## Comparison between Smokers and Nonsmokers Regarding Incidence of Dry Eye Disease

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#### **Abstract:**

TBUT.

ocular surface, induced by tear hyperosmolarity. Smokers have high risk of developing cataract compared to non-smokers and they are believed to complain of ocular surface symptoms more than non-smokers due to the irritant effect of smokers. Aim: This study was prospective cohort study which intended to compare the incidence of dry eye between smokers and nonsmokers of the 3rd and 4th decade, admitted to Ophthalmology Department, Benha University Hospitals. Methods: This prospective cohort study was made on 120 subjects (240 eyes), distributed into: smokers group; included 60 individuals with a history of cigarette smoking, between 30 to 50 years and nonsmokers group; involved 60 individuals without a history of cigarette smoking having matched age and sex. Results: Patients in the smokers group demonstrated significantly higher frequencies of punctate epitheliopathy in both the right and left cornea (P < 0.001 for both). The Schirmer and TBUT values of both eyes among smokers were considerably less than nonsmokers (P<0.001 for all). Smokers had ~28 and 140- fold increased risk of developing dry eye in the right and left eyes, respectively (P<0.001 for both). The multivariate linear regression analysis revealed that the smoking was significantly associated with reduced Schirmer and TBUT values in both eyes (P<0.001 for all). **Conclusion:** Smoking significantly impairs tear production and stability, dramatically elevating the risk of dry eye disease. These findings highpoint the need for targeted smoking cessation strategies in ocular surface disease prevention.

Keywords: Dry eye; Tear film; Smoking; Schirmer's test;

Background: Dry eye is a chronic inflammatory disorder of the

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#### Introduction

Dry eye syndrome (DES)- or keratoconjunctivitis sicca- is an eye condition brought on by dry eyes, which are in turn brought on by either increased tear film evaporation or decreased tear production. Keratitis sicca symptoms are caused by an unstable tear film, which is created when any one of the three layers of tears is aberrant <sup>(1,2)</sup>.

Depending on whether there are any systemic symptoms or indicators, tear deficiency dry eye is classified as either non-Sjogren or Sjogren tear deficiency <sup>(3)</sup>. Keratoconjunctivitis sicca is characterized by dryness, itchy, scratchy, burning, stinging, or gritty eyes, as well as sandy or gritty eye irritation. Additional symptoms include pressure behind the eye, redness, pain, and a feeling of a foreign body or pulling. Pain and sensitivity to intense light are increased as a result of the damage to the eye's surface <sup>(4)</sup>.

Numerous dry eye risk factors were found and examined. Gender, contact lens use, arthritis, thyroid diseases, and steroids and antihistamines intakes are the most prevalent risk factors (5). Male corneal epithelial cells express higher levels of proliferation and repair genes, like EGFR and DNA replication enzymes, whereas, female cells show elevated expression of genes associated with pain sensitivity, inflammation, and keratinization. Androgens promote epithelial mitosis and wound healing, while estrogen can reduce corneal stiffness and increase matrix remodeling via MMPs, potentially leading to epithelial vulnerability (5).

Smoking harms different organs in the body including the eyes. Smokers have high risk of developing cataract compared to non-smokers. They also have increased risk to get age-related macular degeneration than non-smokers. There is a link between smoking and uveitis. The development and progression of diabetic retinopathy is also related to smoking <sup>(6)</sup>.

Dry eye can be diagnosed by symptoms only. Schirmer's test is done in 5 minutes,

with or without anesthesia, using a Whatman 41 filter paper. Tear breakup time (TBUT) test detects the time taken by tears to break up in the eye <sup>(7)</sup>.

Smokers are believed to complain of ocular surface symptoms more than nonsmokers due to the irritant effect of smoke. Many studies have related smoking with dry eye through reporting documenting symptoms and signs respectively, and using clinical tests like but results Schirmer test, controversial (8).

Therefore, the current work intended to compare the incidence of dry eye between smokers and non-smokers. We intended to compare the presence of punctate epitheliopathy between the studied groups; determine the predictors of dry eye occurrence; determine the predictors of Schirmer and determine the predictors of TBUT.

# **Patients and Methods Patients**

This study was prospective cohort study carried out on 120 subjects (240 eyes), attend the Ophthalmology Department of Benha University Hospital, from October 2022 to September 2023. The subjects were divided into two groups: smokers group [comprising 60 individuals (57 males and 3 females) with a history of cigarette smoking, ranged between 30 – 50 years] and non-smokers group [comprising 60 individuals of matched age and sex (57 males and 3 females) without history of smoking].

