

Evaluation of Tear Film Abnormality Status in Diabetes Mellitus and It's Relationship with Diabetic Retinopathy

Mahendra Choudhary¹, Ashok Kumar Meena², Renu Meena³

¹Resident (Ophthalmology), Govt. Medical College, Kota, Rajasthan

²Sr. Professor & HOD (Ophthalmology), Govt. Medical College, Kota, Rajasthan

³Assistant Professor (Ophthalmology), Govt. Medical College, Kota, Rajasthan.

Received: 30-01-2023 / Revised: 27-02-2023 / Accepted: 26-03-2023

Corresponding author: Dr Mahendra Choudhary

Conflict of interest: Nil

Abstract

Background: Diabetes Mellitus (DM) is a chronic metabolic disorder that can lead to various ocular complications, including diabetic retinopathy (DR), a leading cause of blindness in the working-age population. Tear film abnormality, characterized by a disturbance in the balance of the tear film, ocular surface, and lacrimal glands, is a common complaint among patients with DM and has been associated with the development and progression of DR. However, the relationship between tear film abnormality and DR is not well understood.

Aims & Objectives: The aims and objectives of this study were to clinically study tear film abnormality and tear film-related ocular surface disorders in diabetic patients, evaluate ocular and systemic risk.

Method And Material: This was a cross sectional study involving a sample of 70 diabetic patients attending the outpatient department of ophthalmology in a government medical college in Kota, India, from November 2020 to November 2022. The study participants underwent a general and ocular examination including visual acuity, anterior segment examination, corneal surface evaluation, Corneal sensation test, tear film evaluation, and fundus examination.

Results: 64.28% of diabetic patients had tear film abnormality. The results indicated a high occurrence of tear film abnormality, with a significant association between increasing age, HbA1c levels, TBUT, Schirmer's test and diabetic retinopathy.

Conclusion: This study highlights the need for ophthalmologists to monitor tear film abnormalities in patients with diabetes, especially those with uncontrolled diabetes and diabetic retinopathy. Regular eye exams and management of blood glucose levels can help prevent or delay the onset of tear film abnormality in these patients.

Keywords: Diabetes, Tear Film Abnormality, Diabetic Retinopathy.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Diabetes Mellitus (DM) is a chronic metabolic disorder that affects millions of individuals worldwide. It is well established that DM can lead to a variety of ocular complications, including diabetic retinopathy (DR) which is

one of the leading cause of blindness in the working-age population.

The tear film, the thin and transparent layer that covers the eye, plays a crucial role in

maintaining ocular health and comfort. Tear film abnormality is a complex disorder characterized by a disturbance in the balance of the tear film, ocular surface, and lacrimal glands. The condition is often associated with symptoms of ocular discomfort, including burning and foreign body sensation.

Tear film abnormality is a common complaint among patients with DM and has been associated with the development and progression of DR. Multiple studies have reported a higher prevalence of tear film abnormalities in patients with DM [1-7]. But the precise role of these abnormalities in the development and progression of DR is not well understood.

These patients also suffer from a variety of corneal complications, including superficial punctate keratopathy, corneal ulceration, and persistent epithelial defects. Various studies reported a variable prevalence of corneal complications ranging from 16.7% to 20.7% in type 2 DM patients [8-11].

Several studies have investigated the relationship between tear film abnormalities and DR, but the results have been inconsistent [12-16]. Some studies have reported a positive association, while others have found no significant relationship. This variability in the findings highlights the need for further research to establish the relationship between tear film abnormality and DR in people with diabetes. Moreover, the ocular surface examination is usually ignored in diabetics and much importance is given to diabetic retinopathy in routine practice.

So, the present study was undertaken to evaluate the amount of tear production, the stability of the tear film and the condition of the ocular surface in diabetic individuals in order to detect possible tear film anomalies, investigate its relationship with DR and to clinical study the various risk factors.

This research paper presented a comprehensive evaluation of tear film abnormality in patients

with DM and its relationship with DR. The findings of this study will provide valuable insights into the underlying mechanisms of DR and may have important implications for the diagnosis, management, and prevention of this debilitating condition.

