

Original Article

# Association of Meibomian Gland Dysfunction Severity and Glycohemoglobin Levels in Type 2 Diabetic Patients

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## Abstract

**Purpose:** To investigate the association of meibomian gland dysfunction severity and glycated hemoglobin A (HbA1c) levels among type 2 diabetic patients.

**Patients and Methods:** In this cross-sectional study, 40 type 2 diabetic patients with meibomian gland dysfunction (MGD) were studied at Basir Eye Clinic, Tehran, Iran. An expert ophthalmologist determined the MGD stage based on staging scale outlined in American academy of ophthalmology's basic and clinical science course. The HbA1c level was measured applying a standard method, certified by the National Glycohemoglobin Standardization Program (NGSP). We divided patients to two groups based on their HbA1c level; the first group included patients with HbA1c < 6.5 % and the second group included patients with HbA1c ≥ 6.5 %.

**Results:** Our results demonstrated that 12.5 % of the participants had minimal, 52.5 % had mild and 35 % had moderate to severe MGD. We observed that different levels of HbA1c (over or under 6.5 %) were significantly associated with MGD severity (P < 0.013). Moderate to severe MGD stage was observed in 43.7 % of individuals with HbA1c ≥ 6.5 %, while it was found in none of participants with HbA1c < 6.5 %. With increase in HbA1c level, the risk of moderate to severe MGD occurrence increased (OR = 3.57; 95 % CI: 1.05-12.13; P = 0.041). This association was not confounded by age or gender.

**Conclusion:** Meibomian gland dysfunction severity has an association with HbA1c levels in diabetic type 2 patients, and a rise in HbA1c noticeably aggravates the MGD stage.

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## Introduction

Type 2 diabetes mellitus, with increasing number of affected people due to aging, urbanization, physical inactivity and obesity, is a main cause of worldwide socioeconomic burden and mortality. It is more prevalent among 45 to 64 year old and over 64 year old population in developing and developed countries, respectively <sup>1</sup>. According to the first survey of risk factors for non-communicable diseases in Iran (2005) the overall incidence of diabetes had reached 7.7 % among adults aged 25-64 year old <sup>2</sup>.

HbA1c or glycated hemoglobin indicates the mean blood sugar level over the lifetime of red blood cells. HbA1c is considered as the gold standard test for diabetes assessment and management <sup>3</sup>.

Despite the abundance of literature concerning complications of diabetes, there are few studies regarding the relation between diabetes and dry eye. Recent studies have indicated the toxic nature of hyperglycemia and insulin resistance on human meibomian gland epithelial cells <sup>4</sup>. Meibomian glands supply the tear film lipid component and play a major role in ocular surface health <sup>4-6</sup>. Diabetes impairs sebaceous glands function <sup>7-9</sup> and has a key role in development of meibomian gland dysfunction (MGD). MGD blocks meibomian glands openings, increases tear film osmolarity and evaporation and causes an inflammation leading to eye irritation <sup>10-11</sup>. MGD is considered as the most common cause of dry eye and patient visit due to eye irritation and foreign body sensation <sup>12</sup>.

The higher prevalence of dry eye and MGD in diabetes is well-defined in the literature. However, to the best of our knowledge there is no study evaluating the relation between HbA1c in patients with type 2 diabetes and the severity of MGD, so the present cross-

sectional study was conducted to study the correlation between HbA1c levels and the MGD severity among these patients.

## Patients and Methods

The present study was a cross-sectional study including 40 type 2 diabetic patients with MGD. Patients with a history of any refractive surgery, thyroid eye disease, pterygium, and antihistamines and tricyclic antidepressants usage in last one year were excluded. The study was approved by the ethics committee of Basir Eye Health Research Center, Tehran, Iran, and written consent was provided by all participants before entering the study.

The diabetic state was evaluated according to the American Diabetes Association guidelines <sup>13</sup>. The HbA1c level was measured using a standard method, certified by the National Glycohemoglobin Standardization Program (NGSP) <sup>14</sup>.

A single expert ophthalmologist examined all patients and determined the MGD based on staging scale outlined in American Academy of Ophthalmology's Basic and Clinical Science Course (Table 1) <sup>10,15</sup>. Finally, Patients were divided based on their HbA1c level into 2 main groups including HbA1c < 6.5 %, and  $\geq 6.5$  %; then the correlation of HbA1c and MGD stage was evaluated.

## Statistical analysis

Chi-square and multinomial logistic regression tests were used when appropriate to evaluate the data. SPSS version 21 (Armonk, NY: IBM Corp.) was used for statistical analysis. P values less than 0.05 were considered significant.

## Results

The mean age of participants in the present study was  $58.45 \pm 6.32$ . The male to female

**Table 1: Clinical summary of the MGD staging <sup>10</sup>**

Stage	MGD * grade	Symptoms	Corneal staining
1	+ (Minimally altered expressibility and secretion quality)	None	None
2	++ (Mildly altered expressibility and secretion quality)	Minimal to mild	None to limited
3	+++ (Moderately altered expressibility and secretion quality)	Moderate	Mild to moderate; mainly peripheral
4	++++ (Severely altered expressibility and secretion quality)	Marked	Marked: central in addition

ratio was 14/26. The mean age of diabetic females and males were  $58.96 \pm 4.43$  and  $57.50 \pm 8.97$  years, respectively.

