



Association of tobacco smoke exposure with dry-eye symptoms and ocular surface signs

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ABSTRACT

Background: Dry eye disease is a multifactorial ocular-surface disorder. Tobacco smoke exposure has been associated with ocular discomfort and altered tear-film measures, although findings remain inconsistent. This study compared dry-eye symptoms and ocular-surface signs between tobacco smoke-exposed and non-exposed participants.

Methods: This cross-sectional reanalysis used a retrospective, de-identified dataset collected in Gaza in 2023. The sample comprised 81 participants: 40 tobacco smoke-exposed and 41 non-exposed controls. Exposure was defined by a pooled self-reported binary item encompassing cigarette smoking, shisha use, passive smoke exposure, or combinations thereof. Arab Ocular Surface Disease Index (Arab-OSDI) score was the primary outcome; tear break-up time (TBUT), Schirmer I test with topical anesthesia (STT), and corneal fluorescein staining (CFS) were secondary outcomes. All 81 records were analyzed with adjustment for sex and age category. Arab-OSDI, TBUT, and STT used ordinary least-squares regression with HC3 heteroscedasticity-consistent standard errors (SEs); CFS used proportional-odds ordinal logistic regression with HC3 covariance. Sensitivity analyses included median quantile regression for Arab-OSDI, log-transformed TBUT regression, and age-category frequency matching.

Results: Baseline age and sex distributions did not differ significantly between groups ($P > 0.05$ and $P > 0.99$, respectively). Mean (standard deviation [SD]) Arab-OSDI score was 17.18 (16.40) in the exposed group and 10.67 (10.53) in controls. After adjustment, exposure was associated with a 6.77-point higher Arab-OSDI score (HC3 SE, 2.96; 95% confidence interval [CI], 0.96 to 12.57; $P < 0.05$). Associations were not statistically significant for TBUT (regression coefficient [B] = -0.02 s; HC3 SE, 0.71; 95% CI, -1.41 to 1.37; $P > 0.05$) or STT (B = -0.55 mm; HC3 SE, 2.18; 95% CI, -4.82 to 3.73; $P > 0.05$). For CFS, the adjusted proportional-odds ratio for a higher staining category was 0.63 (95% CI, 0.18 to 2.18; $P > 0.05$). Median quantile regression for Arab-OSDI yielded B = 7.05 (95% CI, -0.23 to 14.33; $P > 0.05$), while regression of log-transformed TBUT yielded a ratio of 1.003 (95% CI, 0.775 to 1.299; $P > 0.05$). In the frequency-matched subset (N = 68), the adjusted Arab-OSDI difference was 6.82 points (95% CI, 0.09 to 13.56; $P < 0.05$).

Conclusions: Tobacco smoke exposure was associated with greater dry-eye symptom burden. No statistically significant associations were identified for TBUT, STT, or CFS. Arab-OSDI sensitivity estimates were similar in magnitude and direction, although the median-regression result was not statistically significant. Because exposure pooled cigarette smoking, shisha use, and passive smoke exposure, the findings cannot be interpreted as the isolated effect of active cigarette smoking. Future studies should distinguish these exposure modalities and quantify exposure intensity and duration.

KEYWORDS

dry eye syndromes, tobacco smoking, tobacco smoke pollution, water pipe smoking, Arab-OSDI, tear break-up time, Schirmer I test, corneal fluorescein staining, cross-sectional studies.

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INTRODUCTION

Dry eye disease (DED) is a multifactorial disease of the ocular surface characterized by loss of tear-film homeostasis and accompanied by ocular symptoms [1, 2]. Cigarette smoking is a leading preventable cause of disease and premature mortality worldwide [3] and has also been associated with ocular diseases and ocular-surface abnormalities [4, 5]. Both active smoking and environmental tobacco smoke exposure may adversely affect the ocular surface through direct contact with smoke and the effects of irritant and inflammatory constituents [5, 6].

Clinical studies report differences in dry-eye symptoms, tear-film stability, tear secretion, meibomian-gland morphology and function, and other ocular-surface measures between smokers and nonsmokers [7–14]. However, findings have not been consistent across studies or outcome measures. Lee et al. found no overall association between current smoking and dry-eye severity [15], while more recent epidemiological and genetic studies have likewise reported variable associations between smoking exposure and DED [16, 17]. Systematic reviews and meta-analyses have similarly found that the overall association between smoking and DED remains inconsistent [18, 19]. These findings suggest that smoking may affect specific components of the dry-eye phenotype without producing consistent changes across symptoms and objective ocular-surface signs.

Dry-eye symptoms and ocular-surface abnormalities have also been investigated in Palestinian populations. Studies conducted in Gaza have documented dry-eye symptoms and DED, examining associated demographic, behavioral, clinical, and stress-related factors [20, 21]. The Arabic version of the Ocular Surface Disease Index (Arab-OSDI) has also been validated in a Gazan population, providing a linguistically and culturally adapted measure of dry-eye symptoms [22].

The present study therefore reanalyzed the available participant-level dataset to compare dry-eye symptoms and ocular-surface signs between participants classified as tobacco smoke-exposed and non-exposed. Exposure was defined using a pooled binary item encompassing cigarette smoking, shisha use, passive smoke exposure, or combinations of these exposures; consequently, the analysis does not permit estimation of the isolated effect of active cigarette smoking. The primary hypothesis was that tobacco smoke exposure would be associated with the Arab-OSDI symptom score after adjustment for sex and age category. Secondary analyses examined associations between tobacco smoke exposure and ocular-surface signs, specifically tear break-up time (TBUT), Schirmer I test with topical anesthesia (STT), and corneal fluorescein staining (CFS).

METHODS

This study is a cross-sectional reanalysis of a retrospective, de-identified participant-level dataset collected in Gaza between 15 March and 5 August 2023. The study was conducted in accordance with the Declaration of Helsinki and received ethical approval from the Palestinian Health Research Council (PHRC), Helsinki Committee for Ethical Approval. Written informed consent was obtained before study procedures and data collection. Participation was voluntary, and study data were recorded and analyzed without personally identifying information.

