Ocular Surface Disorders in Type 2 Diabetes Mellitus

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ABSTRACT

Introduction: The Global Burden of diabetes has shown a a significant rise in recent years as estimated by the International Diabetes Federation (IDF). Study aimed to assess the ocular surface disorders in type 2 Diabetes mellitus patients.

Material and methods: In an observational cross sectional study, standardized enrolment criteria were employed, and 182 patients with Type 2 Diabetes Mellitus were selected with duration of diabetes more than 5 years of age. Standardized methods were used to evaluate the Ocular surface damage and Dry eye disease. Clinical tests such as Schirmer's Test, Tear Film breakup Time(TBUT), Tear Meniscus Height Test, Blink Rate Fluorescein staining and Lissamine green Staining were used to diagnose the Dry eye and Ocular surface disorders.

Results: Abnormal Tear film Breakup time was seen in 51% patients, Abnormal Schirmer's test were observed in 61% patients, Abnormal Tear Meniscus height was seen in 45.6% patients. 45.6% patients were diagnosed top have Dry eye disease, and had a positive co-relation with Duration of Diabetes(P=0.01), Diabetic Control(P=0.002) and with Diabetic Retinopathy(P=0.031).

Conclusion: Ocular Surface disorders and dry eye are seen in 45% of patients and are related to factors such as Age of Diabetes and Glycaemic Control of Diabetes.

Keywords: Diabetes Mellitus, Dry Eye, Ocular Surface Disorders.

INTRODUCTION

India has the 2nd largest population of Diabetics in the world after China.[1] Diabetic Retinopathy and Cataract are well known and most researched manifestation of Diabetes, but in recent years there is a well-recognised relationship between Diabetes and Ocular surface disorders.[2]

The alterations described in the tear film and ocular surface of diabetic patients are due to 3 mechanisms a) chronic hyperglycaemia, b) corneal nerve damage and c) impairment on insulin action. These events contribute to tissue injury and may create an environment for inflammation, as a non-specific response that increases and perpetuates the tissue injury. The progressive peripheral neural damage is an example of afferent and efferent neural signaling pathway, that once damaged, as in neurotrophic keratitis interrupts the anti-inflammatory neural feedback.[3,4,5]

The reported percentage of Ocular surface disorders and dry eye have been around 54%.[6] Some other reports report a low prevalence of around 20% in type 2 Diabetic patients.[7]

The purpose of the study was to assess the relationship between Ocular surface damage and dry eye with Diabetes, and its correlation with factors such as Duration of Diabetes and Glycaemic control.

MATERIAL AND METHODS

The Study was a Hospital based Observational Cross sectional study. It included all the Type 2 Diabetic patients with Duration of Diabetes more than 5 years. Study was done between October 2016 to May 2018.

All Type 1 Diabetic subjects, Subjects with congenital lacrimal dysfunction, on any drug treatment, Topical (Betaxolol, Olapatidine, Naphazoline, Miotics or Mydriatics, Ketorolac) or Systemic (Beta blockers anti-hypertensives, anti-histaminics, Anti-psycotics) which produce dry eye, subjects under gone any ocular surgery (Cataract, Refractive surgery, pterygium excision) or Cosmetic Surgery, subjects with any other ocular disorder known to produce dry eye (Allergic eye disease, Vit A deficiency, Post Steven Johnsons, Vernal keratoconjuctivitis, Post ocular chemical burns and with any systemic diseases associated with dry eye other than diabetes mellitus (RA, SLE, CVD, Thyroid disordes) were excluded from the study.

A detailed Medical History and past history were taken. All patients were subjected to a comprehensive ocular examination, which included Visual Acuity, Slit-Lamp Examination and Fundus Examination.

Fundus Examination was performed by an Indirect Ophthalmoscopy with a 20 D And on Slit lamp bio microscope with a 90 D lens.

Tear function was evaluated by Schirmer's test 1, Tear Film Breakup time and Tear Meniscus Height test. Ocular Surface staining was performed by Fluorescein test and Lissamine Green test.

Dry eye was diagnosed if Schirmer's Test 1 values were less than 10 mm, Tear film Break up time was less than 10 seconds and Tear meniscus height was less than 0.25mm

Dry Eye was graded under Mild Moderate and severe according to the DEWS Dry Eye Severity Grading System[8] under following

Mild Dry Eye: Schirmer's Test 1 ≤ 10 mm, TBUT ≤ 10 seconds, Tear Meniscus height <0.25 mm

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Moderate Dry Eye: Schirmer's Test 1 ≤ 5 mm, TBUT ≤ 5 seconds, Tear Meniscus height <0.25 or absent.