The study was approved the Ethical Committee Benha University Hospitals (code no. MS32-12-2022). An informed written consent was gained from the patients.

Patients who did not have any of the inclusion criteria, patients with collagen diseases, ocular surface diseases, ocular surgeries, prolonged computer use and contact lens wear- were excluded.

## Methods

All of the participants were subjected to history taking including (age, sex, occupation and residence, medication, presence of any chronic disease. Slit lamp examination, Visual acuity, Fluorescein staining, Schirmer test and TBUT were performed.

## Fluorescein staining

Fluorescein staining is performed by touching a fluorescein strip to the surface of the eye then ask the patient to blink, wait 1-2 seconds and shines blue light at the eye of the patient. A broad range of corneal superficial punctate epithelial erosions are among the clinical manifestations of fluorescein staining in dry eye. These erosions typically appear in the cornea's lower third and extend throughout the whole surface.

#### Schirmer's test

A single drop of Benoxinate Hydrochloride 0.4 mg % (also known as oxybuprocaine hydrochloride) is used topically to each eye as topical anesthetic for Schirmer's test. Benoxinate blocks sodium ion channels in the neuronal cell membrane, preventing nerve impulse conduction. This leads to a temporary loss of sensation on the ocular surface. This method assesses fundamental function. Making sure not to contact the cornea, a typical Schirmer's strip is folded at the notch and inserted into the inferolateral third of the lower lid. The strip wetness level was measured in millimeters after five minutes. The test gauges how much moisture is present in the eye. It is typical for the filter paper to have more than 10 mm of moisture on it after 5 minutes <sup>(9)</sup>.

In five minutes, those with Sjögren's syndrome moisten <5 mm. Normally, the amount of tears secreted by each eye is equal. The tests were conducted simultaneously on both eyes: Dry eyes (10–15 mm), mild (6–10 mm), moderate (2–5 mm), and severe (0–1 mm)- are the normal range (25–30 mm).

## Tear Break-Up Time

TBUT test is a practical indicator of tear film stability. A single drop of 0.4 mg benoxinate hydrochloride is used to soak a fluorescein strip before applying it to the lower bulbar conjunctiva. Participants were instructed to blink multiple times, and a slit lamp biomicroscope with a broad beam of the slit to study the ocular structures. The tear breakup time is the interval between the final blink and the onset of the first haphazardly placed dry patch on the cornea. Dry spots that form in less than ten seconds are deemed abnormal.

After three iterations of this process, the average value in seconds for each eye was noted. Normal TBUT values are greater than 10 seconds; mild is 8-10 s; moderate is 5-7 s; and severe is < 5 s  $^{(10)}$ .

## Statistical analysis

The sample size was calculated using G\*power software depending on an early research done by Fahmy et al. (11) who stated a medium effect size of TBUT between smokers and non-smokers (d = 0.523) using alpha and beta were adjusted at 0.05 and 0.8, respectively. Statistical analysis were done using Statistical Package for Social Science (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). The data was assessed for normality using the Shapiro-Wilk test and according to normality, numerical data were expressed as using Mann-Whitney U). Categorical data were expressed as numbers and percentages (compared between groups using the Chi-square or Fisher's exact test). Correlations analyses using Pearson's done Spearman's correlations as appropriate.

Multivariate logistic/linear regression analyses calculated the odds ratios (OR) with 95% confidence intervals (95% CI). All statistical tests were two-sided. P<0.05 reflected a significant value.

#### Results

Regarding the demographic data, the study found no substantial variances in age between both groups (p=0.377) and sex (p=0.068). The median duration smoking was 9 years, with a range from 1 to 21 years. Among the smokers, 28.3% smoked fewer than 20 cigarettes per day, while the majority (48.3%) reported smoking between 20 and 40 cigarettes daily. A smaller proportion (23.3%) smoked more than 40 cigarettes per day. **Patients** in the smokers group significantly demonstrated higher frequencies of punctate epitheliopathy in both the right cornea (86.7% vs. 18.3%, P < 0.001) & left cornea (83.3% vs. 3.3%, P < 0.001) than non-smokers, as shown in (Table 1).

Smokers showed significantly reduced tear production as by the Schirmer test in both eyes, than the non-smokers (P < 0.001 for both). Also, Tear film stability evaluated by TBUT was considerably lower in both eyes of smokers than non-smokers (p < 0.001 for both), (**Figures 1, 2**).

