ORIGINAL ARTICLE

A Clinical Study on Meibomian Gland Dysfunction and Dry Eye in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Objective: The objective of the study was to find the occurrence of meibomian gland dysfunction (MGD) and dry eye disorder in patients with type 2 diabetes mellitus (DM) and to assess the profile of MGD in type 2 DM patients. **Materials and Methods:** An observational case-control study was conducted on 100 type 2 diabetes patients and 100 controls who are attending ophthalmology outpatient department with distinct complaints, for example, correction of refractive error. Age and gender matching was done. Tear film evaluation was done for both the groups, lid margin abnormalities were noted under slit lamp biomicroscope, fluorescein staining of ocular surface performed, and pre-corneal tear film was observed for debris. Schirmer's test as well as tear breakup time test was performed. **Results:** Of 100 diabetic patients, dry eye disorder was found in 56 (56%) cases, among which 24 patients had MGD. Twenty-four of 56 that is 42% of dry eye is credited to MGD. Of 100 non-diabetics, 15% had dry eye disorder, among which 6 cases had MGD. **Conclusion:** Diabetes can cause changes in ocular surface with respect to both qualitative and quantitative parameters. Diabetic patients are more susceptible for dry eye disorders when compared to normal subjects. In diabetics, the frequency of MGD is considerably more when compared to nondiabetic group. As the duration of DM increases prevalence and severity of MGD also increases proportionately.

KEY WORDS: Dry eye, meibomian gland dysfunction, Schirmer's test, tear film breakup time.

Introduction

Diabetes mellitus (DM) is defined as a primary disorder of carbohydrate metabolism, secondarily involving the protein and fat metabolism characterized by glycosuria and hyperglycemia.[1] Diabetes affects various organs and of these perhaps, one of the most important is its ocular manifestations. The incidence of DM is hastily increasing in India, diabetes will perhaps appear as one of the foremost cause of ocular disorder by the time we accomplish something in preventing a larger amount of preventable blindness.[2]

DM is found to be associated with several ocular conditions such as acute orbital infection, hordeolum, variations in the refractive error, chronic inflammation of the lid, neovascular glaucoma, ptosis, diabetic retinopathy, and oculomotor nerve palsies, cataract. Deficiency of tear secretion and dysfunction of tear film for chronic period has also been identified in diabetic patients.[3] Studies have proved that deficient production and secretion of tears is due to "autonomic neuropathy," in turn causing disturbance to the nerves that supply the lacrimal gland causes dry eye in majority of the cases of dry eye in association with diabetes.[4]

For dry eye disorders, DM is noted as one among the foremost systemic risk factors.[5] Patientsdiabetic might show symptoms of dry eye due to abnormal lacrimal secretions, metabolic dysfunction, or neuropathy. International Workshop on meibomian gland dysfunction (MGD) tells that MGD might play a significant task in aqueous-deficient dry eye and it is the most prevalent cause of evaporative dry eye.[6] In patients with type 2 diabetes, meibomian gland structure, and dysfunction including meibum expressibility, lid

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margin abnormalities, and meibography scores were found to be appreciably inferior.[7]

Diabetes leads to instability in tear film by reducing the number of goblet cells, in turn inducing damage to conjunctival and corneal epithelial, ocular surface hydrophilic environment, and secretion of mucin is also reduced in diabetes.[8,9] A study from Ding *et al*. established that proliferation of epithelial cells of meibomian gland human meibomian gland epithelial cells is stimulated by insulin, and also showed that high glucose was toxic to these cells.[10] The corneal sensitivity, fluorescein staining score, and the density of corneal epithelial cells and nerve fibers in the diabetic patients show a relationship with the duration of diabetes.[11] Dry eye (keratoconjunctivitis sicca, tear instability) is a disorder of the tear film due to tear deficiency or excessive evaporation and is related to symptoms of discomfort and ocular irritation such as feeling hot, dry, gritty or sandy, burning, smarting sensation, itching, watering, or tearing.[12] The purpose of the study is to evaluate the incidence of dry eye and MGD in type 2 diabetes patients and to compare the results with those of controls.

Materials and Methods

Clearance from Institutional Ethical Committee in accordance with the guidelines of the Declaration of Helsinki was obtained. Purposive sampling method was used. One hundred cases with type 2 DM and 100 nondiabetic controls, which are matched with respect to age and gender who are seeking medical care for correction of refractive error were enrolled from the ophthalmology department. Informed consent was taken by all study participants.

Inclusion criteria

- Type 2 DM patients of both the gender with more than 18 years of age, who have given consent to participate in the study were included in the study.

