Research Square

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Prevalence of Ocular Surface Diseases among Glaucoma Patients attending in an Eye Hospital of Bangladesh

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Abstract

Background

Ocular surface disease (OSD) is a common comorbidity in glaucoma patients receiving topical medications, yet data from low- and middle-income countries like Bangladesh remain limited. This study aimed to determine the prevalence of OSD and assess agreement between subjective symptoms and objective tests among glaucoma patients.

Methodology:

This cross-sectional study enrolled 68 glaucoma patients attending Al-Noor Eye Hospital, Dhaka, from September 2025 to March 2026. Participants completed the Ocular Surface Disease Index (OSDI) questionnaire and underwent Schirmer test and tear break-up time (TBUT) evaluation.

Results

Although 69.1% of patients reported normal OSDI scores, objective tests revealed significantly higher abnormality rates: 54.4% had abnormal Schirmer test results and 76.5% had abnormal TBUT. Poor agreement existed between OSDI and Schirmer test (κ=-0.193, $p = 0.033$), with no agreement between OSDI and TBUT (κ=-0.077, $p = 0.247$). Age was significantly associated with abnormal objective findings ($p = 0.017–0.026$), while prostaglandin analogues and carbonic anhydrase inhibitors showed unexpected protective associations.

Conclusion

Objective ocular surface abnormalities are highly prevalent among Bangladeshi glaucoma patients despite minimal subjective symptoms. Routine objective testing is essential for accurate OSD detection in this population.

Introduction

Glaucoma is a major cause of irreversible blindness around the world, and it is characterized by progressive optic neuropathy and correlative visual field loss (Tham et al., 2014). Since glaucoma is a chronic disease that has to be controlled throughout the lifetime of the patient, the treatment of this disease is mainly aimed at decreasing the level of intra-ocular pressure (IOP) with the help of topical medications, laser, or surgery (Weinreb et al., 2014). Of these, topical anti-glaucoma drugs continue to be the core of treatment and can require a long-term course with one or more classes of anti-glaucoma medications to achieve optimal IOP levels (Conlon et al., 2017).

Ocular surface disease is a spectrum of disorders of the tear film, cornea, and conjunctiva, including dry eye disease, dysfunction of the meibomian glands, and blepharitis (Craig et al., 2017). The prevalence of comorbid dry eye disease (DED) in patients receiving topical therapy for glaucoma may be as high as 60% (Karpecki, 2019). Although five major classes of topical glaucoma drugs such as Prostaglandin analogues (PGAs), Beta-blockers, carbonic anhydrase inhibitors (CAIs), Alpha agonists and Rho kinase inhibitors (RKI) has the potential to disrupt ocular surfaces, the mechanisms of adverse effects differ (Freeman et al., 2009).

The most commonly prescribed first-line therapy, which has been strongly correlated with the ocular surface damage, is the prostaglandin analogues (PGAs), as shown by the finding of abnormal tear break-up times, lower values of the Schirmer test, and malfunction of the meibomian glands in numerous investigations (Fechtner et al., 2009). PGAs are pro-inflammatory, capable of inducing significant meibomian lipoid activity involution and one study reported that over 90% of

patients taking PGAs experienced some type of MGD (Karpecki, 2019). Beta-blockers are linked with a decrease in corneal sensitivity and blinking, and may also increase fibroblasts and inflammatory cells in the conjunctiva, which can cause squamous metaplasia and ocular surface fibrosis (Zhou et al., 2022). Limbal conjunctival follicles, follicular conjunctivitis, and severe allergic conjunctivitis are known to be caused by topical carbonic anhydrase inhibitors (CAIs) (Young, 2023). Substances that may commonly lead to allergic conjunctivitis, follicular reactions, and dry eye symptoms are alpha agonists, especially brimonidine (Monge-Carmona et al., 2025). Rho kinase-inhibitors (RKI) being a relatively new class has also been coupled with negative effects on the ocular surface including conjunctival hyperemia and corneal staining escalation (Freeman et al., 2009).

The cumulative effects are often exacerbated by BAK, an antimicrobial preservative with detergent properties that disrupts the lipid layer of the tear film, leading to evaporative dry eye and epitheliotoxic damage (Karpecki, 2019; Karpecki, 2024). Such cumulative toxic burden may result in lower quality of life, low adherence to medication, and even poor surgical outcomes (Leung et al., 2008; Fechtner et al., 2009).

