

## A Hospital Based Prospective Clinical Study to Correlate the Dry Eye and Diabetic Retinopathy with Duration of Diabetes and Blood Urea and Serum Creatinine Level

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### Abstract

**Aim:** The aim of the present study was to correlate the dry eye and diabetic retinopathy with duration of diabetes and blood urea and serum creatinine level.

**Material & Methods:** A prospective clinical observational study was conducted in department of Ophthalmology for a period of one and half years. A written consent was obtained from the patients before subjecting them for detailed clinical examination. 100 cases of only type 2 diabetes mellitus patients who reported to eye OPD through referral from diabetology OPD and ward, medicine OPD and ward for routine diabetes eye screening were examined.

**Results:** Among 100 patients studied, 65 patients were females and 35 patients were males. The patients diagnosed with diabetes less than 1 year duration were 5%. Majority of population were between 1 to 5 years duration i.e., 60%. 64% had no dry eye symptoms and 36% had dry eye symptoms. 26% of patients had FBS less than 110mg/dl. 74% had FBS more than 110mg/dl. 25 patients had PPBS less than 160 mg/dl. 75 patients had PPBS more than 160 mg/dl. 85 patients had urea level less than 40 mg /dl. 15 patients had urea level more than 40 mg. 90 patients had Creatinine level less than 1 mg/dl. 10 patients had Creatinine more than 1 mg/dl. 30 Schirmer test positive patients, 8 patients had 1 to 5 years of diabetes. 10 of them were 6 to 10 years of diabetes. 8 of them were 11 to 20 years of diabetes. The P value of above comparison was significant. 25 TBUT test positive patients, 4 of them were in 1 to 5 years duration of diabetes, 16 of the were in 6 to 10 years duration and 5 of them were in 11 to 20 years duration of diabetes.

**Conclusion:** There was statistically significant positive correlation between the dry eye and duration of diabetes and severity of retinopathy. Hence, all the diabetic patients should be evaluated and screened at the earliest for retinopathy changes and presence of ocular surface disorders and treated accordingly. Early treatment would prevent complications associated with ocular surface disorders and diabetic retinopathy. They should be emphasized upon on need for regular follow up and maintaining a good glycemic control.

**Keywords:** Dry eye, Diabetes, Diabetic retinopathy, Schirmer test

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### Introduction

Diabetes mellitus is a metabolic disorder characterized by chronic hyperglycemia associated with disturbances of carbohydrate, protein and fat metabolism due to absolute or relative deficiency in insulin action and or secretion. Diabetes is the leading cause of blindness in twenty-to-seventy-four-year age group. [1] Dry eye is the most common problem encountered in patients with diabetes mellitus. [2] Dry eye is defined according to Dry eye workshop (DEWS) Definition (2007) as a multifactorial disease of the tear film and ocular surface resulting in symptoms of visual disturbance, discomfort, tear film instability,

increased osmolarity of tear film and ocular surface inflammation. [3]

The exact mechanism for cause of dry eye in diabetes is not known. [4] Autonomic dysfunction plays a role in causing dry eye. Aldose reductase enzyme which converts glucose to sorbitol also plays a role. [5] Jin et al found that diabetes mellitus type 2 patients are prone to develop dysfunction of tear film. The reduced corneal sensitivity favors the occurrence of dry eye syndrome (DES) by reducing the blink rate, by decreasing the reflex-induced lacrimal secretion and increasing evaporative tear loss. [6]

Hyperglycemia and microvascular damage to the corneal nerves can block the feedback mechanism which controls secretion of tears. The higher the HbA1c values, the higher the rate of dry eye syndrome. [7] When the ocular surface innervation is disrupted; tears are not secreted properly by the lacrimal gland. Hyperglycemia triggers inflammatory alterations, thus reducing tear secretion. Inflammation is not only a cause, but also a consequence of dry eye. Inflammation results in aqueous deficient dry eye or lacrimal insufficiency. [8] The dry eye disease in diabetes mellitus is 15-33%.

Globally, an estimate of 422 million adults are living with diabetes mellitus in 2014 compared to 108 million in 1980 according to the latest 2016 data from the WHO. [9] So lacrimal gland does not secrete tears. [10] 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. [11] Therefore early diagnosis of dry eye syndrome in diabetic patients is important for beginning of treatment in early stages. Increased duration influence the occurrence of DR and its severity was due to prolonged exposure to hyperglycemia. Duration of diabetes is an independent risk factor. The duration of diabetes is an important predictor of DR and its severity. [12] Nevertheless studies to evaluate the prevalence of dry eye syndrome in type 2 diabetic patients are lacking.

