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Original Article

Ophthalmology Section

Comparative Evaluation of Tear Film and Corneal Surface in Chronic Smokers and Non Smokers: A Cross-sectional Study

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ABSTRACT

Introduction: Tobacco smoking is the primary avoidable cause of mortality, resulting in the deaths of seven million people worldwide annually. Tobacco smoke is a well-documented ocular irritant that exacerbates Dry Eye Disease (DED) and its associated symptoms.

Aim: To compare tear film and corneal surface parameters in chronic smokers and non smokers.

Materials and Methods: This cross-sectional study was conducted among chronic smokers and non smokers presenting at a tertiary eye care centre in Northern India. A total of 80 subjects were included in the study and divided into two groups of 40 subjects each, comprising group A (chronic smokers) and group B (non smokers). All participants underwent a series of measurements: Schirmer I test, Tear Breakup Time (TBUT), Central Corneal Thickness (CCT) and endothelial cell count using specular microscopy.

Results: The mean age of smokers was 50.15±6.89 years, whereas the mean age of non smokers was 49.25±6.39 years, with a significant male preponderance. The dry eye parameters, such as the Schirmer I test and TBUT, were significantly lower in smokers compared to non smokers, with a statistically significant difference (p-value <0.001). Similarly, CCT and endothelial cell count were significantly lower in smokers than in non smokers, with a statistically significant difference (p-value <0.001).

Conclusion: The study highlights the detrimental effects of smoking on ocular surface health. Smoking predisposes users to DED due to lower tear production and an unstable tear film.

Keywords: Central corneal thickness, Dry eye, Endothelial cell count, Smoking

INTRODUCTION

Cigarette smoking has a global impact on individuals worldwide. According to the 2018 World Health Organisation (WHO) report, there are approximately 120 million smokers in India, accounting for 12% of the world's smoking population [1]. Tobacco smoking is the primary avoidable cause of mortality, resulting in the deaths of seven million people worldwide annually. It is the most preventable cause of death among the top five risk factors for mortality [2,3].

The heavy metals and hazardous mineral components found in cigarette smoke have the capacity to inflict substantial harm on human health [4]. These dangerous substances have a wide array of negative physiological effects, including significant abnormalities in several organs, including the eyes [5]. The tear film is essential for maintaining the health of the ocular surface by providing lubrication, distributing nutrients and oxygen and facilitating the removal of material from the ocular surface [6,7]. Cigarette smoking has been recognised as a notable risk factor that can induce oxidation of the corneal tear film, which constitutes the outermost layer of the tear film. This specific cause has been considered one of the factors attributed to DED [8]. Based on a demographic study conducted by Chia EM et al., it has been shown that between 25-40% of employees engage in cigarette smoking during their working hours. Furthermore, it has been observed that 25% of these individuals exhibit symptoms often linked with dry eye [9].

To date, limited data is available in the literature regarding the impact of tobacco smoke on the eyes in the Indian population [10]. The assertion that smoking is associated with negative impacts on ocular health lacks conclusive evidence to substantiate this hypothesis [11]. Given the aforementioned factors, this research aimed to investigate the impact of smoking on the tear film and corneal surface in individuals who engage in chronic smoking in the Indian population and compare it with non smokers. This is part of a larger project in which tear film, corneal parameters and retinal nerve fiber layer in chronic smokers and non smokers were evaluated. It is important to note that this manuscript discusses only the effects of smoking on anterior segment parameters, namely the tear film and corneal surface.

MATERIALS AND METHODS

The cross-sectional study was conducted among chronic smokers and non smokers presenting to the outpatient department of the Regional Institute of Ophthalmology, Pt. BD Sharma PGIMS, Rohtak, Haryana, India, from September 2022 to September 2023, after fulfilling the inclusion and exclusion criteria. Approval for the study was granted by the Institutional Ethics Committee with letter no. BREC/22/TH/Ophthal.-10 dated 15/11/22, and informed consent was obtained from all participants.

Inclusion criteria: The study included a total of 40 patients aged 40-60 years who had smoked cigarettes for at least one continuous year and were active smokers at the time of the study as cases. Age-matched 40 non smokers with no history of passive smoking were selected as the control group.

Exclusion criteria: Patients using contact lenses, having a history of any ocular surgery using medications that cause dry eye (such as antiglaucoma drugs, vasoconstrictors and antihistamines) having ocular surface disorders (such as herpes simplex virus infection, varicella zoster virus infection and Stevens-Johnson syndrome), using artificial tears, having chronic allergic eye disease or those with a history of passive smoke exposure or who had spent substantial time in a smoky atmosphere at home or at work within the last six months were excluded from this study.

