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Research Article

Comparative Evaluation of Meibomian Gland Dysfunction in Diabetic and Non-Diabetic Patients at a Tertiary Care Centre in Punjab

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Abstract

Objective: To evaluate and compare meibomian gland dysfunction in diabetic and non-diabetic patients..

Design: This was a prospective study conducted on 400 eyes of 100 diabetic patients (group 1) and 100 non- diabetic patients (group 2) who presented to out-patient department and were diagnosed with meibomian gland dysfunction from January 2019 to January 2020.Meibomain gland dysfunction was evaluated by noting the symptoms, determining the grade of meibomian gland expressibility and meibum quality under slit lamp and ocular surface staining. Clinical staging of meibomian gland dysfunction was obtained and the results were compared in both the groups.

Results: The age range of patients in both the groups was 40 to 65 years. The mean blood sugar level in group 1 was 225.16 ± 53.29 (mg/dl) while in group 2 was 99.64 ± 8.58 (mg/dl). Burning sensation in the eyes was found to be the most common symptom in both the groups. The severity of symptoms was significantly more among the diabetic group compared to non-diabetic group ($p = 0.001$). Meibum quality and expressibility grading was significantly greater in group 1 compared to group 2 ($p < 0.05$). There was statistically significant increase in ocular surface staining in group 1 compared to group 2 ($p < 0.001$).Clinical staging of meibomian gland dysfunction was obtained which showed significantly high stage (stage 3,4) meibomian gland dysfunction in diabetic patients compared to non-diabetic patients ($p < 0.001$).

Conclusion: Our data suggests that meibomian gland dysfunction in diabetic patients is more severe compared to non-diabetic patients.

Keywords: Meibomian Gland; Meibum; Meibomian Gland Dysfunction; Diabetes

Abbreviations

MG: Meibomian Gland; MGD: Meibomian Gland Dysfunction; EDE: Evaporative Dry Eye; DM: Diabetes Mellitus.

Introduction

Meibomian Glands (MGs) play an extremely important role in the health and well-being of the ocular surface. Meibomian glands were first described in detail by German physician Heinrich Meibom (1638-1700) and are named after him [1]. They are modified sebaceous glands present in the tarsal plate of both upper and lower eyelids. There are approximately 25-40 glands in the upper eyelid and nearly 20-30 in the lower eyelid. They are about 5.5 mm long in upper eyelid and 2 mm in lower eyelid. They secrete lipids termed as meibum which forms the superficial layer of the tear film. This meibum reduces tear evaporation, functions as a lubricant for the eyelids during blinking and may provide a barrier to prevent bacteria from entering the tear film [2,3].

Korb and Henriquez coined the term meibomian gland dysfunction (MGD) in a study done on contact lens intolerance and the obstruction of the meibomian gland orifices by desquamated epithelial cells [4]. The International Workshop on Meibomian Gland Dysfunction defined the disease as "a chronic, diffuse abnormality of the meibomian glands, commonly characterized by terminal duct obstruction and/or qualitative/uantitative 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" [5]. Meibomian gland dysfunction, a contributor to evaporative dry eye (EDE), is considered the leading cause of dry eye in clinic and population based studies [6,7]. Meibomian gland dysfunction is influenced by endogenous factors such as age, sex, hormonal disturbance as well as by exogenous factors such as topical medications. Various other factors like contact lens wear, concentrated computer use, PCOD, dyslipidemia, Sjogren's syndrome appears to be associated with meibomian gland dysfunction. Diabetes mellitus (DM) is a significant risk factor for the development of meibomian gland dysfunction [8,9]. The prevalence of type 2 diabetes has increased significantly in recent decades. Recently, a study from Ding J., *et al*. demonstrated that insulin stimulated the proliferation of immortalized human meibomian gland epithelial cells (HMGECs) whereas high glucose was found to be toxic for HMGECs [10]. This suggests that insulin resistance/deficiency and hyperglycemia are deleterious for HMGECs which supports that diabetes may be associated with meibomian gland dysfunction. We conducted a prospective study to evaluate and compare meibomian gland dysfunction in diabetic patients and non-diabetic patients.