The prevalence of ocular surface disease in glaucoma patients varies widely across different populations, ranging from 40% to 60% in various studies (Ghosh et al., 2012; Fechtner et al., 2009). However, limited data exist regarding the burden of OSD among glaucoma patients in low- and middle-income countries, including Bangladesh. Furthermore, the diagnosis of dry eye disease remains challenging due to the often poor correlation between patient-reported symptoms and objective clinical findings (Nichols et al., 2004). The Ocular Surface Disease Index (OSDI) is a validated questionnaire for assessing dry eye symptoms, while the Schirmer test and tear break-up time (TBUT) provide objective measures of tear production and tear film stability, respectively (Schiffman et al., 2000). Previous research has demonstrated variable agreement between these diagnostic modalities, particularly in populations with chronic medication use (Schein et al., 1997).

In Bangladesh, glaucoma is a significant public health concern, yet the ocular surface health status of glaucoma patients undergoing long-term medical therapy remains largely unexplored. Understanding the prevalence of ocular surface abnormalities and the factors associated with their development is essential for optimizing patient care and treatment outcomes. Additionally, identifying the specific anti-glaucoma medications and combination patterns that may contribute to ocular surface damage can guide clinicians in selecting more ocular-surface-friendly treatment regimens.

Therefore, this study was conducted to determine the prevalence of ocular surface diseases among glaucoma patients attending an eye hospital in Bangladesh, to evaluate the agreement between subjective symptoms and objective diagnostic tests, and to identify demographic and treatment-related factors associated with ocular surface abnormalities. The findings of this study aim to provide evidence-based insights for improving the clinical management of glaucoma patients in resource-limited settings.

Methodology

The study was conducted at Al Noor Eye Hospital, Dhaka, operated by Al Basar International Foundation, after approval from the Institutional Review Board (IRB approval no: ABIF/IRB/2025/012 – 04). Data were collected from September 2025 to March 2026, and patients were recruited consecutively. This study was not registered as a clinical trial as it was an observational cross-sectional investigation. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

Eligible participants were adults (≥ 18 years) of either sex with a clinical diagnosis of primary open-angle glaucoma, pseudoexfoliation, or pigment-dispersion glaucoma, or ocular hypertension, who had been using anti-glaucoma medications for at least 3 months and were able to provide informed consent and complete the Ocular Surface Disease Index (OSDI) questionnaire. Glaucoma diagnosis was based on characteristic of visual field defects and/or glaucomatous optic nerve changes, while ocular hypertension was defined as intraocular pressure > 22 mmHg without optic nerve damage. Patients were excluded if they were unable to understand the study, or if they had used cyclosporine or taking

steroids within the past 3 months, were using punctal plugs, had a history of surgery on the cornea or conjunctiva, or glaucoma surgery.

After providing informed consent, qualified patients were asked to complete the 12-item Ocular Surface Disease Index (OSDI) questionnaire (Schiffman et al., 2000). Demographic information, a brief medical history, and information on concomitant medicine use, including use of artificial tears, were obtained from the patient's medical records. After completing the OSDI questionnaire, patients underwent 3 standard clinical tests of the ocular surface in the order listed, including Schirmer test (without anesthesia), and tear break-up time (TBUT). All the questionnaires and examinations were completed in 1 day.

Schirmer test (unaesthetised) - the patients were instructed to look up and the lower eyelid was gently lowered and drawn temporally. The rounded bent end of the sterile strip was hooked in the lower cul-de-sac over the junction of the temporal and central one-third of the lower eyelid margin. The testing period has been started. Minimisation of possible staining of the conjunctiva by this test required the patients to gently close their eyelids after 5 minutes for the removal of the strips. As the tear front would continue advancing a few millimeters after it had been removed from the eyes, the tear front was marked with a pencil after 5 minutes. The amount of wetting was determined by the scale found in a box of strips which showed the amount of wetting. In this case, if the edge of the tear did not travel evenly, an examiner measured the distance from the notch to the center of the diagonal line. If there was a tear front at or above the half millimeter mark, only numbers rounding up to the next whole number were recorded. After Schirmer testing, a 5 µL of a 2% sodium fluorescein solution was instilled into the inferior cul-de-sac. At the end of the delivery micropipette was lightly applied to the lower palpebral conjunctiva. Examination was carried out using slit light at 10x magnifications with the cobalt light used to measure TBUT over the cornea. Patients were asked not to blink and time to TUBT was measured up to 10 seconds.

In each situation, the results were classified into the three categories – normals, mild to moderate, and severe – for each measure. The severity classifications for the Schirmer test were as follows: >10 = normal; 6–10 = mild to moderate; and 0–5 = severe (Baudouin et al., 1998). The severity grades for TBUT were: ≥10s normal; 5s to 9s: mild to moderate; <5s: severe. The 12 items of the OSDI questionnaire were scored on a scale of 0 to 4: 0 = "none of the time" to 4 = "all of the time". The total OSDI score was computed as follows: OSDI = (sum of all the scores on the questions answered) × 100 / (total number of questions answered) × 4). Thus, the OSDI was scored on a scale of 0 to 100. Severity was defined as follows for the OSDI score: 0–5.9 = normal; 6.0–14.9 = mild to moderate; and ≥ 15.0 = severe. The disease severity criteria for the study were previously determined by a prior paper (Leung et al., 2008).