Severe Dry Eye: Schirmer's Test 1 ≤ 2 mm, TBUT ≤ Immediate, Tear Meniscus height <0.25 mm or absent.

Ocular surface Disease index (OSDI)[9] scoring was taken up for each patient and the mean OSDI cores were taken out for each group of Mild moderate and severe dry eye.

Ocular surface staining was undertaken by Fluorescein staining and Lissamine green staining.

Blood sugar levels both Fasting and Post prandial were recorded of each patient on presentation. HbA1c was measured using the ion exchange high-performance liquid chromatography mono S column method by Drew Hb Gold Analyser System.

The Glycaemic control was assessed by HbA1c values> 6.5 were considered to be abnormal.

Diabetic Retinopathy was graded by ETDRS(Early Treatment of Diabetic Retinopathy Study) Classification.[10]

All the patients who experienced symptoms were treated with appropriate Lubricating Eye drops and if confluent staining of ocular surface was present, Antibiotics eye drops and Eye Ointment were started.

STATISTICAL ANALYSIS

The Data collected from the patients were coded and tabulated. All data analysis had been done by using SPSS (version 22) for windows. The initial measures of each group were compared with the final measures of the study period and compared between the groups by using student t test and chi square test.

RESULTS

Out of 182 total subjects included in the study, 148 were more than 50 years of age. Subjects were grouped according to the duration of the diabetes, 30 subjects (16.5%) out of 182 had duration of diabetes between 5-8 years, 21(11.5%) had duration of diabetes between 9-11 years, 73(40%) had duration of diabetes between 12-15 years, and rest 58(32%) had duration of diabetes more than 15 years of age.

According to the duration of diabetes, 8 out of 30 patients (26.6%) with duration of diabetes 5-8 years were diagnosed with dry eye, 8 out of 21 patients (36.3%) between 9-11 years of diabetes had Dry Eye, 32 out of 73 patients(44%) between 12-15 years of diabetes had dry eye, and 35 out of 58(60.3%) with duration of diabetes more than 15 years of age had diabetes. ($P = 0.01$) [Table 1], [Figure 1]

Dry Eye was diagnosed by the tests for tear function, as

Duration of Diabetes	No Dry Eye	Dry Eye (%)	Mild Dry Eye	Moderate Dry Eye	Severe Dry Eye
5-8 years	22	8(26.66%)	06	02	00
9-11 Years	13	8(36.36%)	04	03	01
12-15 years	41	32(43.83%)	16	10	06
>15 Years	23	35(60.34%)	14	11	10
Total	99	83	40	26	17

Table-1: Association of dry eye with duration of diabetes

Dry eye status	No. of Patients	Percentage
No dry eye	99	36.81
Mild	40	30.77
Moderate	26	19.23
Severe	17	13.19
Total	182	100

Table-2: Distribution of patients according to incidence of dry eye

Dry Eye Status	Number of Patients	Mean OSDI Score
No dry Eye	99	7.2 ± 2.6
Mild Dry Eye	40	16 ± 3.4
Moderate Dry Eye	26	27 ± 3.8
Severe Dry eye	17	53.7 ± 16.15

Table-3: Ocular surface disease index score

Severity of Diabetic retinopathy	Total subjects	No Dry Eye	Dry Eye	Mild Dry Eye	Moderate Dry Eye	Severe Dry Eye
No DR	36	26	10	8	2	0
Mild NPDR	38	24	14	9	4	1
Moderate NPDR	66	32	34	16	11	7
Severe NPDR	32	14	18	6	7	5
PDR	10	3	7	1	2	4
Total	182	99	83	40	26	17

