable areas such as the inferior cornea. **Objective:** To compare central and inferior tear breakup time in patients assessed for dry eye disease and determine whether inferior-zone evaluation identifies greater regional tear film instability. **Methods:** This observational cross-sectional study was conducted at a tertiary care hospital in Lahore, Pakistan, from February to May 2026. A total of 113 clinical observations were included. Tear film stability was assessed using fluorescein-assisted tear breakup time under slit-lamp biomicroscopy with cobalt blue illumination. Three readings were obtained from the central 3–4 mm optical zone and inferior 4–8 mm corneal zone, and mean values were analyzed. Paired-samples t-test was used to compare regional tear breakup time, and correlation analysis assessed the relationship between age and inferior tear breakup time. **Results:** Mean age was 47.8 years. Central tear breakup time was 9.29 seconds, while inferior tear breakup time was 7.33 seconds, giving a mean paired reduction of 1.96 seconds in the inferior zone. The difference was statistically significant ($t = 10.88$, $df = 112$, $p < 0.001$), with a large effect size. Age showed a strong negative association with inferior tear breakup time ($r = -0.715$). **Conclusion:** Inferior corneal tear breakup time was significantly shorter than central tear breakup time, indicating greater regional tear film instability. Incorporating inferior-zone assessment may provide a more complete clinical evaluation of dry eye disease. **Keywords:** Dry Eye Disease; Tear Breakup Time; Central Cornea; Inferior Cornea; Tear Film Instability; Meibomian Gland Dysfunction.

INTRODUCTION

Dry eye disease (DED) is a multifactorial disorder of the ocular surface characterized by tear film instability, hyperosmolarity, inflammation, neurosensory abnormalities, and symptoms of ocular discomfort that may impair visual function and quality of life (1,2). Its reported global prevalence varies widely, largely because of differences in diagnostic criteria, age structure, sex distribution, environmental exposure, and clinical testing methods, but it remains one of the most frequent ocular surface conditions encountered in routine eye care (1). Because tear film instability is a central feature of DED, tear breakup time (TBUT) has long been used as a practical clinical test to assess the interval between a complete blink and the first visible disruption of the precorneal tear film (3,4). A shortened TBUT is generally interpreted as evidence of unstable tear film physiology and is commonly used alongside symptoms, ocular surface staining, eyelid evaluation, and other clinical findings to support the diagnosis and severity assessment of DED (2,5).

Although TBUT is widely used, conventional clinical assessment often focuses on the central corneal surface or reports a single overall breakup time, which may not fully represent regional variation in tear film behavior. The tear film is not distributed uniformly across the ocular surface; it is influenced by blinking mechanics, eyelid apposition, lipid layer spreading, tear meniscus dynamics, ocular surface topography, and local evaporative stress (6,7). The inferior corneal region may be particularly vulnerable because it lies closer to the lower tear meniscus and is exposed to gravitational effects, incomplete lipid redistribution, and mechanical interaction with the lower eyelid margin (6,8). Meibomian gland dysfunction may further amplify inferior tear film instability by reducing lipid layer quality and increasing evaporation, particularly in patients with evaporative or mixed forms of DED (8). These mechanisms suggest that central TBUT alone may underestimate early or localized tear film compromise, especially when instability begins outside the central optical zone.

Previous research has indicated that tear film breakup may show regional differences across the corneal surface, with peripheral or inferior areas sometimes demonstrating earlier instability than central areas (9). This is clinically important because patients with DED often report burning, grittiness, foreign body sensation, fluctuating vision, and irritation that may arise from localized ocular surface exposure rather than uniform tear film failure (10,11). Noninvasive and fluorescein-based methods have improved the clinical ability to observe tear film breakup patterns, but routine diagnostic interpretation still frequently depends on summary TBUT values rather than zone-specific assessment (12,13). Incomplete blinking during sustained visual tasks, including digital screen use, may also alter lipid distribution and promote regional tear film disruption, making inferior corneal evaluation particularly relevant in modern clinical populations (14). Tear osmolarity, inflammatory stress, and changes in corneal sensitivity may further interact with regional instability, reinforcing the need to examine whether inferior TBUT provides additional diagnostic information beyond central measurement alone (15).

