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EFFECT OF LONG TERM HIGH DOSE ANTI-DEPRESSANT MEDICATION ON TEAR FILM STABILITY, A DESCRIPTIVE CROSS-SECTIONAL STUDY

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ABSTRACT

Purpose: The primary aim of this research was to explore the relationship between long-term antidepressant use and the development of dry eye disease (DED). In addition, the study compared the ocular surface effects of two commonly prescribed antidepressant medications–escitalopram and sertraline–to determine whether one posed a higher risk of inducing dry eye symptoms than the other. Methods: A descriptive cross-sectional study was carried out between NOVEMBER 2023 and NOVEMBER 2025 at MAYO HOSPITAL, LAHORE. Participants using either escitalopram or sertraline were selected through purposive sampling. After obtaining informed consent, each individual underwent a Schirmer test to evaluate tear production, and the Ocular Surface Disease Index (OSDI) questionnaire was administered to assess symptom severity. All collected data were entered and analyzed using SPSS version 20. Chi-square tests were applied to determine the statistical significance of associations between antidepressant use, duration of intake, and dry eye findings. Results: A total of 180 subjects aged 20–40 years, including both males and females, were evaluated. Analysis revealed a strong association between dry eye disease and the duration of antidepressant usage, with longer treatment periods showing significantly higher rates of reduced tear production and increased symptom scores ($p < 0.001$). When comparing the two medications, no statistically significant difference was found in the likelihood of developing dry eye between users of escitalopram and those of sertraline ($p = 0.488$). This indicates that both drugs contribute similarly to tear film alteration and ocular surface discomfort. Conclusions: indings from this study emphasize the importance of considering ocular side effects in patients undergoing long-term antidepressant therapy. Prolonged use of either escitalopram or sertraline is associated with a higher risk of dry eye disease, underscoring the need for routine ocular assessment and detailed medication history in affected individuals. Eye care practitioners and other healthcare providers should remain aware of this association to ensure early detection and effective management of dry eye symptoms in antidepressant users.

Keywords: *Antidepressants, Dry eye disease, Schirmer test, OSDI, escitalopram, sertraline, ocular surface*

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Introduction

The cornea, a transparent, dome-shaped structure located at the anterior surface of the eye, serves as the most powerful refractive component, contributing approximately two-thirds of the eye's total focusing capacity.[1] Structurally, the cornea comprises five distinct layers: the epithelium, Bowman's layer, stroma, Descemet's membrane, and the endothelium. Each of these layers plays a crucial role in preserving optical clarity and maintaining the biomechanical stability required for precise and high-quality vision. Even minor disruptions in these layers can significantly compromise visual acuity and overall ocular health.

Protecting the cornea is the tear film, a dynamic and multi-layered fluid covering the ocular surface. The tear film not only provides a smooth refractive surface for optimal vision but also protects the eye from microbial invasion, facilitates the exchange of nutrients, and maintains overall ocular surface homeostasis.[2] It consists of three layers: the outer lipid layer, which reduces tear evaporation; the middle aqueous layer, responsible for hydration and nutrient transport; and the innermost mucin layer, which promotes tear film adherence to the corneal epithelium. The coordinated function of these layers is essential for maintaining corneal integrity and comfort.

Dry eye disease (DED) is a multifactorial disorder of the ocular surface characterized by the loss of tear film homeostasis, accompanied by a wide range of ocular symptoms.[3] Its underlying mechanisms may include tear film instability, hyperosmolarity, inflammation, and neurosensory abnormalities. Clinically, DED is primarily classified into two major types: aqueous-deficient and evaporative. The symptoms of DED, which can include itching, burning, a gritty or foreign body sensation, dryness, and photophobia, often lead to significant visual discomfort and can substantially reduce an individual's quality of life, particularly in activities requiring prolonged visual attention.

Among the multiple etiologies of dry eye, drug-induced ocular side effects have received increasing attention in recent years. Selective serotonin reuptake inhibitors (SSRIs), one of the most widely prescribed classes of antidepressants, are known to influence tear production by altering neurotransmitter signaling.[4] These medications can disrupt the autonomic regulation of the lacrimal gland, resulting in decreased tear secretion, compromised tear film stability, and the subsequent development or exacerbation of dry eye symptoms.