The supplied analytical dataset contained 81 participants: 40 classified as tobacco smoke-exposed and 41 as non-exposed. The available records did not contain recruitment-site or regional variables, so the exact recruitment facilities and geographic distribution of participants could not be retrospectively verified. Among the 81 participants represented in the supplied dataset, no post-eligibility exclusions were documented. The number of individuals who declined participation was not separately recorded and could not be retrospectively verified from the available source records.

Eligible participants were aged ≥ 18 years; resided in the study area during the recorded data-collection period; were able to complete the demographic form, Arab-OSDI questionnaire, and clinical assessments; and provided written informed consent. Clinical exclusion criteria applied irrespective of exposure status and included active ocular-surface disease, ocular allergy or infection, eyelid or meibomian-gland disease, Sjogren syndrome or another autoimmune disease, diabetes mellitus, thyroid disease, glaucoma treatment, current topical ophthalmic medication or artificial-tear use, recent ocular surgery, and current contact-lens wear. All participants were assessed by a qualified optometrist with a degree in optometry and more than five years of clinical experience.

For exposure classification, participants completed a structured questionnaire covering demographic characteristics and tobacco smoke exposure. Exposure was assessed using the self-reported binary question, “Are you a cigarette smoker/shisha smoker/passive smoker?”, with response options “Yes” or “No.” A “Yes” response classified the participant as tobacco smoke-exposed if cigarette smoking, shisha (waterpipe or hookah) use, passive smoke exposure, or any combination of these exposures was reported; a “No” classified the participant as non-exposed.

Because the exposure modalities were pooled within a single binary item, cigarette-only smokers, shisha-only users, dual users, and participants exposed only to passive smoke could not be identified separately. The item did not ascertain

a defined exposure period, current versus former exposure, frequency, duration, cumulative intensity, or the setting or intensity of passive exposure. Exposure was self-reported and not biochemically verified.

For outcomes and participant-level ocular measurements, the Arab-OSDI score was the primary outcome. TBUT, STT, and CFS were secondary outcomes (Table 1). No composite DED endpoint was assigned for the primary or secondary analyses. A five-minute interval was maintained between ocular-surface tests to minimize potential interference from the preceding examination, including between fluorescein instillation/TBUT assessment and subsequent CFS grading.

The supplied analytical dataset contained one participant-level value for each ocular outcome (TBUT, STT, and CFS). Because eye-level source data were not available in the supplied dataset, the original method used to derive these participant-level values from bilateral measurements could not be independently reconstructed or verified.

The Arab-OSDI is a validated Arabic adaptation of the OSDI and consists of 12 items addressing ocular symptoms, vision-related function, and environmental triggers [22]. Scores were classified as normal (0–12), mild (13–22), moderate (23–32), or severe (33–100), with an Arab-OSDI score ≥ 13 considered indicative of symptomatic dry eye [22, 23].

TBUT was assessed using a dry fluorescein strip containing 1 mg sodium fluorescein, moistened with one drop of non-preserved sterile saline and gently applied to the bulbar conjunctiva. Participants blinked naturally to distribute the fluorescein and were then instructed to keep their eyes open. Using slit-lamp biomicroscopy with cobalt-blue illumination, TBUT was recorded as the interval in seconds between the last complete blink and the first appearance of a random dark spot or streak indicating tear-film disruption. Three measurements were obtained consecutively for each eye and averaged [7, 21, 24]. The procedural approach is consistent with the referenced fluorescein-based TBUT methods. The manufacturer and specification of the fluorescein strip and the standardized saline-drop volume were not recorded. The examiner was not masked to participants' exposure status during the ocular-surface assessments.

The supplied analytical dataset contained CFS values of 0, 0.5, and 1. The source documentation available for this reanalysis did not define the half-grade or permit reconstruction of the original grading or recoding procedure. Accordingly, no assumption of equal spacing between the three values was made, and CFS was treated as an ordered three-level variable for statistical analysis. A value ≥ 1 was retained as the predefined threshold for a positive individual CFS sign. The ≥ 1 threshold is consistent with the previously reported Gaza DED criteria [21].

Tear production was assessed using the STT [25]. One drop of 0.5% proparacaine hydrochloride solution was instilled into the lower conjunctival fornix of each eye. After a 30-second interval, a standard Schirmer filter-paper strip was inserted laterally into the lower conjunctival fornix without touching the cornea. Participants were instructed to keep their eyes gently closed during testing, and the wetted length was measured in millimeters after 5 minutes. For the present analysis, an STT value < 15 mm/5 min was treated as the predefined threshold for reduced aqueous tear secretion, consistent with the threshold used in the previous Gazan study [21].

The primary analysis included all 81 records in the supplied analytical dataset; an age-category frequency-matched subset was analyzed only as a sensitivity analysis (Figure 1). Arab-OSDI, TBUT, STT, and CFS had no missing values, therefore all 81 participants were included in analyses of the primary and secondary outcomes and no imputation was required. Tobacco smoke exposure was coded as exposed = 1 and non-exposed = 0, and sex as female = 1 and male = 0. Age was modelled categorically, with 18–30 years as reference category.

Statistical analyses were conducted using Python 3.13.5, NumPy 2.3.5, SciPy 1.17.0, and statsmodels 0.14.6. Continuous variables were summarized using mean (standard deviation [SD]) and median with interquartile range (IQR), as appropriate. Age-category distributions were compared between exposure groups using Pearson's chi-square test, and sex distributions using Fisher's exact test. Adjusted analyses of Arab-OSDI, TBUT, and STT used ordinary least-squares regression with HC3 heteroscedasticity-consistent standard errors (SEs). Each model included tobacco smoke exposure, sex, and age-category indicators. Effect estimates were reported as adjusted mean differences with 95% confidence intervals (CIs). CFS was treated as an ordered three-level outcome (0, 0.5, and 1) and analyzed using proportional-odds ordinal logistic regression with HC3 covariance; the exposure effect was reported as an adjusted odds ratio (aOR) with a 95% CI. Sensitivity analyses included median quantile regression for Arab-OSDI, HC3 regression of log-transformed TBUT, and an age-category frequency-matched analysis in which equal numbers of exposed and non-exposed participants were retained within each age category. All statistical tests were two-sided, with statistical significance assessed at $\alpha = 0.05$. Arab-OSDI was the primary outcome; TBUT, STT, and CFS were secondary outcomes. No multiplicity adjustment was applied to secondary or sensitivity analyses: these analyses were interpreted as supportive rather than as independent confirmatory tests.