Correlation analyses were done to explore the association of both Schirmer test and TBUT with different parameters. Schirmer test results in both eyes revealed significant negative correlations with both the number of cigarettes smoked/24hrs (p<0.001 for both eyes) and smoking duration (P<0.001 for both eyes), as shown in **Table (2).** 

TBUT in the right eye demonstrated significant negative correlations with the number of cigarettes/24hrs and smoking period (P<0.001 for both eyes), as shown in **Table** (3).

Multivariate linear regression analysis was

conducted to identify predictors of eye dryness. Smokers had a 28.37-fold increased risk to get dry eye in the right eye (OR=28.37, P<0.001) and a 142.10-fold increased risk in the left eye (OR=142.099, P<0.001), as displayed in **Table (4).** 

Smoking was substantially related to reduced Schirmer values in the right eye (B=-11.278, P<0.001) and the left eye (B=-11.675, P<0.001). For each additional cigarette smoked per day, the Schirmer value significantly decreased by 5.327 mm in the right eye (B=-5.327, p<0.001) and by 5.341 mm in the left eye (B=-5.341, P<0.001).

Similarly, for each additional year of smoking, the Schirmer value decreased by 0.693 mm in the right eye (B=-0.693, p<0.001) and by 0.635 mm in the left eye (B=-0.635, P<0.001), controlling for age and sex, as shown in **Table (5).** 

Multivariate linear regression analysis was made to define predictors of TBUT in both eyes. Smoking was significantly associated with reduced TBUT, with smokers showing a decrease of 3.592 seconds in the right eye (B=-3.592, p<0.001) and 3.604 seconds in the left eye (B=-3.604, p < 0.001). For each additional cigarette smoked per day, TBUT significantly decreased by 1.249 seconds in the right eye (B=-1.249, p<0.001) and by 1.323 seconds in the left eye (B=-1.323, p < 0.001). Additionally, for each additional year of smoking, TBUT was reduced by 0.187 seconds in the right eye (B=-0.187, p<0.001) and by 0.169 seconds in the left eye (B=-0.169, p<0.001), as shown in **Table (6).** 

**Table (1):** Punctate Epitheliopathy between the studied groups.

Punctate epitheliopathy	Smokers (n = 60)	Non-smokers (n = 60)	P
Right cornea n (%)	52 (86.7)	11 (18.3)	<0.001*
Left cornea n (%)	50 (83.3)	2 (3.3)	<0.001*

n: number, \*: Significant P-value.

Table (2): Correlation between Schirmer of both eyes (mm) and different parameters.

Variable		Rt eye			Lt eye	
		p		p		
Age (years)		0.02	0.882	0.145	0.268	
Cigarettes r per day	number	-0.829	<0.001*	-0.85	<0.001*	
•	luration	-0.804	<0.001*	-0.739	<0.001*	

r: correlation coefficient, \*: Significant P-value.

**Table (3):** Correlation between TBUT of both eyes (mm) and different parameters.

Variable		Rt eye		Lt eye	
		r	p	r	p
Age (years)	0.004	0.978	0.082		0.532
Cigarettes number per day	-0.691	<0.001*	-0.756		<0.001*
Smoking duration (years)	-0.753	<0.001*	-0.688		<0.001*

r: correlation coefficient, \*: Significant P-value.

**Table (4):** Multivariate logistic regression analysis to predict dry eye.

Variable	Rt eye		Lt eye		
	OR (95% CI)	P-value	OR (95% CI)	P	
Age	0.99 (0.912 - 1.075)	0.809	1.004 (0.907 - 1.11)	0.944	
(years)					
Sex	0.713 (0.207 - 2.455)	0.592	0.862 (0.163 - 4.565)	0.861	
Smoking	28.37 (10.406 - 77.345)	<0.001*	142.099 (29.411 – 686.543)	<0.001*	

<sup>\*:</sup> Significant P-value.

**Table (5):** Multivariate linear regression analyses to predict Schirmer (mm).

Variable	Rt eye		Lt eye	p
	B (95% CI)†	p	B (95% CI)†	
Smoking	-11.278 (-12.833 9.723)	<0.001*	-11.675 (-13.038 10.312)	<0.001
Cigarettes number per day	-5.327 (-6.3334.321)	<0.001 *	-5.341 (-6.2574.425)	<0.001 *
Smoking duration (years)	-0.693 (-0.840.545)	<0.001 *	-0.635 (-0.790.479)	<0.001 *

B: regression coefficient, †: Controlled for age and sex, \*: Significant p-value.

