RESEARCH ARTICLE

Tear film parameters in females with thyroid eye disease and diabetes: an observational study

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Abstract

Objective: To assess different tear film parameters in female patients with thyroid eye disease and diabetes using a single portable device.

Method: The observational study was conducted at the College of Applied Medical Sciences, King Saud University, Riyadh, Saudi Arabia, from January 12 to April 28, 2022, and comprised women patients with thyroid eye disease in group A, women patients with diabetes in group B, and healthy controls in group C. The sample size was determined with a confidence level of 80% and a significance of 0.05. The participants were subjected first to the Ocular Surface Disease Index, followed by non-invasive tear breakup time, tear meniscus height, and lipid layer pattern tests using EasyTear View+. Data was analysed using SPSS 22.

Results: Of the 120 women, 40(33.33%) with mean age 40.4±11.7 years were in group A, 40(33.33%) with mean age 39.8±12.2 years in group B, and 40(33.33%) controls with mean age 37.2±9.5 years were in group C. Significant differences were found in the median values of Ocular Surface Disease Index, non-invasive tear breakup time, tear meniscus height and lipid layer pattern in group C compared to groups A and B $p<0.00$. The non-invasive tear breakup time score was strongly correlated in group B with the tear meniscus height score ($r=0.559$, $p<0.001$. The lipid layer pattern analysis indicated that grade A was predominant in groups A (35%) and B (45%), while grade D was typical in group C (40%).

Conclusion: Women with thyroid eye disease and diabetes had significantly thin lipid layers and lower tear meniscus height and non-invasive tear breakup time than healthy subjects.

Keywords: Dry eye syndrome, Eye abnormalities, Diabetes complications, Females, Lipids. (JPMA 75: 48; 2025)

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Introduction

The tear film plays an essential role in keeping the ocular system healthy. It removes microorganisms, foreign bodies and debris from the ocular surface. In addition, it lubricates the surface of the ocular system.[1] Disturbance in tear film function leads to problems in vision and ocular diseases, such as dry eye. Dry eye syndrome is common in which the tear film loses its homeostasis.[2] The alteration in the lipid layer of the tear film caused by meibomian gland dysfunction leads to an evaporative dry eye. In contrast, hyposecretory dry eye is caused by inadequate production of tears.[3] Individuals with dry eye (up to one-third of the world population) experience various symptoms, such as ocular inflammation, discomfort, burns, pains and redness.[4] Diagnosing dry eye is challenging to measure different tear film parameters. Therefore, various tests and tools, both invasive and non-invasive, should be used together. Dry eye is commonly assessed using the tear evaporation rate (TER), osmolarity, phenol red thread (PRT), Schirmer, tear meniscus height (TMH), tear ferning (TF), and non-invasive tear breakup time (NITBUT) tests as well as questionnaires.[5-9] Non-invasive devices, such as EasyTear View+, can be used to detect dry eye among smokers and subjects with a high body mass index (BMI).[9]

Hypothyroidism and hyperthyroidism describe a state of under- and over-activity of the thyroid.[10] Thyroid eye disease (TED) causes soft tissue expansion. It leads to hyperosmolarity, high TER, and dry eye.[11] However, the exact mechanism by which TED occurs is complex and possibly involves genetic and environmental factors.

Type 1 diabetes mellitus ((TIDM) is an autoimmune disease involving destroying the Langerhans cells in the pancreas, while type 2 diabetes mellitus (T2DM) is a gene-environment model, and it may be more adequate to capture the essence of the condition.[12] In 2021, there were 537 million people diagnosed with diabetes.[13] The Middle East and North Africa (MENA) region showed the highest

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prevalence of diabetes. In 2021, there were 73 million diabetics in the MENA region, which is expected to increase to 136 million by 2045.[13] The pathogenesis of diabetes disorder is complex. It leads to a high glucose concentration in the blood (hyperglycaemia) due to the disruption of insulin levels. Various diabetic complications could result from long-term hyperglycaemia.[12] Diabetes induces dry eye symptoms and high blood glucose levels, and causes a high prevalence of eye dryness.[14] An association between lacrimal gland dysfunction and diabetes has been identified.[15] Diabetes causes several complications to the ocular system, such as diabetic retinopathy, glaucoma, cataracts, and corneal lesions. In addition, diabetes leads to reduced tear production, and, therefore, induces dry eye symptoms.[16]

The current study was planned to assess different tear film parameters in female patients with TED and diabetes using a single easy-to-use portable device that determines NITBUT, TMH and lipid layer pattern (LLP).