Sample size calculation: The estimated sample size was based on the TBUT among groups. For the sample size calculation, a mean difference of 3.11 with a standard deviation of 4.5, as per the previous study by Bhutia P et al., [12]. The sample size with a 95% confidence interval, 80% power, and an alpha level of 0.05 was calculated.

Comparison of two mean formula:

N=size per group;

SD=Standard Deviation=4.5

δ=mean difference=12.8-9.69=3.11

$Z_{\alpha/2}=Z_{0.05/2}=Z_{0.025}$=1.96-From Z table at type I error of 5

$Z_{\beta}=Z_{0.20}$=0.84-at 80% power

$$N=2\times\frac{(Z_{\alpha/2}+Z_{\beta})^2}{(\delta 0)^2}\times SD^2$$

$=2\ (1.96+0.84)^2\ (4.5)^2/(3.11)^2$

=15.68 * 20.25/9.67

=317.52/9.67

=32.83

=33

The estimated sample size for each group is n1=33 and n2=33. Thus, 40 patients were included in each group, totaling 80 patients.

Study Procedure

A detailed ocular and medical history was taken, including the history of smoking, duration and number of cigarettes smoked per day. For non smokers, a history of passive smoking was recorded. Each patient's complete systemic medical history was also documented. Best-Corrected Visual Acuity (BCVA) using Snellen's chart was assessed to fulfill the inclusion criteria. After this, the Schirmer I test was performed by placing Whatman filter paper 41 (5 mm×35 mm) in the lower conjunctival fornix, at the junction of the outer one-third and inner two-thirds for five minutes. The measurement of wetting (in mm) after five minutes was taken as a measure of aqueous tear secretion. Each eye was tested separately. The eyes were graded based on wetting as normal if >10 mm, mild to moderate if within 6 to 10 mm, and severe if within 0 to 5 mm [12]. Following this, TBUT was assessed using 2% fluorescein dye, which was instilled into the lower fornix of the patient's eye. The eye was examined under a slit lamp with low magnification and a broad beam covering the entire cornea. The lamp was switched to a cobalt blue filter. The patient was asked to blink once and then keep their eyes open. Due to the fluorescein, the tear film appeared green in color. A black spot indicating the dry area appeared a few seconds after each blink. TBUT was defined as the time interval between the last blink and the appearance of the first randomly distributed dry spot. The eyes were classified as normal, marginal, or low grades of dry eye based on the breakup times of >10 seconds, 5 to 10 seconds, or <5 seconds, respectively [13].

Following this, CCT was calculated using a non contact specular microscope. The readings were classified as less than normal, marginal, or normal if the thickness was found to be ≤520 µm, 521 to 570 µm, or >570 µm, respectively [12]. Subsequently, endothelial cell count was measured using the same non contact specular microscope. The mean cell count of a normal cornea was taken as 2445±425 cells per mm^2 [14].

STATISTICAL ANALYSIS

The quantitative variables in both groups were expressed as mean±SD and compared using the Student's t-test. The statistical analysis was performed using the 'R' programming language and/or the Statistical Package for the Social Sciences (SPSS) version 21.0. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 80 subjects were recruited for this study and divided into two groups of 40 subjects each, comprising group A (smokers) and group B (non smokers). The mean age of smokers was 50.15±6.89 years, whereas that of non smokers was 49.25±6.39 years, with a p-value >0.05, which was statistically non significant [Table/Fig-1]. There was a significant male preponderance with a male-to-female ratio of 1.96:1 [Table/Fig-2].

Variable	Smokers (Mean±SD)	Non smokers (Mean±SD)	p-value
Age group (years)	50.15±6.89	49.25±6.39	>0.05

[Table/Fig-1]: Age distribution.

Sex	Smokers	Non smokers	Total
Females	9	18	27
Males	31	22	53
Total	40	40	80

[Table/Fig-2]: Gender distribution of study participants.

Schirmer's test was performed to assess dry eye syndrome [Table/Fig-3]. The mean tear production among smokers was 8.20±4.581 mm in the right eye and 8.55±4.701 mm in the left eye, indicating lower tear production (mild to moderate grade of dry eye). In contrast, non smokers showed significantly higher tear production with a mean of 24.70±6.809 mm in the right eye and 26±6.563 mm in the left eye. The difference in Schirmer's scores was found to be statistically significant (p-value <0.001), suggesting that smoking has a detrimental effect on tear production.

