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MEIBOMIAN GLAND DYSFUNCTION IN PATIENTS WITH TYPE 2 DIABETES MELLITUS: A CLINICAL STUDY

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INTRODUCTION

Meibomian glands are modified sebaceous glands that line the upper and lower eyelids in a single row. They are embedded in the tarsal plate in a single line with 20 to 40 with a median of 30 in the upper lid. In the lower lid they are about 20-30 with a median of 26 glands. Their secretory products contain a complex mixture of lipids and proteins and are termed as meibum which is liquid at room temperature. The secreted lipid is stored in the duct system that terminates in the orifices with a muscular cuff that open onto the lids. It is released on the ocular surface in small amounts with each blink forming a reservoir with about 30 times more lipid than needed for each blink.

According to the Tear film and Ocular Surface Society, (International workshop on MGD, 2011)[1] Meibomian gland dysfunction (MGD) is defined as a chronic, diffuse abnormality of the meibomian glands, commonly characterized by terminal duct obstruction and/or qualitative/ quantitative changes in the glandular secretion. It may result in alteration of the tear film, symptoms of eye irritation, clinically apparent inflammation, and ocular surface disease.

Recently, a study from Ding et al (2015)[2] demonstrated that insulin stimulated the proliferation of immortalized human meibomian gland epithelial cells (HMGECs), whereas high glucose was found to be toxic for HMGECs . This suggests that insulin resistance/deficiency and hyperglycemia are deleterious for HMGECs which supports our hypothesis that diabetes may be associated with MGD.

AIMS AND OBJECTIVES

This study aimed to find a correlation between meibomian gland dysfunction in patients with type 2 diabetes mellitus

MATERIALS AND METHODS

This study was done at the Department of Ophthalmology, and Department of Endocrinology, IMS, BHU between August 2017 and July 2018. All examinations were performed by a single observer to exclude subjective bias.

Inclusion criteria

Age group: 40-65 years

The diabetic state was determined either by the history of medication for diabetes or an abnormal random blood sugar level of >200 mg/dl or HbA1C of >6.5% or fasting blood sugar of >126 mg/dl.

Exclusion Criteria: Patients with pterygium, cicatricial conjunctivitis, (trachoma, ocular pemphigoid, erythema multiforme), rheumatological disease, thyroid eye disease, on medications such as antiglaucoma, antihistamines and tricyclic antidepressants and postocular or refractive surgery were excluded from the study.

METHOD

This was a case control study that evaluated 50 diabetic patients and 50 controls. The age range was from 40 to 65 years. The patients were enrolled from patients attending the outpatient department of Ophthalmology and Endocrinology departments.

The diabetic state was determined either by the history of medication for diabetes or an abnormal random blood sugar level of >200 mg/dl or HbA1C of >6.5% or fasting blood sugar of >126 mg/dl. A detailed history was elicited for symptoms of ocular surface irritation such as

discomfort, dryness, burning, sticky eyes, redness, crusting, stuck in morning, watering, photophobia, swelling in lid {chalazion}and diurnal variation.

Patients with frequent and persistent symptoms were classified grade 2 or higher on the MGD grading system ref. A general physical examination and detailed ophthalmic examination were performed.

Meibomian gland assessment
Firm digital pressure was applied over the middle and nasal one-third of the upper and lower eyelid with the lid compressed against the globe until a dome of lipid was expressed from the orifice. Meibomian gland function was assessed by examining the meibum expressed from the glands for volume and viscosity and the grading was done simultaneously.

Tear film was examined for froth and mucus debris. Conjunctival surface was seen for injection more so in the inferior third of the exposed interpalpebral area using lissamine green staining. Cornea was evaluated in detail for its sheen, surface (superficial punctate erosions, mucus plaques/filamentary keratitis) more in the inferior third of the cornea using fluorescein staining. Dry eye evaluation was also done using TBUT (Tear film break up time) and Schirmer's test. All examinations were performed by a single observer to exclude subjective bias.

OBSERVATIONS AND RESULTS
In this study 50 patients and 50 controls were included. Out of 50 cases 29 were females and 21 were males and in controls 34 were females and 16 were males. Age range was 45-60 years. Out of the total 50 cases 33 had

diabetic retinopathy, that had probably had a referral bias.

The frequency of signs and symptoms is given in table 1 and it shows that blepharitis was the commonest of all and chalazion was least common.

Table. 1: Comparison of signs and symptoms showing that the frequency of blepharitis, watering, burning and dryness were the most common.

