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Original Research Article

Study of association of dry eye with diabetes mellitus

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ABSTRACT

Background: Aim of the study was to evaluate the tear status in diabetes mellitus (DM) patient.
Methods: This study was a prospective observational case control study. Eighty patients with DM aged from 50 to 80 years were compared with a group of 80 normal healthy age matched control group. A general ophthalmological check-up was performed. The main points of comparison were subjective complaints, objective findings on basic Schirmer test, break-up time, Rose Bengal test.
Results: The results show that 27.5% of all diabetic subjects accompanied of dry eye symptoms, as against 6.25% of the control group. A mean BUT value was 15.5s and Standard Error was 0.20. In the control group mean BUT value was 14s and standard error was 0.23. Basic Schirmer test in DM group mean value was 9.50 mm and SE was 0.268. In the control group mean basic Schirmer test value was 15 mm and SE was 0.405. Rose Bengal test score in DM group, normal score (score <3) was found in 80% case and abnormal score (score ≥3) was found in 20%. In the control group, normal score was found in 93.75% and abnormal score was found in 6.25% case. Dry eye percentage in DM group 11.25% had definitive dry eye, 16.25% cases had possible dry eye and 72.5% cases had no dry eye. In control group 2.50% cases had definitive dry eye, 3.75% cases had possible dry eye and 93.75% had no dry eye.
Conclusions: The study shows that dry eye is associated with DM.

Keywords: Dry eye, DM, Tear

INTRODUCTION

Dry eye is a disorder of the ocular surface that results in symptoms such as burning, stinging, grittiness, a sandy feeling, itching, foreign body sensation, and discomfort. This occurs when the quantity or quality of the precorneal tear film is insufficient to maintain the health of the ocular surface.[1] The normal tear film is a complex structure composed of three layers: an outer lipid layer about 0.1 micrometers thick that is formed by secretion from the meibomian gland, which retards evaporation of the aqueous layer and lubricates the eyelids; a 7-micrometer middle aqueous layer, which forms the main bulk of the tear and is secreted by the lacrimal gland and the accessory lacrimal glands of Krause and Wolfring; and an inner mucin layer, which is 0.02-0.05 micrometers thick and secreted by goblet cells in the conjunctiva and by crypts of Henle and glands of Manz, converting the hydrophobic corneal surface to hydrophilic.[2,3]

Dry eye is a common disorder that affects a significant portion of the population, particularly those over 40 years old. The prevalence of dry eye increases with age, though it is not well documented throughout the age spectrum.[4] One of the causes of dry eye is thought to be DM, a clinical syndrome characterized by hyperglycemia due to absolute or relative insulin deficiency, which affects the metabolism of carbohydrates, proteins, and fats, and causes a significant disturbance of water and electrolyte homeostasis.[5] The reported prevalence of dry eye

syndrome (DES) in diabetics is 15-33% in those over 65 years old, and increases with age. It is 50% more common in women than in men and is correlated with the level of glycated hemoglobin, with higher levels leading to a higher incidence of dry eye.[6]

Symptoms of dry eye are typically severe in patients with diabetes whose glycemic control is poor.[6,7] Those with a longer duration of diabetes may report fewer dry eye symptoms, and increased tear osmolarity is negatively correlated with symptoms. However, those without symptoms are unlikely to seek care, as a reduction in corneal sensitivity due to diabetic peripheral corneal neuropathy may result in a lack of symptoms, even with a minimal decrease in corneal sensitivity causing changes in tear secretion.[8,9] In a hospital-based study, a longer duration of diabetes was associated with a lower (less severe) ocular surface disease index.[10]

Diagnosis of dry eye syndrome is typically done using tear break-up time (BUT) and the Schirmer test. Tear osmolality and dynamics may also be used as supplementary diagnostic methods. Severe diabetes-associated dry eye syndrome can lead to visual impairment, corneal scarring, and ulcers, resulting in secondary bacterial infections. The synergistic effect of corneal infection and diabetes can accelerate corneal lesions, changing the ocular surface irreversibly and inducing visual impairment. Tear film dysfunction not only causes dry eye but also exacerbates the ocular surface, leading to a corneal epithelial defect, a common sign in diabetics.[6]

Bangladesh, a developing country, has made remarkable progress in controlling the incidence of DM. However, the rapidly increasing number of patients diagnosed with DM in Bangladesh is a clear indication that its related complications will become a major health burden in the near future. Dry eye symptoms, such as feelings of dryness, burning, grittiness, and discomfort, are common. Other symptoms include stringy discharge, redness, and crusting of the lids. These symptoms can lead to chronic irritation and may result in epithelial erosions or filaments on the corneal surface. The damage to the cornea and conjunctiva can be clinically diagnosed through staining with Rose Bengal. If left untreated, dry eye can cause reduced vision and even lead to blindness. However, the use of artificial tears can help prevent these symptoms and complications. Thus, early diagnosis of dry eye is essential in all diabetic patients. This study aims to evaluate association between dry eye and DM.

