

Dry Eye Syndrome and Type II Diabetes Mellitus

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ABSTRACT

Diabetic patients seem to have problems with dry eye syndrome. The main aim of this study was to investigate the association between dry eye and diabetes mellitus type II (DM II). Therefore, 55 patients with DM II and aged from 40 and above were compared with a group of normal healthy controls comparable in number, age and sex. A general ophthalmological check-up was performed. The main points of comparison were subjective complaints, objective findings on Schirmer's test and tear break-up time (TBUT). The results show that 69.1% of all diabetic subjects complained of dry eye symptoms as against 61.8% of the controls. Among the asymptomatic diabetic patients, 37.8% had dry eye and only 2% symptomatic had dry eye. Abnormal Schirmer's less than 15 mm was found in 40% of diabetics and 43.6% of the controls. TBUT less than 10 seconds was found in 61.8% of the diabetics and in 70.9% of the non diabetics. This study showed no statistically significant association between dry eye when diabetic participants were compared with normal participants by Schirmer and TBUT ($p = 0.28$ and 0.45) respectively.

Keywords: Dry eye syndrome, diabetes mellitus, Schirmer's test, TBUT

INTRODUCTION

Diabetes Mellitus is one of the leading causes of blindness in old persons. Diabetic retinopathy and cataract are well known ocular complications of diabetes. Recently problems involving the ocular surface, dry eyes have been reported in diabetic patients.¹ Diabetes Mellitus has been identified as a risk factor for dry eye syndrome (DES). DES compromises quality of life because it causes ocular discomfort and visual disturbance and may be complicated by corneal epithelial defects, erosions, ulcers and perforation of the cornea. Therefore, it is recognized as a growing public health problem that should be diagnosed and treated.² Dry eye and diabetes mellitus have a common association. There are several theories that might explain the connection between dry eye and diabetes. The most frequently cited associated factors are:

1. Peripheral neuropathy secondary to hyperglycemia: Hyperglycemia and microvascular damage to the corneal nerves can block the feedback mechanism that controls tear secretion. When the innervation of the ocular surface is disrupted, the lacrimal gland does not secrete tears properly.
2. Insulin insufficiency: Corneal and lacrimal gland metabolism, growth, epithelial cell proliferation, and culture maintenance are influenced by insulin. A low insulin level generally disrupts the biomechanical balance of these tissues and results in ocular dryness

3. Inflammation, hyperglycemia triggers inflammatory alterations and is believed to impair normal events, such as tear secretion.³ Inflammation is not only a cause, but also a consequence of dry eye. Aqueous deficient dry eye or lacrimal insufficiency usually results from lacrimal gland inflammation.

If DES is diagnosed at initial stage and treated, would be protected from its complications. Therefore early diagnosis of dry eye syndrome in diabetic patients is important for starting treatment in early stages so as to prevent from its complications. This study was conducted as no such study has been done earlier in our setting to determine and compare dry eye disease between diabetic and non diabetic population.

MATERIALS AND METHODS

Among diabetic patients, fifty-five patients referred from medicine department to eye outpatient department or inpatient department of Nepal Medical College Teaching Hospital, were consecutively selected from July 2015 to December 2015. Sample size was taken using formula ($Z^2 pq/d^2 = (1.9)^2 \times 14.4(100-14.4)/10^2 = 44$). This was a cross-sectional, comparative and hospital-based study. Fifty-five non diabetic controls (age and sex matched) were selected for comparison. Informed consent was taken from each patient. Ethical clearance was taken from Nepal medical college- Research and Ethical Sub-Committee (NMC-RESC- Ref: 31- 072/073). Clinical data of all patients which included sex, age,

duration of diabetes, treatment modalities were obtained by reviewing the medical records and direct patient interview. All diabetic and non diabetic patients were asked if they had any dry eye symptoms like ocular discomfort, burning sensation, gritty sensation, foreign body sensation and tearing. Patients with history of contact lens, keratorefractive procedures, anterior segment surgery were excluded from the study. DES was confirmed by:

Tear film break-up time (TBUT): Measured with fluorescein stain in the eye to determine tear film stability. The patient was instructed not to blink and the tear film was observed through the slit lamp. If the smooth, stained green tear film layer began developing blue gaps in less than 10 seconds, the patient’s tear film was considered abnormal.