Materials and Methods

This present prospective study was conducted on 200 patients (400 eyes) with meibomian gland dysfunction who visited the outpatient department at a tertiary care centre in Punjab. After obtaining informed consent, they were divided into 2 groups comprising 100 patients each, group 1 with Diabetes Mellitus (diabetic group) and group 2 without Diabetes Mellitus (non-diabetic group). This study was conducted after obtaining approval from Institutional Review Board in accordance with Declaration of Helsinki. Patients with the age range from 40 to 65 years were included. 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 fasting blood sugar of >126 mg/dl or HbA1c of >6.5%. Patients with pterygium, thyroid eye disease, history of previous ocular surgery, signs of active ocular infection or inflammation, history of continuous use of topical ocular medications or on medications such as antihistamines and tricyclic antidepressants were excluded from our study.

A detailed history for symptoms of ocular surface irritation such as foreign body sensation, grittiness, dryness, burning sensation, watering and itching was elicited. Symptoms were graded on the basis of its severity as none, mild, moderate and severe. All patients underwent slit lamp examination for meibomian gland assessment. Firm digital pressure was applied over the middle and nasal one-third of the lower eyelid until meibum was expressed from the orifice. The quality of meibum and the expressibilty of meibomian glands was assessed and graded simultaneously. Meibum quality was graded by assessing each of the central 8 meibomian glands as 0 -clear meibum, 1 -cloudy meibum, 2- cloudy with debris, 3 -thick like toothpaste. Similarly, the expressibility of meibomian glands was graded as 0-all glands expressible, 1 -3-4 glands expressible, 2 -1-2 glands expressible, 3 -no glands expressible.

Ocular surface staining by an unquantified method was done, wherein corneal staining of the eyes was done with sodium fluorescein strip containing 1 mg fluorescein. It was applied to the inferior palpebral surface and the staining pattern was observed under slit lamp. Similarly, after an interval of 5 minutes, Lissamine green strip was used for staining of the conjunctiva. Ocular surface staining pattern was graded according to the Oxford grading scale as minimal (grade 1), mild (grade II), moderate (grade III) and severe (grade IV and V).

Clinical staging of meibomian gland dysfunction was obtained by all three of the following criteria: symptoms, meibum quality and gland expressibility and corneal staining (Table 1) [11].

All parameters were analyzed by SPSS® 22.0 version statistical tests. We used chi square test and unpaired t-test for inter-group comparison. p-value < 0.05 was considered as statistically significant in our study.

Stage	MGD Grade	Symptoms	Corneal staining
1	+(minimally altered expressibility and secretion quality: grade ≥2 to 4, Expressibility: 1)	None	None
2	++(Mildly altered expressibility and secretion quality: grade≥ 4 to <8, Expressibility: 1)	Minimal to mild	None to limited
3	+++(Moderately altered expressibility and secretion quality: grade ≥8 to <13, Expressibility: 2)	Moderate	Mild to moderate mainly peripheral
4	++++(Severely altered expressibility and secretion quality: grade ≥ 13 Expressibility: 3)	Marked	Marked; central in addition
'Plus' disease	Co-existing or accompanying disorders of the ocular surface and/or eyelids		

Table 1: Summary of clinical staging of meibomian gland dysfunction.

Results

In our study, 100 diabetic patients and 100 non-diabetic patients were included. Out of 100 patients in group 1, 43% were males and 57% were females and in group 2, 42% were males and 58% were females. The mean age of patients in group 1 was 57.58 ± 7.73 years and in group 2 was 55.94 ± 7.53 years. (Age wise distribution- (Table 2).

