International Journal of Medical Research Professionals
P-ISSN: 2454-6356; E-ISSN: 2454-6364
DOI: 10.21276/ijmrp

Original Research Article.

Clinical Characteristics of Dry Eye Syndrome in Patients with Diabetes Mellitus

Khandaker Khadiza Farhana Ferdaus[1*], Md. Masud Rana[2], Kamruzzaman[3], Obidul Hoque[4]

[1]MBBS, MS(Ophthalmology), Assistant Surgeon,
National Institute of Ophthalmology and Hospital, Dhaka, Bangladesh.
[2]Junior Consultant (Ophthalmology), Long Term Fellowship Trainee in Cornea,
National Institute of Ophthalmology and Hospital, Dhaka, Bangladesh.
[3]MBBS, MS(Ophthalmology), Assistant Professor, Department of Ophthalmology,
Monowara Sikder Medical College and Hospital, Shariatpur, Bangladesh.
[4]MBBS, MS(Ophthalmology), Fellow Department of Retina,
National Institute of Ophthalmology and Hospital, Dhaka, Bangladesh.

ABSTRACT

Background: Dry eyes may be caused by impairment in the tear production or excessive tear evaporation and are associated with photophobia, red eyes, vision impairment, local pain and pruritus. It has been described those patients with Diabetes Mellitus (DM) may have a higher prevalence of dry eyes than normal population.

Purpose: To investigate clinical characteristics of dry eye syndrome in patients with diabetes mellitus.

Methodology: This cross-sectional observational study was conducted in the Department of Ophthalmology, Bangabandhu Sheikh Mujib Medical University from October 2016 to February 2019 to assess relation of Dry Eye Syndrome with type-2 Diabetic Retinopathy patients. Patients attending into Department of Ophthalmology, Bangabandhu Sheikh Mujib Medical University, who were diagnosed as a type-2 diabetic retinopathy were the study population of this study.

Results: We analyzed 95 diabetic retinopathy patients with type 2 diabetes mellitus of which 61.1% patients were male and 38.95% were female. Out of the 95 patients, 66.3% patients had dry eye and 33.7% patients had no dry eye. After categorization according to severity 17.5% patients had mild, 61.9% had moderate and 20.6% patients had severe dry eye. Study findings showed Dry Eye participants mean (SD) age in years was 56.03 (6.63). The reflex secretion of tears, as measured by Schirmer's I method, decreased significantly with increasing age and significant influence was seen in Type 2 diabetes patients after 50 years of age. In the present study, 58.7% of dry eye in diabetic retinopathy patients were males and 41.3%% were females. TBUT was found to be less than 10 second in 66.3% dry eye patients but normal TBUT in 33.7% patients. Most of the dry eye patients (71.4%) with type 2 diabetic retinopathy had very poor control of diabetes. In this study, 7.9% patients of mild NPDR, 17.5% patients of moderate NPDR, 57.1% patients of severe NPDR and 17.5% patients of PDR had dry eye. A statistically significant ($P \leq 0.000$) association was found between type-2 diabetic retinopathy and dry eye.

Conclusion: With the development of biomedical research, additional drugs, as well as gene and stem cell therapies, with specific targets will become available for the treatment of DES in diabetes.

Key words: Diabetes Mellitus, Diabetic Retinopathy, Dry Eye Syndrome, Schirmer's Test, Tear Film Breakup Time.

***Correspondence to:**

Dr. Khandaker Khadiza Farhana Ferdaus,
MBBS, MS(Ophthalmology),
Assistant Surgeon,
National Institute of Ophthalmology and Hospital,
Dhaka, Bangladesh.