Table 1. Interpretive thresholds for dry-eye symptoms and individual ocular-surface signs

Measure	Criterion
Arab-OSDI	Normal: 0–12; Mild: 13–22; Moderate: 23–32; Severe: 33–100
Dry-eye symptoms	Arab-OSDI ≥ 13
TBUT	Positive sign: < 5 s
CFS	Positive sign: ≥ 1
STT	Positive sign: < 15 mm

Abbreviations: Arab-OSDI, Arabic Ocular Surface Disease Index; TBUT, tear break-up time; CFS, corneal fluorescein staining; STT, Schirmer I test with topical anesthesia. Note: Arab-OSDI ≥ 13 denotes symptom positivity. TBUT < 5 s, CFS grade ≥ 1 , and STT < 15 mm/5 min denote positive individual signs. No composite dry-eye-disease diagnosis was assigned in the primary analyses [7, 21–25].

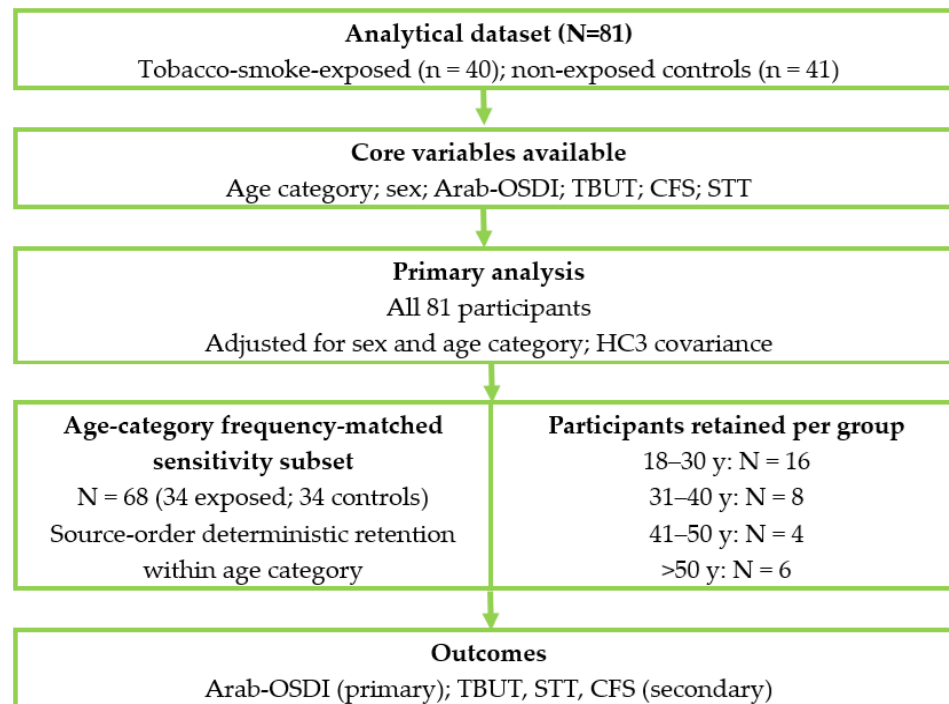


Figure 1. Flow of the supplied analytical dataset and sensitivity-analysis sample. Abbreviations: Arab-OSDI, Arabic Ocular Surface Disease Index; CFS, corneal fluorescein staining; HC3, heteroscedasticity-consistent covariance estimator, type 3; STT, Schirmer I test with topical anesthesia; TBUT, tear break-up time.

RESULTS

Baseline characteristics of the tobacco smoke-exposed and control groups are summarized in Table 2. The supplied analytical dataset contained 81 participants, 40 of them tobacco smoke-exposed and 41 non-exposed controls. Age-category distributions did not differ statistically between groups ($\chi^2(3)=2.65$; $P > 0.05$), and no statistically significant difference in sex distribution was observed (Fisher exact $P > 0.99$). No values were missing for Arab-OSDI, TBUT, CFS, or STT, so the primary and secondary outcome analyses included all 81 participants.

The tobacco smoke-exposed group had a mean Arab-OSDI score of 17.18 (SD, 16.40) and a median of 14.96 (IQR, 4.20–25.78), compared with a mean of 10.67 (SD, 10.53) and a median of 8.33 (IQR, 2.50–13.89) in the non-exposed group. In the adjusted HC3 model, tobacco smoke exposure was associated with a 6.77-point higher Arab-OSDI score (HC3 SE, 2.96; 95% CI, 0.96 to 12.57; $P < 0.05$). Adjusted associations were not statistically significant for TBUT (regression coefficient [B] = -0.02 s; HC3 SE, 0.71; 95% CI, -1.41 to 1.37 ; $P > 0.05$) or STT ($B = -0.55$ mm; HC3 SE, 2.18; 95% CI, -4.82 to 3.73 ; $P > 0.05$). For CFS, the adjusted proportional-odds ratio for a higher staining category was 0.63 (95% CI, 0.18 to 2.18; $P > 0.05$) (Table 3).

Sensitivity analyses are summarized in Table 4. Median quantile regression for Arab-OSDI yielded an adjusted exposure coefficient of 7.05 points (95% CI, -0.23 to 14.33 ; $P > 0.05$). HC3 regression of log-transformed TBUT yielded a ratio of 1.003 (95% CI, 0.775 to 1.299; $P > 0.05$). In the age-category frequency-matched subset ($N = 68$; 34 participants per exposure group), the adjusted Arab-OSDI difference was 6.82 points (95% CI, 0.09 to 13.56; $P < 0.05$) and the adjusted proportional-odds ratio for CFS 0.60 (95% CI, 0.18 to 1.98; $P > 0.05$).