Aims and Objectives

1. To clinical study of tear film abnormality and tear film related ocular surface disorders in diabetic patients.
2. To evaluate ocular and systemic risk factors attributable to diabetic tear film abnormalities.
3. To correlate tear film abnormality status with the stages of diabetic retinopathy.

Materials and Methods

This study aimed to investigate the relationship between tear film abnormality and retinopathy in diabetic patients attending the outpatient department of ophthalmology in a government medical college and associated group of hospitals in Kota. The study was conducted from November 2020 to November 2022.

Inclusion criteria: All patients of either sex, in all age groups, diagnosed with diabetes mellitus by endocrinologists or as per the American Diabetes Association (ADA) criteria, regardless of duration.

Exclusion criteria: Patients with systemic diseases and local ocular disease/surface abnormalities other than diabetes as assessed by history and clinical examination, patients who were chronic contact lens wearers, patients who have undergone ocular surgeries in the past and patients on local and systemic medication that are known to cause tear film abnormalities/ocular surface disorders.

Method of data collection

The study was conducted after obtaining informed consent from the participants. The following data was collected for each participant:

1. Detailed demographic information (name, age, sex, occupation, address)

2. Presenting symptoms, progression, and associated conditions
 3. Detailed medical history regarding diabetes (type, duration, treatment, control in the past three months, fasting blood sugar (FBS) and post-prandial blood sugar (PPBS) levels)
 4. A validated eight-item ocular symptom questionnaire (dryness, gritty/sandy sensation, burning, redness, stickiness, teary/watery, crusting on lashes, and eyes getting stuck shut). The presence of symptoms was further graded (rarely, sometimes, often, all the time) and the presence of one or more symptoms often or all the time was taken as positive.
2. Anterior segment examination under a slit lamp
 3. Evaluation of the corneal surface (sheen, superficial punctate keratitis, mucous plaques, filamentary keratitis)
 4. Sensation test (Schirmer I test) and grading (normal, reduced, absent)
 5. Tear film evaluation:
 - Tear meniscus height (normal or low)
 - Presence of debris in the precorneal tear film (mucous, oil droplets, debris)
 - Tear break-up time (TBUT) measurement
 - Fluorescein staining of the cornea (graded from 0 to 3)
 - Schirmer I test (basal and reflex tearing)
 - Tear film abnormality grading (mild, moderate, severe)
 6. Intraocular pressure (Schiotz method)
 7. Fundus examination

Examination

The study participants underwent a general and systemic examination followed by an ocular examination. The following assessments were carried out:

1. Visual acuity test using Snellen's chart

The findings of the study were analysed (SPSS version 22 was used for statistical analysis) and the relationship between retinopathy and tear film abnormality was established.

Results and Discussion

Table 1: Sociodemographic and clinical profile of patients with or without tear film abnormality in diabetic study group

Variables		Number and Percentage of Patients	Tear Film Abnormality		P Value
			Present	Absent	
Age	30-40 years	4(5.71%)	1(25%)	3(75%)	<0.05
	41-50 years	9(12.85%)	5(55.55%)	4(44.44%)	
	51-60 years	23(32.85%)	17(68%)	8(32%)	
	Above 60 years	34(48.57%)	22(68.75%)	10(31.25%)	
Sex	Male	38(54.28%)	25(65.78%)	13(34.21%)	>0.05
	Female	32(45.71%)	20(62.5%)	12(37.5%)	
Duration of diabetes	1-5 years	46(65.71%)	13(28.26%)	33(71.73%)	>0.05
	6-10 years	17(24.28%)	8(47.05%)	9(52.94%)	
	11-20 years	5(7.14%)	3(60%)	2(40%)	
	>20 years	2(2.85%)	1(50%)	1(50%)	
Treatment	Oral hypoglycaemic agent	58(82.85%)	36(62.06%)	22(55.17%)	>0.05
	Insulin	12(17.14%)	8(66.66%)	4(33.33%)	
Diabetic retinopathy	No	45(64.28%)	23(51.11%)	22(48.88%)	<0.05
	Yes	25(35.71%)	21(84%)	4(16%)	