Article History:

Received: 17-11-2021, **Revised:** 21-12-2021, **Accepted:** 19-01-2022

Access this article online	
Website: www.ijmrp.com	Quick Response code
DOI: 10.21276/ijmrp.2022.8.1.001	

INTRODUCTION

Dry eye syndrome is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance and tears film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface (D.E.W.S., 2007)[1]. Studies have indicated 54% prevalence of asymptomatic and symptomatic DES, in diabetes (Manaviat et al., 2008)[2]. Diabetes mellitus has received widespread attention in that it causes life-

threatening or debilitating complications in heart, kidney, brain, and eye (Smith-Palmer et al., 2014)[3]. In the eye, diabetic retinopathy (DR), cataract, glaucoma, keratopathy, chronic dry eye, and refractive abnormalities are the diseases associated with diabetes (Josifova et al., 2008)[4]. Most cases of dry eye syndrome are thought to be due to an insufficient quantity of the middle aqueous layer, which is normally secreted by a large tear gland (the lacrimal gland). Dry eye can lead to vision deficit, scarring and perforation of the cornea and secondary bacterial infection. If this syndrome is diagnosed at first stage and treated, would be protected from its complications (Riordan-Eva and Whitcher, 2003)[5]. Diabetic retinopathy is predominantly a microangiopathy in which small blood vessels are particularly vulnerable to damage from hyperglycemia. Direct hyperglycemic effects on retinal cells are also likely to play a role (Kanski and Bowling, 2016)[6]. Diabetic retinopathy characterized by exudates, micro aneurysms, and hemorrhages, is the major ocular complication of diabetes (Fong et al., 2004)[7]. DR is also associated with a decrease in tear film function. Tear break-up time (BUT) and Schirmer's test values were significantly decreased in the PDR group (Nepp et al., 2000)[8]. Another hospital-based study showed that DES is more prevalent in individuals with DR and/or clinically significant macular edema and both DES and retinopathy were associated with HbA1c (McKown et al., 2009)[9]. Although DR is one of the major diabetic complications and the leading cause of blindness in the working age population worldwide (Antonetti et al., 2012)[10]. and in Bangladesh prevalence of DR is 21.6% (Lee et al., 2015; Akhter et al., 2013).[11,12]

OBJECTIVES

General Objectives: To investigate clinical characteristics of dry eye syndrome in patients with diabetes mellitus.

Specific Objectives

- To detect dry eye in diabetic retinopathy patients.
- To detect different types of diabetic retinopathy in patients with type -2 diabetes mellitus.
- To explore the relationship of dry eye syndrome with different types of diabetic retinopathy in patients with type -2 diabetes mellitus.

METHODOLOGY

Type of Study: Cross sectional Observational study

Place of Study: Department of Ophthalmology, Bangabandhu Sheikh Mujib Medical University (BSMMU).

Study Period: October 2016 to February 2019.

Study Population: Different types of type-2 diabetic retinopathy Patients of either sex attended in the Department of Ophthalmology, BSMMU.

Sampling Technique: Purposive

Criteria of Study Population: The selection was done on the basis of the following criteria:

Inclusion Criteria

- Both male and female DR patients with DM type-2 wanted to participate in the study.
- Age group = patients of 45years and older had type-2 DM with retinopathy (As adults aged from 45 to 64 years are the most diagnosed age group for type-2 diabetes according to the Centers for Disease Control and Prevention in year 2012).

Exclusion Criteria

- Patients who had undergone ocular surgery in the past.
- Patients who wear contact lens.
- Patients who were on local or systemic medication known to cause dry eye (antihistamines, tricyclic antidepressants, oral contraceptives, hormone replacement therapy and some antihypertensives).
- Patient with other ocular surface disease including meibomian gland dysfunction and systemic disease which known to cause dry eye other than diabetic mellitus. (Allergies, Sjogren's syndrome, Rheumatoid arthritis, Parkinson, Lupus).
- Pregnant women.

Sampling Technique: Purposive sampling technique was applied to collect the sample from the study population**.** The patients, who met the criteria of inclusion, were selected.

Sample Size: In this study around 95 cases were taken because of limited time frame.

