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Prevalence of dry eye disease in type 2 diabetic patients and its co-relation with the duration, glycemic control and retinopathy

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Abstract: *Aims:* To study the prevalence of dry eye disease in type 2 diabetes mellitus patients and to study the various factors associated with dry eye in them. *Methods:* A hospital based cross-sectional clinical study of 100 Type 2 diabetic patients attending a Medical College in Raichur, India was conducted between July 2011 – June 2013. Detailed diabetic history was recorded. Assessment of anterior segment via slit lamp biomicroscopy was done. The examination for dry eyes included Schirmer's test, Tear break up time, Fluorescein and rose Bengal staining and a questionnaire. The grade of retinopathy was examined by ophthalmoscopy and recorded. *Results:* 36% of the diabetic patients had dry eye. Dry eye prevalence increased with increase in the duration of diabetes (p=0.002), poor glycemic control (p=0.005), presence of retinopathy (p=0.002). Meibominitis (53.6%), was found to be the major contributory factor (p=0.00). Mild dry eye was found in 55.5%, moderate dry eye was found in 33.0%, severe dry eye in 11.5%. *Conclusion:* Diabetes and dry eye appears to be a common association. Reduction in modifiable risk factors of dry eye is essential to reduce its prevalence. Statistical correlation was found between dry eye and duration of diabetes, presence of retinopathy, poor glycemic control. Examination for dry eye should be an integral part of the assessment of diabetic eye disease.
Keywords: Dry eye disease, Diabetes mellitus, Meibomian gland disease.

Introduction

Dry eye syndrome is one of the most frequently encountered ocular conditions especially in the elderly population. According to the international dry eye disease workshop (DEWS) [1] in 2007 it is defined as multifactorial disease of the ocular surface resulting in symptoms of ocular discomfort, visual disturbance & tear film instability with potential damage to the ocular surface.

Causal factors of diabetic dry eye [2]: There are several theories that might explain the connection between dry eye and diabetes. The most frequently cited associated factors include:

- *Peripheral Neuropathy Secondary to Hyperglycemia:* Damage to the nerves (peripheral neuropathy) is a key result of diabetes and hyperglycemia. In the eye hyperglycemia and microvascular damage to the corneal nerves can block the feedback mechanism (or loop) that controls tear secretion. This neurotropic like condition may be the result of significant nerve damage to the cornea.
- *Insulin Insufficiency:* Corneal and lacrimal gland metabolism, growth, epithelial cell proliferation and maintenance are influenced by insulin. A low insulin level generally disrupts the biochemical balance of these tissues and results in ocular dryness.
- *Inflammation:* Hyperglycemia triggers inflammatory alterations and is believed to impair normal events, such as tear secretion. Higher levels of NO were found in the aqueous humor of diabetic patients and this leads to inflammatory reaction that cause cell damage.

This study is undertaken to study the prevalence of dry eye in type 2 diabetic patients and to highlight the significance of careful examination for dry eye in these subgroup of patients so as to prevent the adverse complications of dry eye and to symptomatically relieve the patient.

Material and Methods

Design of the study: A cross sectional descriptive study.

Source of data: Institute ethical clearance and written informed consent from 100 cases of type 2 diabetes mellitus was undertaken.

Inclusion criteria: All patients diagnosed as diabetic by a physician irrespective of duration of diabetes, age, glycemic control, symptomatic/ asymptomatic of dry eye were included.

Exclusion criteria:

1. Type I diabetic patients.
2. Secondary diabetic patients.
3. Associated with other diseases-sjogrens syndrome, rheumatoid arthritis, lupus, parkinson's.
4. Patients who have under went ocular surgeries in the past.
5. On medications – anti histaminics, tricyclic anti-depressants, ocps, steroids, ACTH Pregnancy.

Examination: Detailed history regarding diabetes such as type of diabetes, duration, type of treatment, overall control in the past three months (based on sugar levels, Hba1c values if available), FBS and PPBS levels were recorded.

A validated eight item questionnaire [3] of ocular symptoms relating to dry eye was used. The questions included:

- Do your eyes ever feel dry?,
- Do you ever feel gritty or sandy sensation in your eye?
- Do your eyes ever have a burning sensation?
- Are your eyes ever red?
- Do your eyes ever feel sticky?
- Do your eyes ever feel watery or tearing?
- Do you notice much crusting on your lashes?
- Do your eyes ever get stuck shut?