**Table (6):** Multivariate linear regression analyses to predict TBUT (sec).

Variable Right eye		Left eye		
	B (95% CI)†	p	B (95% CI)†	p
Smoking	-3.592 (-4.1093.076)	<0.001*	-3.604 (-4.0533.155)	<0.001*
Cigarettes number per day	-1.249 (-1.6010.897)	<0.001*	-1.323 (-1.6321.015)	<0.001*
Smoking duration (years)	-0.187 (-0.230.144)	<0.001*	-0.169 (-0.2140.124)	<0.001*

B: regression coefficient, †: Controlled for age and sex, \*: Significant P-value.

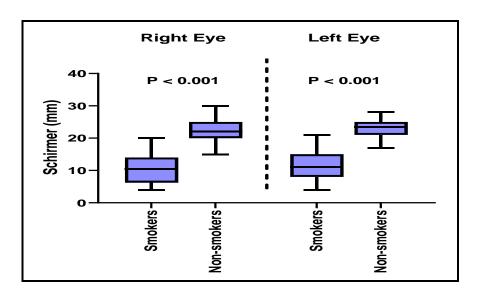
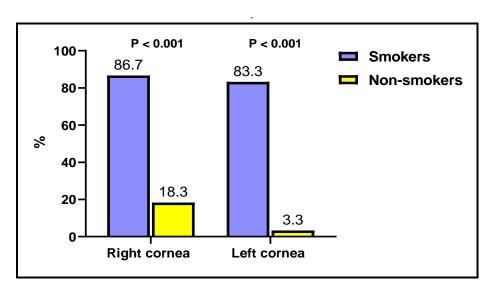


Figure (1): Schirmer Test results between the studied groups



**Figure (2):** Tear Break-Up Time (sec) between the studied groups.

#### **Discussion**

Smoking negatively affects eye health, increasing the risks of cataract, macular degeneration, uveitis, and diabetic retinopathy. Smokers report more dry eye symptoms owing to the irritant effect of smoke. Smoking is linked to dry eye symptoms, clinical signs, and test results, but the relationship remains unclear. Further clarification is required (12). Therefore, this work aims to compare the occurrence of dry eye between smokers and non-smokers.

This study was made at Benha University Hospital and included 120 participants, divided equally into 60 smokers and 60 non-smokers, aged 30 to 50 years. Each participant underwent detailed history taking, clinical examination involving slit lamp evaluation, visual acuity assessment, fluorescein staining, Schirmer test, and TBUT test.

Our study revealed clear alterations in ocular surface health of smokers vs. non-smokers. Smokers showed significantly more frequent signs of punctate epitheliopathy in both eyes, indicating greater corneal epithelial damage. This bilateral pattern suggests that smoking contributes to widespread ocular surface disruption, likely due to the systemic and local toxic influences of smoke on the tear film and corneal epithelium.

The measured tear production was significantly lower in smokers, suggesting impaired tear secretion. This reduction correlated strongly with both the no. of cigarettes/24hrs and the smoking period. TBUT was also considerably shorter in smokers, reflecting reduced tear film stability. These impairments were evident in both eyes, confirming that smoking leads to bilateral compromise in tear production and tear film integrity, worsening of dry eye disease.

Our findings align with Ibrahim et al. evaluated the alterations in the ocular surface in smokers. They included 100 participants of both sexes, aged 18 years

or older. Subjects were divided into two groups: 55 current smokers and 45.

All contributors underwent comprehensive eve examinations, including slit lamp evaluation, Schirmer 2 test, TBUT, and ocular surface staining. Schirmer 2 test were considerably lower means smokers in comparison with non-smokers. Non- smokers had a mean value of 11.5  $\pm$ 2.48 mm, while smokers showed reduced values:  $10.4 \pm 1.33$  mm (mild),  $9.3 \pm 0.99$ mm (moderate), and  $9.4 \pm 1.03$  mm (heavy), with a P < 0.001. TBUT was also meaningfully decreased in smokers (13). Non-smokers recorded  $9.9 \pm 2.99$  seconds.

Non-smokers recorded 9.9  $\pm$  2.99 seconds, compared to 7.7  $\pm$  1.94, 6.4  $\pm$  1.95, 5.9  $\pm$  1.92, and 6.6  $\pm$  1.98 seconds in smokers, with a P < 0.001, and punctate corneal staining was higher in smokers than in non-smokers (P < 0.001). These findings indicate smoking negatively affects tear function and ocular surface integrity (13).