Study Procedure and Design: The study was a cross sectional observational study. The study protocol was adhered to the tenets of the Declaration of Helsinki. Population of the study was type-2 diabetic retinopathy patients attending into the department of ophthalmology, Bangabandhu Sheikh Mujib Medical University. Different types of DR patients with DM type-2 of either sex were screened for dry eye over a period of 15 months. The Individual eyes from study population which met the criteria of inclusion were selected.:

Data Collection, Processing and Analysis: The demographic information, relevant history, examination findings, Investigation reports, fundus examination of all the study subjects were recorded in the data collection sheet. After compilation, the data was presented in the form of tables, figures and graphs, as necessary. Statistical analysis of the results was done by using computer-based software, SPSS (SPSS Inc., Chicago, IL, USA). Descriptive statistics: Mean SD, Frequency and Percentage. A probability 'P' value of 0.05 or less was considered as significant.

RESULTS

The purposive sampling technique was applied to collect sample from the study population, as per inclusion and exclusion criteria. Proper history taking, detailed general physical examination and systemic clinical examination was done for all subjects to exclude the presence of collagen vascular or mucocutaneous disorders. Ocular examinations including evaluation of Visual acuity, Eyelids (to look for blepharitis, trichiasis, meibomitis, ectropion, hordeolum etc.), Conjunctiva (to look for congestion, follicles, papillae, tortuosity of vessels, symblepharon etc.), Lacrimal apparatus (position and patency of punctum and further drainage system, tear film tests), Cornea (surface contour, loss of normal lustre, filaments, vascularization, keratic precipitates), Anterior chamber, Posterior segment (fundus examination using direct and indirect ophthalmoscope and slit lamp biomicroscopy using +90D condensing lens after pupillary dilatation) was done. Retinopathy if present was classified as: Non-Proliferative Diabetic Retinopathy (NPDR) = No DR, Very Mild NPDR, Mild- NPDR, Moderate-NPDR, Severe- NPDR, Very Severe NPDR; Proliferative Diabetic Retinopathy = Mild-Moderate PDR, High risk PDR; Advanced Diabetic Eye Disease. Dry eye syndrome was confirmed with Tear film break up time (TBUT), and Schirmer's test.

Table II presents study participants' age in years. Study findings indicate mean (SD) age in years of Dry Eye group is 56.03 (6.63) and No Dry Eye is 51.94 (6.47) years. These findings are statistically significant.

Table III presents study participants HbA1c level. Mean (SD) HbA1c level 8.79 (.60) for Dry Eye group and 8.10 (.89) for No Dry Eye group and this is highly statistically significant.

Table IV shows study participants' Schirmer's test results. These findings are statistically highly significant.

Table I: Study participants background characteristics (n=95)

Sex	
Male	58 (61.1%)
Female	37 (38.9%)
Eye status	
Dry Eye	63 (66.3%)
No Dry Eye	32 (33.7%)
Sex of the Dry Eye	
Dry Eye (Male)	37 (58.7%)
Dry Eye (Female)	26 (41.3%)
Sex of the No Dry Eye	
No Dry (Male)	21 (65.6%)
No Dry Eye (Female)	11 (34.4%)
Current age	
Mean (SD) Current Age in years	54.65 (6.82)
Mean (SD) Current Age in years (Male)	56.17 (7.57)
Mean (SD) Current Age in years (Female)	52.27 (4.60)
Current age of Dry Eye	
Mean (SD) Current Age in years	56.03 (6.63)
Mean (SD) Current Age in years (Male)	57.97 (7.32)
Mean (SD) Current Age in years (Female)	53.27 (4.26)
Current age of No Dry Eye	
Mean (SD) Current Age in years	51.94 (6.47)
Mean (SD) Current Age in years (Male)	53.00 (7.09)
Mean (SD) Current Age in years (Female)	49.91 (4.70)

Table II: Distribution of study participants according to age (n=95)

Current age	Dry Eye		No Dry Eye	
(in years)	#	%	#	%
<50	12	19.0	17	53.1
50-60	36	57.1	12	37.5
>61	15	23.8	3	9.4
Total	**63**	**100.0**	**32**	**100.0**
Mean (SD)	**56.03 (6.63)**		**51.94 (6.47)**	
	p=.002			

