

# Ocular Surface Changes in patients with Type 2 Diabetes Mellitus: Evidence from Palestine



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## ABSTRACT

**Purpose:** To determine the ocular surface disease in patients with Type 2 diabetes mellitus (DM) by using translated and validated Arabic version of Ocular Surface Disease Index (Arab-OSDI) and the clinical measurements.

**Study Design:** Cross-sectional study.

**Place and Duration of Study:** Faculty of Health and life sciences, management and science university and International Islamic University Malaysia, from March to July 2022.

**Methods:** A total of 30 patients with Type 2DM and 30 non-diabetic controls were included in this study. All participants, who were non-contact lens users, completed the Arab-OSDI questionnaire and underwent clinical evaluations including tear break-up time (BUT), meibomian gland assessments, tear meniscus height (TMH), Marx line (ML), Schirmer II tear test, fluorescein corneal staining (F/S), and lissamine green conjunctival staining (LGS) were recruited. Dry eye (DE) was diagnosed when Arab-OSDI scores were  $\geq 13$  and BUT was  $< 5$  seconds.

**Results:** The DM and non-DM groups demonstrated notable differences in the outcomes of Arab-OSDI ( $p = 0.017$ ) and the evaluations of meibomian gland ( $p = 0.022$ ). Within the DM group, individuals with dry eye showed significantly elevated Arab-OSDI results compared to those without dry eye ( $p = 0.014$ ), whereas the other clinical parameters showed no statistically significant differences.

**Conclusion:** Individuals with Type-2 DM may experience damage to the lacrimal functional unit, leading to tear deficiency or evaporative DE. This altered tear composition may increase DE symptoms, as reflected in elevated Arab-OSDI scores.

**Keywords:** Ocular surface disease, Diabetes Mellitus, Ocular surface disease index.

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## INTRODUCTION

According to projections by the International Diabetes Federation, the global diabetic population is expected

to reach approximately 578 million by 2030, accounting for about 10.2% of the world's adult population.<sup>1</sup> This figure is anticipated to increase further, reaching 700 million (10.9%) by 2045. Diabetes mellitus is widely recognized for causing various pathophysiological alterations that contribute to multi-organ complications involving the ocular, renal, cardiovascular, and nervous systems.<sup>2</sup> Among the ocular complications linked to diabetes are diabetic retinopathy, cataract, glaucoma, and ocular surface abnormalities, including dry eye disease (DE).<sup>3</sup>

In diabetic patients, DE symptoms have been significantly linked to a reduced tear break-up time (BUT), with diabetics suffering from DE exhibiting a markedly shorter BUT compared to those without DE.<sup>4</sup> Furthermore, compromised ocular surface integrity which is a key feature of DE and may be attributed to reduced corneal sensation in diabetes, which diminishes reflex-induced lacrimal secretion and blink rate, leading to an increased susceptibility to evaporative dry eye disease (DED).<sup>5</sup>

A prior study utilizing the translated and validated Arabic version of the Ocular Surface Disease Index (Arab-OSDI) found a dry eye (DE) prevalence of 51.7% among Saudi adults with type 1 or type 2 diabetes.<sup>6</sup> However, the relationship between diabetes and diabetic eye disease (DE) remains unexplored in the Palestinian population—a region marked by sandy coastlines, fluctuating winds, and intermittent rainfall. In Palestine, the prevalence of diabetes is anticipated to rise from 18.4% in 2015 to 21.5% by 2030, underscoring the need to investigate DE among diabetic individuals in this region.<sup>7</sup>

Gaza was selected as the study site due to its high population density, distinct four-season climate with limited rainfall, high summer temperatures, and cold winters. This investigation aims to contribute valuable insights into DE among the Arab population in this region, where current reports on DE evaluation are limited.