Hence the aim was to correlate the dry eye and diabetic retinopathy with duration of diabetes and blood urea and serum creatinine level and to evaluate the risk factors attributed to dry eye and diabetic retinopathy in diabetes mellitus patients and also to study the prevalence of dry eye and diabetic retinopathy in diabetes mellitus patients.

### Material & Methods

A prospective clinical observational study was conducted in department of Ophthalmology, Nalanda Medical College and Hospital, Patna, Bihar, India for a period of one and half years. A written consent was obtained from the patients before subjecting them for detailed clinical examination. 100 cases of only type 2 diabetes mellitus patients who reported to eye OPD through referral from diabetology OPD and ward, medicine OPD and ward for routine diabetes eye screening were examined. These patients were already on oral antidiabetic drugs, insulin or both combined therapy.

### Inclusion Criteria

In this study, both male and female of age group between 35 to 85 years were included. All individuals were only under type 2 diabetes mellitus.

### Exclusion Criteria

The type 2 diabetic patients associated with contact lens wear, long-standing tricyclic antidepressants, beta blockers, antihistaminics. Other causes of dry eye syndrome like rheumatoid arthritis, HIV positive individuals, recent ocular surgeries, lupus, Parkinson disease, ocular cicatrice pemphigoid, Steven Johnson syndrome, keratoconjunctivitis sicca, drugs intake like antipsychiatric drug, beta-blockers, diuretics, antihistaminics, tricyclic antidepressant, post LASIK surgery, meibomian gland dysfunction, pregnancy, vitamin A deficiency, corneal oedema, contact lens wearers, viral keratitis, Hansen, glaucoma individuals were excluded from our study. Type 1 diabetes mellitus cases were also excluded from our study.

### Methodology

Data of all the patients including age, sex, BMI, duration of diabetes, drug history like whether on oral antidiabetic drugs, insulin or both drugs, history of other associated conditions like hypertension, chronic kidney disease, hyperlipidaemia were obtained by reviewing the medical records and direct patient interview. The eye complaint like ocular discomfort, gritty sensation, itching, redness, blurring of vision, which improves with blinking, burning sensation were recorded apart from defective vision. Visual acuity examination by Snellen chart distance and near vision examination, cycloplegic refraction, slit lamp examination, intraocular pressure assessment by applanation tonometer, fundus examination by direct and indirect ophthalmoscope, angle of anterior chamber assessment by Goldmann three mirror gonioscopy, tear breakup time, Schirmer's test I, corneal sensitivity test, blood investigation like fasting and postprandial blood sugar, Hb1AC, blood urea and serum creatinine and blood pressure recording were done in all the individuals.

### Statistical Analysis

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS version 12.0, Chicago IL). Chi square test and t- student test was used to compare discrete variables. Significance was considered to be  $P < 0.05$ . Results were given with their 95% CIs. Data were presented as means  $\pm$  SD.

### Results

**Table 1: Demographic data**

<b>Gender</b>	<b>N%</b>
Male	35 (35)
Female	65 (65)
<b>Duration range</b>	
Less than 1 year	5 (5)
1 to 5 years	60 (60)
6 to 10 years	25 (25)
11 to 20 years	10 (10)
<b>Prevalence of dry eye symptoms</b>	
Absent	64 (64)
Present	36 (36)

Among 100 patients studied, 65 patients were females and 35 patients were males. The patients diagnosed with diabetes less than 1 year duration were 5%. Majority of population were between 1 to 5 years duration i.e., 60%. 64% had no dry eye symptoms and 36% had dry eye symptoms.

**Table 2: Fasting and post prandial blood sugar range**

<b>Fasting blood sugar</b>	<b>N%</b>
FBS < 110	26 (26)
FBS > 110	74 (74)
<b>Post prandial blood sugar</b>	
Up to 160	25 (25)
Above 160	75 (75)

26% of patients had FBS less than 110mg/dl. 74% had FBS more than 110mg/dl. 25 patients had PPBS less than 160 mg/dl. 75 patients had PPBS more than 160 mg/dl.

**Table 3: Blood Urea and Serum Creatinine Range**

<b>Blood Urea</b>	<b>N%</b>
Upto 40 mg /dl	85 (85)
>40 mg /dl	15 (15)
<b>Serum Creatinine</b>	
Upto 1 mg /dl	90 (90)
>1 mg /dl	10 (10)

85 patients had urea level less than 40 mg /dl. 15 patients had urea level more than 40 mg. 90 patients had Creatinine level less than 1 mg/dl. 10 patients had Creatinine more than 1 mg/dl.