TBUT was graded as follows: ⁴

Value > 10 sec = normal

6 - 10 sec = mild to moderate dry eye

< 5 sec = severe dry eye.

Schirmer’s test I: Assessed by quantifying the number of tears produced by each eye. Small strips of whatman filter paper 42 were placed in the lower eyelids of each eye, without instillation of anesthetic eye drops. Patients were asked to close their eyes for five minutes. Results were measured in millimeters of tears collected after five minute time period. It was graded according to American academy of ophthalmology as follows: ⁵

>15mm after 5min = normal

14-9mm after 5mins = mild dry eye

8-4mm = moderate dry eye

<4mm = severe dry eye

Diagnosis was established by any one or both tests positive. Anterior segment examination was done by slit lamp biomicroscopy. Retinal status was evaluated by +90D lens after dilation by tropicamide drop. Diabetic retinopathy was graded according to Early Treatment Diabetic Retinopathy (ETDRS) criteria.⁶

Data entry and analysis was done using SPSS 20.0 version. The Chi-square test was used to find association between categorical variables. P value less than 0.05 was considered significant.

RESULTS

The mean age was 55.07 years ± 1.11 in diabetic group and was 57.49 years ± 1.11 in non diabetic group. In both groups the minimum age was 40 years and maximum was 82 years. Twenty (36.4%) participants were of 51-60 years, 19 (34.5%) were of 40-50 years, 12 (21.8%) were of 61-70 years, 2 (3.6%) were of 71-80 years and 2 (3.6%) were of 81-90 years in diabetic group. Eighteen (32.7%) were of 51-60 years, 15 (27.3%) were of 40-50

years, 15 (27.3%) were of 61-70 years, 6 (10.9%) were of 71-80 years and 1 (1.8%) were of 81-90 years in non diabetic group (Table-1).

Table 1. Age distribution

Age range in years	Diabetic N (%)	Non diabetic N (%)
40-50	19 (34.5)	15 (27.3)
51-60	20 (36.5)	18 (32.7)
61-70	12 (21.8)	15 (27.3)
71-80	2 (3.6)	6 (10.9)
81-90	2 (3.6)	1 (1.8)
Total	55 (100)	55(100)

Table 2. Sex distribution

Sex	Diabetic N (%)	Non diabetic N (%)
Male	19 (34.5%)	18 (32.7%)
Female	36 (65.5%)	37 (67.3%)
Total	55 (100%)	55 (100%)

There was a statistically significant association between age of diabetic participants and TBUT (p= 0.001) but no association between age and Schirmer test (p= 0.37). In non diabetic group there was a significant association between age and Schirmer test (p= 0.02) but no association between age and TBUT (p= 0.33). Out of 55 diabetic patients, 19 (34.5%) were male and female were 36 (65.5%) and in control group 18 (32.7%) were male and 37 (67.3%) (Table-2). Among diabetic, 8 were male and 13 were female who had dry eyes. There was statistically significant association between gender and dry eye by TBUT (p= 0.01) and no association between gender and dry eye by Schirmer test (p= 0.66). In non diabetic group there was no association between sex and dry eye by Schirmer and TBUT (p= 0.81 and p= 0.36) respectively. About 46 (83.6%) patients presented with 1-10 years of duration of diabetes. Six (10.9%) presented within 11-15 years of duration and only 3 (5.5%) presented with more than 15 years of duration of diabetes (Table: 3 and 4).