## METHODS

As part of a wider investigation into the epidemiology and underlying causes of dry eye (DE) disease in southern Palestine, this cross-sectional study was carried out in four provinces of the Gaza Strip.<sup>8</sup> The study was approved by the Institutional review board/Ethical review board (PHRC/HC/883/21). Participants aged above 18 years who were capable of understanding and adhering to the study instructions were recruited. Individuals with active ocular surface conditions (e.g., ocular inflammation), a history of refractive or ocular surface surgery in the past 12 months, or current use of contact lenses were excluded.<sup>9</sup>

Subjective evaluation of dry eye (DE) was assessed with the Arabic version of the Ocular Surface Disease Index (Arab-OSDI) questionnaire. This 12-item tool measures ocular discomfort, symptom severity, and the influence of environmental and visual

factors.<sup>10</sup> Arab-OSDI scores were classified into four categories: normal (0–12), mild (13–22), moderate (23–32), and severe (33–100). Participants scoring 13 or above were considered to have dry eye disease.<sup>11,12</sup>

Objective clinical assessments included the Schirmer Test (ST), Tear Break-up Time (TBUT), Corneal Fluorescein Staining (CFS), Conjunctival Lissamine Green Staining (LGS), Meibomian Gland Dysfunction (MGD), Marx Line (ML) evaluation, and Tear Meniscus Height (TMH). The Schirmer Test was used to assess aqueous tear secretion, while TBUT measured tear film stability. CFS and LGS were employed to evaluate conjunctival and corneal staining, respectively. MGD was examined using slit lamp biomicroscopy and graded from 0 (clear meibum) to 4 (severe obstruction).<sup>14</sup> ML was assessed to evaluate lid margin changes, and TMH was measured by positioning a horizontally oriented slit lamp beam along the lower eyelid margin; values below 0.2 mm indicated reduced tear volume.<sup>13</sup>

Meibomian gland secretions were evaluated using lissamine green-moistened swabs applied to the lower eyelid margin, segmented into outer, middle, and inner thirds. Secretion quality was scored on a 0–3 scale, where 0 indicated no secretion at gland orifices and 3 represented excessive secretion extending beyond the orifices. ML evaluation was performed by applying lissamine green dye to the lower fornix. The eyelid margin was segmented into three zones, with each zone graded on a scale from 0 to 3. A total ML score greater than 3.5 was considered indicative of an abnormal finding.<sup>15</sup>

Conjunctival LGS was rated from 0 to 5 based on the frequency and intensity of stained punctate spots—ranging from absent staining (Grade 0) to extensive staining (Grade 5).<sup>16</sup> TBUT was measured after applying a fluorescein strip moistened with saline to the bulbar conjunctiva; the time between the last blink and the initial appearance of tear film disruption under cobalt blue light was recorded, with three readings averaged. Corneal staining was subsequently assessed via CFS and scored from 0 (no staining) to 3 (severe staining involving more than 50% of the corneal surface).<sup>17</sup> While primarily used to monitor tear film behavior and the overall integrity of the ocular surface, these tests also offer indirect insight into corneal nerve function, as impaired corneal innervation may contribute to reduced tear secretion and staining. Direct corneal sensitivity testing was not performed due to lack of appropriate equipment.

**Table 1:** Comparison of Arab-OSDI overall score and meibomian gland assessment between diabetes mellitus subjects and non-diabetes mellitus.

Variable	DM Subjects (Mean ± (SD))	Non-DM Subjects (Mean ± (SD))	p-value*
Arab-OSDI (score)	27.24 ± 15.20	17.65 ± 15.05	0.017
MGDs (grade)	1.67 ± 15.20	1.10 ± 0.80	0.022

DM: diabetes mellitus; SD: standard deviation; OSDI: ocular surface disease index; MGDs: meibomian gland dysfunctions; \*Mann Whitney U test

**Table 2:** Comparison of Arab-OSDI overall score, CFS, TMH, ST, ML and LGS among diabetes mellitus patients with and without dry eye

Variable	DM with DE (mean ± (SD))	DM without DE (mean ± (SD))	p-value*
Arab-OSDI (score)	32.05 ± 11.54	3.21 ± 3.25	0.014
CFS (grade)	0.86 ± 0.64	0.4 ± 0.42	0.001
TMH (mm)	0.58 ± 0.40	0.50 ± 0.46	<0.001
ST II (mm)	23.04 ± 8.30	25.80 ± 11.03	<0.001
ML (grade)	1.08 ± 0.64	1.2 ± 0.27	0.001
LGS (grade)	3.12 ± 2.54	3.00 ± 2.45	0.046

DM: diabetes mellitus; SD: standard deviation; OSDI: ocular surface disease index; TMH: tear meniscus height; ML: Marx line; LGS: lissamine green staining; CFS: corneal fluorescein staining; ST: Schirmer test; \*Mann Whitney U test

