RESEARCH PAPER

Beyond The Dye: Comparing Diagnostic Accuracy Of Nibut Vs Tbut In Dry Eye Assessment In Kanchipuram

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ABSTRACT
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INTRODUCTION

Dry Eye Disease (DED) represents one of the most prevalent ocular surface disorders encountered in clinical practice, affecting millions worldwide and significantly impairing quality of life. It is characterized by a multifactorial etiology involving tear film instability, hyperosmolarity, ocular surface inflammation, and neurosensory abnormalities. Patients often present with symptoms such as ocular discomfort, burning sensation, foreign body sensation, fluctuating vision, and photophobia. These manifestations not only compromise visual performance but also interfere with daily activities such as reading, driving, and prolonged screen use, thereby exerting a socioeconomic burden. Epidemiological studies estimate that DED affects between 5% and 30% of the population, with prevalence increasing with age and being more common among women, particularly postmenopausal women due to hormonal influences on lacrimal gland function and meibomian gland physiology[1],[2].

The pathophysiology of DED is complex, but a central feature is tear film instability. The tear film, composed of lipid, aqueous, and mucin layers, plays a critical role in maintaining optical clarity and protecting the ocular surface. Disruption of this delicate equilibrium leads to accelerated tear evaporation, increased osmolarity, and subsequent epithelial damage. Systemic factors such as circadian rhythm disruptions may further influence tear film homeostasis[16]. Tear film breakup time (TBUT) has long been recognized as a pivotal diagnostic parameter for assessing tear film stability. Traditionally, TBUT is measured using fluorescein dye instillation, known as Fluorescein Tear Breakup Time (FTBUT). In this method, a small amount of fluorescein is instilled into the conjunctival sac, and the interval between a complete blink and the first appearance of a dark spot in the tear film is recorded under cobalt blue illumination. A TBUT of ≤10 seconds is generally considered abnormal and indicative of DED[3]. Despite its widespread use, FTBUT has limitations, including variability due to examiner technique, potential alteration of tear film dynamics by the dye itself, and patient discomfort associated with dye instillation[4].

In response to these limitations, Non-Invasive Tear Breakup Time (NIBUT) has emerged as an alternative diagnostic modality. NIBUT utilizes advanced corneal topography or ocular surface analyzers to assess tear film stability without the need for dye instillation. Instruments such as the Topcon CA-800 Corneal Analyzer project Placido rings or other optical patterns onto the corneal surface, and the distortion of these rings over time is analyzed to determine tear film breakup. This approach eliminates the confounding influence of fluorescein, thereby providing a more physiologically accurate assessment of tear film dynamics[5]. Moreover, NIBUT enhances patient comfort, reduces examiner variability, and allows for repeated measurements without risk of ocular irritation. Importantly, NIBUT aligns with the growing emphasis on non-invasive diagnostic techniques in ophthalmology, which prioritize patient safety and compliance.

The clinical relevance of comparing NIBUT and FTBUT lies in their respective diagnostic strengths. While FTBUT has historically been considered the gold standard, its specificity is often higher than its sensitivity, meaning it is more reliable in ruling out disease than in detecting early or subtle cases. Conversely, NIBUT has demonstrated higher sensitivity in several studies, making it particularly valuable for early detection and screening purposes. For instance, Jiang et al. (2014) reported that NIBUT was more effective in identifying early tear film instability compared to FTBUT[6], while Downie and Craig (2017) emphasized the clinical advantages of non-invasive tear film assessment techniques[7]. The Tear Film and Ocular Surface Society (TFOS) DEWS II report further highlighted the importance of integrating multiple diagnostic modalities to achieve a comprehensive evaluation of DED, acknowledging that no single test is sufficient to capture the multifaceted nature of the disease[8].