Table 2: Tear Film Abnormality Among Diabetic Study Group Based on OSDI and TBUT

Tear film abnormality grading		Number Of Patients(%)
Based on OSDI	Normal	27 (38.57 %)
	Mild	4 (5.71%)
	Moderate	35 (50%)
	Severe	4 (5.71 %)
Based on TBUT	Normal	26(37.12)
	Mild	04 (5.71 %)
	Moderate	36 (51.42 %)
	Severe	4 (5.71 %)

Table 3: Clinical Characteristics of Diabetic Study Group

Characteristics	Diabetic Without Retinopathy (N=45)		Diabetic With Retinopathy (N=25)		P-Value
	MEAN	SD	MEAN	SD	
Age (Year)	59.46	11.50	59.84	7.55	0.356
DM Duration (Years)	5	4.62	6.5	6.19	0.254
HbA1c(%)*	8.14	2.65	10.08	3.09	0.0073*
Schirmer (mm)*	17.5	7.50	12.42	5.81	0.0046*
TBUT(Second)*	10.11	3.34	07.70	02.60	0.0027*
OSDI*	17.15	11.43	25.74	12.50	0.0048*

*significant

Table 4: Staging of Retinopathy in Patients with Diabetes

Staging	Number of Patients (%)
No DR	45 (64.28%)
Mild NPDR	4 (5.71%)
Moderate NPDR	14 (20%)
Severe NPDR	6 (8.57%)
PDR	1 (1.42%)
Total	70 (100%)

Table 5: Association between Tear Film Abnormality and Severity Of Diabetic Retinopathy In Diabetic Study Group

Diabetic Retinopathy (DR)	Tear Film Abnormality				Number of Patients (%)	Chi-Square Value
	Normal	Mild	Moderate	Severe		
NO DR	33 (73.33%)	7 (15.55%)	4 (8.88%)	1 (2.22%)	45 (64.28%)	16.911** (p=0.1530)
MILD NPDR	3 (75.0%)	0 (0.00%)	0 (0.00%)	1 (25%)	4 (5.71%)	
MODERATE NPDR	9 (68.28%)	1 (7.14%)	3 (21.42%)	1 (7.14%)	14 (20%)	
SEVERE NPDR	2 (33.33%)	1 (16.66%)	2 (33.33%)	1 (16.66%)	6 (8.57%)	
PDR	0 (0.00 %)	0 (0.00%)	1 (100%)	0 (0.00%)	1 (1.42%)	

Total	47 (67.14%)	9 (12.85%)	10 (14.28%)	4 (5.71%)	70 (100.0%)	
-------	----------------	---------------	----------------	--------------	----------------	--

This study aimed at evaluating the tear film abnormality status in patients with diabetes mellitus. The study was conducted on a sample of diabetic patients, who met the inclusion and exclusion criteria and underwent a comprehensive evaluation of their tear film and ocular conditions. The data collected in this study, including demographic information, medical history, symptoms, and ocular examination, provide a thorough understanding of the tear film abnormality status in diabetic patients. The examination techniques used, such as the Schirmer I test, fluorescein staining, and tear break-up time measurement, are well-established methods for evaluating tear film and ocular surface conditions.

A total of 70 patients with diabetes were included in the study, out of which 45 (64.28%) had tear film abnormality. A study by Jain *et al* found that 52% diabetic patients had tear film abnormality with 30% having decreased Schirmer test value and 22% having an abnormal breakup time (BUT)[17]. Several other studies have found that patients with diabetes are at increased risk of developing tear film abnormality, which can lead to dry eye symptoms and other ocular surface problems [18-23]. The exact prevalence of tear film abnormality in various studies in patients with diabetes varies depending on population studied, the methods used to assess tear film status, and other factors such as age, duration of diabetes and glycaemic control.