For each patient, examiner considered the eye that showed worse results for each specific test. If both the eyes had equally severe results on a particular test, then 1 eye was chosen randomly by the flip of a coin.

Bivariate logistic regression model was used to evaluate the relationship between the use of eye drops and results on the OSDI questionnaire and clinical tests of OSD. The results of each test were categorized as normal/abnormal and entered as dependent variables. Drug classes were considered as the independent variables. The model was adjusted for age and sex, also entered as independent variables.

Results

Table 1: Distribution of patients with each result on the OSDI, Schirmer Test and TBUT

In this study of 68 glaucoma patients from eye hospitals in Bangladesh, in the Table 1, the Ocular Surface Disease Index (OSDI) revealed that the majority (69.1%) had normal symptom scores, while 26.5% reported mild-to-moderate and 4.4% severe symptoms. However, objective tests showed notably higher rates of ocular surface abnormalities. The Schirmer test indicated that only 45.6% of patients had normal tear production, with 42.6% classified as mild-to-moderate and 11.8%

Category	OSDI Score	Schirmer	TBUT
Normal	47 (69.1%)	31 (45.6%)	16 (23.5%)
Mild/Moderate	18 (26.5%)	29 (42.6%)	33 (48.5%)
Severe	3 (4.4%)	8 (11.8%)	19 (27.9%)
Total	**68 (100.0%)**	**68 (100.0%)**	**68 (100.0%)**

as severe dry eye. The tear breakup time (TBUT) was even more frequently impaired: just 23.5% of patients had normal tear film stability, while 48.5% showed mild-to-moderate and 27.9% severe dysfunction.

Table 2: Distribution of drug classes (N=68)

Drug Class	n	%
Prostaglandin analogues (PGA)	43	63%
Beta-blockers (BB)	34	50%
Carbonic anhydrase inhibitors (CAI)	38	56%
Alpha agonists (AA)	21	31%
Rho kinase inhibitors (RKI)	7	10%

Because of multiple drugs used, the sum of the participants exceeds the total sample size

Table 2 shows that the most commonly prescribed anti-glaucoma medications among the 68 participants were prostaglandin analogues (63%), followed by carbonic anhydrase inhibitors (56%) and beta-blockers (50%). Alpha agonists were used by about one-third of patients (31%), while rho kinase inhibitors were the least frequently used (10%). This pattern indicates a predominance of prostaglandin-based therapy, which is consistent with their role as first-line treatment in glaucoma management, often complemented by adjunctive agents such as carbonic anhydrase inhibitors and beta-blockers to achieve better intraocular pressure control. The relatively lower use of alpha agonists and rho kinase inhibitors suggests they are more commonly prescribed as second- or third-line options. As multiple medications were used concurrently in many patients, the total exceeds 100%, reflecting combination therapy practices in clinical management. Overall, the findings highlight a high reliance on multidrug regimens, which may have implications for ocular surface health due to cumulative exposure to topical medications.

Table 3: Drug Combination Patterns (N = 68)

Pattern Category	Definition	Frequency (n)	%	Interpretation
Monotherapy	Single drug class	15	22.1%	Moderate
Dual therapy	Two drug classes	30	44.1%	Common
Triple or more therapy	Three or more drug classes	17	25.0%	Moderate
Rho kinase inhibitor–based combination	Regimens containing RKI with other classes	6	8.8%	Less frequent

Table 3 demonstrates that combination therapy is the predominant treatment approach among glaucoma patients in this study. Dual therapy was the most common regimen, used by 44.1% of participants, indicating that nearly half of the patients required two drug classes to achieve adequate intraocular pressure control. Monotherapy was observed in 22.1% of cases, suggesting that a smaller proportion of patients could be managed with a single agent. Additionally, 25.0% of patients were on triple or more drug combinations, reflecting more advanced or difficult-to-control cases requiring intensified treatment. Regimens involving rho kinase inhibitors were relatively uncommon (8.8%), indicating their limited use, possibly as adjunctive or newer therapeutic options. Overall, these findings highlight a substantial reliance on multi-drug therapy in glaucoma management, which may increase the risk of ocular surface disease due to cumulative drug exposure and preservative-related toxicity.

