## INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION



## COMPARATIVE ANALYSIS OF DRY EYE SYNDROME AMONG DIABETIC VERSUS NONDIABETIC PATIENTS PRESENTING TO A TERTIARY CARE HOSPITAL, PESHAWAR. A CASE-CONTROL STUDY.

Original Research

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### ABSTRACT

**Background:** Dry eye syndrome (DES) is a multifactorial ocular surface disorder that is becoming increasingly prevalent with advancing age and rising rates of diabetes mellitus worldwide. Among diabetic individuals, ocular surface abnormalities such as tear film instability and epithelial damage are frequent yet often underdiagnosed complications. The geriatric demographic, especially those with comorbidities, are at a significantly higher risk for DES due to systemic changes and impaired lacrimal gland function.

**Objective:** To compare the prevalence of dry eye syndrome between diabetic and nondiabetic patients attending the ophthalmology outpatient department at a tertiary care hospital in Peshawar.

**Methods:** This case-control study was conducted at the Eye OPD of Lady Reading Hospital, Peshawar, from October 5, 2020, to December 5, 2023. A total of 100 participants were selected using convenience sampling and divided equally into two groups: 50 diabetic patients (cases) and 50 nondiabetic individuals (controls), all above 40 years of age. A comprehensive anterior segment examination was performed using slit lamp biomicroscopy. Dry eye diagnosis was established through two diagnostic tools: the Schirmer test (values <10 mm considered dry; <5 mm considered severely dry) and fluorescein staining (presence of more than three stained cells indicating surface damage). Data were processed using SPSS version 25 and EPI Info 16, with significance assessed via chi-square analysis.

**Results:** Among diabetic patients, 12 out of 50 (24%) were diagnosed with DES, compared to 26 out of 50 (52%) in the nondiabetic group. The calculated odds ratio was 7.90 at a 95% confidence interval, with a statistically significant p-value of 0.004943 (p < 0.05), indicating a notable association between diabetes and DES.

**Conclusion:** The study indicates a significant association between diabetes mellitus and the development of dry eye syndrome, emphasizing the need for early ocular screening in diabetic patients for timely intervention.

Keywords: Diabetes Mellitus, Dry Eye Syndrome, Fluorescein Staining, Ocular Surface, Schirmer Test, Tear Film, TBUT.

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## **INTRODUCTION**

Dry eye syndrome (DES) is a multifactorial ocular surface disease characterized by discomfort, visual disturbance, and tear film instability, often accompanied by inflammation. It is increasingly recognized as a global health issue due to its high prevalence and impact on quality of life, particularly in the elderly population. Epidemiological evidence suggests a rising incidence of DES with advancing age. In Italy, for instance, the condition affects approximately 11.59% of individuals aged 50 and above (1), while a population-based study in Salisbury reported persistent dry eye symptoms in 14.6% of individuals aged 65 and older (2). Similar findings were noted in the Australian Community Dry Eye Study, where more than half of the 926 participants aged 40 to 97 showed both reduced Schirmer test results and elevated rose Bengal staining, indicating a high prevalence of DES in middle-aged and older adults (3). Contributing factors to dry eye disease in this demographic include refractive surgeries, systemic autoimmune diseases, hormonal changes, and prolonged contact lens use (4). These risks are further amplified by the increasing life expectancy and the growing proportion of elderly individuals worldwide. Notably, studies show a higher burden of DES in women compared to men, with prevalence rates of 5.7% in women under 75 years and 9.8% in those above 75 years (5). In contrast, men exhibit a slightly lower prevalence, ranging from 3.90% to 7.67% between ages 50 and over 80 (2,4). More alarmingly, most individuals report prolonged suffering, with symptoms persisting for an average of over seven years and a majority experiencing progressive worsening over time (5).