Presence of a symptoms from the dry eye questionnaire was further graded as rarely (at least once in 3-4 months) sometimes (once in 2-4wks), often (at least once a week) or all the time. Presence of one more symptoms often or all the time was taken as positive. Ocular examination included recording visual acuity with snellens chart. Detailed anterior segment examination was done under slit lamp.

Meibomian gland status was graded as follows [4]:

- Grade 0- No disease.
- Grade 1- Plugging with translucent serous secretion when compressing the lid margins.
- Grade 2- Plugging with viscous or waxy white secretion when compressing the lid margin.
- Grade 3- Plugging with no secretion when compressing the lid margin.

Tear meniscus height was recorded as normal or low (under slit lamp thin beam). Tear film break up time of less than 10 seconds are taken as abnormal. Fluorescein staining of cornea was graded according to NEI workshop grading system. The maximum staining score is 15 for the cornea with values above 3 considered abnormal [3]. Schirmers test 1(basal and reflex tearing) was performed by using a precut strip of filter paper (contacare ophthalmics & diagnostics vadodara) and the amount of wetting of the paper strip after 5 mins noted. Rose Bengal stain was carried out in the end. A moistened strip of rose Bengal containing 1.5mg (contacare ophthalmics and diagnostics, Vadodara) was applied to the inferior cul-de sac, under no anaesthesia. The NEI workshop grading system was used to grade the conjunctival staining. The maximum score is 18 for each eye with values above 3 being abnormal [3].

Dry eye was defined as having one or more symptoms (often or all the time present) along with one or more positive clinical findings (based on slit lamp examination) and one or more positive clinical tests (tear break up time of less than or equal to 10 seconds,schrimers test score of less than or equal to 10mm, fluorescein score of > or equal to 3, rose Bengal score of > or equal to 3 [3]. Asymptomatic patients with positive signs or positive tests were also considered in the diagnosis.

Dry eye was graded into three types mild, moderate and severe according to DEWS

definition and classification [1]. Detailed fundus examination (under mydriasis) was done under direct and indirect ophthalmoscopy and 90D slit lamp examination. Retinopathy if present was classified as per (ETDRS Classification) The data after coding entered on excel spread sheet, was further processed &analyzed using SPSS statistical software version 17.0 the mean standard deviation and proportions were computed based on type of data. The test of significance used were chi-square test & unpaired t test.

Results

Table-1: Correlation of duration of diabetes mellitus and presence of dry eye disease			
Duration of diabetes	**Patients with dry eye disease**	**Total no. of patients**	**Pearson chi square test**
<5 yrs	19 (25.3%)	75	P=0.00
5-10 yrs	13 (61.9%)	21	
10-15 yrs	02 (100%)	02	
>15 yrs	02 (100%)	02	
Total	36	100	

Prevalence of dry eye disease is increasing with increase in the duration of diabetes

Table-2: Correlation between severity of retinopathy and presence of dry eye disease			
Grades of retinopathy (ETDRS)	**Total no. of patients**	**No. of patients with dry eye**	**Pearson chi square test**
No retinopathy	15	3(20%)	Value =14.7 Df=3 P=0.002
Mild NPDR	37	8(21.6%)	
Moderate NPDR	44	21(47.7%)	
Severe NPDR Advanced diabetic disease	4	4(100%)	
Total	100	36(36%)	

This table shows that as the severity of retinopathy increased the prevalence of dry eye in the patients also increased. Dry eye was seen in all the patients with severe NPDR and advanced diabetic eye disease. This was found to be statistically significant. (p=0.002).

Table-3: Correlation of glycemic control and Dry eye disease

Table-3a: Mean FBS in patients with dry eye disease and no dry eye disease.				
Dry eye disease	**Mean FBS**	**Standard deviation**	**Standard error mean**	**Levine test for variation**
Absent (64)	142.5	29.00	3.62	P=0.05
Present(36)	160.8	33.7	5.62	

Mean FBS was 142.5 +/-29.0 in patients with no dry eye disease.
Mean FBS was 160.8 +/- 33.7 in patients with dry eye disease.
Applying Levine test for equality of variances this was significant. (p=0.005)

Table-3b: Mean PPBS levels in patients with dry eye disease and no dry eye disease				
Dry eye disease	**Mean**	**Standard deviation**	**Standard error mean**	**Levine test of variation**
Absent(64)	206.18	34.43	4.30	P=0
Present(36)	242.19	40.64	6.77	

Mean PPBS levels was 206.18 +/- 34.43 in patients with no dry eye disease.
Mean PPBS levels was 242.19 +/- 40.6 in patients with dry eye disease.
This was statistically significant (p=0.0)

Table-4: Correlation between meibomian gland disease and dry eye disease in diabetic patients			
Meibomian gland disease	**Pts with dry eye**	**Patients without dry eye**	**Total**
Present	30(53.6%)	26(46.4%)	56
Absent	61(13.6%)	38(86.4%)	44
Total	36(36%)	64	100
Pearson chi square test = value-17.05, df=1, p<0.01			

This table shows that out of 36 patients with dry eye 30 patients had meibomian gland disease.
This was statistically significant (p<0.01).