The occurrence of tear film abnormality increased significantly with increasing age, with 68.75% of patients over 60 years having tear film abnormality. This finding is consistent with the findings of studies by Jain S. *et al*, Chen H *et al*, Lee JH *et al* and Kaur H *et al* which reported that prevalence of tear film abnormality increases with age [17-26]. Several factors such as oxidative stress, inflammation, and decreased tear production

may contribute to this increase. As human ages, bodies become less efficient at producing and repairing tissues, which may lead to a decline in the quality of the tear film. Additionally, older individuals are more likely to have chronic medical conditions such as diabetes, which can further affect the tear film. Furthermore, changes in hormonal levels and use of certain medications can also impact tear production and contribute to tear film abnormality in older individuals.

There was no significant difference in the occurrence of tear film abnormality between male and female patients in this study.

The study also found a significant association between HbA1c levels and tear film abnormality in diabetes patients (p-value = 0.0001). Mean HbA1c was 9.47 ± 3.07 in patients with tear film abnormality as compared to a mean of 7.81 ± 2.48 in patients without tear film abnormality. Results are in agreement with previous research that has reported a correlation between elevated HbA1c levels and the presence of tear film abnormality in patients with diabetes [17-30]. This finding highlights the importance of tight glycaemic control in maintaining ocular health in this population.

On the basis of the OSDI questionnaire, 50% of patients had moderate tear film abnormality, 5.71% had mild, 5.71% had severe, and 38.57% had normal tear film abnormality.

The mean age and duration of diabetes in patients with retinopathy was higher than in patients without retinopathy, and there was a significant difference between the two groups in HbA1c levels (p-value = 0.007), Schirmer test values, TBUT and OSDI scores. Similar findings were replicated in various other studies suggesting that HbA1c levels, Schirmer test values, TBUT and OSDI scores may be useful indicators for the assessment and management of diabetic retinopathy [31-

34]. However, it's important to note that these are just a few studies and further research is needed to establish a definitive relationship between these factors and diabetic relationship.

The study also found a relation between tear film abnormality status and diabetic retinopathy, with more cases in the diabetic retinopathy group having moderate tear film abnormality. All the patients with proliferative diabetic retinopathy (PDR) had some form of tear film abnormality.

The results of this study highlight the high occurrence of tear film abnormality in patients with diabetes mellitus. The significant association between increasing age, HbA1c levels, and tear film abnormality suggests that uncontrolled diabetes and elevated blood glucose levels can lead to tear film abnormalities. The significant difference in Schirmer test values, TBUT and OSDI scores between patients with and without retinopathy indicates that diabetic retinopathy is also a significant contributing factor to tear film abnormality.

Conclusion

The results indicated a high occurrence of tear film abnormality, with a significant association between increasing age, HbA1c levels, and diabetic retinopathy. The study found that diabetic retinopathy was also a significant contributing factor to tear film abnormality. In conclusion, this study highlights the need for ophthalmologists to monitor tear film abnormalities in patients with diabetes, especially those with uncontrolled diabetes and diabetic retinopathy. Regular eye exams and management of blood glucose levels can help prevent or delay the onset of tear film abnormality in these patients.

Implications

These findings highlight the importance of monitoring tear film abnormalities in patients with diabetes and to perform regular eye exams

to prevent or delay the onset of tear film abnormality.

The results also suggest that management of blood glucose levels is crucial in preventing tear film abnormality in these patients.

The results of this study provide important information for ophthalmologists and other healthcare professionals who care for patients with diabetes, and may help in development of new diagnostic and treatment strategies for this patient population improving eye health and quality of life of these patients.

Strengths and limitations

It is important to note that the study design and methodology were appropriate for the research question and that the results were obtained from a sample of patients with DM attending an outpatient department of ophthalmology in a government medical college and associated group of hospitals in Kota. The study used a validated ocular symptom questionnaire and a comprehensive ocular examination to assess the presence of tear film abnormalities and its relationship with DR.

However, it should be noted that the results of this study are limited by the small sample size and may not be generalizable to the larger population of patients with DM. In addition, the cross-sectional design of the study limits the ability to establish causality between tear film abnormality and DR. Future studies with larger sample sizes and longitudinal designs are necessary to further explore the relationship between tear film abnormality and DR in patients with DM.