Similarly, to find out how smoking a tobacco waterpipe affected the surface of the eyes, Bakkar et al. (14) undertook a study. The Ocular Surface Disease Index, tear osmolarity, tear film break-up time, and corneal staining were used to evaluate the ocular health of 33 exclusive waterpipe smokers and 31 age-matched non-smokers.

The findings indicated that smokers had considerably lower tear film break-up time  $(5.82 \pm 3.77 \text{ s})$  than non-smokers  $(8.32 \pm$ 3.46 s), and significantly higher tear osmolarity and corneal staining (314.64 ± 15.24 mOsm/L and  $0.73 \pm 0.94$ ) than nonsmokers (306.42  $\pm$  13.48 mOsm/L and  $0.10 \pm 0.30$ ). There was no significant difference in OSDI ratings. Compared to non-smokers (35.5%), smokers had a significantly higher prevalence of dry eye disease (57.6%). These studies demonstrated that Waterpipe smoking could have a considerable effect on tear film characteristics and be associated with dry eye illness (14).

Similarly, Mohidin and Jaafar <sup>(15)</sup> studied how smoking affected the cornea's ocular surface and tear stability in students

between the ages of 19 and 25.

They used fluorescein tear break-up time and non-invasive tear break-up time to assess tear film stability. The Efron grading scale was used to determine corneal staining. When compared to the non-smoking group, the smoker group showed a statistically significant decrease in tear film stability (P<0.0001). The mean TBUT was substantially lower in smokers, averaging  $3.24 \pm 1.05$  seconds, while non-smokers showed a higher mean TBUT of  $5.51 \pm 1.44$  seconds. Smokers' nasal and temporal corneal regions showed statistically significant increased levels of corneal staining (p < 0.05). These results show that tobacco smoke significantly affects the stability of the tear film, as evidenced by smokers' lower tear stability values.

The association between smoking and dry eye in adults was assessed by Khalil et al. (16). The 500 male patients in their study were split equally between 250 smokers and 250 non-smokers. Slit lamp and fundus examinations, the Schirmer 2 test (with topical anesthetic), and TBUT were all part of the ocular evaluation. Smokers' Schirmer 2 test results were considerably those of nonsmokers lower than (P=0.017).

In smokers, the mean value of Schirmer 2 test was 13.91±6.81 mm, whereas in nonsmokers it was 16.58±7.41 mm. TBUT values of the smokers were significantly lower in smokers than in nonsmokers (P=0.035). It averaged 11.9±5.8 s in smokers and 14.9±5.5 s in nonsmokers. Additionally, a linear negative correlation was detected between smoking index of smokers and their Schirmer 2 test and TBUT values. These findings indicate that smoking negatively affects tear film and stability, leading secretion increased eye irritation and a higher likelihood of dry eye among smokers. Moreover, the severity of dry eye is greater in smokers, with a clear negative correlation between smoking intensity and tear function parameters (16).

Also, Agrawal et al. (17) evaluated the consequences of smoking on ocular surface clinically. The study evaluated 100 patients aged 18–50 years, including 50 smokers and 50 non-smokers, matched in age. Smokers were characterized as mild (<10/day), moderate (10-20/day), and heavy (>20/day). Mean TBUT was 14.71 ± 4.34 seconds in non-smokers versus  $11.25 \pm 2.29$  in smokers (p=0.0001). Schirmer's test averaged  $12.58 \pm 2.79$ seconds in non-smokers and  $10.40 \pm 2.64$ in smokers (p=0.001). These findings suggest that smoking is a substantial risk factor in the development of dry eyes and ocular surface condition defined by squamous metaplasia and loss of goblet cells. Additionally, there is a favorable association between the amount of smoking and the severity of dry eyes.

Supporting our results, Bhutia et al. (18) investigated the impacts of lasting smoke on dry eye parameters. From 80 eyes of smokers, TBUT of less than 10 seconds was recorded in (42.5%) of eyes, compared to 22.5%) of non-smokers eyes. The mean TBUT in smokers was  $9.69 \pm 3.96$  seconds, significantly lower than the  $12.8 \pm 1.93$  seconds observed in non-smokers (P < 0.0001), indicating a clear reduction in tear film stability due to smoking.