Table 4: Agreement between dry eye diagnostic tests with corresponding Bland–Altman analyses

Comparison	Kappa (κ)	Std. Error	t-value	p-value	Interpretation
OSDI vs Schirmer	-0.193	0.085	-2.128	0.033	Significant poor (inverse) agreement
OSDI vs TBUT	-0.077	0.072	-1.159	0.247	No agreement
Schirmer vs TBUT	0.031	0.083	0.387	0.699	No agreement

The agreement analysis in table 4 and Figure1(A, B, C) demonstrated poor concordance among the three dry eye diagnostic tests. The Ocular Surface Disease Index (OSDI) showed a statistically significant but weak inverse agreement with Schirmer test (κ = −0.193, p = 0.033), indicating that higher symptom scores were not aligned with tear production measurements. In contrast, OSDI and Tear Break-Up Time (TBUT) demonstrated no significant agreement (κ = −0.077, p = 0.247), and similarly, Schirmer and TBUT also showed no agreement (κ = 0.031, p = 0.699). The Bland–Altman plots further support these findings, showing wide limits of agreement and substantial dispersion of data points around the mean differences for all comparisons. Although most observations fall within the 95% limits of agreement, the presence of outliers and the broad spread indicate poor consistency and lack of interchangeability between these tests.

Table 5. Associations Between OSDI, Schirmer Test, and TBUT

Variable	OSDI (Absent) (N=47)	OSDI (Present) (N=21)	Pearson χ^2 (df)	p-value	Fisher's Exact (2-sided)	Phi	Cramer's V	**Spearman's rho with OSDI**	**Spearman p-value**
Schirmer test									
(Absent)	18 (38.3%)	13 (61.9%)	3.261 (1)	0.071	0.113	−0.219	0.219	−0.219	0.073
(Present)	29 (61.7%)	8 (38.1%)							
TBUT									
(Absent)	9 (19.1%)	7 (33.3%)	1.623 (1)	0.203	0.228	−0.154	0.154	−0.154	0.208
(Present)	38 (80.9%)	14 (66.7%)							

The analysis indicates that subjective dry eye symptoms measured by the Ocular Surface Disease Index (OSDI) were not significantly associated with objective clinical findings among glaucoma patients. For the Schirmer test, a greater proportion of symptomatic participants had abnormal tear production (61.9%) compared to asymptomatic individuals (38.3%), while normal tear production was more common among those without symptoms (61.7%). However, this association was not statistically significant (χ^2 = 3.261, p = 0.071; Fisher's exact p = 0.113), though it approached borderline significance. The correlation analysis also showed a weak negative relationship (Spearman's ρ = −0.219, p = 0.073), suggesting that higher symptom scores may be associated with lower tear production, but without statistical confirmation. Similarly, for Tear Break-Up Time (TBUT), abnormal TBUT was more frequent among symptomatic participants (33.3%) than asymptomatic ones (19.1%), yet the association remained non-significant (χ^2 = 1.623, p = 0.203; Fisher's exact p = 0.228). The Spearman correlation also indicated a weak negative relationship (ρ = −0.154, p = 0.208). Overall, both association and correlation analyses consistently demonstrate weak and non-significant relationships between subjective symptoms and objective test results, highlighting a discrepancy between patient-reported outcomes and clinical measures in this population.

Table 6: Binary logistic regression analysis for predictors of Ocular Surface Disease Index (OSDI) with the Schirmer and Tear Break-Up Time test

Predictor	B	S.E.	Wald	df	Sig.	Exp(B)	95% CI for Exp(B)
Schirmer	−0.877	0.550	2.545	1	0.111	0.416	(0.142, 1.222)*
TBUT	−0.581	0.612	0.900	1	0.343	0.560	(0.169, 1.857)*
Constant	0.063	0.547	0.013	1	0.908	1.065	–

Binary logistic regression analysis was done, where absent and present of dry eye based on OSDI questionnaire regarded as the dependent variable, and Schirmer and TBUT test results categorized as the independent variables.

The binary logistic regression analysis showed that neither the Schirmer test nor the Tear Break-Up Time (TBUT) significantly predicted the presence of dry eye symptoms as measured by the Ocular Surface Disease Index (OSDI). Although both predictors had negative regression coefficients (Schirmer: B = −0.877; TBUT: B = −0.581), suggesting that abnormal test results may be associated with lower odds of reporting symptoms, these relationships were not statistically significant (Schirmer: p = 0.111; TBUT: p = 0.343). The odds ratios further support this lack of association, with Schirmer (Exp(B) = 0.416; 95% CI: 0.142–1.222) and TBUT (Exp(B) = 0.560; 95% CI: 0.169–1.857) both having confidence intervals that cross 1.0, indicating no meaningful predictive effect. The constant was also non-significant (p = 0.908). Overall, the model suggests that objective measures of tear production and tear film stability do not significantly influence the likelihood of experiencing subjective dry eye symptoms among glaucoma patients, reinforcing the observed discrepancy between clinical signs and patient-reported outcomes.