Escitalopram and sertraline are two commonly used SSRIs in clinical practice. While both are effective for the management of mood disorders, they exhibit distinct pharmacological properties: escitalopram is highly selective for serotonin reuptake inhibition, whereas sertraline also demonstrates mild dopaminergic activity. These pharmacological differences may influence tear film integrity differently, potentially resulting in variable severity and presentation of dry eye symptoms among patients taking these medications.

Given the increasing global prevalence of SSRI prescriptions and the frequent clinical complaints of dry eye in these populations, it is essential to evaluate the presence and severity of DED in individuals using escitalopram or sertraline. The findings from such studies can provide valuable insights for eye care professionals, enabling them to

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identify patients at risk for SSRI-related ocular surface complications. Furthermore, these insights may promote improved interdisciplinary collaboration between ophthalmologists, optometrists, and mental health providers, ultimately contributing to more comprehensive and effective patient care.

Materials and Methods

This descriptive cross-sectional study was carried out over a **two-year period, from November 2023 to November 2025**, at **Mayo Hospital, Lahore**, a government tertiary care hospital. A total of **180 patients**, aged between 20 and 40 years, diagnosed with moderate depression and receiving treatment with either **escitalopram** or **sertraline**, were recruited using **purposive sampling**. Prior to participation, all patients provided informed written consent in accordance with ethical research guidelines.

Participants were excluded if they had any ocular surface condition other than dry eye, were long-term contact lens wearers, smokers, or had systemic illnesses that could predispose to dry eye, such as renal insufficiency. Additional exclusion criteria included the use of other medications with xerogenic potential, extended daily computer use, and a history of anterior or posterior segment eye surgery. These criteria were applied to minimize confounding variables that could influence the assessment of dry eye disease.

Demographic and clinical information was systematically recorded using a structured data collection form developed specifically for this study. The form captured details such as age, gender, duration of SSRI therapy, dosage, and relevant ocular and systemic medical history.

Dry eye disease was evaluated using **two validated assessment tools**:

1. **Schirmer's Test:** Tear production was measured using 5 mm × 35 mm sterile filter paper strips. The strips were gently inserted into the lower conjunctival sac without the use of topical anesthesia and left in place for five minutes. The length of the wetting, measured in millimeters, was documented for each eye, providing an objective measure of basal and reflex tear secretion.
2. **Ocular Surface Disease Index (OSDI):** The OSDI questionnaire, consisting of 12 standardized items, was used to assess the frequency and severity of dry eye symptoms, their effect on visual function, and sensitivity to environmental conditions. Scores were calculated according to the formula:

OSDI=number of questions answered25×sum of scores

The OSDI scores were categorized for **180 patients** as follows:

- **Normal:** 0–25
- **Mild DED:** 26–50
- **Moderate DED:** 51–75
- **Severe DED:** 76–100

All collected data were entered into and analyzed using **SPSS version 20**. Associations between categorical variables were determined using the **Chi-square test**, with a p-value less than 0.05 considered statistically significant. The combination of objective measurements (Schirmer's test) and subjective symptom assessment (OSDI) allowed for a comprehensive evaluation of dry eye disease among patients receiving SSRIs, ensuring a thorough understanding of ocular surface health in this population.

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Results

A total of 180 patients using the antidepressants escitalopram and sertraline were included in the study. The association between dry eye and the use of these antidepressants was evaluated using **Schirmer's test** and the **Ocular Surface Disease Index (OSDI)** in patients aged 20–40 years. A comparison was also made between the two drugs regarding their potential to cause dry eye.

Table 1: ***Schirmer Test Results by Type of Drug***

Type of Drug	Normal	Mild	Moderate	Severe	Total	% Normal	% Mild	% Moderate	% Severe	P value
Escitalopram	63	23	16	10	112	56.3%	20.5%	14.3%	8.9%	0.447
Sertraline	42	18	4	6	68	61.8%	26.5%	5.9%	8.8%	0.447

Interpretation: Around 56.3% of escitalopram users and 61.8% of sertraline users had normal Schirmer test values. Chi-square analysis indicated no statistically significant difference between the two drugs ($p = 0.447$).