Table III: Distribution of study participants HbA1c level (n=95)

HbA1c Level	Dry Eye		No Dry Eye	
	#	%	#	%
<7.50	2	3.2	4	12.5
7.50-8.50	16	25.4	21	65.6
>8.50	45	71.4	7	21.9
Total	**63**	**100.0**	**32**	**100.0**
Mean (SD)	**8.79 (.60)**		**8.10 (.89)**	
	p=.000			

Table IV: Distribution of study participants Schirmer's test findings (n=95)

Findings	Dry Eye		No Dry Eye	
	#	%	#	%
Normal	0	0.0	32	100.0
Mild	11	17.5	0	0.0
Moderate	39	61.9	0	0.0
Severe	13	20.6	0	0.0
Total	**63**	**100.0**	**32**	**100.0**
	p=.000			

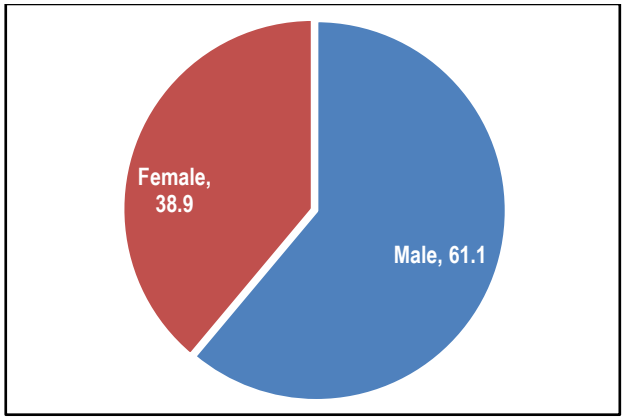

Fig 1: Study participants according to sex

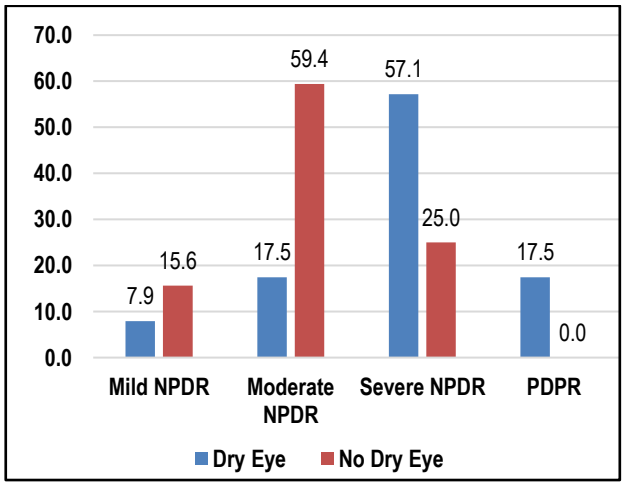

Fig 2: Bar diagram of distribution of study participants Fundus findings/ status

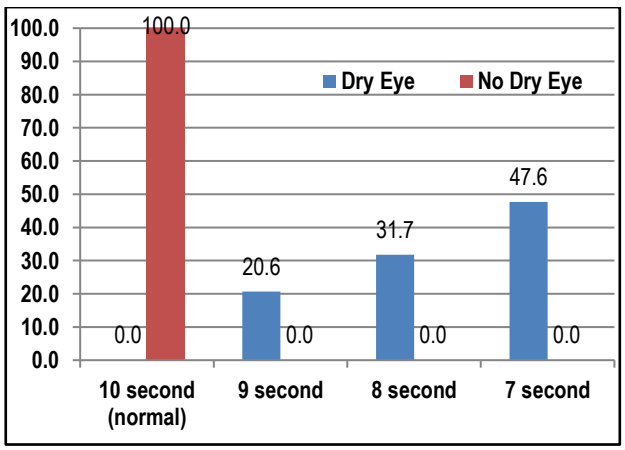

Fig 3: Bar diagram of study participants Tear Film Break up Time status

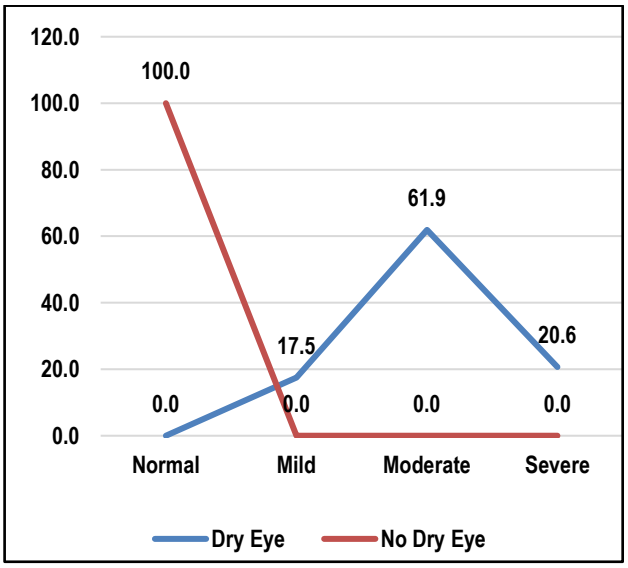

Fig 4: Line chart of study participants Schirmer's test findings

DISCUSSION

Current study analyzed 95 diabetic retinopathy patients with type - 2 diabetes mellitus and found 66.3% of patients had dry eye syndrome and 33.7% patients had no dry eye. Various studies had previously reported increased incidence of dry eye syndrome in diabetic patients. Manaviat et al. in 2008 found that 54.3% of patients with type-2 diabetic retinopathy suffered from dry eye syndrome and which was higher than patients without diabetic retinopathy[2]. A study by Seifart and Strempel in1994 showed that 52.8% of diabetic subjects complained of dry eye symptoms[13]. They concluded that close monitoring of diabetic patients and good blood sugar regulation was important for the prevention of dry eye syndrome and retinopathy. High prevalence of dry eye disorder could be explained by low tear production in DM patients related to dysfunction of the autonomic nervous system[14]. After categorization according to Schirmer's test current study showed that 17.5% patients had mild, 61.9% had moderate and 20.6% patients had severe dry eye.