Additionally, Erginturk Acar et al. reported notable differences in dry eye indicators between chronic smokers and non-smokers. Schirmer test scores, TBUT, symptom severity scores were significantly worse in smokers: 35.85 ± 24.01 points for OSDI,  $14.25 \pm 5.94 \text{ mm}$ for Schirmer test, and  $5.17 \pm 2.85$  seconds for TBUT. In contrast, non-smokers showed better values across parameters:  $15.20 \pm 12.93$  points for OSDI,  $15.48 \pm 7.01$  mm for Schirmer test, and  $10.03 \pm 3.44$  seconds for TBUT. These findings further support the negative impact of smoking on tear secretion and tear film stability.

Furthermore, Thomas et al. (20) assessed how smoking affected smokers' tear films

and ocular surfaces. 50 age- and gender-matched non-smokers (100 eyes) and 51 smokers (102 eyes) participated in the study. Compared to non-smokers (11.28  $\pm$  1.27 s; p=0.0001), smokers exhibited a lower mean TBUT (7.26  $\pm$  1.86 s).

Additionally, 56.9% of smokers had superficial punctate staining of the cornea, whereas the control group had no staining at all. Nonetheless, there was no significant difference in the mean Schirmer's II test value between smokers  $(20.21 \pm 6.62 \text{ mm/5 min})$  and nonsmokers (19.12  $\pm$  5.93 mm/5 p=0.22), suggesting that while smoking negatively impacts tear film stability and corneal health, it might not significantly affect basic tear production concerning Schirmer's test. This discrepancy could be due to differences in the sample size, smoking intensity, or methodology used in the two studies (20).

Additionally, Matsumoto et al. (21) investigated how the chronic smoking affects ocular surface and tear functions. They involved 15 chronic smokers (20 cigarettes daily for 20 years, aged 36–47) and (20 non-smokers, aged 38–43). Participants underwent various ocular tests, including TBUT, Schirmer's test, and corneal fluorescein staining.

They found that the mean TBUT was considerably decreased among smokers  $(3.2\pm0.7 \text{ s})$  than non- smokers  $(14.2\pm2.4 \text{ s}; P<0.0001)$ . On the other hand, there was no significant difference in Schirmer's test values between smokers  $(13.3\pm2.1 \text{ mm})$  and non-smoker controls  $(17.1\pm2.6 \text{ mm}; P>0.05)$ . This inconsistency may arise from differences in the methodology, such as variations in sample size, smoking habits (number of cigarettes or duration), or environmental factors (21).

Moreover, Altinors et al. (22) conducted a prospective, comparative, interventional case series to explore how smoking affects the ocular surface. The study included 60 smokers (33 men and 27 women) and 34 healthy non-smokers (18 men and 16 women), excluding individuals with

systemic or ophthalmic diseases, prior ocular surgery, or contact lens use. The average duration of smoking among participants was 13.1 years, ranging from 5 to 35 years. Smokers demonstrated a mean Schirmer 1 test value of 10.8 mm (range: 8–14 mm), which, although within the lower limits of normal, suggests a trend toward reduced tear production among chronic smokers. The mean TBUT was 5.3 seconds (range: 1–10 seconds), indicating significantly decreased tear film stability. While the difference in Schirmer 1 test values between smokers and nonsmokers was non-significant (P > 0.05), the shortened TBUT reflects a clear disruption of tear film integrity in smokers. This imbalance in tear quantity and quality confirms the influence of smoking on ocular surface health. particularly through compromised tear film dynamics.

Contrary to the findings of our study, Yoon et al. (23) found no discernible difference between smokers and non-smokers in TBUT, corneal staining, or symptom scores. This discrepancy can result from their study's smaller sample size.

#### Conclusion

Smoking significantly impairs tear production and stability, dramatically elevating the risk of dry eye disease. These findings highpoint the need for targeted smoking cessation strategies in ocular surface disease prevention.

The study's single-center design, which might restrict the findings' applicability to a larger population, is one of the work's primary limitations. **Variations** healthcare practices, patient demographics, and environmental factors in different settings could influence the outcomes. In addition, excluding younger and older populations may experience different tear film responses and smoking-related ocular effects not captured in this study. Smoking habits were self-reported by participants, who introduces potential recall

reporting bias and may impact the accuracy of exposure-related correlations in the findings.

However, multicenter studies should be conducted involving diverse geographical locations and populations to improve the generalizability of findings. Adolescents and the elderly should be included, to determine whether smoking affects tear production differently across age-related physiological changes.

Also, biochemical verification methods like cotinine testing should be used to objectively measure tobacco exposure and improve the reliability of smoking-related data in future research.

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