Patients and Methods

The observational study was conducted at the women's campus of the College of Applied Medical Sciences, King Saud University, Riyadh, Saudi Arabia, from January 12 to April 28, 2022, and comprised women patients with TED in group A, women patients with diabetes in group B, and healthy controls in group C. Group A was subdivided into patients with hyperthyroidism A1 hypothyroidism A2. Group B was subdivided into patients with controlled diabetes having glycated haemoglobin (HbA1c) level 5.8-6.5% in subgroup B1 and those with uncontrolled diabetes having HbA1c level >6.5% in subgroup B2.[17]

After approval from the institutional ethics review board, the sample size was determined with a confidence level of 80% and a significance of 0.05 using the OpenEpi online sample size calculator,[18] based on the mean prevalence of the diseases in Saudia Arabia. A non-probability sampling technique was used, and the subjects were selected based on non-random factors. Those excluded from patient groups A and B were individual with body mass index (BMI) $^{3}25kg/m^{2}$, hypertension, anaemia, history of ocular surgery, smokers, wearers of contact lens, pregnant or lactating women, those with cholesterol levels >4mmol/L, and patients with vitamin A or D deficiency. For control group C, probable subjects were tested with the Ocular Surface Disease Index (OSDI)[5] and with OSDI score <13 were included. Since the study was conducted at a women's campus, male subjects had to be excluded due to cultural restrictions. Written informed consent was obtained from all the enrolld participants.

All the participants were subjected to 12-item OSDI , which covers symptoms, vision, and triggers for dry eyes, and is used to assess ocular irritation and inflammation caused by dry eyes quickly, with dry eye cut-off being a score >13.[5]

This was followed by NITBUT, TMH and LLP tests, which were carried out in the right eye of each subject, and a 5-minute gap was allowed between the tests.

The tear film parameters were assessed using EasyTear View+ (EasyTear SRL, Maioliche, Trento, Italy), which evaluated the NITBUT and TMH, and visualised the interference of the tear film with the lipid phase. It used white, blue and infrared light-emitting diode (LED) lighting, minimising film tear drying or alteration during measurements. One examiner performed the NITBUT and TMH measurements in triplicate, and the averages were calculated.

The time (in seconds) between the appearance of the first dry spot on the tear film and the last blink was recorded as the NITBUT. Dry eye was assigned for <10 seconds.[9]

The height of the triangular cross-section between the margin of the lower lid and the cornea was recorded (in millimetres) as the TMH. Dry eye was assigned for a height <0.2mm.[9]

The lipid layer thickness (LLT) was cateogirsed as grade A for LLT 13-15nm having gray appearance, grade B for LLT 30-50nm having a more compact apperance, grade C for LLT 50-80nm having grey waves, grade D for LLT around 80nm having a dense white-blue layer, and grade E for LLT 90-140nm having variable colours. Grades A, B, C, D and E were replaced by scores of 1, 2, 3, 4 and 5, respectively, to allow for statistical analysis.[9]

Data was analysed using SPSS 22. Data was not normally distributed, with Kolmogorov-Smirnov test score being $p<0.05$. Therefore, data was expressed as median with interquartile range (IQR) values. The association between scores was tested using the Spearman rank correlation coefficient. $p<0.05$ was considered significant.

Results

Of the 120 women, 40(33.33%) with mean age 40.4±11.7 years were in group A, 40(33.33%) with mean age 39.8±12.2 years in group B, and 40(33.33%) controls with mean age 37.2±9.5 years were in group C. In group A, 8(20%) patients were in subgroup A1 and 32(80%) in A2. In group B, 19(47.5%) patients were in subgroup B1 and 21(52.5%) in subgroup B2. Significant differences were found in the median values of OSDI, NITBUT, TMH and LLP in group C compared to groups A and B ($p<0.001$) (Table 1).

LLP analysis indicated that grade A was predominant in groups A (35%) and B (45%), while grade D was typical in group C (40%) as shown in Figure 1.

Table-1: Median scores with interquartile range (IQR) for OSDI, NITBUT, TMH and LLP in the study groups

Parameter	TED	*p*-Value	Diabetes	*p*-Value	Control
OSDI*	43.5 (29.4)	< 0.001	14.6 (14.7)	< 0.001	10.4 (14.0)
NITBUT (sec)*	7.4 (4.5)	< 0.001	7.9 (1.3)	< 0.001	9.4 (5.7)
TMH (mm)*	0.08 (0.03)	< 0.001	0.17 (0.01)	0.001	0.20 (0.10)
LLP*	2 (2)	< 0.001	2 (2)	< 0.001	4 (2)

OSDI: Ocular Surface Disease Index, NITBUT: Non-invasive tear breakup time, TMH: Tear meniscus height, LLP: Lipid layer pattern.
* Significant difference (Mann–Whitney test).

Table-2: Median values with interquartile range (IQR) for OSDI, NITBUT, TMH and LLP in hyperthyroidism and hypothyroidism subgroups.

Parameter	Hyperthyroidism (n = 8)	Hypothyroidism (n = 32)	*p*-Value
OSDI score*	25.0 (24.4)	43.2 (28.5)	0.048
NITBUT (sec)	9.7 (8.6)	7.4 (4.2)	0.339
TMH (mm)	0.08 (0.04)	0.10 (0.04)	0.121
LLP grade	2 (4)	2 (2)	0.961

OSDI: Ocular Surface Disease Index, NITBUT: Non-invasive tear breakup time, TMH: Tear meniscus height, LLP: Lipid layer pattern.
* Significant difference (Mann–Whitney test).

Table-3: Median values with interquartile range (IQR) for OSDI, NITBUT, TMH and LLP in controlled and uncontrolled diabetes subgroups.