There were certain aspects of tear physiology change with age, such as tear volume, tear film stability, and reflex secretion by the lacrimal gland. The secretion of tears, decreased significantly with increasing age was observed by Schirmer in 1903. Kaiserman et al. in 2005 have reported that the prevalence of dry eye increased with age[15]. In the beaver dam eye study, the ageing effect was significant after 65 years of age[16]. Current study findings indicated that mean (SD) age of dry eye patients was 56.03 (6.63) year and significant influence was seen in Type-2 patients after 50 years of age. The majority (57.1%) of diabetic retinopathy in Type-2 DM patients in the age group of 50-60 years had dry eye syndrome. Therefore, in the present study, increased of dry eye in age group 50-60 could be because of DM.

In current study, out of 95 diabetic retinopathy patients with type-2 diabetes mellitus 61.1% patients were male and 38.95% patients were female. Among the patients with dry eye syndrome in DR in type-2 DM, 58.7% were male and 41.3% were female which was similar to the finding of a population study done by Lee et al. in 2002 that showed the prevalence of dry eye was 1.4 times higher for men than women[17]. But Moss et al. in 2000 reported a higher incidence (16.7%) of dry eye syndrome in type-2 diabetic women[18]. Higher incidences DES in male in this study could be as female diabetic retinopathy patients using OCP and hormone replacement therapy were ruled out.

Most of the dry eye syndrome patients (71.4%) with type 2 diabetic retinopathy had very poor control of diabetes. This finding was similar to the study done by Chulyoon et al. in 2004 that suggested poor metabolic control, presence of diabetic retinopathy stages were risk factors for tear film and ocular surface disorder in DM[19].