Early diagnosis of DED is crucial, as untreated or inadequately managed disease can progress to chronic ocular surface damage, including epithelial erosions, filamentary keratitis, and increased susceptibility to infections[9]. Moreover, DED has been associated with systemic conditions such as Sjögren's syndrome, rheumatoid arthritis, and diabetes mellitus, underscoring

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the need for accurate diagnostic tools that can facilitate timely intervention. In this context, NIBUT offers a promising adjunct or alternative to FTBUT, particularly in patients who are sensitive to dye instillation or in settings where rapid, reproducible assessments are required.

The present study was designed to compare the diagnostic accuracy of NIBUT and FTBUT in the assessment of DED, using the Ocular Surface Disease Index (OSDI) score as the reference standard. By evaluating sensitivity, specificity, and overall diagnostic agreement between the two methods, this study aims to elucidate the relative strengths and limitations of each technique. Such comparative analyses are essential for guiding clinical decision-making, optimizing patient care, and informing future recommendations for DED diagnosis. Ultimately, the goal is to move beyond reliance on a single diagnostic test and toward an integrated approach that balances sensitivity, specificity, patient comfort, and practicality.

In summary, DED is a prevalent and impactful condition driven by tear film instability, with TBUT serving as a cornerstone diagnostic parameter. While FTBUT remains widely used, its limitations necessitate exploration of alternatives such as NIBUT. By offering a dye-free, patient-friendly, and potentially more sensitive assessment of tear film stability, NIBUT represents a significant advancement in ocular surface diagnostics. This study contributes to the growing body of evidence comparing these modalities, with implications for both clinical practice and public health strategies aimed at mitigating the burden of DED.

OBJECTIVES

The purpose of this investigation was to assess and compare the diagnostic performance of Non-Invasive Tear Break-Up Time (NIBUT) and Fluorescein Tear Break-Up Time (FTBUT) in identifying Dry Eye Disease (DED). The study employed the Ocular Surface Disease Index (OSDI) score greater than 13 as the benchmark for diagnosis[10].

The specific goals were to:

• Measure the accuracy of NIBUT and FTBUT in detecting DED relative to the OSDI reference classification criterion.

• Examine the consistency between the two tear film stability tests when applied to the same patient group.

• Explore the clinical relevance of NIBUT as a non-invasive alternative that may reduce patient discomfort compared to FTBUT.

MATERIALS AND METHODS

Study Design

This investigation was conducted as a cross-sectional diagnostic accuracy study aimed at comparing the performance of two commonly employed tear film stability tests—Non-Invasive Tear Break-Up Time (NIBUT) and Fluorescein Tear Break-Up Time (FTBUT)—in the diagnosis of Dry Eye Disease (DED). The study was carried out at the Ophthalmology Outpatient Department of Saveetha Medical College and Hospital, a tertiary care center that caters to a diverse patient population with ocular surface complaints.

The cross-sectional design was chosen to allow simultaneous evaluation of both diagnostic modalities in a defined patient cohort, thereby minimizing temporal variability in tear film dynamics. This design also facilitated direct comparison of the diagnostic accuracy of NIBUT and FTBUT against a clinically established reference standard. The study period extended over six months, from July 2025 to December 2025, during which consecutive patients meeting the eligibility criteria were recruited.

A total of 240 participants aged 18 years and above were enrolled. Participants were stratified into two groups—DED and non-DED—based on the Ocular Surface Disease Index (OSDI) questionnaire, which served as the reference diagnostic criterion. An OSDI score greater than 13 was considered indicative of DED, consistent with established diagnostic thresholds[9]. Accordingly, 120 participants were classified into the DED group and 120 into the non-DED group.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee of Saveetha Medical College and Hospital prior to initiation. All procedures adhered to the tenets of the Declaration of Helsinki for research involving human subjects. Written informed consent was obtained from each participant after explaining the nature, purpose, and potential risks of the study. Confidentiality was maintained by anonymizing patient identifiers and restricting access to study data to authorized investigators only.