The mean blood sugar level was 225.16 ± 53.29 mg/dl in group 1 whereas 99.64 ± 8.58 mg/dl in group 2. The mean of HbA1c value was found to be 7.75 ± 0.93 % in group 1 and 4.99 ± 0.34 % in group 2.

Burning sensation in eyes was found to be the most common symptom in both the groups. In group 1, 73% eyes had burning sensation followed by watering of eyes (48%), itching (34.5%), foreign body sensation (19%).In group 2, 64% eyes had burning sensation followed by watering of eyes (43.5%), itching (33.5%). There was no significant difference in the type of symptoms between the two groups but the severity of symptoms was found to be highly significant among the diabetic group compared to non-diabetic group (p-value=0.001) (Figure 1).

Age (Years)	GROUP		Total
	Group I (Diabetic)	Group II (Non -diabetic)	
40-45	3 (3.0%)	11 (11.0%)	14 (7.0%)
46-50	12 (12.0%)	18 (18.0%)	30 (15.0%)
51-55	12 (12.0%)	14 (14.0%)	26 (13.0%)
56-60	35 (35.0%)	25 (25.0%)	60 (30.0%)
61-65	38 (38.0%)	32 (32.0%)	70 (35.0%)
Total	100 (100.0%)	100 (100.0%)	200 (100.0%)

Table 2: Age-wise distribution.

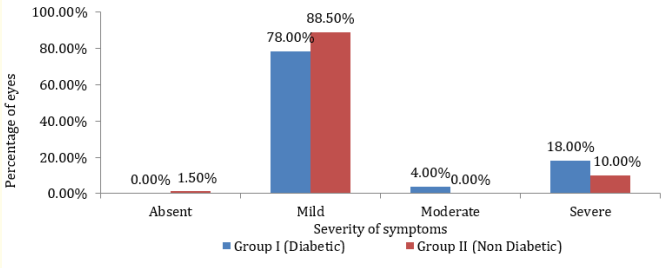

Figure 1: Showing severity of symptoms.

On comparing the meibum quality, it was observed that grading of meibum quality was significantly greater in the diabetic group as compared to non-diabetic group (p-value= 0.002). Grade 2 and 3 meibum quality was found in 42% eyes of group 1 compared to 25% eyes of group 2 (Table 3).

Grading of meibomian gland expressibility was observed to be significantly higher in group 1 compared to group 2 ($p < 0.001$). Grade 2 and 3 meibomian gland expressibility was found in 45% eyes of group 1 compared to 26% eyes of group 2 (Table 4).

On ocular surface staining, it was seen that there was statistically significant increase in ocular surface staining in diabetic group as compared to non-diabetic group (p-value <0.001).Moderate to marked ocular surface staining was found in 27.5% eyes in group 1 compared to 10% eyes in group 2 (Table 5).

Meibum quality score(MQS) grade	Group		Total
	Group I (Diabetic)	Group II (Non-diabetic)	
0 (Clear meibum)	22(11.0%)	20(10.0%)	42(10.5%)
1 (Cloudy meibum)	94(47.0%)	130(65.0%)	224(56.0%)
2 (Cloudy with debris)	62(31.0%)	34(17.0%)	96(24.0%)
3 (Thick like toothpaste)	22(11.0%)	16(8.0%)	38(9.5%)
Total eyes	200(100.0%)	200(100.0%)	400(100.0%)

Table 3: Showing meibum quality grading under slit lamp examination.

Meibum expressibility score(MES) grade	Group		Total
	Group I (Diabetic)	Group II (Non-diabetic)	
0 (All glands expressible)	40(20.0%)	73(36.5%)	113(28.2%)
1 (3-4 glands expressible)	70(35.0%)	75(37.5%)	145(36.3%)
2 (1-2 glands expressible)	66(33.0%)	39(19.5%)	105(26.3%)
3 (No glands expressible)	24(12.0%)	13(6.5%)	37(9.3%)
Total eyes	200(100.0%)	200(100.0%)	400(100.0%)

Table 4: Showing meibomian gland expressibility under slit lamp examination.