In the current study, TBUT was found to be less than10 second in 66.3% dry eye syndrome patients of which 47.6% patients had 7 second, 31.7% had 8 seconds and 20.6% had 9 seconds of TBUT but normal TBUT in 33.7% no dry eye patients. Devi and Gowda in 2016 showed that TBUT was found to be less than10 second in 65% patients which was similar to current study finding[16]. In Jin study 100 patients with type-2 diabetes were compared with 80 normal healthy controls and TBUT was significantly lower in type 2 diabetic patients[20].

In Goebbels study, Schirmer test and tearing reflex was significantly lower in diabetic patients compared with control group [21]. Jain in 1998 reviewed the cases of 400 patients with dry eyes referred to a tertiary referral center and found that 80 patients (20%) had diabetes, only two (2.5%) of these patients had Sjogren's syndrome, which could account for the dry ocular surface. In all the other patients, no other conditions were found to be a risk factor for dry eye syndrome, and it was therefore presumed to be of diabetic origin. Deterioration of tear film status was found to be significantly associated with severity of diabetic retinopathy by Ozdemir et al. in 2003[22]. Khurana et al. in 2017 showed that the patients with diabetic retinopathy had 6.65 times more chance of having Schirmer's value less than10 mm than those without diabetic retinopathy[23]. Also, patients with diabetic retinopathy had 6.37 times more chance of having TBUT less than10 seconds than those without diabetic retinopathy.

In the present study, 7.9% patients of mild NPDR, 17.5% patients of moderate NPDR, 57.1% patients of severe NPDR and 17.5% patients of PDR had dry eye (Fig 2). In a study by Manaviat et al. in 2008 showed that Dry eye syndrome was more frequent in diabetic patients with DR ($P = 0.02$)[2]. They found 17.1% patients with mild NPDR, 17.1% patients with moderate NPDR, 11.1% patients with severe NPDR and 25.1% patients with PDR which was more than the current study. Najafi et al. in 2013 found in her study that dry eye disease was more prevalent in PDR which was different from current study finding. This could be due to autonomic neuropathy as well as reduced density of corneal nerve fibers with scattered distribution and tortuous axonal trajectory observed by confocal microscopy. In this study, statistically significant relation was found between diabetic retinopathy and dry eye syndrome ($P \leq 0.000$ %).

CONCLUSIONS

DM and dry eyes appear to have common association. Statistically significant correlation was found between dry eye and diabetic retinopathy. In clinical practice, more awareness of chronic pain syndromes might help in understanding the discrepancy between signs and symptoms in dry eye disease. With the development of biomedical research, additional drugs, as well as gene and stem cell therapies, with specific targets will become available for the treatment of DES in diabetes.