Following the application of topical anesthesia, the Schirmer test was conducted by placing the strips

laterally in the lower fornix. The extent of strip wetting was measured in millimeters after five minutes, with values under 15 mm indicating reduced aqueous tear production.<sup>18</sup>

Statistical comparisons between diabetic and non-diabetic participants, as well as between diabetic individuals with and without DE, were carried out using the Mann–Whitney U test. Information regarding diabetes type (type 1 or type 2) was obtained through participant self-report and verified using online records from the Palestinian Ministry of Health (PMOH).<sup>19</sup> However, data on diabetes severity (proliferative vs. non-proliferative) were unavailable in the current dataset retrieved from PMOH records.

## RESULTS

A total of 30 patients with Type 2 DM and 30 non-diabetic controls were included in this study. When comparing DM to non-DM groups, significant differences were observed in the overall Arab-OSDI scores ( $p = 0.017$ ) and meibomian gland assessments ( $p = 0.022$ ), as detailed in Table 1. Within the DM group, those with DE exhibited significantly higher Arab-OSDI scores ( $p = 0.014$ ), along with notable differences in the Schirmer test ( $p < 0.001$ ), Marx's line grading ( $p = 0.001$ ), tear meniscus height ( $p < 0.001$ ), and corneal fluorescein staining

( $p = 0.001$ ), as shown in Table 2. The remaining clinical tests did not show any significant differences.

Most parameters show statistically significant differences between the groups, supporting that diabetic patients with dry eye exhibit more severe symptoms and signs, particularly regarding corneal staining, tear secretion, and subjective discomfort.

## DISCUSSION

Our research team has observed similar significant differences in clinical DE measurements in a retrospective Malaysian study.<sup>4</sup> Consistent with these results, elevated HbA1c levels have been significantly correlated with the incidence of DE.<sup>20</sup> Similarly, early-stage DM is associated with corneal neuropathy which may contribute to DE.<sup>21</sup> Chronic hyperglycemia in diabetics is linked to trigeminal nerve damage, leading to decline in corneal sensitivity, diminished corneal nerve fiber, and increased symptoms of DE.<sup>22</sup> This is reflected by the significant differences in Arab-OSDI scores between DM and non-DM subjects in our study. Damaged corneal nerves can impair reflex tear production, which is vital for maintaining the morphological and functional condition of the ocular surface.<sup>23,24</sup>

Our study further supports these findings through observations of diminished tear volume, increased corneal staining, and compromised Marx's line. The participants in the current study had type 2 DM, a

condition suggested to contribute to meibomian gland dysfunction by altering epithelial cell proliferation and lipid metabolism. This imbalance in tear lipid composition may lead to excessive tear evaporation.<sup>25</sup>

Moreover, alterations in corneal nerve fibers implicated in DE have also been linked to diabetic retinopathy (DR). Evidence indicates that corneal nerve damage can precede DR onset in Type 2 DM, and that corneal nerve fiber length may predict DR progression in Type 1 DM over time.<sup>25</sup> Given that neuronal degeneration in the cornea and retina can occur early in diabetes, it is recommended to assess corneal nerve health even in the absence of overt DR signs. Consequently, DE symptoms and signs resulting from compromised corneal nerves due to neuropathy may serve as valuable indicators for estimating DM severity, particularly in pre-diabetic individuals.

Limitations of the study include small sample size, cross-sectional design, limited assessment of glycemic control and absence of longitudinal follow-up.

## CONCLUSION

Diabetic patients exhibit significantly higher overall Arab-OSDI scores compared to non-diabetic individuals, indicating more pronounced dry eye symptoms. Moreover, diabetic subjects showed notable impairments in meibomian gland function. Significant differences were also observed in measurements of Arab-OSDI, ML, TMH, and CFS when comparing diabetics with and without dry eye. These findings highlight the importance of further investigation to deepen our understanding of diabetes-related ocular complications, especially within Arab populations.

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**Patient's Consent:** Researchers followed the guide lines set forth in the Declaration of Helsinki.

**Conflict of Interest:** Authors declared no conflict of interest.

**Ethical Approval:** The study was approved by the Institutional review board/Ethical review board (PHRC/HC/883/21).

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### Authors Designation and Contribution

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