Table 7. Binary Logistic Regression Results for Three Outcomes

Predictor	**OSDI (Present vs Absent)**			**Schirmer Test (Present vs Absent)**			**TBUT (Present vs Absent)**		
	B (SE)	OR	p-value	B (SE)	OR	p-value	B (SE)	OR	p-value
Gender	0.313 (0.702)	1.368	0.656	−0.017 (0.672)	0.983	0.980	−1.234 (1.044)	0.291	0.237
Age	−0.021 (0.018)	0.979	0.243	0.044 (0.020)	1.045	**0.026**	0.087 (0.037)	1.091	**0.017**
PGA	0.191 (0.958)	1.211	0.842	−2.185 (1.046)	0.112	**0.037**	−3.733 (1.853)	0.024	**0.044**
BB	0.630 (0.761)	1.878	0.408	0.744 (0.740)	2.105	0.315	−2.319 (1.387)	0.098	0.095
CAI	1.253 (0.789)	3.501	0.112	−2.036 (0.843)	0.130	**0.016**	−1.910 (1.123)	0.148	0.089
AA	1.060 (1.036)	2.886	0.306	1.615 (0.978)	5.027	0.099	−3.099 (1.706)	0.045	0.069
RKI	−0.245 (1.292)	0.783	0.850	0.181 (1.479)	1.199	0.902	−1.217 (1.765)	0.296	0.491
Constant	−1.475 (1.525)	0.229	0.333	−0.411 (1.499)	0.663	0.784	4.557 (2.206)	95.326	**0.039**

OR = Odds Ratio; SE = Standard Error; PGA = Prostaglandin Analogues; BB = Beta-blockers; CAI = Carbonic Anhydrase Inhibitors; AA = Alpha Agonists; RKI = Rho Kinase Inhibitors

The multivariable binary logistic regression analysis demonstrated differing patterns across subjective and objective measures of ocular surface disease. For symptoms assessed by the Ocular Surface Disease Index (OSDI), none of the predictors including gender, age, or any anti-glaucoma drug class showed a statistically significant association (all $p > 0.05$), indicating that these variables did not meaningfully influence the likelihood of reporting dry eye symptoms. In contrast, for the Schirmer test, age was a significant predictor ($B = 0.044$, $p = 0.026$; OR = 1.045), suggesting that increasing age was associated with higher odds of abnormal tear production. Additionally, the use of prostaglandin analogues (PGA) ($p = 0.037$; OR = 0.112) and carbonic anhydrase inhibitors (CAI) ($p = 0.016$; OR = 0.130) were significantly associated with lower odds of abnormal Schirmer results, indicating a potential protective or less harmful effect on tear secretion. Similarly, for Tear Break-Up Time (TBUT), age remained a significant predictor ($B = 0.087$, $p = 0.017$; OR = 1.091), reflecting worsening tear film stability with advancing age. Prostaglandin analogues were also significantly associated with reduced odds of abnormal TBUT ($p = 0.044$; OR = 0.024). Other drug classes such as beta-blockers, alpha agonists, and CAIs showed non-significant trends but did not reach statistical significance. Gender and rho kinase inhibitors were not associated with any of the outcomes. Overall, these findings suggest that while demographic and treatment factors do not significantly predict subjective symptoms, age and certain medications are significantly associated with objective measures of tear production and stability, highlighting a discrepancy between patient-reported symptoms and clinical signs in glaucoma patients.

Discussion

This study of 68 glaucoma patients attending an eye hospital in Bangladesh revealed three major findings. First, while subjective symptoms measured by the Ocular Surface Disease Index (OSDI) suggested that the majority of patients (69.1%) had normal ocular surface health, objective tests demonstrated substantially higher rates of ocular surface abnormalities, with only 45.6% showing normal tear production on Schirmer testing and merely 23.5% having normal tear film stability on TBUT. Second, there was poor agreement between subjective symptoms and objective clinical examination with negative agreement between OSDI and Schirmer test ($\kappa = -0.193$, $p = 0.033$) and no agreement between OSDI and TBUT ($\kappa = -0.077$, $p = 0.247$). Third, age proved to be an important factor associated with the likelihood of being identified as having abnormal objective test results, and anti-glaucoma medications were unexpectedly associated with a lower odds of abnormal tear function tests, specifically prostaglandin analogues and carbonic anhydrase inhibitors.

The frequency of ocular surface abnormalities in this study, especially those demonstrated on the objective tests, is consistent with previous studies of patients with glaucoma receiving topical therapy. Karpecki (2019) reported that the prevalence of comorbid dry eye disease in patients receiving topical therapy for glaucoma may be as high as 60%. Likewise, the studies by Ghosh et al. (2012) and Fechtner et al. (2010) reported 40–60% of prevalence in different population groups. In the present study 76.4% found to have abnormal TBUT and 54.4% with abnormal Schirmer test result suggests that the burden of objective OSD may be higher in the Bangladeshi population of glaucoma patients when compared with these estimates.