Exclusion criteria

The following criteria were excluded from the study:

- Not given consent
- History of ocular surgery
- Contact lens wearers
- Patients on topical treatment that found to cause or worsen dry eye such as apraclonidine, brimonidine, dipivefrin, olopatadine, emedastine, acyclovir, idoxuridine, trifluridine, betaxolol, carteolol, levobunolol, metipranolol, timolol, brinzolamide, dorzolamide, pilocarpine, ecothiopate, naphazoline, tetryzoline, dapiprazole, cyclopentolate, tropicamide, hydroxyamfetamine, bimatoprost, latanoprost, travoprost, unoprostone, cocaine proxymetacaine, tetracaine, bromfenac, diclofenac, ketorolac, and nepafenacd
- Cases who are on systemic or local drugs such as oral contraceptives, antidepressants, antihistamines, diuretics, which are associated with causation of dry eye
- Cases with systemic diseases such as rheumatoid arthritis, Sjogren's syndrome, Parkinson's disease, and systemic lupus erythematosus and other ocular surface disorders associated with dry eye
- Smokers
- Cases with Vitamin A deficiency
- Patients having pseudoexfoliation syndrome
- Pregnant women
- Patients with a history of cranial nerve injury or active ocular inflammation or infection.

The study participants were asked regarding subjective symptoms, ocular surface disease index (OSDI) score was calculated and recorded, and all were subjected to ophthalmologic examination, which includes detailed ocular surface examination with slit lamp to examine the condition of eyelid, meibomian gland, pre-corneal tear film, conjunctival, and corneal surface was evaluated using fluorescein stain.

Tear film assessment was done as follows:

- Lid margin alterations were recorded: Lid margin irregularity, vascular engorgement, anterior, or posterior displacement of the mucocutaneous junction, whether any obstructed orifices of meibomian glands noted
- Pre-corneal tear film was observed for debris
- Tear breakup time (TBUT) test carried out
- Schirmer's test (SchT) test done.

A minimum interval of 10 min left between any two tests. All the patients were examined by the same ophthalmologist to avoid interobserver bias. Grading of MGD was done based on guidelines tailored from "The international workshop on meibomian gland dysfunction" Diagnosis of dry eye disorder was made according to the recommendation by TFOS DEWS II report, in which OSDI score of ≥ 13 and either TBUT <10 s or ocular surface staining showing >5 corneal spots, >9 conjunctival spots, and lid margin

(≥2 mm length and ≥25% width) was diagnosed as dry eye.

Data were entered in Excel Sheet using SPSS software Chi-square statistical test was applied to compare the results between two groups.

Results

- Fifty-six of 100 cases with diabetes that is 56% had dry eye, MGD was noted in 24 cases, 24 of 56 (42%) of dry eye is ascribed to MGD. About 6% had MGD of 100 nondiabetic cases
- About 20% of diabetics and 3% of nondiabetics showed Grade 1 MGD. About 3% of diabetics and 2% of nondiabetics showed Grade 2 MGD. About 1% of diabetics and 1% in nondiabetics displayed Grade 3 MGD. The distribution of various grades of MGD is not statistically significant with $P = 0.2154$ at 5% level of significance
- Notable difference in distribution of MGD among females and males is present in our study. In diabetic group, 8% of males have MGD, whereas it is noted in 16% of females
- Distribution of the proportion of various grades of fluorescein staining in nondiabetics and diabetics shows that in diabetic group Grade 0 staining was noted in 14% of subjects, Grade 1, 2, and 3 were noted in 26%, 24%, and 36% of the subjects, respectively. Whereas in nondiabetic group, Grade 0 staining was noted in 53%, Grade 1, 2, and 3 were noted in 27%, 13%, and 7% of the subjects, respectively. Chi-square test was applied for above data, and there is a statistically significant difference noted between two groups with $P = 0.0076$, with diabetic group showing proportionately more fluorescein staining of ocular surface
- Distribution of MGD in diabetics in relation to the duration of diabetes shows that among males with 5 years duration of diabetes 12.5% had MGD, whereas 50% of males with 16–20 years duration of diabetes had MGD. Among females with 5 year duration of diabetes, 6% had MGD. Moreover, 56% of females with 16–20 years of diabetes had MGD (Tables 1-3 and Figures 1-4).

Discussion

There is a substantial variation in incidence of MGD in various studies, incidence varies from 3.5% to 70% in relation to different geographic locations.