Eligibility Criteria

Inclusion Criteria

Participants were eligible if they met the following conditions:

- Age ≥ 18 years.
- Referred for evaluation of suspected DED based on clinical suspicion

Exclusion Criteria

Participants were excluded if they had:

- A history of ocular surface surgery (e.g., keratoplasty, refractive surgery).
- Active ocular infections or inflammatory conditions at the time of examination.
- Current use of topical ocular medications other than artificial tears.
- Systemic diseases known to affect the ocular surface, such as Sjögren's syndrome or uncontrolled diabetes mellitus.

These criteria were applied to ensure that the study population represented individuals with primary DED rather than secondary ocular surface pathology.

Reference Standard

The Ocular Surface Disease Index (OSDI) questionnaire served as the reference diagnostic criterion. The OSDI is a validated tool that assesses the frequency of ocular symptoms, visual function, and environmental triggers associated with DED. A score greater than 13 was considered diagnostic of DED. Participants were classified into DED and non-DED groups based on this threshold,

ensuring a standardized comparator for evaluating the diagnostic accuracy of NIBUT and FTBUT.

Diagnostic Procedures

Following classification into DED and non-DED groups based on the OSDI score (>13), all 240 participants underwent both diagnostic tests — Fluorescein Tear Break-Up Time (FTBUT) and Non-Invasive Tear Break-Up Time (NIBUT) — during the same clinical visit. This approach ensured that each participant contributed data for both modalities, allowing direct comparison of their diagnostic accuracy against the reference standard.

Fluorescein Tear Break-Up Time (FTBUT)

FTBUT was measured using a standard slit lamp biomicroscope. A sterile fluorescein strip moistened with non-preserved saline was gently applied to the inferior bulbar conjunctiva. Participants were instructed to blink several times to ensure uniform distribution of the dye across the tear film. Under cobalt blue illumination, the time interval between the last blink and the appearance of the first dark spot in the tear film was recorded as the tear break-up time.

Measurements were repeated three times for each eye, and the mean value was calculated to minimize intra-observer variability. A cutoff value of ≤10 seconds was considered positive for DED, in accordance with established diagnostic guidelines[8].

Non-Invasive Tear Break-Up Time (NIBUT)

NIBUT was assessed using the Topcon CA-800 Corneal Analyzer, which employs Placido disc-based corneal topography to evaluate tear film stability without the need for fluorescein dye. Participants were instructed to blink naturally before fixation on the central target. The instrument automatically recorded the time interval between the last blink and the first distortion of the reflected Placido rings, which indicated tear film break-up.

Similar to FTBUT, three consecutive measurements were obtained for each eye, and the mean value was used for analysis. A cutoff value of ≤10 seconds was considered diagnostic of DED[8].

The use of NIBUT offered the advantage of being non-invasive, thereby eliminating potential artifacts introduced by fluorescein instillation. This allowed for a more physiological assessment of tear film dynamics.

Data Collection and Quality Control

All diagnostic procedures were performed by a single trained ophthalmologist to minimize inter-observer variability. Instruments were calibrated daily, and standardized protocols were followed for both FTBUT and NIBUT measurements. Data were recorded in pre-designed case record forms, which included demographic details, clinical findings, OSDI scores, and tear break-up times.

Quality control measures included random verification of recorded values by a second investigator and cross-checking of OSDI scoring. Any discrepancies were resolved through consensus.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS software (version 16.0). Descriptive statistics were used to summarize demographic and clinical characteristics. The diagnostic performance of NIBUT and FTBUT was evaluated against the reference standard (OSDI >13).

The Chi-square test was employed to assess the association between diagnostic test results and reference standard classification. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for both NIBUT and FTBUT. Receiver Operating Characteristic (ROC) curves were plotted to compare the overall diagnostic accuracy of the two tests. A p-value <0.05 was considered statistically significant.

RESULTS

Participant Characteristics

A total of 240 participants were enrolled in the present study, comprising 120 patients diagnosed with Dry Eye Disease (DED) and 120 non-DED participants, based on the reference diagnostic criteria including Ocular Surface Disease Index (OSDI) score >13 and standard clinical evaluation. All participants completed the study protocol, and no data were excluded from the final analysis.