Most commonly prescribed medications were prostaglandin analogues (63%), beta-blockers (50%) and carbonic anhydrase inhibitors (56%), which is indicative of global treatment pattern, with PGAs being first-line therapy treatment (Conlon et al., 2017; Weinreb et al., 2014). The high rate of patients on dual therapy (44.1%) and those on triple therapy or more (25.0%) suggest that combination therapy is often needed to achieve efficient intraocular pressure (IOP) control, which can exacerbate ocular surface toxicity by cumulative exposure to preservatives (Karpecki, 2019; Baudouin et al., 2010).

One intriguing result of this study is the lack of correlation between patient-reported symptoms and objective measures of the presence of OSD. The high degree of inverse correlation between OSDI and the Schirmer test ($\kappa = -0.193$, $p = 0.033$) and

the absence of agreement between OSDI and TBUT (κ= –0.077, p= 0.247) showed that a high percentage of asymptomatic eyes had objective tear dysfunction, and that a significant percentage of those eyes with objective abnormalities were asymptomatic. The finding is consistent with previous research reported by Nichols et al. (2004) which noted that the diagnosis of dry eye disease is often difficult as there is poor correlation between subjective and objective clinical findings. Likewise, Schein et al. (1997) showed varying levels of agreement between diagnostic modalities in population-based studies.

This discrepancy was further supported by the binary logistic regression analysis where neither the Schirmer test nor the TBUT were significant predictors of the presence of dry eye symptoms based on the OSDI (Schirmer test: p = 0.111; TBUT: p = 0.343). This finding has important clinical implications, as reliance on patient symptoms alone would substantially underestimate the true burden of ocular surface disease in this population. Therefore, objective testing must be performed in patients with glaucoma in low resource settings such as Bangladesh with a low threshold, even if the patient does not report ocular discomfort.

The significant association of age with abnormal Schirmer test results (B = 0.044, p = 0.026, OR = 1.045) and abnormal TBUT (B = 0.087, p = 0.017, OR = 1.091) results suggest that older age is an independent factor contributing to exacerbation of tear production and tear film stability. Some of these physiological changes that occur with age may account for this age-related reduction in ocular surface function such as decrease in lacrimal gland function, meibomian gland dysfunction, and decrease in corneal sensitivity (Craig et al., 2017). The combination of this predilection of glaucoma for the older population and the fact that the incidence of clinically significant ocular surface disease is significantly greater with age, means that the elderly population of glaucoma patients is generally at a higher risk of developing clinically significant ocular surface disease as a result of the additive effect of their old age and exposure to chronic topical medication use (Tham et al., 2014).

In contrast to previous studies, the use of prostaglandin analogue was associated with lower odds of abnormal Schirmer test result (OR = 0.112, p = 0.037) and abnormal TBUT (OR = 0.024, p = 0.044). Various studies have shown the pro-inflammatory nature of PGAs and caused severe MGDs, while one study states that more than 90% of patients who use PGAs develop at least one type of MGD (Karpecki, 2019). Likewise, the use of carbonic anhydrase inhibitors was found to be associated with reduced odds of abnormal Schirmer results (OR = 0.130, p = 0.016), although there was known evidence to support the associations with limbal conjunctival follicles and allergic conjunctivitis (Young, 2023).

There could be a number of reasons behind these surprising discoveries. Moreover, this cross-sectional study design does not prove causality, and it is possible that patients with more baseline tear function were more likely to receive PGAs as first-line therapy, while other patients who had predisposing ocular surface disease were more likely to receive other agents. Second, the relatively small sample size (N=68) and the wide confidence intervals (PGA for Schirmer: 0.142–1.222; CAI for Schirmer: 0.130–0.148) suggest that these estimates may be unstable and should be interpreted with caution. Third, limited data on medication usage duration, day-to-day drop numbers and specific preservative concentrations diminishes the capacity to determine cumulative exposures to toxicity. Fourth, there might have been differences in preservative-free formulation across individuals in this study, significantly impacting the ocular surface toxicity profile (Baudouin et al., 2010).The use of beta blockers, alpha agonists, and rho kinase inhibitors was not associated with any of the outcome measures, though beta blockers exhibited a trend towards association with abnormal TBUT (p = 0.095) and alpha agonists (p = 0.069). This could be possibly attributed to inadequate power of the samples with the smaller number of patients using these agents, especially in the case of RKI (10% of patients) (Freeman et al., 2009).