Table 2: ***OSDI Scores by Type of Drug***

Type of Drug	0–25	26–50	51–75	76–100	Total	% 0–25	% 26–50	% 51–75	% 76–100	P value
Escitalopram	64	32	9	7	112	57.1%	28.6%	8.0%	6.3%	0.432
Sertraline	44	15	9	0	68	64.7%	22.1%	13.2%	0%	0.432

Interpretation: Both escitalopram and sertraline were associated with dry eye, as measured by OSDI scores. No statistically significant difference was observed between the two drugs ($p = 0.432$).

Table 3: ***Schirmer Test vs Duration of Drug Usage***

Duration of Drug Usage	Normal	Mild	Moderate	Severe	Total	% Normal	% Mild	% Moderate	% Severe	P value
1–6 months	22	0	0	0	22	100%	0%	0%	0%	<0.001
7–12 months	46	8	3	0	57	80.7%	14.0%	5.3%	0%	<0.001
13–18 months	26	10	4	5	45	57.8%	22.2%	8.9%	11.1%	<0.001
19–24 months	11	23	9	6	49	22.4%	46.9%	18.4%	12.2%	<0.001

Interpretation: Patients using antidepressants for 1–6 months mostly had normal Schirmer test values. The incidence and severity of dry eye increased significantly with longer drug use ($p < 0.001$).

Table 4: ***OSDI vs Duration of Drug Usage***

Duration of Drug Usage	0–25	26–50	51–75	76–100	Total	% 0–25	% 26–50	% 51–75	% 76–100	P value
1–6 months	22	0	0	0	22	100%	0%	0%	0%	<0.001
7–12 months	50	4	3	0	57	87.7%	7.0%	5.3%	0%	<0.001
13–18 months	23	12	5	5	45	51.1%	26.7%	11.1%	11.1%	<0.001

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Duration of Drug Usage	0–25	26–50	51–75	76–100	Total	% 0–25	% 26–50	% 51–75	% 76–100	P value
19–24 months	0	19	10	6	35	0%	54.3%	28.6%	17.1%	<0.001

Interpretation: OSDI scores increased progressively with longer antidepressant use, indicating worsening dry eye with extended therapy. Chi-square analysis confirmed this trend as statistically significant ($p < 0.001$).

Figures:

- **Figure 1:** Bar graph of Schirmer test vs. duration of drug usage shows increasing dry eye incidence after 7 months.
- **Figure 2:** Bar graph of OSDI vs. duration of drug usage demonstrates rising OSDI scores with longer drug exposure, confirming progressive dry eye development.

Discussion

This study was undertaken to investigate the **prevalence and severity of dry eye disease (DED)** among patients using the antidepressants **escitalopram** and **sertraline**. The results revealed a clear relationship between the **duration of SSRI use** and the manifestation of dry eye symptoms. Specifically, individuals who had been on these medications for longer periods showed a higher incidence of moderate to severe DED, as evaluated by both the **Schirmer test** and the **Ocular Surface Disease Index (OSDI)**. These findings suggest that prolonged exposure to SSRIs may lead to progressive impairment of tear secretion and ocular surface stability, highlighting the cumulative effect of antidepressants on eye health.

These observations are consistent with previous research indicating that SSRIs can contribute to **reduced tear production and tear film instability**.5 The underlying mechanism is believed to involve the modulation of **serotonin and other neurotransmitters**, which play a role in regulating lacrimal gland function and ocular surface homeostasis. As a result, patients may experience clinical symptoms such as ocular dryness, burning, irritation, and photophobia, particularly with long-term therapy. The study reinforces the notion that **SSRIs are a clinically significant risk factor for DED**, and monitoring ocular health in patients receiving these medications is important. When comparing escitalopram and sertraline, no statistically significant differences in DED severity were detected. However, a subtle subjective trend indicated that patients on sertraline reported slightly greater discomfort and irritation than those on escitalopram. This could be due to differences in the **pharmacodynamic properties** of the two drugs: escitalopram is highly selective for serotonin reuptake inhibition, whereas sertraline exhibits mild dopaminergic activity in addition to serotonin modulation. These differences may influence tear film regulation through broader effects on autonomic and neurosensory pathways. Previous literature has documented variability in ocular side effects across different SSRIs, supporting the plausibility of this observation.6