Globally, DES affects 5% to over 30% of the population, translating to an estimated 25–30 million people (6). Ethnicity appears to have minimal impact on DES prevalence, but gender-based differences remain prominent, with women at higher risk (7). Additional risk groups include individuals with rheumatoid arthritis—where keratoconjunctivitis sicca affects up to 20%—and those with extended screen exposure, long-term contact lens use, or Helicobacter pylori infections (8). Dry eye is also increasingly recognized among patients with type 2 diabetes, a condition affecting 6.28% of the general population and up to 22% of those above 70 years (9). Diabetes-related ocular surface changes such as corneal insensitivity, goblet cell loss, and lacrimal gland dysfunction contribute to the high prevalence of DES, reported in up to 55% of diabetic patients (10). Studies have found a higher incidence of dry eye in diabetic women compared to non-diabetic women, and lower rates in diabetic men (11). Furthermore, DES has been linked with worsening symptoms of diabetic retinopathy, compounding ocular morbidity in diabetic individuals (12). In one study, 52.9% of patients with diabetes or prediabetes were found to have clinically significant dry eyes, emphasizing the close association between metabolic disorders and ocular surface health (13). Locally, in India, dry eye prevalence has been reported at around 32% (14), underscoring regional variations influenced by environment, healthcare access, and diagnostic criteria. A clinical cohort aged 24 to 93 years, primarily composed of women over 50, showed DES as a prevalent complaint, with arterial hypertension being a common comorbidity (10). Despite numerous international studies, limited data exists from Pakistan on the comparative burden of DES in diabetic and non-diabetic individuals. Given the high prevalence of diabetes in the region and the ocular complications it can entail, a focused investigation is warranted to inform screening and management strategies. Therefore, this study aims to compare the prevalence of dry eye syndrome in diabetic versus non-diabetic patients above 50 years of age attending a tertiary care ophthalmology outpatient clinic in Peshawar, a region known for its high diabetic patient load.

## **METHODS**

This case-control study was conducted in the Ophthalmology Department of Lady Reading Hospital, Peshawar, following approval from the Institutional Ethical Review Board. A total of 100 participants of both sexes and varying regional and ethnic backgrounds were recruited through convenience sampling over the study period from October 5, 2020, to December 5, 2023. The participants were divided equally into two groups: 50 diabetic patients aged above 40 years served as the case group, while 50 nondiabetic individuals of similar age served as controls. Informed consent was obtained from all participants, and confidentiality of data was maintained through de-identification protocols. Inclusion criteria required participants to be aged 40 years or older. Diabetic individuals included in the case group were diagnosed according to established clinical parameters, whereas the control group comprised age-matched nondiabetic patients. Participants with known causes of secondary dry eye were excluded. These exclusions covered individuals using systemic medications such as antihistamines, antidepressants, beta-blockers, or oral contraceptives, all of which may induce dry eye. Additionally,



patients with thyroid disorders, rheumatoid arthritis, systemic lupus erythematosus, or those unwilling to participate were also excluded to ensure sample homogeneity and avoid potential confounders.

A comprehensive ophthalmologic evaluation was conducted on all participants. Initial assessment included measurement of visual acuity using a Snellen chart at a distance of six meters, followed by detailed history-taking encompassing personal and familial medical records with specific reference to ocular history. The anterior segment of the eye was examined using a slit lamp biomicroscope. To diagnose dry eye syndrome, a series of standardized tests were conducted, including Tear Break-Up Time (TBUT), Schirmer's test, and fluorescein staining. TBUT was assessed using fluorescein dye and a slit lamp, with the interval measured from the last complete blink to the first appearance of a gap in the pre-corneal tear film. A TBUT of less than 3 seconds was considered indicative of dry eye. The Schirmer's test was performed by placing filter paper strips into the tarsal conjunctiva of the lower eyelid. Following a five-minute period after the patient sipped water, the wetting of the strip was measured. A tear film reading of less than 10 mm was diagnostic of dry eye, while values below 5 mm indicated severe dry eye. Fluorescein staining was also used to evaluate the integrity of the ocular surface, where more than three stained epithelial cells denoted dry eye-related epithelial damage (15). All relevant data were collected using a predesigned Performa. The statistical analysis was performed using SPSS version 25. Descriptive statistics, including frequencies and percentages, were calculated for categorical variables such as sex and group assignment. For continuous variables, means and standard deviations were reported. The association between categorical variables was analyzed using the chi-square test, and the results were interpreted using EPI Info version 16.