Clinical Implications

The results of this study have practical implications for the treatment of glaucoma in low-and middle-income country contexts such as Bangladesh. The prevalence of objective problems of the cornea despite limited complaints suggests that routine objective testing should be incorporated into the monitoring protocol for glaucoma. The OSDI questionnaire is

not enough to identify the presence of OSD in this group of patients, and should be supplemented by other routine tests, specifically a Schirmer and TBUT should be conducted even in asymptomatic patients. Second, combination therapy is used by the majority of patients (77.9% on dual or triple therapy) emphasizing the need for ocular surface friendly prescription. If clinically appropriate, preservative free formulations should be considered especially for patients with multiple medications (Baudouin et al., 2010; Karpecki, 2024). Also, if medications are therapeutically equivalent, choosing those with less ocular surface toxicity can minimize cumulative effects of all topical treatments.

Third, with glaucoma, there is significant association between age and objective manifestations of OSD, therefore elderly glaucoma patients should be carefully monitored for OSD, even in the absence of symptoms. Assessment of tear production and tear film stability should be routine for older people who are taking chronic topical glaucoma therapy.

Strengths and Limitations

The strengths of this study include its prospective design, use of validated diagnostic instruments (OSDI questionnaire, Schirmer test, and TBUT), and focus on an understudied population in Bangladesh. Utilization of multiple diagnostic modalities provided a comprehensive view of ocular surface status to permit test agreement analysis.

There are several restrictions we should note. The sample size of 68 patients was adequate to obtain some of the primary prevalence estimates but did not meet the statistical power requirements for secondary analyses and may have been a reason for the broad confidence intervals used in the regression model. Secondly, the single-center study setting could restrict the generalizability to other parts of Bangladesh or primary care settings. Third, the study failed to account for specific factors that may influence the cumulative toxicity to the eye's surface, such as duration of glaucoma therapy use, systemic and daily counts of the number of glaucoma drops, and the concentrations of specific glaucoma preservatives. Fourth, as a cross-sectional study, this study does not allow for causal inferences to be made about how certain medications correlate with the outcomes of the ocular surface. Lastly, the study did not directly measure meibomian gland dysfunction, but the factor is known to have a role in OSD associated with glaucoma (Karpecki, 2019). Thirdly, artificial tear uses and other concurrent ocular medications have not been reported and might have confounded observed association.

Recommendations for Future Research

In the future, the findings of this study will be expanded by larger, multi-center, prospective cohorts that will provide detailed medication histories with respect to length of use, frequency of drop, and preservative status. Future causal studies are required to determine if particular anti-glaucoma medications increase the risk of developing an ocular surface disease over a prolonged period of time. Further, study to assess the effect of preservative-free medication, topical anti-inflammatory agents on the outcomes of the surface of the eye in the Bangladeshi glaucoma patients would also be useful information for treatment guidelines. Last but not least, cost-effectiveness studies between the routine objective OSD-screening and symptom-based OSD-screening would guide resource allocation in LMICs.

Conclusions

This study revealed that majority of glaucoma patients visiting a glaucoma clinic are also suffering from ocular surface disease (OSD) from objective parameters of tear production and tear film stability. The close match between subjective illness perception and objective clinical parameters highlights the need for routine objective tests in this group since the subjective self-reported illness would drastically underestimate the burden of disease. While age is an important factor in objective indices of ocular surface dysfunction, the unexpected relationships with certain medications suggest that one should be careful with interpretation and more research should be conducted. The results offer insights into the clinical management of glaucoma patients in a resource constrained environment, highlighting the importance of frequent objective assessment of the ocular surface and the need to employ preservative-free management options.

Declarations

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Authors contribution

The study was conceptualized and designed by Salman Ahmed Tahed Hamid, while data acquisition was carried out by Farzanur Rahman and Zinatus Sama. Data analysis and interpretation, along with the writing of the original draft, were jointly performed by Md Mahmudul Hasan and Imtiaj Hossain Chowdhury, who also took sole responsibility for preparing the final manuscript. The manuscript underwent critical revision by Salman Ahmed Tahed Hamid, Farzanur Rahman, and Zinatus Sama, ensuring a thorough and collaborative refinement of the work

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Data Availability Statement

All the data are available upon request to the corresponding author through email.

Ethics Approval

Ethical approval was granted by the Institutional Review Board (IRB) of Al-Basar International Foundation (IRB approval no: ABIF/IRB/2025/012-04). The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. All human-related procedures were performed in accordance with institutional guidelines and the Declaration of Helsinki.