Table 2. Baseline characteristics available in the supplied 81-participant analytical dataset

Characteristic	Tobacco smoke-exposed (N = 40)	Non-exposed controls (N = 41)	P-value
Age category, n (%)			
18–30 years	19 (47.5)	16 (39.0)	0.448
31–40 years	8 (20.0)	11 (26.8)	
41–50 years	4 (10.0)	8 (19.5)	
>50 years	9 (22.5)	6 (14.6)	
Sex (Male / Female), n (%)	38 (95.0) / 2 (5.0)	38 (92.7) / 3 (7.3)	>0.99

Abbreviations: n, number of participants; %, percentage. Note: The age-distribution *P*-value is from Pearson's chi-square test. The sex *P*-value is from Fisher's exact test. Recruitment region, site, stress, sleep, and screen-time variables were not present in the supplied analytical file.

Table 3. Primary adjusted associations between tobacco smoke exposure and dry-eye outcomes

Outcome	Exposed	Controls	Adjusted estimate	HC3 SE	95% CI	P-value
Arab-OSDI (score), Median (IQR)	14.96 (4.20–25.78)	8.33 (2.50–13.89)	B = 6.77	2.96	0.96 to 12.57	0.022
TBUT (s), Median (IQR)	6.60 (4.65–8.04)	6.50 (5.00–9.83)	B = −0.02	0.71	−1.41 to 1.37	0.979
STT (mm), Median (IQR)	26.50 (17.50–35.00)	27.00 (19.00–33.00)	B = −0.55	2.18	−4.82 to 3.73	0.802
CFS (grade), Median (IQR)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	OR = 0.63	log-OR SE = 0.63	0.18 to 2.18	0.464

Abbreviations: HC3, heteroscedasticity-consistent covariance estimator, type 3; CI, confidence interval; Arab-OSDI, Arabic Ocular Surface Disease Index; B, regression coefficient; TBUT, tear break-up time; s, seconds; IQR, interquartile range; STT, Schirmer I test with topical anesthesia; mm, millimeters; CFS, corneal fluorescein staining; OR, odds ratio. Note: *P*-value < 0.05 is shown in bold. Arab-OSDI, TBUT, and STT estimates are adjusted mean differences from HC3 linear regression; the CFS estimate is an adjusted proportional-odds ratio from HC3 ordinal logistic regression. All models are adjusted for sex and age category.

Table 4. Sensitivity analyses were conducted to assess robustness to alternative outcome modelling and age-category frequency matching

Sensitivity analysis	Estimate	95% CI	P-value	Note
Arab-OSDI median quantile regression	B = 7.05	−0.23 to 14.33	0.058	Adjusted
Log-transformed TBUT, HC3	Ratio = 1.003	0.775 to 1.299	0.980	Adjusted geometric mean ratio
Age-category frequency-matched Arab-OSDI (N = 68)	B = 6.82	0.09 to 13.56	0.047	34/group
Age-category frequency-matched CFS (N = 68)	OR = 0.60	0.18 to 1.98	0.399	Ordinal HC3

Abbreviations: CI, confidence interval; Arab-OSDI, Arabic Ocular Surface Disease Index; B, regression coefficient; TBUT, tear break-up time; HC3, heteroscedasticity-consistent covariance estimator, type 3; CFS, corneal fluorescein staining; OR, odds ratio. Note: *P* value < 0.05 is shown in bold. All *P* values are two-sided and unadjusted for multiplicity. Ratio denotes exp(B), the exponentiated regression coefficient from the log-transformed TBUT model. N = 68 denotes the age-category frequency-matched sensitivity subset, with 34 participants in each exposure group.

DISCUSSION

In this study, tobacco smoke exposure was associated with a higher Arab-OSDI symptom score after adjustment for sex and age category, with an adjusted mean difference of 6.77 points (HC3 SE, 2.96; 95% CI, 0.96 to 12.57; *P* < 0.05). In contrast, the secondary analyses did not identify statistically significant associations with TBUT, STT, or ordinal CFS. The median quantile-regression sensitivity analysis for Arab-OSDI produced an estimate of similar magnitude and direction, although its CI included zero, while the age-category frequency-matched subset yielded an adjusted Arab-OSDI difference similar to that observed in the full sample. Because the sensitivity analyses were supportive and not adjusted for multiplicity, they should not be regarded as independent confirmation of the primary result. The overall pattern is therefore most appropriately interpreted as an association between the pooled tobacco smoke exposure measure and greater self-reported ocular symptom burden, without corresponding statistically significant associations across the three objective ocular-surface measures examined. This study did not assign a composite DED diagnosis and does not establish that tobacco smoke exposure causes DED.

The symptom finding in the current study is compatible with other – albeit not all – previous clinical evidence. Bhutia et al. [7] reported higher OSDI scores among smokers together with lower Schirmer II, tear meniscus height, and

TBUT measurements, while Khalil et al. [13] found higher eye-irritation indices among smokers in addition to lower TBUT and Schirmer II measurements. In contrast, Yoon et al. [14] observed shorter TBUT, reduced basal tear secretion, lower corneal sensitivity, and greater conjunctival squamous metaplasia among smokers, but found no significant differences in symptom score, keratoepitheliopathy score, or goblet-cell density. Lee et al. [15] likewise found no general association between current smoking and dry-eye severity among patients attending a specialist dry-eye clinic. Importantly, their study examined variation in severity within an established dry-eye population rather than differences in symptom burden between exposed and non-exposed participants and is therefore not directly comparable with the present analysis.

Two meta-analyses found no statistically significant overall association between current smoking and DED: Tariq et al. [18], comparing current and former smoking, with results remaining consistent across subgroup analyses; and Xu et al. [19], comparing current and ever smoking, although an association emerged when their analysis was restricted to general-population studies. More recently, Mendelian randomization analyses associated genetically predicted regular and lifetime smoking with DED, but not smoking intensity or cessation, and alternative Mendelian randomization estimators did not consistently reproduce the primary associations [16]. These differences across studies [18, 19] indicate that the relationship between smoking and dry-eye outcomes is unlikely to be captured adequately by a single exposure definition or outcome measure [16, 26, 27].