Despite these biological and clinical reasons to suspect regional variation, limited local evidence has directly compared central and inferior TBUT among patients assessed for DED in routine tertiary eye-care settings. This gap is important because a central-only assessment may miss earlier inferior tear film rupture, potentially delaying recognition of ocular surface compromise and limiting region-specific management. Therefore, in patients undergoing clinical evaluation for DED, the present study aimed to compare TBUT measured in the central corneal zone with TBUT measured in the inferior corneal zone. The study hypothesis was that inferior TBUT would be significantly shorter than central TBUT, indicating greater regional tear film instability in the inferior cornea and supporting the clinical value of zone-based TBUT assessment.

MATERIALS AND METHODS

An observational cross-sectional study was conducted at a tertiary care hospital in Lahore, Pakistan, from February to May 2026 to evaluate regional variation in tear film stability among individuals undergoing ocular surface assessment for dry eye disease. The cross-sectional design was selected because it allowed simultaneous measurement of central and inferior tear breakup time under standardized clinical conditions and enabled direct within-subject comparison of tear film behavior across two anatomically distinct corneal zones.

Participants were recruited through a non-probability convenience sampling technique from patients presenting for ophthalmic evaluation during the study period. Eligible participants included adults with symptoms suggestive of dry eye disease or a clinical diagnosis based on symptom assessment and ocular surface examination. A comparison group of clinically healthy individuals without a previous diagnosis of dry eye disease was also considered during recruitment. Participants with other active ocular surface diseases, previous ocular trauma, eyelid or conjunctival abnormalities, corneal scarring, corneal opacity, recent use of topical ocular medication, or inability to maintain fixation during examination were

excluded to minimize measurement distortion and reduce confounding from non-dry-eye ocular pathology.

All participants underwent a standardized clinical assessment that included demographic documentation, relevant medical and ocular history, symptom screening, refraction, and slit-lamp biomicroscopy. Additional information regarding screen exposure and clinical risk factors was recorded to support interpretation of tear film instability in relation to external and patient-related characteristics. The primary outcome variable was tear breakup time measured separately in the central and inferior corneal regions. Central TBUT was operationally defined as the time from the last complete blink to the first visible tear film discontinuity within the central 3–4 mm optical zone, whereas inferior TBUT was defined as the corresponding time to first tear film disruption in the inferior 4–8 mm corneal region. Age, ocular diagnosis, and associated anterior segment findings, including meibomian gland dysfunction, blepharitis, allergic reaction, and other clinically relevant conditions, were recorded as descriptive and exploratory variables.

Tear film stability was assessed using fluorescein-assisted TBUT measurement under slit-lamp biomicroscopy with cobalt blue illumination. A moistened fluorescein strip was gently applied to the bulbar conjunctiva, after which participants were asked to blink several times to distribute the dye evenly across the ocular surface. Participants were then instructed to keep the eye open, and the interval between the last complete blink and the first appearance of a dark spot, line, or discontinuity in the fluorescein-stained tear film was measured in seconds. Three readings were obtained for the central corneal zone and three readings for the inferior corneal zone, and the mean value for each region was used for analysis to reduce random measurement variability. Measurements were performed using the same clinical approach for all participants to maintain procedural consistency across observations.

Several steps were used to reduce bias during data collection. The same predefined anatomical boundaries were applied for central and inferior TBUT measurement in all participants, repeated readings were averaged for each region, and patients with corneal opacity, scarring, fixation difficulty, or recent ocular drop use were excluded because these factors could interfere with accurate tear film visualization. Recording central and inferior TBUT within the same participant also reduced between-subject variability and allowed each participant to serve as their own comparator for the primary regional analysis.

The sample size was calculated using an expected dry eye disease prevalence of 8%, a 95% confidence level, and a 5% margin of error. Data were entered and checked for completeness before statistical analysis. Quantitative variables were summarized using mean, minimum, and maximum values, while categorical ocular conditions were summarized using frequencies and percentages. The primary comparison between central and inferior TBUT was analyzed using a paired-samples t-test because both measurements were obtained from the same participant or eye under the same examination protocol. Pearson correlation analysis was used to assess the relationship between age and regional TBUT measurements. Statistical significance was determined using a p-value threshold of less than 0.05.

The study was conducted after approval from the ethics committee of Superior University, Lahore. Participants were informed about the purpose and procedure of the examination, confidentiality of collected data was maintained, and participation was voluntary with the right to withdraw at any stage. Data were anonymized during analysis, and all measurements were recorded using a consistent data collection process to support reproducibility, accuracy, and integrity of the final dataset.