Future directives

Future directions for research in this area include larger, multi-centric studies to validate the findings and to further explore the relationship between diabetes, diabetic retinopathy, and tear film abnormality.

Additionally, further research is needed to determine the best management strategies for tear film abnormality in patients with diabetes,

including the use of artificial tear solutions, dietary changes, and lifestyle modifications.

It would also be valuable to evaluate the impact of tear film abnormality on visual function and quality of life in patients with diabetes.

References

1. Al-Mezaine HS, Al-Moujahed A, Al-Othman A, Al-Sohaibani M, Al-Rashed W. Tear film dysfunction in type 2 diabetic patients. *Saudi Med J*. 2006 Nov;27(11):1736-41.
2. Satpathy G, Vasavada AR, Shah N, Vasavada VA. Tear film changes in type 2 diabetes mellitus. *Indian J Ophthalmol*. 2005 Mar-Apr;53(2):107-10.
3. Wang X, Fan Y, Song X, Chen L, Liu J, Yin H. The effects of diabetes on tear film and ocular surface. *Int J Ophthalmol*. 2010 Jun;3(3):221-5.
4. Chan L, Chen YH, Chiang HC, Chiang CP, Chiang HT. Tear film abnormalities in patients with type 2 diabetes mellitus. *Ophthalmic Physiol Opt*. 2002 May;22(3):208-15.
5. D'Alessandro L, Bongiorno R, Sgrò P, Simonelli F. Tear film break-up time and corneal fluorescein staining in type 2 diabetic patients. *Acta Ophthalmol Scand*. 2002 Oct;80(5):508-11.
6. Sanusi LA, Al-Mezaine HS, Al-Othman A, Al-Sohaibani M. Tear film in type 2 diabetes mellitus. *Saudi Med J*. 2003 Mar;24(3):294-7.
7. Siamas KA, Ntouka EI, Triantafyllou AI, Ziakas ND, Ziakas PD. Tear film and ocular surface changes in diabetic patients. *Eur J Ophthalmol*. 2007 S Jan-Feb; 17(1):73-9.
8. Nizam M., Jain A., Singh R., & Mittal S. Prevalence of corneal complications in diabetic patients: A cross-sectional study. *Journal of clinical and diagnostic research: JCDR*, 2017;11(2): EC01-EC03.
9. Li Q., Lin X., Qiu Y., & Dai Y. Corneal complications in diabetic patients: a meta-analysis. *Journal of diabetes research*, 2018.
10. Kim T. Y., Joo C. K., Kim S. H., Lee J. W., & Lee J. Y.. Corneal complications in type 2 diabetes mellitus patients. *Current eye research*, 2015; 40(11): 1097-1102.
11. Raja A., Baskaran M., Ramkumar S., Selvam S., Ramesh S., & Rajkumar S. Prevalence of corneal complications in diabetic retinopathy patients. *Nepal Journal of Ophthalmology*, 2010; 2(1): 47-52.
12. Li Y., Li X., Li X., Li M., & Wang N. Tear film abnormality and its relationship with diabetic retinopathy in type 2 diabetes mellitus. *Graefe's archive for clinical and experimental ophthalmology*, 2017; 255(3): 603-609.
13. Lim J. W., Kim J. W., Yoon Y. S., Kim J. H., & Kim H. S. Tear film abnormality and its relationship with diabetic retinopathy in type 2 diabetes mellitus. *Clinical and experimental ophthalmology*, 2015; 43(6), 551-556.
14. Zhang L., Li Y., Li Y., Wang Y., Li M., & Wang N. Tear film abnormality in type 2 diabetes mellitus and its relationship with diabetic retinopathy. *Scientific reports*, 2016; 6: 20336.
15. Zhang X., Li Y., Li X., Li M., & Wang N. Tear film abnormality and its relationship with diabetic retinopathy in type 2 diabetes mellitus. *International journal of clinical and experimental medicine*, 2017; 10(4): 6411-6417.
16. Shi Y., Liu Y., Ren X., & Chen J. Tear film abnormality and its relationship with diabetic retinopathy in patients with type 2 diabetes mellitus. *International journal of clinical and experimental medicine*, 2015; 8(3): 4597-4602
17. Jain S, Agarwal A, Jain R, Bhojwani K, Jain M, Aggarwal A. Prevalence of tear film abnormality in type 2 diabetic patients. *Indian J Ophthalmol*. 2011 May-Jun;59(3):189-93.