METHODS

A case control study was conducted for a period of one year (December 2020 to November 2021) at Sir Salimullah medical college Mitford hospital in Dhaka, Bangladesh in collaboration with the department of ophthalmology at the Bangladesh institute of research and rehabilitation for diabetes, endocrine and metabolic disorder (BIRDEM) in Shahbag, Dhaka, Bangladesh. The 80 patients fulfilling the inclusion criteria (age >50 years and diabetic with a duration of >2 years) were included in the diabetic group (case) and 80 age and gender matched healthy subjects were included in the healthy control group. The patients were selected through purposive sampling. The exclusion criteria included systemic disease other than diabetes, chronic blepharitis, keratitis, conjunctivitis, dacryocystitis, ocular surgery, chemical injury of the eye, collagen vascular disorder, corneal surface irregularities, eyelid abnormalities, history of using eye drops, and use of sulfonamide, beta blockers, amitriptyline, diazepam, nitrazepam, and antihistamines. Clinical assessment included a history of dry eye symptoms and diabetes duration, drug history (topical/systemic), and ocular injury/surgery and a clinical examination of visual acuity, anterior segment, tear status (basic Schirmer test, tear film break up time, and Rose Bengal test).[11,12] Dry eye was diagnosed with presence of dry eye symptoms, positive vital dye staining of the ocular surface (Rose Bengal score > 3), and abnormalities of tear dynamics (Schirmer test <5 mm or tear break up time <10 sec). If all three criteria were met, the diagnosis was definite dry eye. If only two criteria were met, the diagnosis was probable dry eye. The statistical analysis was done using SPSS software and ethical clearance was obtained from the institutional review board.

RESULTS

Table 1 shows age distribution in DM group and healthy control. There were 41 (51.25%) patients of age group 50-65 years in DM group and 38 (47.5%) in healthy control group. In age group 66-80 years 39 (48.75%) patients were in DM group and 42 (52.5%) patients were in control group. Mean age distribution was 65 years (SE=0.575) in DM group and 66 years (SE=0.618) in healthy control. Age distribution in both study groups were almost similar making study more representative.

Among total 160 patients, male patients were 81 and female patients were 79. In DM group, among 80 patients 39 (48.75%) patients were male and 41 (51.25%) patients were female. In the healthy control 42 (52.50%) patient were male and 38 (47.50%) were female. Sex distribution in both study groups were almost similar making the study more representative.

In DM group among 80 patients, 15 (18.75%) patients were farmer, 10 (12.50%) were grocer, 15 (18.75%) were officer worker, 20 (25%) were involved in household duties and 20 (25%) were passing their retired life. In the healthy control among 80 patients 18 (22.5%) were farmer, 12 (15%) were grocer, 16 (20%) were office worker, 18 (22.5%) were involved in house hold duties and 16 (20%) were passing their retired life. In DM group among 80 patients 15 (18.75%) were from urban residential area, 15 (18.75%) from urban industrial area, 20 (25%) from slum area and 30 (37.50%) from rural

area. In the healthy control among 80 patients 16 (20%) from urban residential area, 14 (17.50%) from urban industrial area, 18 (22.50%) from slum area and 32 (40%) from rural area. Patients from almost similar geographical distribution were participated in the study making the study more representative.

Table 1: Baseline characteristics of the patients in DM group and healthy control.

Variables	DM group, n (%)	Healthy control, n (%)	P value
Age (Years)			
50-65	41 (51.25)	38 (47.5)	>0.05^{ns}
66-80	39 (48.75)	42 (52.5)	
Mean ± SE	65±0.575	66±0.618	
Sex			
Male	39 (48.75)	42 (52.50)	>0.05^{ns}
Female	41 (51.25)	38 (47.50)	
Occupation			
Farmer	15 (18.75)	18 (22.5)	>0.05
Grocer	10 (12.50)	12 (15)	
Office work	15 (18.75)	16 (20)	
House hold duties	20 (25)	18 (22.5)	
Retired life	20 (25)	16 (20)	
Living area			
Urban residential area	15 (18.75)	16 (20)	>0.05
Urban industrial area	15 (18.75)	14 (17.50)	
Slum area	20 (25)	18 (22.50)	
Rural area	30 (37.50)	32 (40)	

Unpaired t-test and Chi-square was done, ns=not significant

Table 2: Dry eye symptoms in DM group and healthy control.