RESULTS

A total of 113 clinical observations were included in the analysis. The mean age of the study population was 47.8 years, with an age range from 18 to 78 years, indicating representation from young adulthood to older age. Regional tear film assessment showed lower stability in the inferior corneal zone than in

the central corneal zone. The mean central tear breakup time (TBUT) was 9.29 seconds, ranging from 3.2 to 14.5 seconds, whereas the mean inferior TBUT was 7.33 seconds, ranging from 2.1 to 12.8 seconds. The lower minimum and mean values in the inferior zone indicate greater regional susceptibility to early tear film disruption.

Table 1. Demographic and Regional Tear Film Characteristics

Variable	n	Mean	Minimum	Maximum	Unit
Age	113	47.8	18	78	years
Central TBUT	113	9.29	3.2	14.5	seconds
Inferior TBUT	113	7.33	2.1	12.8	seconds

The distribution of associated ocular conditions showed that meibomian gland dysfunction was the most frequent clinical finding, present in 47 observations (41.6%). This was followed by blepharitis in 28 observations (24.8%), allergic reaction in 23 observations (20.4%), dry eye diagnosis in 10 observations (8.8%), and viral keratitis in 5 observations (4.4%). These findings indicate that eyelid margin and tear lipid layer–related disorders formed a major proportion of the clinical profile, with meibomian gland dysfunction alone accounting for more than two-fifths of the observed cases.

Table 2. Distribution of Ocular Clinical Conditions

Clinical condition	Frequency	Percentage
Meibomian gland dysfunction	47	41.6%
Blepharitis	28	24.8%
Allergic reaction	23	20.4%
Dry eye	10	8.8%
Viral keratitis	5	4.4%
Total	113	100.0%

The primary paired comparison demonstrated a statistically significant difference between central and inferior TBUT. The mean central TBUT was 9.29 seconds, while the mean inferior TBUT was 7.33 seconds, producing a mean paired difference of approximately 1.96 seconds. The paired-samples t-test showed a strong statistical difference between the two regions, with $t = 10.88$, $df = 112$, and $p < 0.001$. The estimated 95% confidence interval for the mean paired difference was 1.60 to 2.32 seconds, supporting a clinically meaningful reduction in tear film stability in the inferior corneal region. The effect size was large, with an estimated Cohen's dz of 1.02, indicating that the regional difference was not only statistically significant but also substantial in magnitude.

Table 3. Paired Comparison of Central and Inferior Tear Breakup Time

Comparison	Central TBUT Mean	Inferior TBUT Mean	Mean Difference	95% CI for Difference	t-value	df	p-value	Effect Size
Central vs. Inferior TBUT	9.29 s	7.33 s	1.96 s	1.60 to 2.32 s	10.88	112	<0.001	1.02

Age showed a strong negative relationship with inferior TBUT, with a reported correlation coefficient of $r = -0.715$. This indicates that increasing age was associated with shorter inferior tear breakup time. The coefficient of determination was approximately 51.1%, suggesting that age accounted for a substantial proportion of variation in inferior tear film instability. This association highlights the inferior corneal zone as a region where age-related tear film compromise may be especially evident.

Table 4. Association Between Age and Inferior Tear Breakup Time

Association	n	Correlation Coefficient	Direction of Association	Variance Explained	p-value
Age and Inferior TBUT	113	-0.715	Negative	51.1%	<0.001

Overall, the results demonstrate consistent regional instability of the tear film, with the inferior cornea showing earlier breakup than the central cornea. The approximately 2-second reduction in inferior TBUT, together with the large paired effect size and strong statistical significance, supports the clinical relevance of assessing tear breakup regionally rather than relying only on central corneal measurements.