Table-4: Association of Dry Eye with Severity of Diabetic Retinopathy

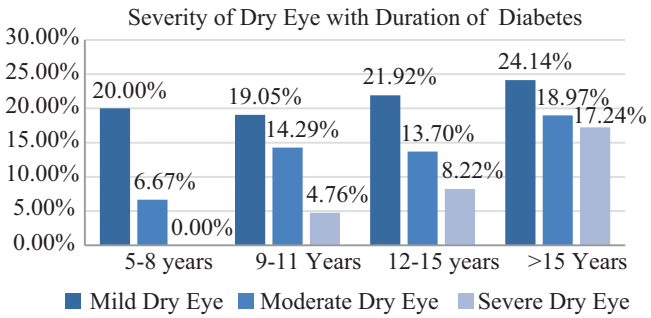

Figure-1: Severity of dry eye with duration of diabetes

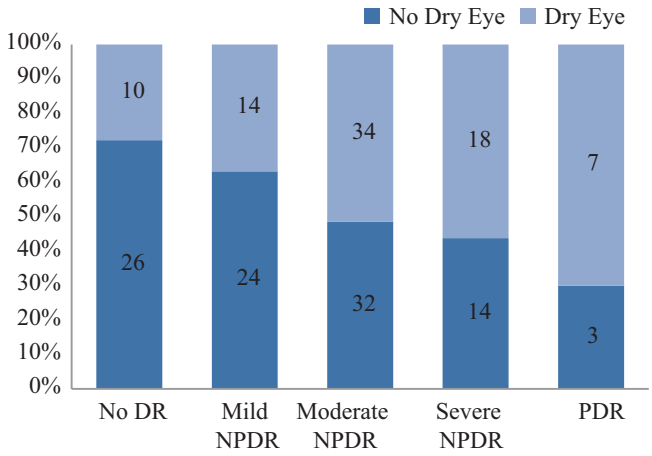

Figure-2: Dry Eye in association with Diabetic Retinopathy

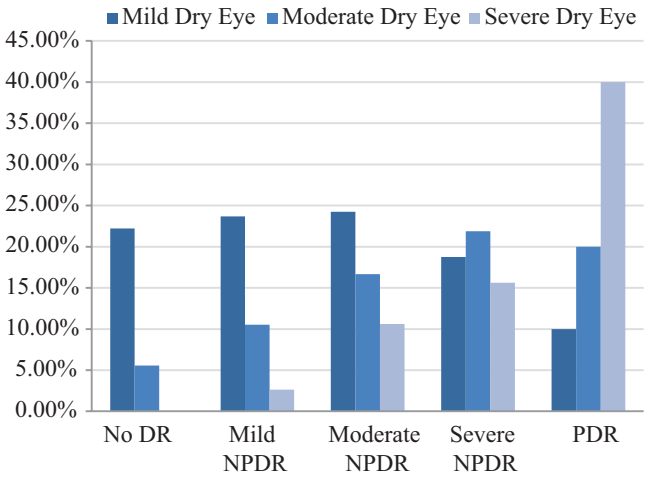

Figure-3: Severity of Dry Eye with Severity of Diabetic Retinopathy

mentioned above, and was grouped under mild moderate and severe. Dry eye was diagnosed in 83 subjects (45.6%), out of them, 40(22%) had Mild Dry eye, 26(14.2%) had Moderate Dry eye and 17(9.3%) had Severe Dry Eye. [Table 2]

The most common complaints of the subjects were Foreign body sensation (116 subjects) followed by Itching(78 subjects) and watering of Eye(67 subjects).

The mean OSDI scores according the severity of the dry eye were, 7.2 ± 2.6 in the group of subjects with No dry eye, 16 ± 3.4 amongst the Mild Dry Eye group, 27 ± 3.8 amongst the Moderate Dry eye group and 53.7 ± 16.15 amongst the Severe dry eye group (P <0.001). These results showed a significant rise of OSDI scores according the severity of Dry eye.[Table 3]

There was a significant rise in the Dry Eye subjects with a poor glycaemic control, 56 out of 108 subjects(52%) and 27 out 74 subjects (36.5%) with a good glycaemic control were diagnosed with Dry eye. (P = 0.04).

Diabetic Retinopathy was present in 146 subjects. 38 out of them had Mild NPDR, 66 had moderate NPDR, 32 had Severe NPDR and 10 patients had PDR. Diagnosis of dry eye showed significant concurrence with increasing grades of Diabetic Retinopathy. 10 out of 36 patients (27%) with no Diabetic Retinopathy had dry eye, 14 out of 38 patients(37%) with mild NPDR had dry eye, 34 of 66 patients(51.5%) with Moderate NPDR had dry eye, 18 out of 32 patients(56.2%) with severe NPDR had dry eye and 7 out of 10 patients(70%) with PDR had dry eye. Also the severity of Dry Eye increased with Severity of Diabetic Retinopathy. (P = 0.031) [Table 4], [Figure 2, Figure 3]

Ocular surface staining tests, fluorescein staining was positive in 42 subjects(23%) and lissamine green staining was positive in73 patients(40%).