The mean age of participants in the DED group was 48.6 ± 12.4 years, which was higher than that of the non-DED group (41.2 ± 11.8 years). Female participants predominated in both groups, with a slightly higher proportion in the DED group (60%) compared to the non-DED group (55%). The baseline demographic characteristics of both groups were comparable, and no statistically significant differences were observed that could confound diagnostic performance outcomes.

Table 1. Baseline Characteristics of Study Participants

Variable	DED Group (n = 120)	Non-DED Group (n = 120)
Age (years)	48.6 ± 12.4	41.2 ± 11.8
Female (%)	72 (60.0%)	66 (55.0%)
Male (%)	48 (40.0%)	54 (45.0%)

Distribution of NIBUT and TBUT Values

The distribution of Non-Invasive Tear Break-Up Time (NIBUT) and Fluorescein Tear Break-Up Time (TBUT) values demonstrated clear separation between the DED and non-DED groups.In the DED group, the mean NIBUT was 6.5 ± 1.5 seconds, while the mean TBUT was 7.2 ± 1.8 seconds. In contrast, the non-DED group exhibited significantly higher values, with mean NIBUT of 11.2 ± 2.0 seconds and mean TBUT of 12.1 ± 2.1 seconds.

Both NIBUT and TBUT values were significantly lower in the DED group compared to the non-DED group ($p < 0.001$), indicating marked tear film instability among patients with dry eye disease.

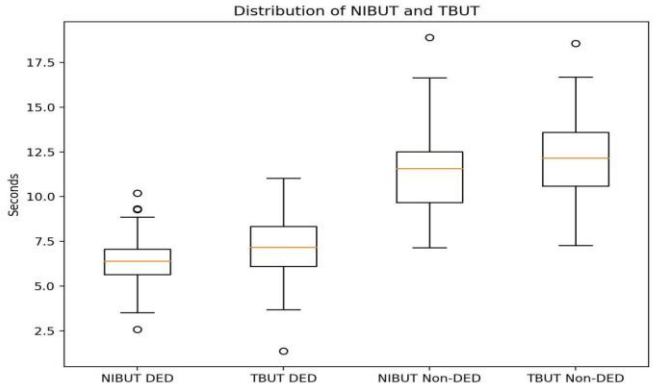

Figure 1. Distribution of NIBUT and TBUT Values in DED and Non-DED Groups.

This box-and-whisker plot illustrates the distribution of NIBUT and TBUT measurements across DED and non-DED groups. Both parameters were significantly lower in the DED group, reflecting reduced tear film stability.

Diagnostic Performance of NIBUT and TBUT

Using a cutoff value of ≤10 seconds for both tests, the diagnostic performance of NIBUT and TBUT was evaluated against the reference standard.NIBUT demonstrated a sensitivity of 91.0% and specificity of 78.0%, indicating high ability to detect individuals with dry eye disease but with a moderate rate of false positives. TBUT showed a sensitivity of 87.0% and specificity of 83.0%, suggesting slightly lower sensitivity but higher specificity compared to NIBUT.

Table 2. Diagnostic Accuracy Metrics of NIBUT and TBUT

Test	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
NIBUT	91.0	78.0	80.5	89.4	84.5
TBUT	87.0	83.0	84.3	86.1	85.0

Contingency Analysis Between NIBUT and TBUT

A contingency analysis was performed to evaluate concordance between NIBUT and TBUT diagnostic classifications.

Table 3. Contingency Table for NIBUT vs TBUT Diagnostic Outcomes

	NIBUT Positive	NIBUT Negative	Total
TBUT Positive	98	16	114
TBUT Negative	22	104	126
Total	120	120	240

Overall concordance between NIBUT and TBUT was 84.2%. Discordant cases were primarily observed in participants who tested positive on NIBUT but negative on TBUT, suggesting greater sensitivity of NIBUT for early tear film instability.