Study group	Dry eye symptoms present, n (%)	Dry eye symptoms absent, n (%)	P
Case	22 (27.5)	58 (72.5)	<0.01
Control	05 (6.25)	75 (93.75)	

*=Significant (p<0.01) done with chi-square test.

Table 2 show dry eye symptoms in DM group and healthy control. In DM group 22 (27.5%) patients complained of dry eye symptoms (e.g., burning, stringing, grittiness and discomfort) whereas in the healthy control 5 (6.25%) patients complained of dry eye symptoms out of 80 persons. No complaints of dry eye symptoms were noted in 58 (72.50%) cases in DM group and in 75 (93.75%) cases in the healthy control. These findings showed that dry eye symptoms had a significant (p<0.01) association with DM.

Table 3 shows mean basic Schirmer test value in DM and healthy control. In DM group mean value was 9.50 mm and SD=0.268. Healthy control means basic Schirmer test value=15 mm and SD=0.405. Thus, basic Schirmer test value reduced significantly in DM compared to control.

Table 3: Basic Schirmer test value.

Group	N	Mean ± SD	P value
DM group	80	9.50±0.268	<0.001
Control group	80	15.00±0.405	

Significant (P<0.001) done with 't' unpaired test.

Table 4: Abnormal value (<5 mm) by basic Schirmer test in DM group and healthy control.

Study group, (n=80)	Abnormal value (<5 mm), n (%)	Normal value (≥5 mm), n (%)	P value
DM group	7 (8.75)	73 (91.25)	0.05*
Healthy control	1 (1.25)	79 (98.75)	

Chi-square test was done.

Table 4 shows abnormal value <5 mm by basic Schirmer test in DM group and healthy control group. In DM group abnormal mean value <5 mm was 7 (8.75%) in number. In the healthy control abnormal value was 1 (1.25%) in number out of 80 cases.

Table 5: Break up time (BUT) value: in study subjects.

DM group, (n=80)		Healthy group, (n=80)		P value
Mean value (sec)	**SD**	**Mean value (sec)**	**SD**	
12.50	0.20	14	0.23	<0.001*

Unpaired t- test was done to observe the significant difference.

Table 5 shows mean break up time (BUT) value in DM group and healthy control. In DM group, mean break up time (BUT) value was 12.50 seconds and SE was 0.20. In the healthy control mean Break up time (BUT) value was 14.00 seconds and SE was 0.23. Thus, BUT value found to be significantly (p<0.001) low in DM group.

Table 6: Abnormal value (<10 sec) of BUT in study subjects, (n=160).

Study group	Abnormal value (<10 sec.), n (%)	Normal value (≥10 sec.), n (%)	P value
DM group	8 (10)	72 (90)	<0.05
Control group	2 (2.5)	78 (97.5)	

Significant (P<0.05) done with chi-square test.

Table 6 shows abnormal value (<10 sec) of BUT in DM group and healthy control group. In DM group abnormal value (<10 sec) was 8 (10%) out of 80 cases. In healthy control abnormal BUT= 2 (2.5%) out of 80 cases.

Table 7: Distribution of Rose Bengal test score in DM group and healthy control.

Study group, (n=80)	Abnormal score (score >3), n (%)	Normal score (score ≤3), n (%)	P value
DM group	16 (20)	64 (80)	<0.05
Control group	05 (6.25)	75 (93.75)	

Significant (p<0.05) done with chi-square test.

Table 7 shows Rose Bengal test score in DM group and healthy control group. In DM group normal score (score ≤3) was found in 64 (80%) cases and abnormal score (score >3) was found in 16 (20%) cases. In the healthy control normal score was found in 75 (93.75%) and abnormal score was found in 05 (6.25%) cases. Thus, it was evident that DM was significantly (p<0.05) associated with abnormal Rose Bengal test score.

Table 8: Distribution of dry eye percentage in DM group and healthy control group.

Study group, (n=80)	Dry eye, n (%)	No dry eye, n (%)	P value
DM group	22 (27.5)	58 (72.5)	<0.01
Healthy group	5 (6.25)	75 (93.75)	

Significant (p<0.0l) with chi-square test.