Recent evidence further illustrates the heterogeneity of smoking-related dry-eye findings. Power et al. [26] reported higher OSDI scores and more than twofold greater odds of both aqueous-deficient and evaporative DED among current smokers, together with poorer tear meniscus height, lipid-layer quality, and corneal staining; however, the non-invasive TBUT did not differ significantly between smokers and non-smokers. Wanees Nakhla et al. [27] likewise found markedly higher OSDI scores and shorter non-invasive TBUT in chronic smokers, with poorer lipid-layer and eyelid findings, but no significant differences in tear meniscus height, meibomian-gland loss, or corneal staining compared to non-smokers [27]. In contrast, Wei et al. [28] found that an apparent inverse association between current smoking and DED disappeared after multivariable adjustment (adjusted OR = 0.83; 95% CI, 0.38 to 1.81), while smokers showed longer non-invasive TBUT but greater meibomian-gland loss. These studies are consistent with our finding of greater Arab-OSDI symptom burden but variable objective signs, suggesting that differences in exposure definition, population characteristics, confounder adjustment, and tear-film measurement [16, 18, 19, 29] may partly explain the discordant findings.

The secondary ocular-surface findings also need to be interpreted in this context. Studies of active cigarette smokers report shorter TBUT than in nonsmokers [7, 9, 10, 12–14], whereas the adjusted TBUT coefficient in the present study was close to zero and remained so after log transformation. A recent study further reported associations between greater smoking exposure, meibomian-gland abnormalities, and reduced non-invasive tear-film stability [8]. The study also highlighted an important methodological issue: TBUT findings may vary according to whether fluorescein-based or non-invasive measurement is used [8]. The present study used fluorescein TBUT, and differences in measurement technique [29, 30], participant characteristics [31], and smoking-exposure characteristics—including definitions of chronic smoking and exposure intensity [8, 26, 27, 32]—may contribute to variation between studies; the current data cannot determine which of these factors accounts for the difference.

Evidence concerning tear secretion and ocular staining is similarly non-uniform [7, 9–13]. Lower Schirmer measurements among smokers have been reported by Bhutia et al. [7], Sayin et al. [9], Panon et al. [10], Uchino et al. [11], and Khalil et al. [13]. In contrast, Thomas et al. [12] found no statistically significant difference in Schirmer II results despite shorter TBUT and greater punctate corneal staining among smokers. Comparisons are further complicated by differences among studies in Schirmer I versus Schirmer II testing, use of topical anesthesia, and the thresholds used to define abnormal tear production. Ocular-surface staining has also varied across reports: Yoon et al. [14] found no significant difference in fluorescein staining despite abnormalities in tear stability and secretion; Khalil et al. [13] found no difference in rose-bengal staining; and Thomas et al. [12] reported greater punctate staining among smokers [12]. Hence the absence of a statistically significant CFS association in the present dataset is not without precedent and reinforces the lack of a uniform relationship between smoking exposure and individual ocular-surface signs.

The difference between the Arab-OSDI and objective-sign findings in the current study should not be regarded as intrinsically contradictory. Dry eye is heterogeneous, and symptom severity often correlates only weakly with individual clinical signs, a discordance well documented in the DED literature [2, 21, 33–35]. The use of the Arab-OSDI is particularly relevant in this population because the instrument has been specifically validated in a Gazan sample [22].

One possible interpretation is that tobacco smoke exposure may contribute to ocular discomfort through ocular-surface sensory irritation without necessarily producing detectable parallel changes in TBUT, STT, or CFS at a single examination; previous clinical and review evidence has linked direct ocular exposure to tobacco smoke with conjunctival irritation and related ocular-surface symptoms [5, 14]. This remains a hypothesis rather than a mechanism demonstrated by the present data. Residual confounding, exposure misclassification, variability in clinical testing [36], time-of-day variation in symptoms [37], or differences in exposure intensity [8, 26, 27] could also account for part of the symptom-sign divergence.

The exposure variable is particularly important in this respect [38]. In the present study, cigarette smoking, shisha use, passive smoke exposure, and combinations thereof were collapsed into a single binary exposure category. By contrast, a recent cross-sectional study of 305 Saudi adults classified participants separately as nonsmokers, passive smokers, or active cigarette smokers and evaluated Schirmer test results, tear meniscus height, non-invasive keratographic break-up time, and frequency and severity of dry-eye symptoms [17]. Significant differences in Schirmer, tear meniscus height, and tear-film-stability classifications persisted across smoking-status groups after adjustment for age and sex, while active smokers generally reported more frequent and severe dry-eye symptoms; passive smokers also differed from nonsmokers in symptom measures [17]. These findings illustrate the potential importance of distinguishing exposure modalities when examining ocular-surface outcomes. Pooling active cigarette smoking, shisha use, and passive exposure in the present study may have attenuated or obscured modality-specific associations and, importantly, precludes attribution of the observed Arab-OSDI association specifically to active cigarette smoking. Residual confounding by other unmeasured environmental and occupational exposures cannot be ruled out either, as dry-eye symptoms have been associated with adverse conditions such as excessive wind, air conditioning or heating, and cooking fumes, in addition to cigarette smoke exposure [39, 40].

The present study contributes population-specific evidence from Gaza by evaluating a locally validated symptom instrument alongside three clinically relevant ocular-surface signs and by distinguishing a full-sample primary analysis from sensitivity analyses addressing outcome distribution and age-category balance. Its strengths include complete data for Arab-OSDI, TBUT, STT, and CFS in all 81 participants, adjustment for sex and age category using heteroscedasticity-consistent SEs, ordinal modelling of the observed CFS scale, and consistency in magnitude of the Arab-OSDI estimate in the age-category frequency-matched subset. Some limitations nevertheless constrain interpretation. The cross-sectional design prevents determination of temporal sequence or causality. Exposure was self-reported through a single pooled binary item, with no information on current versus former exposure, frequency, duration, cumulative intensity, passive-exposure setting, or biochemical verification. The examiner was not masked to tobacco smoke exposure status during ocular-surface assessments, introducing the possibility of observer-related measurement bias in the secondary clinical outcomes. The sample was modest and included few women, limiting precision and generalizability, and the available records did not permit verification of the exact recruitment facilities or geographic distribution. CFS was restricted to the observed categories 0, 0.5, and 1, and the original derivation of the half-grade could not be reconstructed. STT values clustered at 35 mm, but true right-censoring could not be established; accordingly, no censored-data sensitivity analysis was retained. Secondary and sensitivity analyses were not adjusted for multiplicity and should remain supportive. Future studies should use larger and more demographically balanced samples; distinguish between active cigarette smoking, shisha use, and passive exposure; quantify exposure duration and intensity, ideally with biochemical verification where feasible; and apply standardized, reproducible ocular-surface measurements. Longitudinal designs would be particularly useful for determining whether changes in exposure precede changes in symptoms or objective ocular-surface findings.