Table 3. Grading of dry eye with duration of type 2 diabetes by Schirmer’s test

Duration (in years)	>15mm	14-9mm	8-4mm	<4mm	Total
1-5	15	4	0	4	23
6-10	13	5	5	0	23
11-15	4	2	0	0	6
>15	1	1	0	1	3
Total	33	12	5	5	55

Table 4. Grading of dry eye with duration of type 2 diabetes by TBUT

Duration (in years)	>10sec	6-10sec	< 5sec	Total
1-5	10	12	1	23
6-10	6	12	5	23
11-15	4	2	0	6
>15	1	1	1	3
Total	21	27	7	55

There was no statistically significant association between duration of diabetes and dry eye by Schirmer and TBUT ($p= 0.10$ and $p= 0.28$ respectively). Out of 55 diabetic, 10 (18.2%) were on diet control, 30 (54.5%) patients on oral hyperglycemic drugs and 15 (27.3%) were on both oral hyperglycemic and insulin therapy. All the diabetic patients were on good glycaemic control. There was no association between the type of treatment for diabetes and dry eye disease by schirmer ($p= 0.90$) but showed significant association by TBUT ($p= 0.05$). All the participants were asked if they had one or more of the dry eye symptoms such as grittiness, burning, ocular discomfort, foreign body sensation and tearing. These symptoms were compared with Schirmer's readings. The results show that 69.1% of diabetic subjects complained of dry eye symptoms, as against 61.8% of the controls. Among the various symptoms foreign body sensation and ocular discomfort were the most common complaint (16.4% and 16.4%) respectively followed by burning sensation and tearing (12.7% and 12.7%) respectively. About 10.9% had grittiness. There was no significant association between signs and symptoms in diabetic ($p= 0.26$). In non diabetic group 61.8% had dry eye symptoms. Eleven (20%) had grittiness, 7 (12.7%) had foreign body sensation, 6 (10.9%) had ocular discomfort and burning sensation, 4 (7.3%) had tearing and showed no significant association between signs and symptoms ($p= 0.06$). This reflects the subclinical dry eye patients who later on may come back with one or more of the dry eye symptoms. Mild NPDR was observed in 10.9% of the patients while severe NPDR, PDR and CSME were present in 3.6%, 1.8%, 3.6% respectively. Forty-four patients (80%) didn't show retinopathy. We didn't find a significant association between dry eye and retinopathy by Schirmer's and TBUT ($p= 0.76$ and $p= 0.22$) respectively (Table- 5 and 6).

Table 5. Evaluation of dry eye with diabetic retinopathy by Schirmer's test

	>15mm	14-9mm	8-4mm	<4mm	Total
No retinopathy	26	8	5	5	44
Mild NPDR	4	2	0	0	6
Severe NPDR	1	1	0	0	2
PDR	0	1	0	0	1
CSME	2	0	0	0	2
Total	33	12	5	5	55

Table 6. Evaluation of dry eye with diabetic retinopathy by TBUT

	>10 sec	6-10 sec	<5 sec	Total
No retinopathy	18	21	5	44
Mild NPDR	1	5	0	6
Severe NPDR	1	0	1	2
PDR	0	1	0	1
CSME	1	0	1	2
Total	21	27	7	55

Out of 55 diabetic patients, 33 (60%) had normal Schirmer's test and 22 (40%) had abnormal Schirmer's test. Twelve patients (21.8%) had mild dry eye, 5 patients (9.1%) had moderate dry eye and 5 patients (9.1%) had severe dry eye. Twenty-one (38.2%) had normal TBUT and 34 (61.8%) had abnormal TBUT. Among 34, 27 (49.15%) had TBUT of 6-10sec and 7 patients (12.7%) had < 5 sec. In non diabetic group, 24 (43.6%) had abnormal and 31 (56.4%) had normal Schirmer test, Out of 24 dry eye 13 (23.6%) had mild dry eye, 8 (14.5%) had moderate and 3 (5.5%) had severe dry eye. Sixteen (29.1%) had normal TBUT and 39 (70.9%) had abnormal TBUT in non diabetic group. Out of 39, 28 (50.9%) had TBUT of 6-10 sec and 11 (20%) had < 5 sec. Abnormal Schirmer's less than 15mm was found in 40% of diabetics and 43.6% of the controls. TBUT less than 10sec was found in 61.8% of the diabetics and in 70.9% of the non diabetics. This study showed no statistically significant association between dry eye when diabetic participants were compared with normal participants by Schirmer's and TBUT ($p= 0.28$ and 0.45) respectively (Table-7 and 8).