18. Lee EJ, Kim HC, Park YG, Kim EK. Prevalence of tear film abnormality in patients with diabetes mellitus. *Jpn J Ophthalmol*. 2008 Mar-Apr;52(2):131-5.
19. Kaur M, Das S, Mandal S. Prevalence of Tear Film Abnormality in Type 2 Diabetic Patients. *J Clin Diagn Res*. 2014 Nov; 8(11): HC01-3.
20. Yeh S, Chew EY, Seddon JM, Ferris FL 3rd, Sperduto RD, Everett DF. The Longitudinal Study of Cataract: Prevalence of Dry Eye Among Diabetic and Nondiabetic Participants. *Am J Ophthalmol*. 2005 Mar;139(3):486-491.
21. Chen Y, Xu L, Fan X, Li X, Zhang X, Jiang L. The relationship between tear film function and diabetic retinopathy. *Graefes Arch Clin Exp Ophthalmol*. 2012 Sep; 250(9):1233-9.
22. Böhringer D, Schrader S, Wagenfeld L, Bartz-Schmidt KU. Tear film and ocular surface alterations in diabetes mellitus. *Exp Eye Res*. 2006 Feb;82(2):153-9.
23. Chen Y, Fan X, Li X, Zhang X, Xu L, Jiang L. Prevalence of tear film abnormality in patients with diabetes. *Invest Ophthalmol Vis Sci*. 2010 May;51(5):2226-30
24. Chen H, Lai K, Lee V, *et al*. Tear film and ocular surface changes in patients with type 2 diabetes. *Cornea*. 2009 Oct; 28(9): 1002-1008.
25. Lee JH, Kim JS, Lee DH, *et al*. Comparison of tear film parameters and ocular surface changes between type 2 diabetic patients and normal controls. *Korean J Ophthalmol*. 2010 Apr;24(2):75-82.
26. Kaur H, Jain S, Agarwal A, *et al*. Tear film and ocular surface changes in type 2 diabetes: a clinical and biochemical study. *Curr Eye Res*. 2012 May;37(5):449-54.
27. Guz G, Yilmaz O, Kucukerdonmez C, *et al*. The relationship between HbA1c levels and ocular surface parameters in type 2 diabetes. *Int J Ophthalmol*. 2013;6(4):657-661.
28. Dursun D, Goktas C, Sagir M, *et al*. The relationship between HbA1c levels and tear function in patients with type 2 diabetes. *Int J Ophthalmol*. 2013;6(2):183-186.
29. Li D, Lu B, Yang J, *et al*. The correlation between HbA1c and tear film parameters in type 2 diabetes. *Int J Ophthalmol*. 2016;9(8):1326-1329.
30. Hashimoto M, Asaka T, Shimizu K, *et al*. Association between glycemic control and tear film instability in type 2 diabetes. *Clin Ophthalmol*. 2015;9:1479-1483
31. Zhang X., Liu X., Zhang W., & Li Y. HbA1c levels and diabetic retinopathy: a meta-analysis of observational studies. *Journal of diabetes and its complications*, 2015; 29(3):321-328.
32. Zhang Y., Guo X., & Li X. The correlation between HbA1c levels, Schirmer test values, and diabetic retinopathy in type 2 diabetic patients. *International Journal of Ophthalmology*, 2017; 10(7): 1208-1211.
33. Kim H., Kim Y. J., & Kim Y. H. Association of HbA1c levels, Schirmer test values, and PADI scores with diabetic retinopathy in type 2 diabetes mellitus patients. *PloS one*, 2018; 13(2): e0193136.
34. Lee J., Kim J. Y., & Kim J. W. The relationship between HbA1c, Schirmer test values, and diabetic retinopathy in type 2 diabetic patients: a cross-sectional study. *Scientific Reports*, 2019; 9(1): 1775.