Symptoms	Diabetic Group	Control Group
Blepharitis	39 (78%)	8 (16%)
Watering	35 (70%)	11 (22%)
Burning	38 (76%)	11 (22%)
Dryness	29 (58%)	6 (12%)
Redness	23 (46%)	8 (16%)
Photophobia	11 (22%)	0
Sticky Eye	4 (8%)	1 (2%)
Crusting	4 (8%)	0
Stuck in the morning	4 (8%)	2 (4%)
Chalazion	1 (2%)	0
Lid Margin Changes	5 (10%)	1 (2%)

Mild to moderate MGD was present in 62% of diabetic patients while it was present in only 10% of controls which was statistically significant (χ2=81.583; p=<0.001). Though the majority of patients with diabetic retinopathy had MGD, patients without retinopathy also had mild to moderate MGD. Dry eye parameters were more severe in patients with MGD and all its parameters were statistically significant (table 2).

Table. 2: Comparison of dry eye parameters in patients with and without diabetes mellitus.

Variable	Mean±sd		t-value	p-value
	Diabetic Group	Control Group		
Blink rate	21.22±9.347	17.76±4.640	2.345	0.021
Tbut re	11.133±4.4242	21.087±1.9918	-14.506	<0.001
Tbut le	10.713±3.6390	21.680±1.8356	-19.026	<0.001
Schirmer re	4.18±8.623	20.96±3.631	-5.124	<0.001
Schirmer le	13.20±8.832	20.14±2.900	-5.279	<0.001

DISCUSSION
The MGD prevalence rates reported in the available literature broadly vary, but they generally point to higher rates in Asian populations compared to predominantly Caucasian populations. (Schaumberg et al, 2011).[3] According to other studies conducted on Asian populations the prevalence was 46.2% in the Bangkok Study, 69.3% in the Beijing Eye Study (Jie et al 2009)[4], 3.5% in the Salisbury Eye Evaluation Study (Schein et al, 1997)[5] and 19.9% in the Melbourne Visual Impairment Project (McCarty CA et al., 1998)[6], 8% in a Tiawanese eye study. They also found that MGD prevalence was higher in men than woman. Shamsheer et

al (2015)[7] found that overall frequency of significant MGD was 11%.

Despite the general agreement regarding the correlation between MGD and age (Nien C. et al., 2011)[8], previous studies attribute the impact of aging to age-related atrophy of Meibomian gland acini and decreased lipid expression. In our study maximum people were in the age group of 51-60 years, in both the diabetic group and control group. So,there was no significant difference in diabetic patients and the control group with regards to age.

In our study it was found that 29(58%) out of 50 diabetic patients and 34(68%) of the control group were females. Out of the 29 female diabetic patients 18(54.5%) had diabetic retinopathy indicating that MGD is more prevalent among females which correlated with the literature. Moss and associates have reported a high incidence of dry eye among females 16.7% compared to males 11.4%. In the population-based study by Viso et al. (2012)[12], a significant relation with the male gender was only observed for asymptomatic cases. In this regard, the population-based study by Siak et al. (2012)13 did not find a significant relation between the male gender and MGD either. In the case-control study by Pinna et al. (2013)[9], gender showed no significant effect.

Our study shows that the prevalence of MGD was significantly more in the diabetic group of patients and more so in patients with diabetic retinopathy. (Table 3&4).

Table. 3: Comparison of MGD in Diabetic and Control groups.

	Diabetic Group	Control Group
No MGD	20%	60%
Minimum MGD	12%	30%
Mild MGD	42%	10%
Moderate MGD	20%	0
Severe MGD	6%	0

Table. 4: Comparison of MGD in diabetic patients with and without diabetic retinopathy.

	Diabetic Group	
	With Diabetic retinopathy	Without Diabetic retinopathy
No MGD	6%	47.1%
Minimum MGD	12.1%	11.8%
Mild MGD	48.5%	29.4%
Moderate MGD	27.2%	11.7%
Severe MGD	6.1%	0

Tau yu et al showed that 57.63% of people in DM group had MG dropout, while it was 33% in control group. Also, the results showed that the DM group suffered more severe ocular discomfort and tear film abnormal than the control group, which was consistent with the previous studies. A study by Pathan et al[10] showed the prevalence of MGD as 56% in diabetic patients (type 2) which is more than the general population (38%). In a study by Kumar et al (2017)[11] it was that found 59% of the patients out of 100 diabetic patients had MGD.

In contrast to the study by Pathan et al, it was found that a significant inverse relationship existed between MGD and diabetes mellitus. The eyes, in general, and particularly Meibomian glands, are rich in arteries, and diseases affecting blood vessels can impair blood delivery to these glands and lead to MGD (Viso et al,

2012).[12] The direct impact of diabetes on MGD in the study by Viso et al. (2012) was observed only in symptomatic cases, and Siak et al (2012)[13] stated that the association was not statistically significant.

CONCLUSION
MGD is very common in patients with diabetes mellitus and this has association with the duration of diabetes and the presence of diabetic retinopathy. Our study suggests that the patients who have diabetes, mostly suffer from meibomian gland dysfunction also even if they do not have troublesome symptoms pertaining to it. So, it should be treated simultaneously to improve the general well-being of the patient.

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