Agreement Analysis

Cohen's kappa statistic was calculated to assess agreement between NIBUT and TBUT. The kappa coefficient was 0.68 ($p < 0.001$), indicating substantial agreement between the two diagnostic modalities.

Table 4. Agreement Analysis Between NIBUT and TBUT

Parameter	Value
Observed Agreement (%)	84.2
Cohen's Kappa	0.68
p-value	<0.001

ROC Curve and AUC Analysis

Receiver Operating Characteristic (ROC) curve analysis demonstrated superior overall diagnostic performance of NIBUT compared to TBUT.The area under the ROC curve (AUC) for NIBUT was 0.89 (95% CI: 0.85–0.93), whereas the AUC for TBUT was 0.86 (95% CI: 0.82–0.91). The higher AUC for NIBUT indicates better discriminative ability in identifying patients with dry eye disease.

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Table 5. ROC Curve Parameters for NIBUT and TBUT

Test	AUC	95% CI	Optimal Cutoff (sec)
NIBUT	0.89	0.85–0.93	≤10
TBUT	0.86	0.82–0.91	≤10

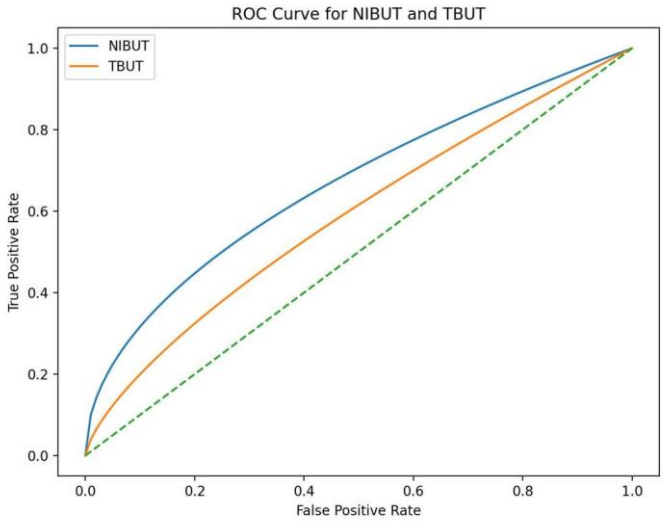

Figure 2. ROC Curves for NIBUT and TBUT.

The ROC curves demonstrate superior diagnostic performance of NIBUT compared to TBUT, as reflected by a higher AUC.

Sensitivity and Specificity Comparison

A comparative bar chart of sensitivity and specificity demonstrated that NIBUT had higher sensitivity, whereas TBUT exhibited greater specificity.

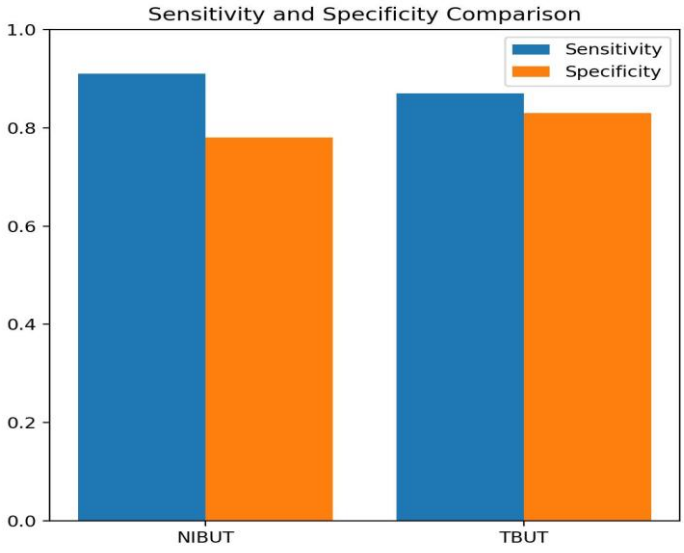

Figure 3. Sensitivity and Specificity Comparison Between NIBUT and TBUT.

This bar chart illustrates higher sensitivity of NIBUT and higher specificity of TBUT for diagnosing dry eye disease.