### RESULTS

A total of 100 participants were included in the study, comprising 53 females and 47 males, reflecting a gender distribution of 53% and 47%, respectively. The diabetic group consisted of 50 individuals with a mean age of 62 years (SD  $\pm$ 5 years) and an average diabetes duration of 8 years (SD  $\pm$ 3 years). Among them, 24 were males (48%) and 26 were females (52%). In the diabetic group, dry eye syndrome was diagnosed in 12 participants, accounting for a prevalence of 24%. Of these, 5 were males (33.3%) and 7 were females (66.6%). Aqueous tear deficiency was the more prevalent subtype, identified in 6 participants (66.6%)—2 males (33.3%) and 4 females (66.6%). Evaporative dry eye syndrome was found in 3 cases (44.4%)—1 male (33.3%) and 2 females (66.6%). In contrast, the control group also included 50 individuals, of which 12 were males (36.6%) and 14 were females (63.6%). Dry eye syndrome was identified in 26 individuals within this group, indicating a prevalence of 52%. Aqueous tear deficiency was observed in 17 participants (77.2%)—6 males (35.2%) and 11 females (64.8%). The evaporative subtype was identified in 5 participants (22.7%).

The mean prevalence score for dry eye syndrome across both groups was 2.36 with a standard deviation of  $\pm 0.871$ . Statistical analysis using the chi-square test demonstrated a significant association between diabetes and dry eye syndrome, with an odds ratio of 7.90 at a 95% confidence interval and a P-value of 0.004943, confirming significance at the P < 0.05 level. In the diabetic group, 12 out of 50 individuals were diagnosed with dry eye syndrome, resulting in a prevalence of 24%. Among the non-diabetic group, 26 participants were affected, yielding a prevalence of 52%. When stratified by age brackets, diabetic patients showed the highest number of dry eye cases in the 40–49 age group (5 cases), followed by 4 cases in the 50–59 group and 3 in the 60–69 group. In contrast, the non-diabetic groups. These findings suggest a paradoxical distribution, with a higher prevalence in the non-diabetic group, which may indicate potential biases in participant selection, classification errors, or confounding environmental and behavioral factors not accounted for in this study.

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Gender	Frequency	Percentage (%)	
Female	53	53%	
Male	47	47%	
Total	100	100%	

#### Table 1: Gender-wise Distribution of Participants

#### Table 2: Dry Eye Prevalence by Group

Group	<b>Total Participants</b>	Dry Eye Cases	Prevalence (%)
Diabetic	50	12	24.0%
Non-Diabetic	50	26	52.0%



#### Table 3: Dry Eye Subtypes by Gender and Group

Group	Subtype	<b>Total Cases</b>	Males	Females
Diabetic	Aqueous	6	2	4
Diabetic	Evaporative	3	1	2
Non-Diabetic	Aqueous	17	6	11
Non-Diabetic	Evaporative	5	2	3

#### Table 4: Age-wise Distribution of Dry Eye Cases by Group

Age Group	Dry Eye Cases (Diabetic)	Dry Eye Cases (Non-Diabetic)	
40–49	5	2	
50–59	4	10	
60–69	3	9	
70+	0	5	