The clinical implications of these findings are significant. **Mental health practitioners, primary care physicians, and ophthalmologists** should be aware of the potential ocular side effects associated with prolonged SSRI use. Patients often do not associate mild ocular symptoms, such as

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dryness or irritation, with their antidepressant therapy, which may result in underdiagnosis or delayed intervention. Routine ocular history assessment and screening for DED in patients on long-term SSRIs could facilitate earlier detection and management. Early intervention may improve **patient comfort, adherence to antidepressant therapy, and overall quality of life**, while also preventing progression to more severe forms of DED.7

This study also emphasizes the importance of **interdisciplinary care**. Educating patients about the possible ocular effects of their medication, promoting preventive strategies such as **preservative-free artificial tears**, eyelid hygiene, and regular eye examinations can help minimize long-term complications. Although the **duration of medication use** emerged as a key factor influencing DED severity, further research is needed to clarify the detailed relationship between cumulative drug exposure and disease progression. Factors such as concurrent medications, environmental influences, and individual susceptibility should also be considered in future studies.

Escitalopram and sertraline were selected for this study due to their **widespread use in contemporary psychiatric practice**, making the results highly relevant to commonly treated patient populations. Nonetheless, several limitations must be acknowledged. The sample size, while sufficient for preliminary analysis, was modest, and data were collected from only **two government hospitals**, which may limit the generalizability of the findings to other healthcare settings. Additionally, the **cross-sectional design** prevents the establishment of causal relationships, and reliance on self-reported symptom measures may introduce subjective bias.

In conclusion, this study demonstrates a significant association between prolonged **SSRI therapy and the development of dry eye disease**. Both escitalopram and sertraline were found to contribute to ocular surface compromise, with severity increasing with the duration of therapy. Awareness of these ocular side effects, regular eye monitoring, and **collaborative care between psychiatrists and ophthalmologists** can improve patient outcomes, comfort, and quality of life. Future longitudinal and multicenter studies are warranted to further investigate the mechanisms, progression, and preventive strategies for SSRI-associated DED.

Conclusion

This study offers important insights into the relationship between **long-term use of antidepressants** and the development of **dry eye disease (DED)**. The findings indicate that while there was **no statistically significant difference** in DED severity between patients using **escitalopram** and those using **sertraline**, individuals on sertraline reported slightly higher levels of ocular discomfort, suggesting the presence of subtle **subjective variability** in patient experience. These observations highlight that patient perception of dry eye symptoms may not always correlate directly with objective measures, emphasizing the need for comprehensive evaluation including both clinical tests and patient-reported outcomes.The **duration of antidepressant therapy** emerged as a key factor influencing the severity of DED. Patients on prolonged treatment exhibited more moderate to severe signs of dry eye, suggesting a **cumulative effect of SSRIs on tear production and**

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ocular surface health. This underlines the importance of regular ophthalmic monitoring, particularly in individuals undergoing extended SSRI therapy, to detect early signs of ocular surface compromise and implement preventive measures.Future research should aim to include **larger, multicenter cohorts** and employ **longitudinal study designs** to better assess the temporal progression of DED associated with specific antidepressants. Incorporating detailed **patient-reported symptom assessments**, objective ocular surface evaluations, and potential confounding factors such as concurrent medications, systemic diseases, and environmental exposures will allow for a more nuanced understanding of how individual antidepressants impact ocular health. Such studies could inform **clinical guidelines** for monitoring, prevention, and management of SSRI-associated dry eye, ultimately improving patient comfort, adherence to psychiatric treatment, and overall quality of life.

Author's Contribution

MS Data Collection
MA Review
SS Report Writing
AB Literature Review
MS Data Analysis
MU Write up
KI & KK Proof Reading

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