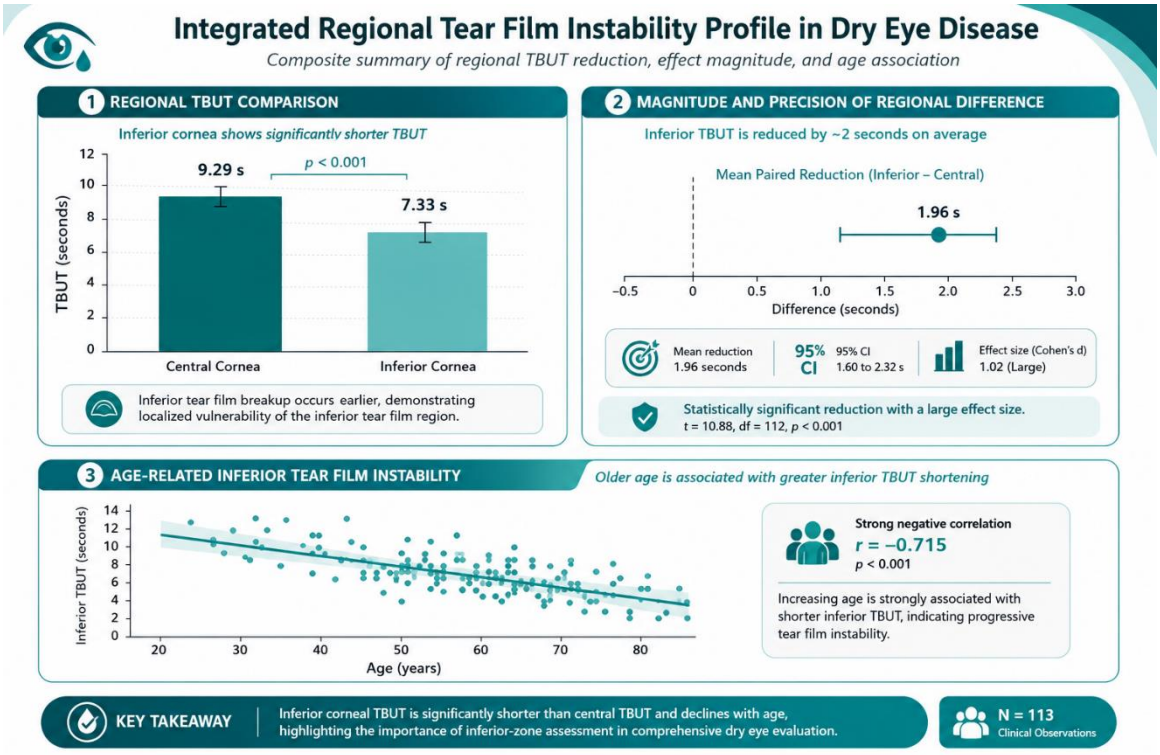

Figure 3. Integrated Regional Tear Film Instability Profile in Dry Eye Disease.

This multidimensional composite figure illustrates the significant regional variation in tear film stability between the central and inferior corneal zones among patients evaluated for dry eye disease. The left panel demonstrates significantly shorter inferior tear breakup time (TBUT) compared with central TBUT (7.33 s vs. 9.29 s; $p < 0.001$), indicating greater inferior corneal vulnerability to tear film disruption. The upper-right panel summarizes the magnitude and precision of the paired regional difference, showing a mean reduction of 1.96 seconds with a 95% confidence interval of 1.60–2.32 seconds and a large effect size (Cohen's d = 1.02). The lower panel presents the strong negative association between age and inferior TBUT ($r = -0.715$, $p < 0.001$), demonstrating progressive age-related deterioration in inferior tear film stability. Overall, the figure highlights the clinical importance of inferior-zone TBUT assessment as a complementary approach for identifying localized tear film instability in dry eye disease.

DISCUSSION

The present study demonstrated a clear regional difference in tear film stability, with the inferior corneal zone showing a shorter mean tear breakup time than the central corneal zone. Central TBUT averaged 9.29 seconds, whereas inferior TBUT averaged 7.33 seconds, producing an approximate paired reduction of 1.96 seconds in the inferior region. This difference was statistically significant and clinically relevant, indicating that tear film instability in dry eye disease is not uniformly distributed across the corneal surface. The finding supports the concept that a single central TBUT value may not fully capture localized tear film compromise, particularly when early rupture occurs in the lower corneal region. Because TBUT is commonly used as a practical indicator of tear film instability, incorporating regional observation may improve the clinical interpretation of ocular surface status, especially in patients whose symptoms are disproportionate to central corneal findings (5,12).

The greater vulnerability of the inferior cornea can be explained by several anatomical and physiological mechanisms. The inferior tear film is positioned close to the lower tear meniscus and is influenced by eyelid movement, tear redistribution, gravitational effects, and local variation in lipid layer spread. Blinking plays a major role in resurfacing the tear film and distributing meibomian lipids across the ocular surface; therefore, incomplete or inefficient blinking can leave the inferior cornea less protected,

allowing faster evaporation and earlier tear film rupture (7,14). This mechanism is particularly relevant in individuals with prolonged visual tasks or reduced blink quality, where tear film replenishment may be delayed and regional drying may occur before a central defect becomes apparent. The observed inferior TBUT reduction therefore reflects a plausible clinical pattern rather than a random measurement difference.