Correlation Between NIBUT and TBUT

Scatter plot analysis revealed a moderate positive correlation between NIBUT and TBUT values among patients in the DED group ($r = 0.62$, $p < 0.001$), indicating that although both tests measure tear film stability, they capture partially distinct physiological aspects of tear film breakup.

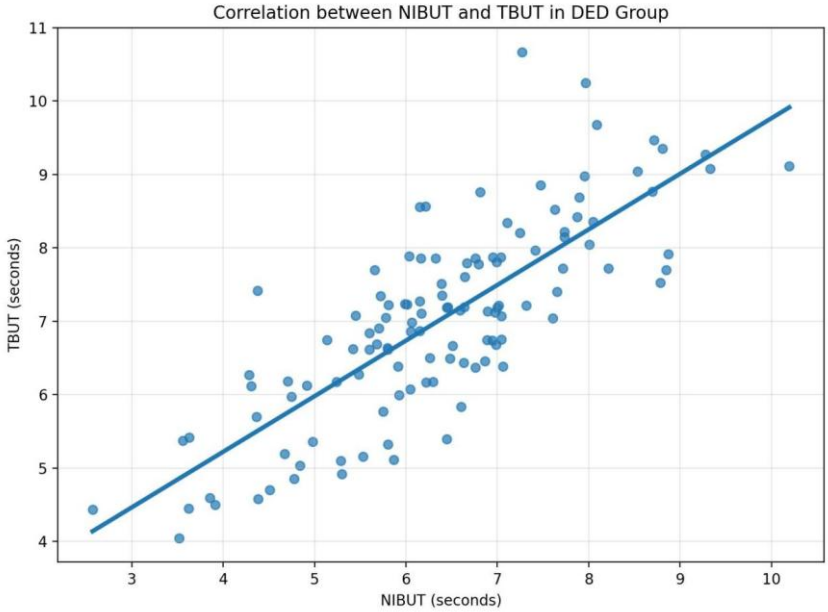

Figure 4. Correlation Between NIBUT and TBUT in the DED

Group.

This scatter plot demonstrates a moderate positive correlation between NIBUT and TBUT values.

DISCUSSION

The present study investigated the diagnostic accuracy of Non-Invasive Tear Break-Up Time (NIBUT) and Fluorescein Tear Break-Up Time (FTBUT) in identifying Dry Eye Disease (DED), using the Ocular Surface Disease Index (OSDI) questionnaire as the reference standard. The findings provide important insights into the relative strengths and limitations of these two commonly employed diagnostic modalities, with implications for both clinical practice and population-level screening strategies.

Diagnostic Accuracy of NIBUT and FTBUT

In this study, NIBUT demonstrated a sensitivity of **91%** and specificity of **78%**, outperforming FTBUT, which showed a sensitivity of **87%** and specificity of **83%** (Table 2). High sensitivity is particularly important for early detection of DED, as it ensures that most individuals with the condition are correctly identified, minimizing false-negative results. This is especially relevant for subtle tear film instability that may not yet manifest as clinical symptoms. The higher sensitivity of NIBUT observed in this study aligns with prior research suggesting that non-invasive methods capture tear film instability more physiologically, without interference from fluorescein dye[11].

Conversely, FTBUT exhibited higher specificity than NIBUT, reflecting its greater ability to correctly identify individuals without DED and reduce false-positive diagnoses. This conservative diagnostic profile supports the role of FTBUT as a confirmatory test, in line with TFOS DEWS II recommendations emphasizing the importance of specificity in avoiding unnecessary treatment and patient anxiety[12]. The observed trade-off between sensitivity and specificity highlights the complementary roles of NIBUT and FTBUT in clinical practice.

Clinical Implications of NIBUT's Non-Invasive Approach

Beyond diagnostic accuracy, NIBUT offers practical advantages due to its non-invasive methodology. Unlike FTBUT, which requires instillation of fluorescein dye, NIBUT uses corneal topography to assess tear film stability, eliminating variability from dye concentration, volume, and distribution. This approach enhances patient comfort and compliance, particularly in individuals sensitive to ocular procedures, and allows for repeated measurements without risk of irritation. These attributes make NIBUT well-suited for mass screening programs where efficiency, reproducibility, and patient acceptability are essential[13].