CONCLUSIONS

In this cross-sectional reanalysis, tobacco smoke exposure was associated with a higher Arab-OSDI symptom score after adjustment for age category and sex, with no statistically significant associations observed for TBUT, STT, or ordinal CFS. The Arab-OSDI sensitivity analyses produced estimates of similar magnitude, although the median-regression result was not statistically significant. Because exposure was assessed using a pooled binary item combining cigarette smoking, shisha use, and passive smoke exposure, the observed association cannot be attributed specifically to active cigarette smoking. These findings suggest that tobacco smoke exposure may be more clearly reflected in reported ocular symptoms than in the objective ocular-surface measures evaluated here. Further studies should distinguish exposure modalities and quantify exposure intensity and duration to clarify these relationships.

ETHICAL DECLARATIONS

Ethical approval: The study was conducted in accordance with the Declaration of Helsinki and received ethical approval from the Palestinian Health Research Council (PHRC), Helsinki Committee for Ethical Approval. Written informed consent was obtained before study procedures and data collection. Participation was voluntary, and study data were recorded and analyzed without personally identifying information.

Conflict of interest: None.

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REFERENCES

1. Craig JP, Nichols KK, Akpek EK, Caffery B, Dua HS, Joo CK, Liu Z, Nelson JD, Nichols JJ, Tsubota K, Stapleton F. TFOS DEWS II Definition and Classification Report. *Ocul Surf*. 2017 Jul;15(3):276-283. doi: [10.1016/j.jtos.2017.05.008](https://doi.org/10.1016/j.jtos.2017.05.008). Epub 2017 Jul 20. PMID: [28736335](https://pubmed.ncbi.nlm.nih.gov/28736335/).
2. Tsubota K, Pflugfelder SC, Liu Z, Baudouin C, Kim HM, Messmer EM, Kruse F, Liang L, Carreno-Galeano JT, Rolando M, Yokoi N, Kinoshita S, Dana R. Defining Dry Eye from a Clinical Perspective. *Int J Mol Sci*. 2020 Dec 4;21(23):9271. doi: [10.3390/ijms21239271](https://doi.org/10.3390/ijms21239271). PMID: [33291796](https://pubmed.ncbi.nlm.nih.gov/33291796/); PMCID: [PMC7730816](https://pubmed.ncbi.nlm.nih.gov/PMC7730816/).
3. Samet JM. Tobacco smoking: the leading cause of preventable disease worldwide. *Thorac Surg Clin*. 2013 May;23(2):103-12. doi: [10.1016/j.thorsurg.2013.01.009](https://doi.org/10.1016/j.thorsurg.2013.01.009). Epub 2013 Feb 13. PMID: [23566962](https://pubmed.ncbi.nlm.nih.gov/23566962/).
4. Cheng AC, Pang CP, Leung AT, Chua JK, Fan DS, Lam DS. The association between cigarette smoking and ocular diseases. *Hong Kong Med J*. 2000 Jun;6(2):195-202. PMID: [10895144](https://pubmed.ncbi.nlm.nih.gov/10895144/).
5. Karimi S, Nouri H, Mahmoudinejad-Azar S, Abtahi SH. Smoking and environmental tobacco smoke exposure: implications in ocular disorders. *Cutan Ocul Toxicol*. 2023 Mar;42(1):1-7. doi: [10.1080/15569527.2022.2144874](https://doi.org/10.1080/15569527.2022.2144874). Epub 2022 Nov 17. PMID: [36369835](https://pubmed.ncbi.nlm.nih.gov/36369835/).
6. Lois N, Abdelkader E, Reglitz K, Garden C, Ayres JG. Environmental tobacco smoke exposure and eye disease. *Br J Ophthalmol*. 2008 Oct;92(10):1304-10. doi: [10.1136/bjo.2008.141168](https://doi.org/10.1136/bjo.2008.141168). Epub 2008 Jul 25. PMID: [18658170](https://pubmed.ncbi.nlm.nih.gov/18658170/).
7. Bhutia P, Sen S, Nath T, Shamshad MA. The effect of smoking on ocular surface and tear film based on clinical examination and optical coherence tomography. *Indian J Ophthalmol*. 2021 Jul;69(7):1693-1696. doi: [10.4103/ijo.IJO_2840_20](https://doi.org/10.4103/ijo.IJO_2840_20). PMID: [34146008](https://pubmed.ncbi.nlm.nih.gov/34146008/); PMCID: [PMC8374799](https://pubmed.ncbi.nlm.nih.gov/PMC8374799/).
8. Chen T, Wang R, Liang S, Feng J. Impact of smoking exposure on meibomian gland morphology and tear film stability: a cross-sectional study. *Front Med (Lausanne)*. 2025 Nov 19;12:1711567. doi: [10.3389/fmed.2025.1711567](https://doi.org/10.3389/fmed.2025.1711567). PMID: [41346990](https://pubmed.ncbi.nlm.nih.gov/41346990/); PMCID: [PMC12672861](https://pubmed.ncbi.nlm.nih.gov/PMC12672861/).
9. Sayin N, Kara N, Pekel G, Altinkaynak H. Effects of chronic smoking on central corneal thickness, endothelial cell, and dry eye parameters. *Cutan Ocul Toxicol*. 2014 Sep;33(3):201-5. doi: [10.3109/15569527.2013.832688](https://doi.org/10.3109/15569527.2013.832688). Epub 2013 Oct 22. PMID: [24147943](https://pubmed.ncbi.nlm.nih.gov/24147943/).
10. Panon N, Tongchit T, Borvonshivabhum S, Sudsaweang P, Pratoomsuwan P, Jehsoh S, Kade S, Phetlor S, Vincent JE, Chotimol P, Tungtrakanpoung J, Kongjaidee P, Jenchitr W. Comparison of ocular parameters and dry eye measurements between Thai male smokers and non-smokers. *Journal of Current Science and Technology*. 2021 May 27;11(2):181-7. doi: [10.14456/jcst.2021.19](https://doi.org/10.14456/jcst.2021.19).
11. Uchino Y, Uchino M, Yokoi N, Dogru M, Kawashima M, Komuro A, Sonomura Y, Kato H, Argüeso P, Kinoshita S, Tsubota K. Impact of Cigarette Smoking on Tear Function and Correlation between Conjunctival Goblet Cells and Tear MUC5AC Concentration in Office Workers. *Sci Rep*. 2016 Jun 14;6:27699. doi: [10.1038/srep27699](https://doi.org/10.1038/srep27699). PMID: [27297822](https://pubmed.ncbi.nlm.nih.gov/27297822/); PMCID: [PMC4906346](https://pubmed.ncbi.nlm.nih.gov/PMC4906346/).
12. Thomas J, Jacob GP, Abraham L, Noushad B. The effect of smoking on the ocular surface and the precorneal tear film. *Australas Med J*. 2012;5(4):221-6. doi: [10.4066/AMJ.2012.1035](https://doi.org/10.4066/AMJ.2012.1035). Epub 2012 Apr 30. PMID: [22848314](https://pubmed.ncbi.nlm.nih.gov/22848314/); PMCID: [PMC3395277](https://pubmed.ncbi.nlm.nih.gov/PMC3395277/).
13. Khalil HE, Aboud SA, Azzab MA. Comparative study between smokers and nonsmokers regarding dry eye. *Delta Journal of Ophthalmology*. 2018 Jan 1;19(1):9-13. doi: [10.4103/DJO.DJO_25_17](https://doi.org/10.4103/DJO.DJO_25_17).
14. Yoon KC, Song BY, Seo MS. Effects of smoking on tear film and ocular surface. *Korean J Ophthalmol*. 2005 Mar;19(1):18-22. doi: [10.3341/kjo.2005.19.1.18](https://doi.org/10.3341/kjo.2005.19.1.18). PMID: [15929482](https://pubmed.ncbi.nlm.nih.gov/15929482/).
15. Lee SY, Petznick A, Tong L. Associations of systemic diseases, smoking and contact lens wear with severity of dry eye. *Ophthalmic Physiol Opt*. 2012 Nov;32(6):518-26. doi: [10.1111/j.1475-1313.2012.00931.x](https://doi.org/10.1111/j.1475-1313.2012.00931.x). Epub 2012 Sep 7. PMID: [22958181](https://pubmed.ncbi.nlm.nih.gov/22958181/).