REFERENCES

1. D.E.W.S. The definition and classification of dry eye disease: Report of the definition and classification Subcommittee of the international dry eye workshop, The Ocular Surface 2007;5(2): 76.
2. Manaviat, M.R., Rashidi, M., Afkhami-Ardekani, M. and Shoja, M.R. Prevalence of dry eye syndrome and diabetic retinopathy in type 2 diabetic patients. BMC ophthalmology 2008; 8(1):10.
3. Smith-Palmer, J., Brändle, M., Trevisan, R., Federici, M.O., Liabat, S. and Valentine, W. Assessment of the association between glycemic variability and diabetes-related complications in type 1 and type 2 diabetes. Diabetes research and clinical practice 2014; 105(3): 273-84.
4. Josifova, T., Schneider, U., Henrich, PB., Schrader, W. Eye disorders in diabetes: potential drug targets. Infect Disord Drug Targets 2008; 8(2): 70-5.
5. Riordan-Eva, P. and Whitcher, J. eds., 2008. Vaughan & Asbury's general ophthalmology. Lange Medical Books/McGraw-Hill Medical Pub. Division, pp. 308-10.
6. Kanski and bowling. 2016, Knaski's Clinical Ophthalmology: Retinal vascular disease, 8th ed, pp. 522.
7. Fong, D.S., Aiello, L.P., Ferris, F.R., Klein, R. Diabetic retinopathy. Diabetes Care 2004; 27(10): 2540-53.
8. Nepp, J., Abela, C., Polzer, I., Derbolav, A. and Wedrich, A. Is there a correlation between the severity of diabetic retinopathy and keratoconjunctivitis sicca?. Cornea 2000; 19(4): 487-91.
9. McKown, R. L., Wang, N., Raab, R. W. Lacritin and othernew proteins of the lacrimal functional unit, Experimental Eye Research 2009; 88(5): 848–58.
10. Antonetti, D.A., Klein, R., Gardner, T.W. Diabetic retinopathy. N Engl J Med 2012; 366(13): 1227-39.
11. Lee, A.J., Lee, J., Saw, S.M., Gazzard, G., Koh, D., Widjaja, D. Prevalence and risk factors associated with dry eye symptoms: A population-based study in Indonesia 2002; 86(12): 1347-51.
12. Akhter, A., Fatema, K., Ahmed, S. F., Afroz, A., Ali, L., Hussain, A. Prevalence and associated risk indicators of retinopathy in a rural Bangladeshi population with and without diabetes. Ophthalmic Epidemiol 2013; 20(4): 220–7.
13. Seifart, U. and Strempel, I. The dry eye and diabetes mellitus. Der Ophthalmologe: Zeitschrift der Deutschen Ophthalmologischen Gesellschaft 1994; 91(2): 235-9.
14. Ramos-Remus, C., Suarez-Almazor, M. and Russell, A. S. Low tear production in patients with diabetes mellitus is not due to Sjogren's syndrome, Clinical and Experimental Rheumatology 1994; 12(4): 375–380.
15. Kaiserman, I., Kaiserman, N., Nakar, S., Vinker, S. Dry eye in diabetic patients. Am J Ophthalmol 2005; 139: 498-503.
16. Devi, R.S.U., Gowda, M.S.S. Dry Eye in Diabetes Mellitus Patients and its Relationship with Diabetic Retinopathy. Int J Sci Stud 2016; 4(8): 67-72.
17. Lee, R., Wong, T.Y. and Sabanayagam, C. Epidemiology of diabetic retinopathy, diabetic macular edema and related vision loss. Eye and vision 2015; 2(1): 17.
18. Moss, S.E., Klein, R., Klein, B.E. Prevalence of and risk factors for dry eye syndrome. Arch Ophthalmol 2000; 118: 1264-8.
19. Chulyoon, K. Kyuim, S. Seo, M. Changes of Tear Film and Ocular Surface in Diabetes Mellitus 2004; 18(2): 168-174.
20. Jin, J., Chen, L.H., Liu, X.L., Jin, G.S., Lou, S.X., Fang, F.N. Tear film function in non insulin dependent diabetics. Zhonghua Yan Ke Za Zhi 2003; 39: 10-3.
21. Goebbels, M. Tear secretion and tear film function in insulin dependent diabetics. Br. J Ophtalmol 2000; 84: 19-21.
22. Ozdemir, M., Buyukbese, M.A., Cetinkaya, A., Ozdemir, G. Risk factors for ocular surface disorders in patients with diabetes mellitus. Diabetes Res Clin Pract 2003; 59: 195-99.
23. Khurana, G., Khurana, D., Jain, R. Dry Eye in Patients with Diabetic Retinopathy: A Clinical Study. Delhi J Ophthalmol 2017; 27: 190- 3.

Source of Support: Nil.

Conflict of Interest: None Declared.

Cite this article as: Khandaker Khadiza Farhana Ferdaus, Md. Masud Rana, Kamruzzaman, Obidul Hoque. Clinical Characteristics of Dry Eye Syndrome in Patients with Diabetes Mellitus. Int J Med Res Prof. 2022 Jan; 8(1): 001-05.
DOI:10.21276/ijmrp.2022.8.1.001