Ocular Surface Staining	Group		Total
	Group I (Diabetic)	Group II (Non-diabetic)	
None	0(0.0%)	3(1.5%)	3(0.8%)
Minimal	81(40.5%)	129(64.5%)	210(52.5%)
Mild	64(32.0%)	48(24.0%)	112(28.0%)
Moderate	19(9.5%)	0(0.0%)	19(4.8%)
Marked	36(18.0%)	20(10.0%)	56(14.0%)
Total	200(100.0%)	200(100.0%)	400(100.0%)

Table 5: Showing ocular surface staining.

Clinical staging of meibomian gland dysfunction was obtained by symptoms, meibum quality, meibomian gland expressibility and ocular surface staining. A statistically significant difference was observed in the severity of meibomian gland dysfunction in group 1 as compared to group 2 (p-value <0.001). Stage 3 and 4 meibomian gland dysfunction was found in 59.5% eyes in group 1 compared to 34% eyes in group 2 (Figure 2).

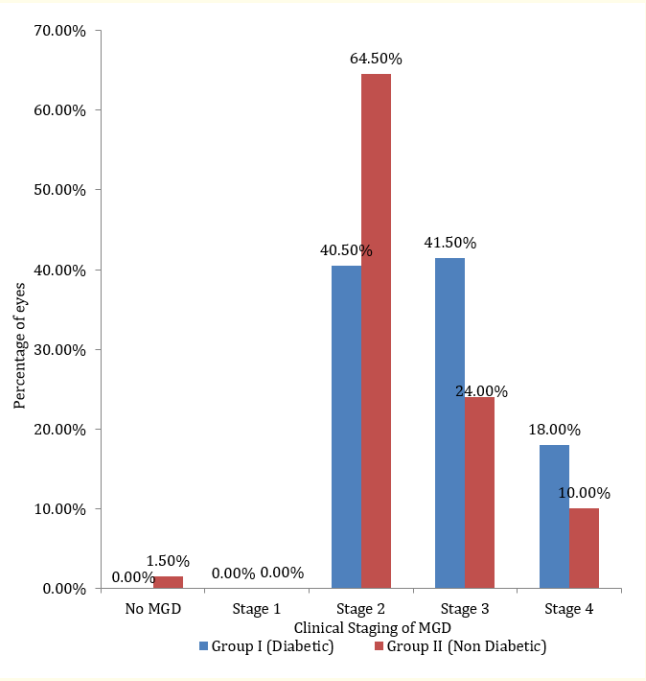

Figure 2: Showing clinical staging of meibomian gland dysfunction (MGD).

Discussion

Meibomian gland dysfunction is a multifactorial, commonly encountered ophthalmic disorder. The International Workshop on Meibomian Gland Dysfunction suggests that meibomian gland dysfunction is the most common cause of evaporative dry eye and may play a role in aqueous-deficient dry eye.

The present prospective study was conducted on 200 patients (400 eyes) of meibomian gland dysfunction who presented to our

out-patient department from January 2019 to January 2020. Group 1 comprised of 100 diabetic patients (200 eyes) with meibomian gland dysfunction while group 2 comprised of 100 non-diabetic patients (200 eyes) with meibomian gland dysfunction. In our study, patients in the age of 40 to 65 years were enrolled. The mean age for group 1 was 57.58 ± 7.73 years and in group 2 was 55.94 ± 7.53 years. Higher incidence was noted in elderly patients which is similar to that reported in a study done by Nien CJ., *et al*. in 2011 [12]. Studies attribute that the aging process is accompanied with functional and morphological meibomian gland alterations [12,13]. In group 1, 43% were males and 57% were females while in group 2, 42% were males and 58% were females. There was no significant difference regarding age and gender wise distribution among the two groups.