16. Yang K, Zhang H, Wang Y, Yan Y, Yang Z, Wan S, Yang W, Yang Y. Evaluating the impact of smoking on the risk of dry eye disease: a two-sample Mendelian randomization study. *Sci Rep.* 2024 Dec 30;14(1):32043. doi: 10.1038/s41598-024-83795-5. PMID: 39738480; PMCID: PMC11685925.
17. Alghamdi A, Zieried FM, Kwarteng MA, Ezinne NE, Anyatonwu OP, Osuagwu UL. The effect of smoking on dry eye disease and corneal thickness in the Saudi population: a cross-sectional study. *Discover public health.* 2025 Apr 17;22(1):168. doi: 10.1186/s12982-025-00532-7.
18. Tariq MA, Amin H, Ahmed B, Ali U, Mohiuddin A. Association of dry eye disease with smoking: A systematic review and meta-analysis. *Indian J Ophthalmol.* 2022 Jun;70(6):1892-1904. doi: 10.4103/ijo.IJO_2193_21. PMID: 35647954; PMCID: PMC9359251.
19. Xu L, Zhang W, Zhu XY, Suo T, Fan XQ, Fu Y. Smoking and the risk of dry eye: a Meta-analysis. *Int J Ophthalmol.* 2016 Oct 18;9(10):1480-1486. doi: 10.18240/ijo.2016.10.19. PMID: 27803868; PMCID: PMC5075666.
20. Aljarousha M, Alghamdi WM, Che Azemin MZ, Mahmud M. Epidemiology of ocular surface symptoms and their association with stress levels among the Gazan population in crowded shelters during the 2023 Israel war. *Cont Lens Anterior Eye.* 2025 Jul;48(4):102403. doi: 10.1016/j.clae.2025.102403. Epub 2025 Mar 17. PMID: 40102140.
21. Aljarousha M, Badarudin NE, Che Azemin MZ, Aljeesh Y, Amer A, Abdul Rahim MAS. Prevalence and Risk Factors of Dry Eye Disease in the South of Palestine. *Malays J Med Sci.* 2024 Apr;31(2):72-97. doi: 10.21315/mjms2024.31.2.8. Epub 2024 Apr 23. PMID: 38694574; PMCID: PMC11057840.
22. Aljarousha M, Badarudin NE, Che Azemin MZ, Aljeesh Y, Amer A, Abdul Rahim MAS. The validity and reliability of the Arabic version of the ocular surface disease index (OSDI) questionnaire in a sample of the Gazan population: a study from Palestine. *Int Ophthalmol.* 2023 Apr;43(4):1303-1316. doi: 10.1007/s10792-022-02528-7. Epub 2022 Sep 26. PMID: 36156181.
23. Alhamyani AH, Kalakattawi RM, Kalakattawi AM, Alhamyani AH, Alsquati FA, Al-Shehri LA, Assery MS, Alzahrani AA. Prevalence of dry eye symptoms and its risk factors among patients of King Abdulaziz Specialist Hospital (Taif), Saudi Arabia. *Saudi Journal for Health Sciences.* 2017 Sep 1;6(3):140-4. doi: 10.4103/sjhs.sjhs_90_17.
24. Tsubota K. Short Tear Film Breakup Time-Type Dry Eye. *Invest Ophthalmol Vis Sci.* 2018 Nov 1;59(14):DES64-DES70. doi: 10.1167/iovs.17-23746. PMID: 30481808.
25. Li N, Deng XG, He MF. Comparison of the Schirmer I test with and without topical anesthesia for diagnosing dry eye. *Int J Ophthalmol.* 2012;5(4):478-81. doi: 10.3980/j.issn.2222-3959.2012.04.14. Epub 2012 Aug 18. PMID: 22937509; PMCID: PMC3428545.
26. Power B, Wang MTM, Xue AL, Craig JP. Association of tobacco smoking with aqueous deficient and evaporative dry eye disease subtypes: a prospective registry-based case-control study. *Ocul Surf.* 2025 Oct;38:53-55. doi: 10.1016/j.jtos.2025.06.001. Epub 2025 Jun 13. PMID: 40518014.
27. Wanees Nakhla MT, El Din Shalash AB, Edris NA, ElSheikha OZ. Assessment of dry eye disease and retinal nerve fiber layer thickness in chronic smokers. *Cont Lens Anterior Eye.* 2025 Apr;49(2):102602. doi: 10.1016/j.clae.2025.102602. Epub 2026 Jan 2. PMID: 41483742.
28. Wei YL, Cao K, Zhang Q, Tang JY, Tian L, Jie Y. Apparent protective associations between smoking, alcohol consumption, and dry eye disease: evidence from a community-based Adult Dry Eye Cohort (ADEC) in Beijing. *BMC Public Health.* 2026 Jun 20. doi: 10.1186/s12889-026-28009-5. Epub ahead of print. PMID: 42321718.
29. Lan W, Lin L, Yang X, Yu M. Automatic noninvasive tear breakup time (TBUT) and conventional fluorescent TBUT. *Optom Vis Sci.* 2014 Dec;91(12):1412-8. doi: 10.1097/OPX.0000000000000418. PMID: 25343685.
30. Wang MTM, Craig JP. Comparative Evaluation of Clinical Methods of Tear Film Stability Assessment: A Randomized Crossover Trial. *JAMA Ophthalmol.* 2018 Mar 1;136(3):291-294. doi: 10.1001/jamaophthalmol.2017.6489. PMID: 29392287; PMCID: PMC5885903.
31. Ayaki M, Negishi K. Decrease of tear break-up time at Japanese eye clinics during five consecutive years. *Sci Rep.* 2022 Apr 27;12(1):6848. doi: 10.1038/s41598-022-11035-9. PMID: 35477771; PMCID: PMC9043507.
32. Satıcı A, Bitiren M, Ozardali I, Vural H, Kilic A, Guzey M. The effects of chronic smoking on the ocular surface and tear characteristics: a clinical, histological and biochemical study. *Acta Ophthalmol Scand.* 2003 Dec;81(6):583-7. doi: 10.1111/j.1395-3907.2003.00158.x. PMID: 14641258.
33. Sullivan BD, Crews LA, Messmer EM, Foulks GN, Nichols KK, Baenninger P, Geerling G, Figueiredo F, Lemp MA. Correlations between commonly used objective signs and symptoms for the diagnosis of dry eye disease: clinical implications. *Acta Ophthalmol.* 2014 Mar;92(2):161-6. doi: 10.1111/aos.12012. Epub 2012 Dec 28. PMID: 23279964.
34. Vehof J, Sillevs Smitt-Kamminga N, Nibourg SA, Hammond CJ. Predictors of Discordance between Symptoms and Signs in Dry Eye Disease. *Ophthalmology.* 2017 Mar;124(3):280-286. doi: 10.1016/j.ophtha.2016.11.008. Epub 2016 Dec 23. PMID: 28024826.