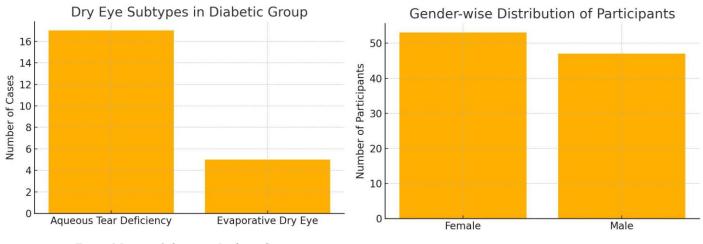


Figure 1 Dry eye Subtypes in Diabetic Group



## DISCUSSION

Dry eye syndrome remains one of the most frequently encountered conditions in ophthalmologic practice, driven by evolving lifestyle patterns and environmental exposure. The findings of the present study reinforce previous global estimates of dry eye prevalence, which range from 18.1% to 70%, and further affirm the burden this condition imposes on both diabetic and nondiabetic populations. Despite its insidious onset and sometimes incongruent symptomatology, particularly in diabetic individuals, dry eye disease exhibits a clearly definable clinical profile when subjective complaints are paired with objective measures such as Schirmer's test, tear film break-up time (TBUT), and fluorescein staining. The study revealed a higher prevalence of dry eye syndrome among nondiabetic participants (52%) compared to diabetic individuals (24%). While this may appear to contradict the known association of diabetes with ocular surface disease, it potentially reflects limitations in sampling, diagnostic inconsistency, or unmeasured environmental exposures among the control group (16,17). Other studies have consistently reported a significant prevalence of dry eye in individuals with type 2 diabetes, with contributory mechanisms involving reduced corneal sensitivity, goblet cell depletion, and lacrimal gland neuropathy. These pathophysiological alterations underscore the silent progression of dry eye disease in diabetics, where signs may be minimal or absent despite clinically meaningful tear dysfunction (18,19).

The present study also identified a gender disparity in dry eye prevalence, with 63.6% of cases occurring in females. Although no statistically significant association between sex and dry eye was found, prior literature has attributed this pattern to hormonal influences, particularly around menopause (20). Estrogen imbalance, whether due to natural menopause or hormone replacement therapy, has been



implicated in altered tear production. However, conflicting reports suggest both estrogen deficiency and supplementation may exacerbate dry eye symptoms, indicating the complexity of hormonal regulation on the ocular surface (21,22). Aqueous tear deficiency emerged as the predominant subtype among both groups, consistent with previous studies that highlight this form as a hallmark of diabetic keratoconjunctivitis sicca (23). Nonetheless, evaporative dry eye, often resulting from meibomian gland dysfunction, also contributed to the burden of disease, especially among younger participants with fewer surface signs but notable discomfort. This subtype is frequently underdiagnosed and contributes to persistent symptoms such as stinging, burning, photophobia, and blurred vision, which affect a substantial portion of the global population, particularly women (24,25).

A notable strength of this study is its structured application of validated diagnostic tools, which enhanced the accuracy of identifying subclinical cases of dry eye. The inclusion of both subjective symptom assessment and objective testing added robustness to case identification. Moreover, the study population drawn from a high-volume ophthalmology center provides a relevant snapshot of clinical realities in diabetic eye care. However, the study is not without limitations. The use of convenience sampling introduces selection bias, and the cross-sectional design precludes causal inferences. Furthermore, the absence of standardized grading for symptom severity or a stratified analysis of medication use, environmental exposure, and glycemic control among diabetics limits the granularity of interpretation. Potential misclassification may also have occurred, particularly in participants with atypical presentations or coexisting ocular pathologies. Future research should focus on longitudinal follow-up to track the progression of subclinical dry eye in diabetics and to evaluate the impact of systemic disease control on ocular surface parameters. Expanding the scope to include tear osmolarity, meibography, and inflammatory biomarkers may also refine diagnostic precision. Recognizing the heterogeneity of dry eye syndrome, integrating multi-modal diagnostic criteria and targeting interventions based on subtype-specific pathology may lead to more effective management strategies, especially in vulnerable populations such as postmenopausal women and individuals with long-standing diabetes.