Kamel *et al*. showed that in type 2 DM patients and in poorly controlled diabetic patients, there is reduced Schirmer's I and the TBUT test results (70% in both Schirmer and TBUT).[13] In our study, there is a reduction in the tear film parameter results such as SchT and TBUT in the diabetic patients as compared to controls. This could be due to damage to lacrimal gland microvasculature, causing impaired functioning, moreover, also due to reduced

Table 1: Age and gender-matched distribution of non-diabetics and diabetics

Age (years)	Non-diabetics			Diabetics		
	Females	Males	Total	Females	Males	Total
40–45	3	7	10	3	7	10
46–50	7	14	21	7	14	21
51–55	16	16	32	16	16	32
56–60	6	20	26	6	20	26
61–65	5	6	11	5	6	11
	37	63	100	37	63	100

Table 2: Frequency of various grades of fluorescein staining among 2 groups

Grade	Diabetics			Non-diabetics		
	Females	Males	Total (%)	Females	Males	Total (%)
0	6	2	8 (14)	5	3	8 (53)
1	5	10	15 (26)	1	3	4 (27)
2	4	9	13 (24)	1	1	2 (13)
3	13	7	20 (36)	2	1	1 (7)

corneal and conjunctival sensitivity in diabetics. One more important contributor is mucin layer of the tear film, which plays integral role in wetting and spreading of tear film, deficiency of which may reduce TBUT value tear film stability, especially in diabetic patients.

Table 3: Distribution of various grades of MGD among 2 groups

Grade of MGD	Diabetics	Non-diabetics
Grade 1	20	3
Grade 2	3	2
Grade 3	1	1

Quality and quantity of the meibomian gland secretion, nature of expressibility, and corneal staining are the key parameters used to grade MGD in our study. Evaporative dry eye can be caused by the qualitative and quantitative alterations in the lipid layer, caused by dysfunction in meibomian glands.