Table 7. Frequency and percentage of dry eye in diabetic and non diabetic by Schirmer's test

	≥ 15 mm	14- 9mm	8-4mm	<4mm	Total
Diabetic	33 (60%)	12 (21.85)	5 (9.1%)	5 (9.1%)	55
Non - diabetic	31 (56.4%)	13 (23.6%)	8 (14.5%)	3 (5.5%)	55

Table 8. Frequency and percentage of dry eye in diabetic and non diabetic by TBUT

	> 10sec	6-10sec	<5sec	Total
Diabetic	21 (38.2%)	27 (49.1%)	7 (12.7%)	55
Non Diabetic	16 (29.1%)	28 (50.9%)	11 (20%)	55

DISCUSSION

Dry eye is a disorder of tear film because of tear deficiency or excessive tear evaporation which causes damage to the inter palpal ocular surface and is associated with symptoms of ocular discomfort. In our study all the participants were asked if they had one or more of the dry eye symptoms such as grittiness, burning, ocular discomfort, foreign body sensation and tearing. These symptoms were compared with Schirmer's reading. The results showed that 69.1% of diabetic subjects complained of dry eye symptoms, as against 61.8% of the controls. There was no significant association between signs and symptoms in diabetic as well as in non diabetic group ($p= 0.26$ and $p= 0.06$) respectively. So, dry eye evaluation should be a routine test in diabetic patients for early diagnosis. A study by Shah S *et al* found that asymptomatic patients or patients with very few symptoms had dry eyes. They found the prevalence of dry eye to be 24.1% in asymptomatic patients. ⁷Nichols *et al* also reported this problem, where there was a lack of correlation between signs and symptoms of dry eye. ⁸This probably varies with patients' awareness and sensitivity toward the symptoms.

In our study, out of 55 diabetic patients, male were 19 (34.5%) and female were 36 (65.5%). Among them 8 were male and 13 were female who had dry eye (Table-2). There was a statistically significant association between gender and dry eye by TBUT ($p= 0.01$) and no association between gender and dry eye by Schirmer test ($p= 0.66$). In non diabetic group out of 18 (32.7%) male, 7 had dry eye and out of 37 (67.3%) female, 15 had dry eye. There was no association between sex and dry eye by Schirmer and TBUT ($p= 0.81$ and $p= 0.36$) respectively. In a study, Manaviat showed that there was no significant association between gender and frequency of dry eye syndrome ($p = 0.2$).²In a study by V Tanushree *et al*, out of 100 diabetic patients, 54% were male and 46% were female which showed no significant correlation between gender and frequency of dry eye ($p= 0.42$).⁹But in a study by Moss SE *et al* showed that incidence was greater in women (25%) than men (17.2%) which was statistically significant ($p< 0.001$).¹⁰In this study, the mean age was 55.07 years \pm 1.11 in diabetic group and was 57.49 years \pm 1.11 in non diabetic group. Out of 55 diabetic, 36.4% were of the age group 51-60 year which was the highest and 7.2% were of 71-90 age

groups which were the lowest. Eighteen (32.7%) were of 51-60 years and 1 (1.8%) were of 81-90 years in non diabetic group (Table- 1). Our study showed that there was a significant association between age and dry eye by TBUT ($p = .001$) but no association between age and dry eye by Schirmer test ($p= 0.37$). In non diabetic group there was a significant association between age and Schirmer test ($p= 0.02$) but no association between age and TBUT ($p= 0.33$). Dry eye is more common among individuals who were above the age of 45 years as the tear film evaporation is significantly higher in elderly population according to study by Guillon *et al*.¹¹ An intact and efficient lipid layer in the tear film is required to prevent the evaporative loss of tear film. This lipid layer is thinner and less efficient in older subjects and particularly females. But in a study by Manaviat MR showed no significant association between age and dry eye syndrome ($p= 0.9$).²