**Table 4: Schirmer Test and Duration of Diabetes**

<b>Schirmer Test</b>	<b>Less than 1 year</b>	<b>1 to 5 years</b>	<b>6 to 10 years</b>	<b>11 to 20 years</b>
Positive	0	8	10	8
Negative	5	52	15	2
Total	5	60	25	10

30 Schirmer test positive patients, 8 patients had 1 to 5 years of diabetes. 10 of them were 6 to 10 years of diabetes. 8 of them were 11 to 20 years of diabetes. The P value of above comparison was significant.

**Table 5: TBUT and Duration Of Diabetes Mellitus**

<b>TBUT</b>	<b>Less than 1 year</b>	<b>1 to 5 years</b>	<b>6 to 10 years</b>	<b>11 to 20 years</b>
Positive	0	4	16	5
Negative	5	56	9	5
Total	5	60	25	10

25 TBUT test positive patients, 4 of them were in 1 to 5 years duration of diabetes, 16 of the were in 6 to 10 years duration and 5 of them were in 11 to 20 years duration of diabetes.

**Discussion**

Dry eye is defined according to Dry eye workshop (DEWS) Definition (2007) as a multifactorial disease of the tear film and ocular surface resulting in symptoms of visual disturbance, discomfort, tear

film instability, increased osmolarity of tear film and ocular surface inflammation. [13] The reduced corneal sensitivity favors the occurrence of dry eye syndrome (DES) by reducing the blink rate, by decreasing the reflex-induced lacrimal secretion and increasing evaporative tear loss. [14] Many theories explain the connection between dry eye and diabetes. Hyperglycemia and microvascular damage to the corneal nerves can block the feedback mechanism which controls secretion of tears. When the ocular surface innervation is

disrupted; tears are not secreted properly by the lacrimal gland. Hyperglycemia triggers inflammatory alterations, thus reducing tear secretion. Inflammation is not only a cause, but also a consequence of dry eye. Inflammation results in aqueous deficient dry eye or lacrimal insufficiency. [8]

Among 100 patients studied, 65 patients were females and 35 patients were males. The patients diagnosed with diabetes less than 1 year duration were 5%. Majority of population were between 1 to 5 years duration i.e., 60%. 64% had no dry eye symptoms and 36% had dry eye symptoms. In a study by Manaviat et al, prevalence of dry eye syndrome in diabetics was 54.3%. Significant association was noted between dry eye syndrome and duration of diabetes and was more frequent in diabetics with DR. [15] In a study by Pradeep et al, prevalence of dry eye was 32% among type 2 diabetics and showed the prevalence being high in older age groups and with >10 years of duration of diabetes mellitus. [16] The reduced corneal sensitivity in diabetic patients is believed to be a symptom of generalised polyneuropathy that occurs in these patients. [17] Corneal complications of diabetes including superficial punctate keratitis, persistent epithelial defects and corneal endothelial damage have been linked to tear secretion abnormality, decreased corneal sensitivity and poor adhesion between epithelial cells and their basement membrane. [18] Reduced corneal sensitivity is related to the severity of their diabetes, patients with this symptoms were reported to exhibit more severe retinopathy and to have a longer disease duration. [19] Reduced corneal sensitivity contributes to dry eye, as described earlier, it also predisposes patients to corneal trauma leads to greater risk of developing trophic corneal ulcers [20] and adversely affects corneal wound healing. [21]

26% of patients had FBS less than 110mg/dl. 74% had FBS more than 110mg/dl. 25 patients had PPBS less than 160 mg/dl. 75 patients had PPBS more than 160 mg/dl. 85 patients had urea level less than 40 mg /dl. 15 patients had urea level more than 40 mg. 90 patients had Creatinine level less than 1 mg/dl. 10 patients had Creatinine more than 1 mg/dl. 30 Schirmer test positive patients, 8 patients had 1 to 5 years of diabetes. 10 of them were 6 to 10 years of diabetes. 8 of them were 11 to 20 years of diabetes. The P value of above comparison was significant. 25 TBUT test positive patients, 4 of them were in 1 to 5 years duration of diabetes, 16 of the were in 6 to 10 years duration and 5 of them were in 11 to 20 years duration of diabetes. Corneal neuropathy and microvascular complications associated with diabetes could significantly decrease the tear film function and corneal sensitivity. Tear film changes in diabetic

patients after cataract surgery remains largely unexplored.