Consent to participate

Informed consent was obtained from all individual participants included in the study. Before commencing data collection, each participant was provided with detailed information regarding the study purpose, potential risks, and expected benefits. Participants were informed that their participation was voluntary and that they could withdraw at any time without affecting their treatment. Written informed consent was obtained from all participants. For participants under 18 years of age, informed consent was obtained from their parents or legal guardians. The consent process ensured that participants were fully aware of the study procedures, the voluntary nature of participation, and their right to confidentiality. All human-related procedures were performed in accordance with institutional guidelines and the Declaration of Helsinki.

Consent for Publication

Informed consent to publish was obtained from all participants (or their parents/legal guardians for participants under 18 years of age). Participants were informed that their anonymized data might be published in scientific journals, and they provided consent for the publication of their data in an aggregated, non-identifiable format. The participants were assured that their identities would remain confidential and would not be disclosed in any publication.

Competing Interest

None

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Figures

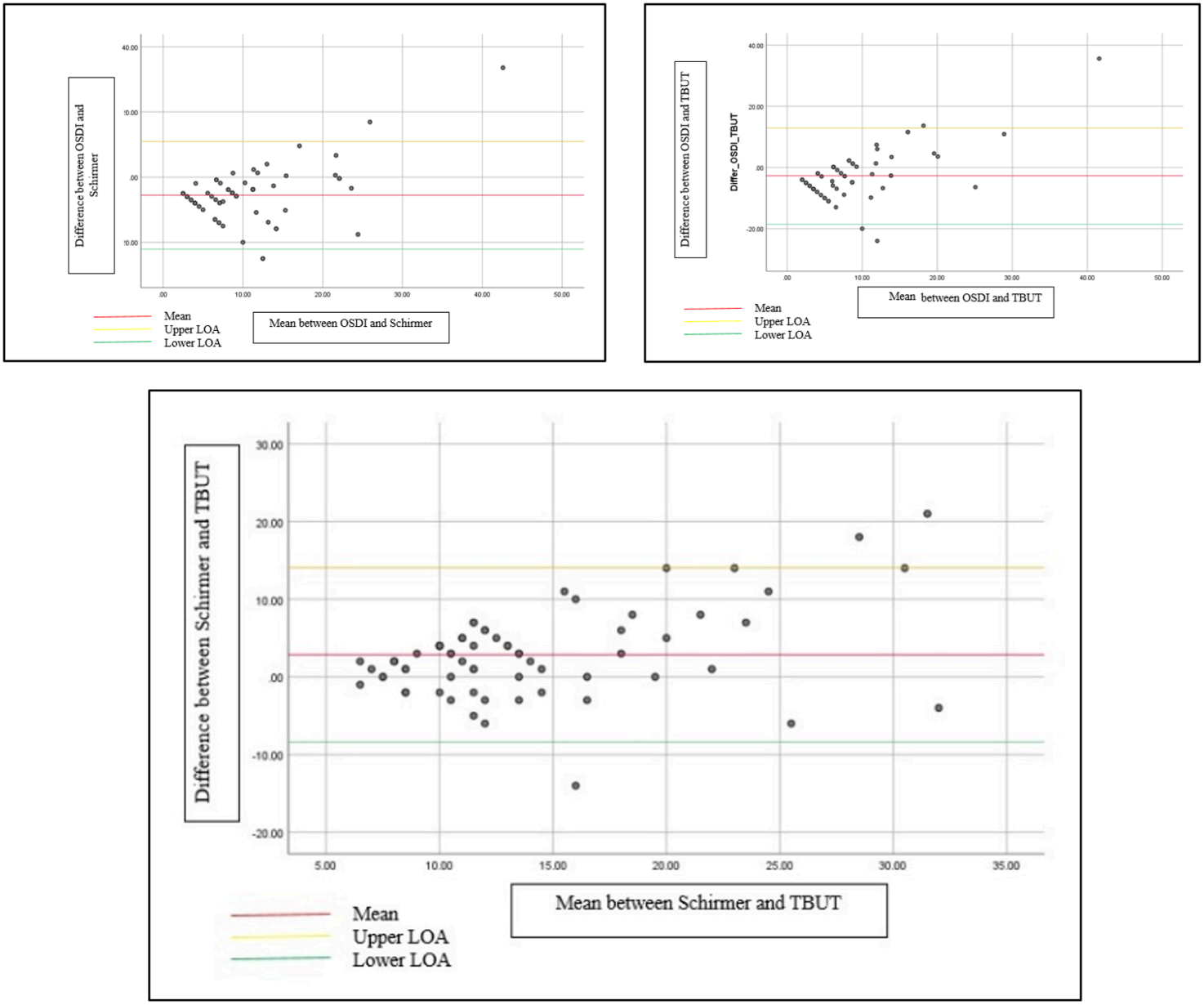


Figure 1

Difference and Mean between OSDI and Schirmer test; B- Difference and Mean between OSDI and TBUT; C- Difference and Mean between Schirmer test and TBUT