Parameter	Controlled diabetes (n = 19)	Uncontrolled diabetes (n = 21)	*p*-Value
OSDI score	14.2 (25.7)	15.0 (12.5)	0.641
NITBUT (sec)	7.5 (0.8)	8.1 (0.8)	0.832
TMH (mm)*	0.17 (0.06)	0.18 (0.03)	0.001
LLP grade*	2 (2)	2 (3)	0.047

OSDI: Ocular Surface Disease Index, NITBUT: Non-invasive tear breakup time, TMH: Tear meniscus height, LLP: Lipid layer pattern.
* Significant difference (Mann–Whitney test).

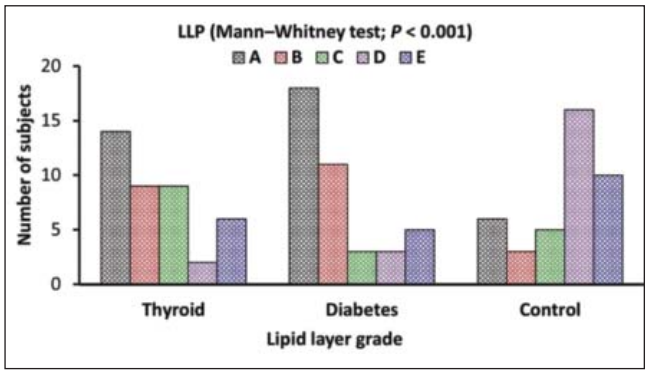

Figure: Lipid layer pattern (LLP) representation in the 3 study groups.

In group A, a weak negative correlation was found between OSDI and NITBUT scores (r=-0.349, p=0.025), and a weak correlation (r=0.354, p=0.023) was found between NITBUT and LLP scores. In group B, OSDI had a medium negative correlation with NITBUT (r=-0.474, p=0.002) and TMH (r=-0.428, p=0.006) scores. NITBUT score was strongly correlated in group B with TMH score (r=0.559, p<0.001).

No significant difference in age was found between A1 and A2 subjects (p>0.05). Median OSDI score was significantly lower in A1 patients than A2 patients (p=0.048). No significant differences were found with respect to NITBUT, TMH and LLP scores between A1 and A2 subgroups (Table 2). The NITBUT score was strongly correlated (r=0.865, p=0.006) with LLP grade in subgroup A2. A medium negative correlation (r=-0.430, p=0.013) was found between OSDI and NITBUT scores in A2 subgroup.

In group B, no significant difference in age was found between subgroups B1 and B2 (p>0.05). Significant differences were found in the median TMH (p=0.001) and LLP (p=0.047) scores between the subgroups (Table 3). No significant difference was found between the median OSDI and NITBUT scores between the subgroups (p>0.05). A strong correlation (r=0.547, p<0.001) was found between the NITBUT and TMH scores in subgroup B2.

Discussion

The current study indicated that dry eye is more prevalent in subjects with TED and diabetes than those with healthy eyes. A similar observation was made based on OSDI scores.

The study showed an association between dry eye and TED, which agrees with the literature.[19] A study conducted on subjects with TED (8 with hypothyroidism and 12 with hyperthyroidism) showed that PRT and NITBUT measurements were significantly lower (p<0.05) compared to the other group. In addition, the TF grades were significantly (p<0.05) higher in thyroid gland patients than in normal eye subjects.[20] Moreover, Schirmer test scores (p= 0.013) and LLT (p=0.012) were significantly lower in patients with TED than in healthy subjects.[21]

The current study using EasyTear View+ suggested an association between dry eye and diabetes. The results agreed with those reported using different techniques and tests.[5,16,22-25]Diabetes is known to cause a thin lipid layer that disrupts the blinking rate, leading to high TER and dry eye symptoms.[26]

In the light of the findings, attention should be paid to increasing people's awareness about these TED and diabetes, and the problems they might cause. In addition, early detection and proper diagnosis are essential to reduce the risk of ocular surface complications.

The current study has limitations, like recruiting only females due to cultural restrictions on recruiting both genders simultaneously. Also, the sample size was relatively small, and the sample was recruited only from one centre. Future studies need to have a large sample size comprising subjects from both genders preferably from different locations across Saudi Arabia.

Conclusions

EasyTear View+ efficiently evaluated LLP, TMH and NITBUT scores. Females with TED and diabetes had significantly thinner lipid layers and lower TMH and NITBUT than the healthy subjects. The OSDI score was significantly higher in subjects with TED and diabetes than in healthy individuals. TED and diabetes were found to be risk factors for dry eye.

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Conflict of Interest: None.

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Author Contribution:
MAA and GAEH: Conceptualization, methodology, investigation, supervision.
MAA, AA, AAAM, MAB, MSA, AAAH, and **GAEH**: Validation. Visualisation.
MAB and MSA: Formal analysis.
MAA, AA, AAAM and GAEH: Data curation.
MAA, MAB, MSA and GAEH: Writing and original draft preparation.
MAA, MAB, MSA, AA and GAEH: Writing, review and editing.
MAA and GAEH: Funding acquisition.