DISCUSSION

The present study was aimed to derive a relationship between Ocular surface disorders, dry eye and Diabetes. It was unique in that it incorporated both, the quantitive analysis of symptoms (by OSDI scores) and diagnosis of dry eye based on symptoms and the clinical tests. The previous studies the Dry eye diagnosis was done on the bases of symptoms, and the severity of dry eye was not a consideration in them. As the study was conducted in the tropical dry region, the symptom based approach could have given a bias and false positive cases would have been abundant. The study also included ocular surface staining techniques by fluorescein staining for corneal erosions and lissamine green staining for conjunctival erosions. The previous studies rarely used the staining techniques.

The prevalence of dry eye was 45.6% in the study. In a similar study by Nepp[11], the Dry eye was seen in 43% of patients, in other various studies by Nora Burda[12] and Masood Reza Manaviat[6], dry eye was diagnosed in 53% and 54% patients respectively.

It was observed that the presence of dry eye was more frequently seeing in subjects with an increased duration of diabetes, with 60% of patients with duration of diabetes more than 15 years and 44% patients with duration of diabetes between 12-15 years were diagnosed with dry eye. Similar association was observed in other studies by Kyung-Chul Yoon[13] where the values of test parameters were significantly out of normal ranges in subjects with diabetes more than 10 years of age. In a study by Masoud Reza Manaviat[6], the mean age of diabetic patients diagnosed with dry eye was 11.48 ± 7.4 years. The duration of diabetes was significantly associated with dry eye. (P = 0.01)

Analysis of the data showed that, the dry eye was more commonly seen in patients with Uncontrolled diabetes (52%) as compared to patients with controlled diabetes (36.5%). A good glycaemic control has shown to decrease the progression of diabetes and has been a consistent thing

in the present study with statistical significance ($P = 0.04$). Seifart[14] in his showed a correlation between the HBA1c values and the presence of dry eye syndrome. The higher the HBA1c values, the higher the rate of dry eye syndrome. In the study by Dogru[15], it was demonstrated that a significantly lower values of testing parameters in patients with peripheral neuropathy and poor metabolic control. Kyung-Chul Yoon[13] found that poor metabolic control, presence of diabetic neuropathy, and advanced DR stage are risk factors for tear film and ocular surface disorder in diabetes mellitus.

The OSDI scores seemed to significantly associated with the grades of the Dry eye. The mean scores significantly correlated with the grades of dry eye. In a study by Nicole Langelier[16], the correlation between osmolarity score and OSDI score was significant among the diabetic cases. The OSDI scoring is a standardized tool to evaluate symptoms and can be easily performed. The results in our tests showed that OSDI scores are a positive predictor and reliable tool to diagnose Dry eye disease.

In the study the Ocular surface damage was evaluated by Lissamine green and fluorescein staining. These results demonstrated a significant increase in fluorescein and lissamine green staining in patients with diabetes mellitus. Similar results were observed in study by David L DeMill[17] where lissamine green staining was positive in about 40% and fluorescein staining was positive in 33% of patients with Diabetes with/without peripheral neuropathy.

The results in the studies demonstrate a concurrent increase in Dry eye with increasing grades of Diabetic retinopathy with about 73 out of 146(50%) diabetic subjects diagnosed with Dry Eye, also the severity of dry eye increased with the increasing severity of Diabetic Retinopathy. In Similar studies by Masoon Reza Manaviat[6], 59% of patients with Diabetic Retinopathy had dry eye, and in a study by Uma Devi[18], 47.8% patients with diabetic retinopathy had dry eye. These results show a parallel occurrence of diabetic retinopathy and ocular surface disorders.

CONCLUSION

A proper Evaluation of Ocular surface damage and Dry Eye should be done in all cases of Diabetes, and should be included in the screening protocol with Diabetic retinopathy. Proper treatment with lubricating Eye drops and antibiotic eye drops should be done according to the severity of the ocular surface disease.

Limitation

The limitations of the study include the following issues. The study could not document the follow up data to determine the progress and improvement. The sample size of 182 seems to be insufficient comparing the large pool of Diabetic Individuals in the country. The modern tests such Impression cytology could not be undertaken considering the study was done in the outpatient department of a tertiary care hospital with limited facilities.

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