## CONCLUSION

This study concludes that dry eye syndrome frequently coexists with diabetes, particularly in individuals with type 2 diabetes, where the condition often presents with mild to moderate severity. The findings highlight the importance of incorporating routine ocular surface evaluations in the clinical care of diabetic patients to ensure early detection and intervention. Recognizing the subtleties of dry eye manifestations, even in the absence of overt signs, can improve patient outcomes and quality of life. The study underscores the value of a comprehensive diagnostic approach and supports the need for increased awareness among clinicians regarding the ocular implications of systemic metabolic diseases.

Author	Contribution
Bilal Khan	Substantial Contribution to study design, analysis, acquisition of Data
	Manuscript Writing
	Has given Final Approval of the version to be published
	Substantial Contribution to study design, acquisition and interpretation of Data
Nuzhat Rahil*	Critical Review and Manuscript Writing
	Has given Final Approval of the version to be published
Muhammad Idris	Substantial Contribution to acquisition and interpretation of Data
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Arib Malik	Contributed to Data Collection and Analysis
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Ramin Ali	Contributed to Data Collection and Analysis
	Has given Final Approval of the version to be published
Muhammad Israr	Substantial Contribution to study design and Data Analysis
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#### AUTHOR CONTRIBUTION



## REFERENCES

 Albdaya, N. A., Binyousef, F. H., Alrashid, M. H., Alajlan, A. A., Alsharif, F. A., Alfouzan, S. K., & Alhuthail, R. R. (2022). Prevalence of Dry Eye Disease and Its Association With the Frequent Usage of Eye Cosmetics Among Women. *Cureus*, *14*(7), e27142.
 Calli, U., Ozturk, Y., & Demir, G. (2022). The Effect of Fluorosecein on Corneal Endothelial Structure and Morphology in

Diabetic Retinopathy Patients undergone Fundus Fluoresecein Angiography. Beyoglu Eye J, 7(1), 35-38.

3. Huang, R., Su, C., Fang, L., Lu, J., Chen, J., & Ding, Y. (2022). Dry eye syndrome: comprehensive etiologies and recent clinical trials. *Int Ophthalmol*, *42*(10), 3253-3272.

4. Khan, M. A. B., Hashim, M. J., King, J. K., Govender, R. D., Mustafa, H., & Al Kaabi, J. (2020). Epidemiology of Type 2 Diabetes - Global Burden of Disease and Forecasted Trends. *J Epidemiol Glob Health*, *10*(1), 107-111.

5. Pan, L. Y., Kuo, Y. K., Chen, T. H., & Sun, C. C. (2022). Dry eye disease in patients with type II diabetes mellitus: A retrospective, population-based cohort study in Taiwan. *Front Med (Lausanne)*, *9*, 980714.

6. Papas, E. B. (2021). The global prevalence of dry eye disease: A Bayesian view. *Ophthalmic Physiol Opt*, *41*(6), 1254-1266.

7. Qian, L., & Wei, W. (2022). Identified risk factors for dry eye syndrome: A systematic review and meta-analysis. *PLOS ONE*, *17*(8), e0271267.

8. Schaumberg, D. A., Sullivan, D. A., & Dana, M. R. (2002). Epidemiology of dry eye syndrome. *Lacrimal Gland, Tear Film, and Dry Eye Syndromes 3: Basic Science and Clinical Relevance Part A and B*, 989-998.

9. Tashbayev, B., Chen, X., & Utheim, T. P. (2024). Chalazion Treatment: A Concise Review of Clinical Trials. *Curr Eye Res*, 49(2), 109-118.

10. Zhang, X., Wang, L., Zheng, Y., Deng, L., & Huang, X. (2020). Prevalence of dry eye disease in elderly individuals: A protocol of systematic review and meta-analysis. *Medicine (Baltimore)*, *99*(37), e22234.

11. Zou, X., Wang, S., Zhang, P., Lu, L., & Zou, H. (2020). Quantitative Proteomics and Weighted Correlation Network Analysis of Tear Samples in Adults and Children With Diabetes and Dry Eye. *Transl Vis Sci Technol*, *9*(13), 8.