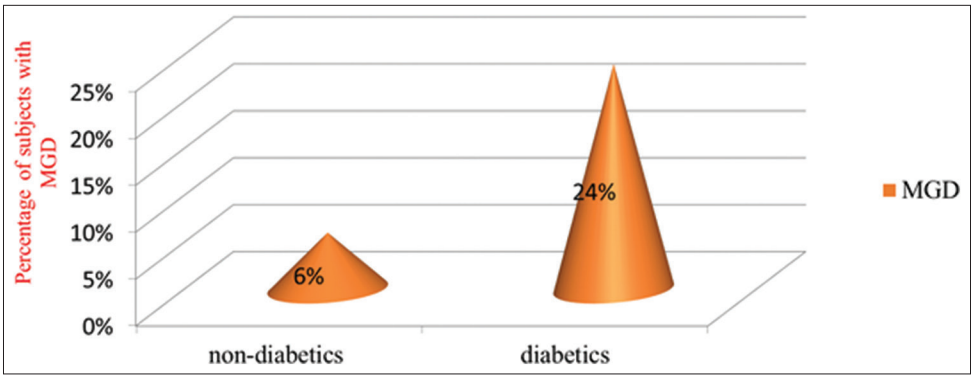

Figure 1: Frequency of MGD among 2 groups

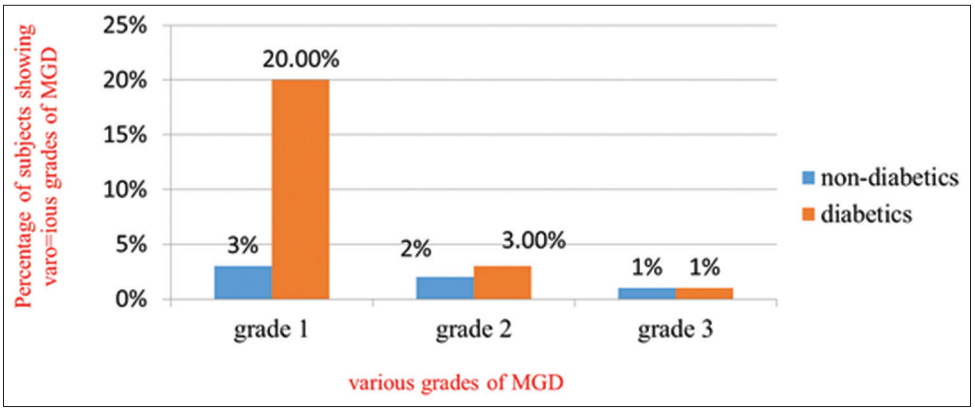

Figure 2: Frequency of grades of MGD among 2 groups

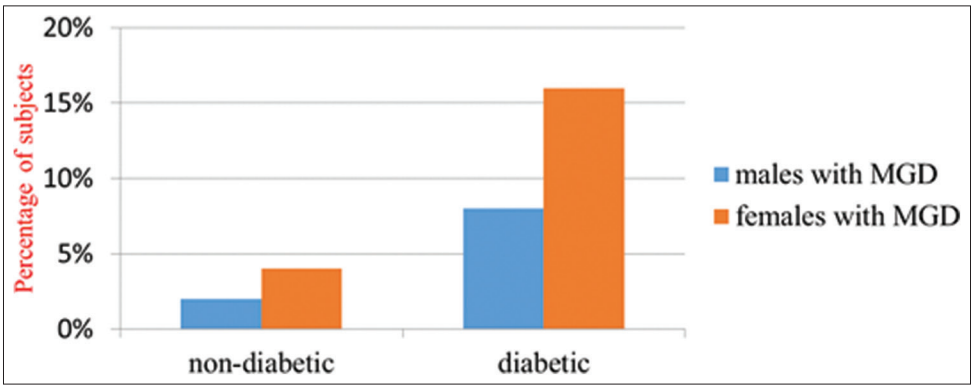

Figure 3: Occurrence of MGD with respect to gender among 2 groups

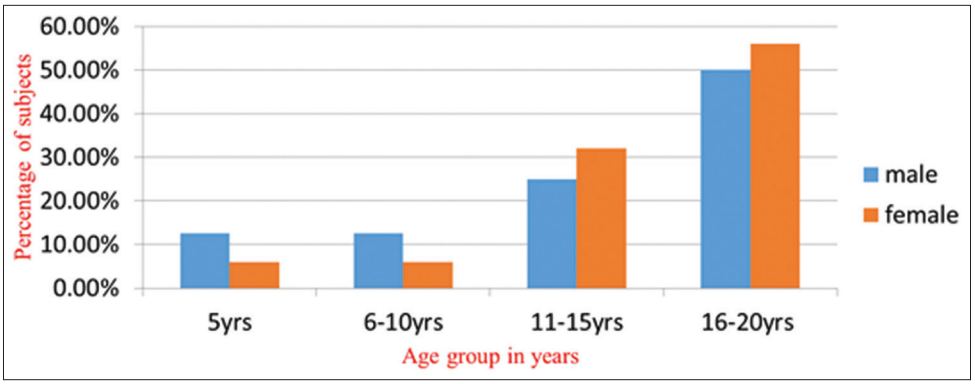

Figure 4: Occurrence of MGD in diabetic group in relation to duration of diabetes mellitus

Devi and Gowda in their study found that patients aged 50 years (53.6%) showed maximum prevalence rate of dry eye, most of the type II patients, that is, 48.8% of cases were lying in age group between 51 and 60 years.[14] The diabetic patients show higher frequency of the more severe form of MGD.

Shamsheer and Arunachalam in their study establish that the diabetic group which comprises 58 eyes showed the highest number of eyes with Grade I–IV lissamine green and fluorescein staining which was a statistically significant difference when compared to the control group with 14 eyes (Chi-square = 32.79, $P < 0.0005$).[15] In our study, 36% of diabetics with MGD showed Grade 3 fluorescein staining, whereas only 7% of nondiabetic controls showed Grade 3 staining.

A European Community study[16] accomplished that in tear film disorders, objective diagnostic tests and subjective assessments have clinical usefulness as diagnostic tools, aqueous tear disease is interrelated to ocular surface disease.

Moss and Klein[17] in their study reported that diabetic women (16.7%) showed a higher incidence of dry eyes in comparison with males (11.4%). In our study, among the cases with 16–20 years of duration of DM, 56% of female and 50% of male cases exhibited MGD. Estrogen deficiency leading to deficient tear secretion in postmenopausal women has been hypothesized to explain gender differences. Paradoxically, Schaumberg *et al*.[18] In their study on hormone replacement therapy and dry eye syndrome, reported that there is an increased risk of dry eye found in women on hormone replacement therapy.

The limitation of the present study is, we have not given special consideration to female cases and controls who had attained menopause, which alone can contribute to dry eye disorder.

Conclusion

- Diabetic patients are more susceptible for suffering from dry eye disorder than normal population
- Diabetes can lead to ocular surface alterations with quantitative and qualitative tear film disorders
- The frequency of MGD in DM is more as compared to diabetics
- The prevalence and severity of MGD increases with increase in the duration of DM
- Reduction in the modifiable risk factors of dry eyes is essential to reduce its prevalence
- Females show preponderance for MGD
- Evaluation for dry eyes must be included as an integral part of the examination of diabetic eye disease.

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