Discussion

In this study 100 type 2 (diagnosed by the physicians) diabetic patients attending a medical college were randomly selected, to study the prevalence of dry eye in them and also the associative factors which makes this group more susceptible to dry eye. Of the 100 subjects studied, 36 patients (36%) had dry eye. Similarly Seifart. U et al [5] in 1994 studied 92 diabetic patients, 57% of type2 diabetics had proven dry eye.

Prevalence of dry eye in diabetes reported in various studies		
Authors	**Diabetic**	**Non -diabetic**
Seifart et al[5]	57% in type 1 & 70%type2	
Moss et al[6]	18.1% (0.1=1.38)	14.1%
Li et al[7]	19.8%	
Masoud R Manvieat et.al[8]	54.3%	
Nepp et al[9]	43%	
Maruti et al[10]	35%	
Present study	36%	

Duration of diabetes in this study ranged from 4days to 20yrs. Mean duration of 3.6yrs+-3.9yrs.As the duration increased the prevalence of dry eye also increased, this was found to be statistically significant (p=.001). The prevalence increased from 25.3% in diabetics of less than 5 yrs to about 100% in diabetics of more than 15 yrs. Manaviat. et. al [8] in 2008 also found a significant association between duration and dry eye prevalence. In clinical geriatric medicine Tumosa [11] 2008 also signifies the duration of diabetes and its complications like dry eye.

The reason for this being the slow microangiopathy and neuropathy of the diabetic disease process causing lacrimal gland dysfunction and reduced corneal sensitivity. The prevalence of Dry eye was 20% in patients with no retinopathy, 21.6% in patients with mild retinopathy, 47.75 in moderate retinopathy, 100% in severe retinopathy. This increase in the prevalence of dry eye with the grade of retinopathy is found to be statistically significant. (p=0.002). Saito.et.al 2003 [12] also correlated reduced corneal sensation with the stage of Retinopathy, which may explain the increase in dry eye in diabetics of higher grade of Retinopathy. The mean FBS among those with dry eye disease was 160mg%+_33.75 than those with no Dry eye disease(140+_ 29)

which was found to be statistically significant association (p=.005). The mean PPBS was 206.18±34.43 in patients with dry eye disease. This was also statistically significant (p=0.00). So it implies that glycemic status of the patient definitely had an impact on the prevalence of dry eye disease in diabetics. Similarly Nepp. J et al [9] 2000 also noted that severity of dry eye disease correlated with glycemic control. 53.6% of the diabetics with dry eye had Meibomian gland disease and in diabetics with no dry eye the disease of meibomian gland was 13.6%. This was statistically significant (p=0.00). So Meibomian gland disease was an important contributory factor to cause dry eye disease in this study.

The lid flora is important in the development of meibomian gland dysfunction. Diabetic patients may be at an increased risk for opportunistic colonization of the eyelids, resulting in blepharitic presentations. These developments lead to a compromised tear film lipid layer with increased evaporation, decreased tear breakup time and increased osmolarity. Previous studies have confirmed that diabetes may be a possible predisposer for blepharitis. (Ghasemi H et al2008) [13], but this study signifies that more than peripheral neuropathy causing aqueous deficiency dry eye meibominitis causing evaporative dry eye is also very important in diabetics.

Conclusion

- This study confirms that both tear secretion and tear film stability are affected in type 2 diabetics and so dry is a common association in them.
- Symptoms and signs of dry eye do not correlate, a symptomatic patient may not have signs of dry eye and vice versa. Careful examination of asymptomatic patients for signs of dry is necessary.
- Meibomian gland disease is the most common causative factor for dry eye in diabetics.
- Modifiable factors to prevent dry eye in diabetics apart from good glycemic control would be lid hygiene and use of ocular lubricants.

In our study more confirmatory tests for meibomian gland disease and also dry eye were not used which is a drawback

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