Table 8 shows distribution of dry eye percentage in DM group and healthy control. In DM group among 80 cases 22 (27.5%) had dry eye and 58 (72.5%) had no dry eye. Among 80 in the healthy control, 5 (6.25%) had dry eye and 75 (93.75%) had no dry eye. These findings showed that DM significantly (p<0.01) associated with dry eye.

DISCUSSION

DM is a metabolic disease characterized by hyper-glycaemia due to absolute or relative deficiency of insulin. It is the most common endocrine disease and is world-wide in distribution. Lack of insulin affects in metabolism of carbohydrate, protein and fat and causes a significant disturbance of water and electrolyte homeostasis. This disease affects the eyes, kidneys, nerve and blood vessels as long-term complications.

Dry eye is a disorder of ocular surface that causes burning, stinging, foreign body sensation and discomfort. This disorder occurs when the quantity or the quality of the three layered pre-corneal tear films insufficient to ensure the well-being of ocular surface. Outer lipid layer is secreted by the Meibomiam gland, intermediate aqueous layer is secreted by the lacrimal gland and the accessory lacrimal glands of Krause and Wolfring. The inner mucin layer secreted by the goblet cells in conjunctiva that converts hydrophobic corneal surface to hydrophilic one, aqueous layer spreads evenly over the ocular surface. Dry eye is a common disorder affecting a significant percentage of population, particularly those older than 40 years and thought to increase with age.[11] Diabetic patient often complains of symptoms of dry eye. Hyndiuk et al described neurotrophic corneal ulceration in DM. Schultz et al indicates that 47% to 64% of diabetic patients have primary corneal lesions during their life time.[13,14] Schuta el al in describing the abnormality in corneal epithelium of diabetic patients were the first to attribute the reduction of corneal sensitivity to a manifestation of diabetic neuropathy.[15] Epithelial fragility microscopic oedema and bleb formation, superficial punctate keratopathy, persistent epithelial defect, recurrent corneal erosions, delayed epithelial healing have been described by Saina and Khandalava.[16] Sanchez described the state of cornea in DM; dry eye, filamentary keratitis has been mentioned as a corneal complication.[19]

In this study 80 diabetic patients who were suffering for more than 10 years and age between 60-80 years of mean 65±SE 0.575, among them 39 male and 41 female were included as case in DM group. Eighty healthy age matched persons with a mean age of 66 years ± SE 0.618 were taken as control, among them 42 were male and 38 were female. These 80 diabetic patients were compared with 80 age matched control group. The parameter of comparison were symptoms of dry eye, mean tear film break-up time, mean Schirmer test value, abnormal Rose Bengal test scoring.

The mean basic Schirmer test value in DM group was 9.50±SE 0.26 mm, which was significantly low in comparison with the control group value of 15±SE 0.40 mm. This Schirmer test value was similar with the study of Dogru et al whose average Schirmer test value in DM group was 7.4±0.38 mm versus 13.53±0.50 mm in the control subjects.[17] In DM group abnormal Schirmer test (<5 mm) value was in 8.75% patients in contrast to 1.25% of control group.

The mean BUT value also showed a marked difference between the group, in DM group it was 12.50±SE 0.20 sec compared with 14±SE 0.23 sec in control group. The difference was statistically significant (p<0.001). Our BUT result was almost similar to that of Dogru et al in which mean BUT was 8.83 sec in DM group and 12.96 sec in control group (p<0.001).[17] In this study 10% of DM group showed abnormal BUT value in contrast to 2.5% in the control group.

Rose Bengal test in this study showed statistically significant difference in abnormal score of >3 between the groups. Sixteen (20%) patients showed abnormal Rose Bengal score in DM compared with 6.25% in control group. Van Bijsterveld scoring system for Rose Bengal dye was used in this study.[18] This scoring system divides the ocular surface into three zones: nasal bulbar conjunctiva, cornea and temporal bulbar conjunctiva. Each zone is given a score ranging zero to 3, zero indicating no staining, 1 indicating few spots of staining,

2 indicating multiple spots and 3 indicating essentially confluent staining. For each eye a possible maximum total is 9, any reading 3 or above was regarded as abnormal scoring.

In this study 22 patients i.e., 27.50% had dry eye in DM group and 5 persons i.e., 6.2% in control group. The difference between the number of dry eyes was statistically significant.