The mean HbA1c was  $7.92 \pm 2.15$  with a mean blood glucose level of  $190.45 \pm 53.10$ . We observed that HbA1c levels significantly differed in each MGD stage ( $P < 0.013$ ) (Table 2). Moderate to severe MGD stage was observed in 43.7 % of individuals with  $HbA1c \geq 6.5$  %, while it was found in none of participants with  $HbA1c < 6.5$  % (Table 2). With increase in HbA1c level, the risk of moderate to severe MGD occurrence increased remarkably (OR = 3.57; 95 % CI: 1.05-12.13;  $P = 0.041$ ). This association was not confounded by age or gender.

### Discussion

In the present study MGD severity was found to be associated with HbA1c levels among type 2 diabetic patients. Subsequently, higher HbA1c levels predicted more severe MGD, independent of age and sex of the participants. Some previous studies have compared the prevalence of dry eye in patients suffering from diabetes mellitus and normal population. Diabetes is a known risk factor for impairment of sebaceous glands function since hyperglycemia and insulin resistance pose a dose-dependent toxic effect on human meibomian gland epithelial cells <sup>9,16</sup>. The prevalence of dry eye has shown a correlation with higher values of glycated hemoglobin <sup>17</sup>.

**Table 2: Association between HbA1c level and MGD stages**

HbA1c level		MGD			Total	P value *
		Minimal	Mild	Moderate to severe		
< 6.5 %	Count	3	5	0	8	
$\geq 6.5$ %	Count	2	16	14	32	0.013
Total	Count	5	21	14	40	

\*Chi-Square test

Moreover, diabetes aggravates peripheral neuropathy, which leads to impairment of corneal sensation and the consequent decline in tear production<sup>18</sup>. Shamsheer et al.,<sup>6</sup> compared the prevalence and severity of MGD between diabetic patients and non-diabetic individuals. They reported that corneal staining and meibomian gland secretion volumes are significantly deteriorated in diabetic patients. However, they did not evaluate HbA1c or blood sugar levels<sup>6</sup>.

Studies on MGD frequency have shown a wide range due to lack of consensus on standardized clinical criteria for MGD. However, in most studies MGD is measured based on frequency of eye dryness, gritty/sandy sensation, burning sensation, sticky sensation, watering/tearing, redness, crusting/discharge, and eyes stuck shut<sup>6</sup>. The prevalence of MGD differs in the literature from 3.5% to 70% of population with the greatest incidence in Asian population<sup>19</sup>. Hom et al.,<sup>19</sup> reported 38.9% prevalence of MGD in a group of 398 randomly selected, apparently normal, participants presenting for routine vision examinations<sup>19</sup>. We found that 87.5% of our patients with type 2 diabetes had self-reported, clinically relevant mild to severe MGD.

Although our results revealed that the severity of MGD is significantly increased when higher HbA1c levels are present, the mechanism of this phenomenon is yet to be fully understood. It is known that peripheral neuropathy gradually damages A $\delta$  and unmyelinated C-class small nerve fibres<sup>20</sup>. Deterioration of corneal nerves might result in reduction of subbasal nerve density and branching, which together will reduce the corneal sensitivity<sup>21</sup>. This reduced corneal sensitivity lowers the blink rate, which might subsequently cause increased tear evaporation<sup>22</sup>. Decreased corneal sensitivity might also influence the

control of orbicularis and Riolan's muscles, which are responsible for the delivery of the lipid to the lid margin<sup>23</sup>; and this change might be a reason for increased frequency of MGD in type 2 diabetic patients. The other proposed mechanism is that MGD might be induced by the concomitant inflammatory response in patients with diabetes. It is well-documented that in diabetic patients free fatty acids (FFAs) in plasma create insulin resistance<sup>24</sup> and enhance the expression and release of pro-inflammatory cytokines<sup>25</sup>. Further studies are needed to link increased FFA in meibomian glands with accumulation of meibum leading to meibomitis in diabetic patients.

To the best of our knowledge, the present study was the first study evaluating the correlation between HbA1c levels in type 2 diabetic patients and MGD severity. The HbA1c is the most worldwide accepted marker for measuring glycemic control and providing long-term metabolic monitoring in patients with diabetes<sup>26</sup>.

The present study had some limitations including the small sample size and not taking into account the blood sugar levels or the clinical severity of diabetes. Moreover, we collected our data during a cold-weather period, which might have aggravated dry eye conditions among our patients<sup>27</sup>.

## Conclusion

Meibomian gland dysfunction severity has an association with HbA1c levels in diabetic type 2 patients, and a rise in HbA1c noticeably aggravates the MGD stage.

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#### Footnotes and Financial Disclosures

#### Conflict of interest:

The authors have no conflict of interest with the subject matter of the present study.