### Conclusion

There was statistically significant positive correlation between the dry eye and duration of diabetes and severity of retinopathy. Hence, all the diabetic patients should be evaluated and screened at the earliest for retinopathy changes and presence of ocular surface disorders and treated accordingly. Early treatment would prevent complications associated with ocular surface disorders and diabetic retinopathy. They should be emphasized upon on need for regular follow up and maintaining a good glycemic control.

### References

1. Harrison TR: Diabetes Mellitus. In Harrison Principle of Internal Medicine. 15th edition.
2. Cousen P, Cackett P, Bennett H, et al. Tear production and corneal sensitivity in diabetes. *J Diabetes Complications*. 2007 Nov-Dec; 21(6):371-3.
3. Definition DE. Classification Subcommittee. The definition and classification of dry eye disease: report of the Definition and Classification Subcommittee of the International Dry Eye WorkShop. *Ocul Surf*. 2007; 5:75-92.
4. Scultz RO, Horn DLV, Peters MA, Klewin KM, Schutten WH: Diabetic keratopathy. *Trans A Ophthalmol Soc* 1981, 79:180
5. Fujishima H, Shimazaki J, Yagi Y, Tsubota K. Improvement of corneal sensation and tear dynamics in diabetic patients by oral aldose reductase inhibitor, ONO-2235: a preliminary study. *Cornea*. 1996 Jul 1;15(4):368-75.
6. Achtsidis V, Eleftheriadou I, Kozanidou E, Voumvourakis KI, Stamboulis E, Theodosiadis PG, Tentolouris N. Dry eye syndrome in subjects with diabetes and association with neuropathy. *Diabetes care*. 2014 Oct 1;37(10): e210-1.
7. Seifart U, Stempel I: The dry eye syndrome and diabetes mellitus. *Ophthalmologie* 1994, 91(2):235-239.
8. Alves MD, Carvalheira JB, Módulo CM, Rocha EM. Tear film and ocular surface changes in diabetes mellitus. *Arquivos brasileiros de oftalmologia*. 2008; 71:96-103.
9. Global report of diabetes. Geneva: World Health Organization 2016.
10. Chous P. Dry eyes and diabetes often go hand in hand.
11. Riordan-Eva, Asbury T, Whitcher JP: Vaughan and Asbury's General Ophthalmology. 16th edition. USA, McGraw-Hill Medical; 2003: 308-310.
12. Bamashmus MA, Gunaid AA, Khandekar RB: Diabetic retinopathy, visual impairment and

- ocular status among patients with diabetes mellitus in Yemen: a hospital-based study. *Indian J Ophthalmol* 2009, 57:293-298.
13. International Dry Eye Workshop Subcommittee. The definition and classification of dry eye disease: report of the definition and classification subcommittee of the International Dry Eye Workshop (DEWS - 2007). *Ocul Surf* 2007; 5:75-92.
  14. Achtsidis V, Eleftheriadou L, Kozanidou E, Voumvourakis K.I., Stamboulis E, Theodosiadis P.G., Tentolouris N. Dry Eye Syndrome in Subjects with Diabetes and Association with Neuropathy. *Diabetes Care* 2014;37(10):e210–e211.
  15. Manaviat MR, Rashidi M, Afkhami-Ardekani M, Shoja MR. Prevalence of dry eye syndrome and diabetic retinopathy in type 2 diabetic patients. *BMC ophthalmology*. 2008 Dec; 8:1-5.
  16. Pakalapati P, Sharmila AG, Nalinodbhavi B. Clinical association between Dry eye and diabetes mellitus. *Indian Journal of Applied Research*. 2015;5(6):474-8.
  17. Fujishima H, Shimazaki J, Yagi Y, et al. Improvement of corneal sensation and tear dynamics in diabetic patients by oral aldose reductase inhibitor ONI-2235: a preliminary study. *Cornea* 1996;15(4):368-375.
  18. Ramos-Remus C, Suarez-Almazor M, Russell AS. Low tear production in patients with diabetes mellitus is not due to Sjogren's syndrome. *Clin Exp Rheumatol* 1994;12(4): 375-380.
  19. Schultz RO, Matsuda M, Yee RW, et al. Corneal endothelial changes in type I and type II diabetes mellitus. *Am J Ophthalmol* 1984; 98(4):401-410.
  20. Schultz RO, Peters MA, Sobocinski K, et al. Diabetic keratopathy as a manifestation of peripheral neuropathy. *Am J Ophthalmol* 1983 ;96(3):368-371.
  21. Schwartz DE. Corneal sensitivity in diabetics. *Arch Ophthalmol* 1974;91(3)174-178.