12. Dai S, Long J, Han W, Zhang L, Chen B. Alleviative effect of probiotics and prebiotics on dry eye in type 2 diabetic mice through the gut-eye axis. Ocul Surf. 2025;36:244-60.

13. Ogawa K, Urata K, Maeda S, Ohno Y, Satoh K, Yamada Y, et al. Blueberry Leaf Extract Prevents Lacrimal Hyposecretion in Sjögren's Syndrome-like Model of Non-obese Diabetic Mice. In Vivo. 2023;37(1):149-62.

14. Ogawa K, Ohno Y, Tagashira A, Urata K, Satoh K, Fujimoto N, et al. Blueberry Stem Extract Prevents Lacrimal Hyposecretion in Non-obese Diabetic Mice via Activation of AMPK. In Vivo. 2023;37(3):1003-15.

15. Sun Y, Zhang Y, Shi F, Li Y, Wang C, Yu F, et al. Characterization and Role of Glucagon-Like Peptide 1 Receptor in the Lacrimal Gland: Novel Insights into Diabetic Dry Eye Pathogenesis. Am J Pathol. 2025;195(4):797-810.

16. Fu Z, Wan M, Jin T, Lai S, Li X, Sun X, et al. Electroacupuncture modulates the TLR4-NF-κB inflammatory signaling pathway to attenuate ocular surface inflammation in dry eyes of type 2 diabetic rats. Cell Mol Biol (Noisy-le-grand). 2024;70(5):111-8.

17. Zhang S, Wang Q, Qu M, Chen Q, Bai X, Zhang Z, et al. Hyperglycemia Induces Tear Reduction and Dry Eye in Diabetic Mice through the Norepinephrine- $\alpha(1)$  Adrenergic Receptor-Mitochondrial Impairment Axis of Lacrimal Gland. Am J Pathol. 2023;193(7):913-26.

18. Qu M, Wan L, Dong M, Wang Y, Xie L, Zhou Q. Hyperglycemia-induced severe mitochondrial bioenergetic deficit of lacrimal gland contributes to the early onset of dry eye in diabetic mice. Free Radic Biol Med. 2021;166:313-23.

19. Pei X, Ba M, Yang T, Xuan S, Huang D, Qi D, et al. Leptin Receptor Deficiency-Associated Diabetes Disrupts Lacrimal Gland Circadian Rhythms and Contributes to Dry Eye Syndrome. Invest Ophthalmol Vis Sci. 2025;66(1):19.

20. Schicht M, Farger J, Wedel S, Sisignano M, Scholich K, Geisslinger G, et al. Ocular surface changes in mice with streptozotocin-induced diabetes and diabetic polyneuropathy. Ocul Surf. 2024;31:43-55.

21. Chen S, Barnstable CJ, Zhang X, Li X, Zhao S, Tombran-Tink J. A PEDF peptide mimetic effectively relieves dry eye in a diabetic murine model by restoring corneal nerve, barrier, and lacrimal gland function. Ocul Surf. 2024;32:1-12.

22. Hwang JS, Shin YJ. Role of Choline in Ocular Diseases. Int J Mol Sci. 2021;22(9).

23. Dogru M, Kojima T, Simsek C, Nagata T, Tsubota K. Salivary and Lacrimal Gland Alterations of the Epidermal Fatty Acid-Binding Protein (E-FABP) in Non-Obese Diabetic Mice. Int J Mol Sci. 2022;23(7).

24. Debreceni IL, Chimenti MS, Serreze DV, Geurts AM, Chen YG, Lieberman SM. Toll-Like Receptor 7 Is Required for Lacrimal Gland Autoimmunity and Type 1 Diabetes Development in Male Nonobese Diabetic Mice. Int J Mol Sci. 2020;21(24).

25. Diaz D, Sassani JP, Zagon IS, McLaughlin PJ. Topical naltrexone increases aquaporin 5 production in the lacrimal gland and restores tear production in diabetic rats. Exp Biol Med (Maywood). 2024;249:10175.