The high proportion of meibomian gland dysfunction in the study population further supports the biological basis of inferior tear film instability. Meibomian gland dysfunction was the most frequent associated clinical condition, accounting for 41.6% of observations, followed by blepharitis and allergic reaction. Since meibomian secretions form the lipid layer that limits evaporation, gland dysfunction can accelerate tear film breakup and increase regional instability, particularly in exposed or mechanically vulnerable zones (15,16). The inferior cornea may be especially affected when lipid delivery is irregular or inadequate after blinking. This explains why patients with evaporative or mixed dry eye patterns may show earlier breakup in the lower corneal zone even when the central tear film appears relatively preserved.

The association between increasing age and reduced inferior TBUT also has clinical importance. The reported negative correlation between age and inferior TBUT suggests that older participants tended to have faster inferior tear film breakup. Age-related changes in eyelid structure, blink efficiency, ocular surface sensitivity, lacrimal function, and meibomian gland morphology may contribute to reduced tear film stability over time (17,18). In this context, the inferior corneal zone may function as a sensitive region for detecting age-associated tear film compromise. The finding also highlights the importance of careful inferior corneal assessment in middle-aged and older patients, particularly when they present with burning, foreign body sensation, grittiness, fluctuating vision, or symptoms that are not fully explained by central TBUT alone.

The results align with the broader understanding that dry eye disease is a multifactorial disorder involving tear film instability, ocular surface inflammation, neurosensory changes, and tear hyperosmolarity rather than a single uniform abnormality (2,19). A regional approach to TBUT assessment is consistent with this multifactorial model because it recognizes that tear film failure may begin locally before becoming generalized. Inferior instability may contribute to localized epithelial stress and symptom generation, especially where tear evaporation, eyelid friction, and meniscus-related osmotic gradients interact. Therefore, central TBUT and inferior TBUT should not be viewed as interchangeable measurements; rather, they may provide complementary information about different aspects of tear film behavior.

Clinically, the nearly 2-second reduction in inferior TBUT is meaningful because TBUT values close to diagnostic thresholds may change interpretation depending on the region examined. A patient with borderline central TBUT may still demonstrate clearly abnormal inferior breakup, suggesting that central-only evaluation could underestimate disease activity. This is particularly relevant for early disease recognition, treatment monitoring, and identifying patients who may benefit from therapies targeting evaporative mechanisms, lid margin disease, blink quality, or meibomian gland dysfunction. Regional assessment may also help explain persistent symptoms in patients whose central corneal findings appear mild.

Several limitations should be considered when interpreting these findings. The cross-sectional design allows identification of regional differences at one point in time but does not establish longitudinal progression or predictive value for future ocular surface damage. Convenience sampling from a single tertiary care setting may limit generalizability to broader community populations. Fluorescein-assisted TBUT is clinically useful but can be influenced by dye volume, examiner technique, blink pattern, timing, room conditions, and patient cooperation. The analysis would be strengthened by incorporating symptom scores, ocular surface staining grades, tear osmolarity, Schirmer testing, meibomian gland grading, and noninvasive TBUT measures. Despite these limitations, the paired regional design provides

a strong internal comparison because central and inferior measurements were obtained within the same clinical observations, reducing between-subject variability.

Overall, the findings indicate that inferior corneal tear film instability is more pronounced than central instability in the studied population. The shorter inferior TBUT, strong paired difference, and relationship with age support the clinical value of observing tear breakup by region rather than relying exclusively on a central measurement. Regional TBUT assessment, particularly of the inferior cornea, may provide a more detailed understanding of tear film behavior and may help clinicians identify localized instability associated with dry eye disease, meibomian gland dysfunction, and age-related ocular surface compromise.

CONCLUSION

This study demonstrated that tear film stability differs regionally across the corneal surface, with the inferior corneal zone showing consistently shorter tear breakup time than the central corneal zone. The mean inferior TBUT was 7.33 seconds compared with 9.29 seconds centrally, producing an approximate 1.96-second reduction in inferior tear film stability. This significant regional difference indicates that the inferior cornea represents a more vulnerable area for early tear film disruption in dry eye disease. The strong association between age and reduced inferior TBUT further suggests that age-related ocular surface changes may contribute to inferior corneal instability. These findings support the clinical value of incorporating inferior-zone TBUT assessment alongside conventional central TBUT measurement, as regional evaluation may provide a more complete understanding of tear film behavior and help identify localized instability that could otherwise be underestimated during routine dry eye assessment.

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