Dry eye was diagnosed on the basis of three criteria described by Tseng and Tsubota which were as follows: presence of chronic dry eye symptoms; positive vital dye staining of ocular surface.[12] That is, a Rose Bengal score >3; abnormalities of tear dynamics a Schirmer test <5 mm or tear break up time, <10 sec. If all the three criteria are met, the diagnosis is definite dry eye. If only the first and second or first and third criteria are met the diagnosis is possible dry eye. In this study dry eye includes both the definite dry eye and possible dry eye.

The tests used in the diagnosis of dry eye were performed very carefully. In tear film break up time test artificially induced rapid break up time were associated with mechanically holding the lids open widely. The cobalt blue filter used in observing tear film break up should be clean as the dust on the filter can give false impression of dry spot. To be reliable repeated reading were taken. Mucin deficient states especially cause a rapid break up time. To prove mucin deficiency conjunctival goblet cell population study in DM patient should be done. False positive and false negative values are a considerable problem with the Scirmer test.[19,20] So, Schirmer test was done in all the cases in same environmental condition.

CONCLUSION

The study concludes that dry eye is significantly associated with DM. Tear film is quantitatively reduced and its stability is also reduced in DM patient.

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REFERENCES

1. Lemp MA, Foulks GN. Definition and classification of dry eye disease. Ocul Surf. 2007;5(2):75-92.
2. Foulks GN. Correlation between tear film lipid layer and dry eye disease. Survey of Ophthalmol. 2007;52(4):369-74.
3. Conrady CD, Joos ZP, Patel BC. Lacrimal gland and its role in dry eye. J Ophthalmology 2016;2016.
4. Sharma A, Hindman HB. Aging as a predisposition to dry eyes. J Ophthalmology 2014;2014.
5. American Diabetes Association (ADA). Diagnosis and classification of diabetes mellitus. Diabetes Care. 2010;33(1): 62-69.
6. Zhang X, Zhao L, Deng S, Sun X, Wang N. Prevalence, etiology, and clinical characteristics of dry eye syndrome in diabetes mellitus patients. J Ophthalmol. 2016;2016.
7. Kaiserman I, Kaiserman N, Nakar S, Vinker S. Dry eye in diabetic patients. Am J Ophthalmol 2005;139(3):498-503.
8. Imam S, Elagin RB, Jaume JC. Diabetes-associated dry eye syndrome in new humanized transgenic model of type 1 diabetes. Molecular Vision. 2013;19:1259.
9. Fuerst N, Langelier N, Massaro-Giordano M, Pistilli M, Stasi K, Burns C et al. Tear osmolarity and dry eye symptoms in diabetics. Clin Ophthalmol (Auckland, NZ). 2014;8:507.
10. Manaviat MR, Rashidi M, Afkhami-Ardekani M, Shoja MR. Prevalence of dry eye syndrome and diabetic retinopathy in type 2 diabetic patients. BMC Ophthalmol. 2008;8(1):10.
11. Lemp MA. Diagnosis and treatment of tear deficiencies. In: Tasman W, Jaeger EA, Schwab IR, Tessler HH (eds). Duane's Clinical Ophthalmology, vol 4. Revised ed. Philadelphia: Lippincott Williams and Wilkins. 2003;1-17.
12. Tseng SC, Tosubota K. Current concepts in ocular surface disease. Cornea and External Disease Congress, Gold Coast, Australia. 1993:10-12.
13. Hyndiuk RA, Kazarian EL, Schultz RO, Seideman S. Neurotrophic corneal ulcers in diabetes mellitus. Arch Ophthalmol. 1977;95(12):2193-6.
14. Schultz RO, Van Horn DL, Peter MA. Diabetic keratopathy. Trans Am Ophthalmol Soc. 1981;79:180-99.
15. Schultz RO, Peter MA, Sobocinski, Nassif K, Schultz KJ. Diabetic keratopathy as manifestation of peripheral neuropathy. Am J Ophthalmol. 1983;96:368-71.
16. Saini JS, Khandalavla B. Corneal epithelial fragility in diabetes mellitus. Can J Ophthalmol. 1995;30(3):142-6.
17. Dogru M, Katakami C, Inoue M. Tear function and ocular surface changes in noninsulin-dependent diabetes mellitus. Ophthalmology. 2001;108(3):586-92.
18. Van Bijsterveld OP. Diagnostic tests in sicca syndrome. Arch Ophthalmol. 1985;82(1):10.
19. Sanchez JC. The cornea in diabetes mellitus. Int Ophthalmol Clin. 1998;38(1):19-36.
20. Gilbard JP, Farris RL. Tear osmolarity and ocular surface disease in keratoconjunctivitis sicca. Arch Ophthalmol. 1979;97(9):1642-6.

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