Burning sensation in eyes was found to be the most common symptom in both the groups. In group 1, 73% eyes had burning sensation as compared to 64% eyes in group 2. Other symptoms reported were watering of eyes, itching, foreign body sensation, dryness and grittiness. This is in accordance with a study conducted by Kumar J., *et al*. in 2017 who reported that the most common symptom was burning sensation in eyes [14]. In our study, in group 1, 78% eyes presented with mild symptoms, 4% eyes with moderate and 18% eyes with severe symptoms. In group 2, 1.5% eyes had no symptoms, 88.5% had mild symptoms and 10 % severe symptoms. Symptoms were significantly more and severe among the diabetic group. The result is similar to a study done by El Sawy NN., *et al*. who found that symptoms were increased significantly in diabetics compared with controls [15]. Another study done by Pathan R reported that the symptoms of meibomian gland dysfunction in type 2 diabetes were highly significant especially burning (46.9%) and dryness (23.5%) [16].

The quality of meibum under slit lamp examination was found significantly abnormal and of greater grade in group 1 when compared to group 2. 11% eyes in group 1 and 8% eyes in group 2 had thick tooth paste like meibum quality (grade 3).Cloudy meibum with debris (grade 2) was found in 31% eyes in group 1 and 17% in group 2. Similar results were obtained by Shamsheer and Arunachalam in a study where they found that frequency of abnormal meibomian gland expression scale (volume and viscosity) was significantly greater in the diabetic group as compared to the control group patients [17].

It was observed that no meibomian glands were expressible (grade 3) in 12% eyes in group 1 and 6.5 % eyes in group 2. 33% eyes in group 1 while 19.5% eyes in group 2 had 1-2 glands expressible (grade 2). When compared to group 2, significantly greater grading was found in group 1. These results were similar to a study done by Lin X., *et al*. in which they found that the number of expressible meibomian glands was significantly lower in the diabetic group [18].

In our study, 27.5% eyes in group 1 had moderate to marked ocular surface staining as compared to 10% eyes in group 2. There was statistically significant increase in ocular surface staining in the diabetic group as compared to non-diabetic group. This was comparable to a study done by Ozdmeir M., *et al*. in 2003 who observed that in diabetic group, significantly more subjects had abnormal fluorescein and rose bengal staining than in control group [19].

The clinical staging of meibomian gland dysfunction in our study was evaluated on the basis of symptoms, quality of secretion of the meibomian glands, altered expressibility and ocular surface staining. Out of 200 eyes in group 1, 18% eyes were stage 4 and 41.5% were stage 3 while In group 2, 10% eyes were stage 4 and 24% eyes were stage 3. Stage 2 was found in 40.5% eyes in group 1 and 64.5% in group 2. All patients were symptomatic, so, none of the patient in our study was stage 1. 1.5% eyes out of 200 eyes in group 2 had no meibomian gland dysfunction. A statistically significant difference was observed in the severity of meibomian gland dysfunction in diabetics compared to non-diabetic group. Group 1 presented with higher stage of meibomian gland dysfunction compared to group 2.This is in accordance with the study done by Sandra Johanna GP., *et al*. in 2019 which concluded that meibomian gland dysfunction in type 2 diabetic patients is more severe compared with non-diabetic patients [20]. Another study conducted by El Sawy NN., *et al*. in 2019 also found that meibomian gland dysfunction in type 2 diabetic patients is more severe compared with non-diabetic patients [15]. In contrast to our study, Siak JJ., *et al*. demonstrated that the association of diabetes with meibomian gland dysfunction was not statistically significant [21]. A limitation of this study was an access to meibography to study the morphological changes in the meibomian glands and hence meibomian gland dropout couldn't be studied. Another limitation was

that only symptomatic patients with meibomian gland dysfunction were included in our study.

Conclusion

This study concludes that meibomian gland dysfunction is more severe in patients with diabetes mellitus compared to non-diabetic patients. It should be noted at an early stage and treated appropriately to improve the general well-being of the patient.

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