35. McMonnies CW. Why the symptoms and objective signs of dry eye disease may not correlate. *J Optom.* 2021 Jan-Mar;14(1):3-10. doi: [10.1016/j.optom.2020.10.002](https://doi.org/10.1016/j.optom.2020.10.002). Epub 2020 Nov 23. PMID: [33243674](https://pubmed.ncbi.nlm.nih.gov/33243674/); PMCID: [PMC7752964](https://pubmed.ncbi.nlm.nih.gov/PMC7752964/).
36. Nichols KK, Mitchell GL, Zadnik K. The repeatability of clinical measurements of dry eye. *Cornea.* 2004 Apr;23(3):272-85. doi: [10.1097/00003226-200404000-00010](https://doi.org/10.1097/00003226-200404000-00010). PMID: [15084861](https://pubmed.ncbi.nlm.nih.gov/15084861/).
37. Bair JA, Khan AZ, Yazdani M, Ræder S, Uttheim TP, Fineide FA. Impact of Time of Day on Dry Eye Disease: Findings from a Large Dry Eye Clinic Cohort. *Clin Ophthalmol.* 2026 Jun 3;20:593926. doi: [10.2147/OPTH.S593926](https://doi.org/10.2147/OPTH.S593926). PMID: [42261474](https://pubmed.ncbi.nlm.nih.gov/42261474/); PMCID: [PMC13242849](https://pubmed.ncbi.nlm.nih.gov/PMC13242849/).
38. Miglio F, Naroo S, Zeri F, Tavazzi S, Ponzini E. The effect of active smoking, passive smoking, and e-cigarettes on the tear film: An updated comprehensive review. *Exp Eye Res.* 2021 Sep;210:108691. doi: [10.1016/j.exer.2021.108691](https://doi.org/10.1016/j.exer.2021.108691). Epub 2021 Jul 2. PMID: [34224681](https://pubmed.ncbi.nlm.nih.gov/34224681/).
39. Li J, Zheng K, Deng Z, Zheng J, Ma H, Sun L, Chen W. Prevalence and risk factors of dry eye disease among a hospital-based population in southeast China. *Eye Contact Lens.* 2015 Jan;41(1):44-50. doi: [10.1097/ICL.0000000000000064](https://doi.org/10.1097/ICL.0000000000000064). PMID: [25232992](https://pubmed.ncbi.nlm.nih.gov/25232992/).
40. Li Y, Yang J, Xie T, Xiang P, Kong L, Liu H. Indoor Environmental Exposures and Dry Eye Disease: Mechanisms, Clinical Impact, and Prevention Strategies. *Toxics.* 2026 Aug 12;14(8):711. doi: [10.3390/toxics14080711](https://doi.org/10.3390/toxics14080711). PMID: [42646993](https://pubmed.ncbi.nlm.nih.gov/42646993/); PMCID: [PMC13517088](https://pubmed.ncbi.nlm.nih.gov/PMC13517088/).