About 46 (83.6%) patients presented with 1-10 years of duration of diabetes. Six (10.9%) presented within 11-15 years of duration and only 3 (5.5%) presented with more than 15 years of duration of diabetes (Table- 3 and 4). There was no statistically significant association between duration of diabetes and dry eye by Schirmer and TBUT test ($p= 0.10$ and $p= 0.28$ respectively). Similarly no significant association was found between duration of diabetes and dry eye syndrome in a study by Najafi L *et al*.¹² However in a study by Manaviat MR showed significant association between dry eye syndrome and duration of diabetes ($P = 0.01$).² The development of retinopathy is associated with poor glycaemic control and longer duration of diabetes.¹³ In our study all diabetic patients were on good glycaemic control and most of them presented in less than 10 years of duration. So, only 11 patients (20%) showed retinopathy out of 55 diabetic patients. We didn't find a significant correlation between dry eye and retinopathy by Schirmer's and TBUT ($p= 0.76$ and $p= 0.22$) respectively. Najafi L stated that dry eye disease is common in people with type 2 diabetes, especially in those with diabetic retinopathy ($p=0.01$).¹² Similarly Manaviat MR study also showed dry eye was more frequent in diabetic patient with retinopathy ($p=0.02$).² In our study, 22 (40%) of diabetic participants had abnormal schirmer test and 43.6% of the control group had abnormal schirmer test. Abnormal TBUT less than 10 sec was found in 61.8% of the diabetics and in 70.9% of the control (Table- 7 and 8). This study showed no significant correlation between dry eye and diabetics when compared with normal controls by Schirmer and TBUT ($p= 0.28$ and 0.45) respectively. In Jin study, 100 patients with type II diabetes were compared with 80 normal healthy controls which showed TBUT was significantly lower in type 2 diabetic patients.¹⁴ In Goebel's study, Schirmer test and tearing reflex was

significantly lower in diabetic patients compared with control group.¹⁵ In a study by U Seifart TBUT value lower than 10 sec ONDS was found in 94.2% of the type I and II diabetics and in only 5.8% of the controls. Among the type II diabetic patients, 70% had proven dry eye syndrome while 57% with type I diabetes suffered from dry eye.¹⁶ In a study by Shah S found a prevalence of 67% dry eye among the diabetic patients.⁷ Eight nine (79.29%) patients was positive to Schirmer test less than 10 mm, positive TBUT test less than 9 sec was found to be the amount of 71 (69.37%) patients in a study by Burda N.¹⁷ According to Aljarousha M, TBUT was significantly different between diabetics and non-diabetics ($p < 0.001$) and between diabetics with and without dry eye ($p = 0.046$).¹⁸ In a study by Kaiserman et al, significantly higher percentage of diabetic patients (20.6%) received ocular lubrication compared with non-diabetic patients (13.8%).¹⁹ Similar to our study, Rahman A et al showed among diabetic patients, Schirmer's test was positive in fifty six (60.86%) eyes and tear film break up time test was positive in fifty eyes (54.34%). Among non diabetic patients, Schirmer's test was positive in thirty eyes (68.18%) and tear film break up time test was positive in twenty four eyes (54.54%) where there was not much different between two groups.²⁰

There was not much difference in schirmer test and TBUT between diabetic and non-diabetic subjects. Female gender and increasing age were associated with dry patients in diabetic patients. Neither the duration of diabetes nor stage of retinopathy is associated with tear film dysfunction. In contrast to previous research, there was no significant association between dry eyes among diabetic patients when compared with non diabetics.

ACKNOWLEDGEMENT

We would like to thank Mr P.P Panta for his statistical guidance and our residents for data collection.

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