Age and Gender Associations with DED

Demographic analysis revealed that the mean age in the DED group was **48.6 ± 12.4 years**, compared to **41.2 ± 11.8 years** in the non-DED group (Table 1), confirming the well-established trend of increased DED prevalence with advancing age[14]. Gender distribution further reflected epidemiological patterns, with **60%** of the DED group being female compared to **55%** in the non-DED group (Table 1). Hormonal factors, particularly in postmenopausal women, likely contribute to this female predominance, along with autoimmune predisposition and systemic medication use. These findings reinforce the importance of targeted screening in older adults and female populations who are at higher risk for DED[1],[2].

Integrating NIBUT and FTBUT in Diagnostic Protocols

Although NIBUT demonstrated higher sensitivity and FTBUT higher specificity, combining both tests may

enhance overall diagnostic accuracy. For instance, NIBUT could serve as a primary screening tool to detect the majority of DED cases, while FTBUT could function as a confirmatory test to reduce false positives. Integrating these tests with corneal staining techniques or other objective measures, such as tear osmolarity, could further strengthen diagnostic reliability, reflecting the multifactorial nature of DED[12],[15]. The moderate positive correlation observed between NIBUT and TBUT ($r = 0.62$, $p < 0.001$) suggests that while both tests assess tear film stability, they capture partially distinct aspects of tear film physiology, supporting their complementary use.

Comparison with Previous Literature

The findings of this study align with prior research indicating that NIBUT is more sensitive for detecting early tear film instability, while FTBUT offers higher specificity[11,12,17]. The greater number of positive cases detected by NIBUT in this cohort is consistent with studies reporting that non-invasive methods may identify subtle tear film irregularities overlooked by fluorescein-based techniques. This underscores the importance of contextual interpretation of test results, particularly when balancing sensitivity and specificity in clinical decision-making.

Strengths and Limitations

A key strength of this study is the direct comparison of NIBUT and FTBUT within the same patient cohort, allowing for robust evaluation of diagnostic performance. The use of the OSDI questionnaire as a validated reference standard further strengthens the reliability of the findings. Limitations include the modest sample size of 240 participants, which may limit generalizability, and the cross-sectional design, which precludes assessment of longitudinal changes in tear film stability or treatment response. Future studies should explore the utility of these tests in monitoring disease progression and response to therapy.

Future Directions

Future research could investigate the role of NIBUT in community-based screening programs, particularly in high-risk populations such as older adults and women. Comparative analyses involving additional diagnostic modalities, such as tear osmolarity, meibography, and inflammatory biomarkers, may refine diagnostic algorithms. Cost-effectiveness analyses would also help evaluate the feasibility of widespread NIBUT adoption. Emerging technologies such as artificial intelligence (AI) may further enhance diagnostic efficiency and precision, supporting personalized treatment strategies[18],[19].

CONCLUSION

In summary, this study demonstrated that NIBUT offers higher sensitivity than FTBUT, making it valuable for early detection of DED, while FTBUT provides greater specificity, reducing false-positive diagnoses. The non-invasive nature of NIBUT enhances patient comfort and compliance, supporting its use in mass screenings. Age and gender associations observed in this cohort align with established epidemiological trends, reinforcing the importance of targeted screening in older adults and women.

The complementary strengths of NIBUT and FTBUT suggest that integrated diagnostic protocols combining both tests, along with additional objective measures, may provide the most accurate and clinically useful approach to DED diagnosis. These findings contribute to the growing body of evidence supporting multimodal strategies for managing this prevalent and multifactorial ocular condition.

SCIENTIFIC REVIEW BOARD:

SRB approval has been granted at the institutional level with number **463/06/2025/PG/SRB/SMCH**

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