Schirmer I test (mm)	Smokers Mean±SD	Non smokers Mean±SD	t-value	p-value
Right Eye (RE)	8.20±4.581	24.70±6.809	-12.715	<0.001*
Left Eye (LE)	8.55±4.701	26±6.563	-13.67	<0.001*

[Table/Fig-3]: Comparison of Schirmer I test between smokers and non smokers.

Similarly, the TBUT was performed to assess the stability of the tear film, with lower values indicating faster tear film breakup and potential dry eye symptoms. Smokers showed a mean value of 6.68±2.615 seconds in the right eye and 6.70±2.989 seconds in the left eye (marginal grade of dry eye), while non smokers had a mean of 11.78±2.939 seconds in the right eye and 12.88±3.252 seconds in the left eye. The difference was found to be statistically significant (p-value <0.001), indicating that the tear film stability of group A is significantly worse than that of group B [Table/Fig-4].

TBUT (sec)	Smokers Mean±SD	Non smokers Mean±SD	t-value	p-value
Right Eye (RE)	6.68±2.615	11.78±2.939	-8.198	<0.001*
Left Eye (LE)	6.70±2.989	12.88±3.252	-8.842	<0.001*

[Table/Fig-4]: Comparison of Tear Breakup Time (TBUT) between smokers and non smokers.

The CCT was measured by specular microscopy. Smokers had a lower mean CCT of 490.88±33.761 µm in the right eye and 495.83±32.220 µm in the left eye, both of which fall in the category of less CCT as per the classification. In contrast, non smokers had a significantly higher mean CCT of 531.88±16.746 µm in the right eye and 533.70±13.838 µm in the left eye, which fall in the category of marginal CCT as per the classification. The differences in mean CCT values between smokers and non smokers were substantial and statistically significant (p-value <0.001), indicating that smokers had significantly thinner CCT compared to non smokers [Table/Fig-5].

CCT (µm)	Smokers Mean±SD	Non smokers Mean±SD	t-value	p-value
Right Eye (RE)	490.88±33.761	531.88±16.746	-6.881	<0.001*
Left Eye (LE)	495.83±32.220	533.70±13.838	-6.831	<0.001*

[Table/Fig-5]: Comparison of Central Corneal Thickness (CCT) between smokers and non smokers.

The endothelial cell density was calculated by specular microscopy. Smokers had a lower mean endothelial cell density of 2299.20±425.386 cells/mm^2 in the right eye and 2339.10±430.404

cells/mm^2 in the left eye, whereas non smokers exhibited a significantly higher mean density of 2775.88±345.417 cells/mm^2 in the right eye and 2839.95±357.885 cells/mm^2 in the left eye. The difference in endothelial cell density between the two groups was statistically significant (p-value <0.001), suggesting that smoking has a negative impact on corneal endothelial health [Table/Fig-6].

Endothelial cell count (cells/mm^2)	Smokers	Non smokers	t-value	p-value
	Mean±SD	Mean±SD		
Right Eye (RE)	2299.20±425.386	2775.88±345.417	-5.502	<0.001*
Left Eye (LE)	2339.10±430.404	2839.95±357.885	-5.659	<0.001*

[Table/Fig-6]: Comparison of endothelial cell count between smokers and non smokers.

DISCUSSION

The DED is characterised by ocular discomfort and instability of the tear film, all of which have the potential to harm the afflicted individual's ocular surface. An elevated osmolarity of the tear film, together with inflammation of the external surface of the eye, is among the most common symptoms associated with DED [15,16]. It is a multifactorial problem that may be influenced by several variables, including environmental conditions, lifestyle choices, age, gender, medication use and the presence of systemic disorders [8]. The findings of the Blue Mountain Eye Study suggest a correlation between current active smoking and a prior smoking history in relation to a higher prevalence of DED [9].

While the harmful effects of smoking on ocular health are well established, there is still a need for further research, especially in third-world countries like India, where tobacco use is very common [17]. Therefore, it is crucial to conduct a comprehensive study to evaluate the effects of smoking on different components of ocular health in chronic smokers compared to non smokers [4]. In the present study, the mean age of smokers was 50.15±6.89 years, whereas the mean age of non smokers was 49.25±6.39 years. These results were consistent with the findings from Bhutia P et al., who concluded that the mean age of the smoker group was 39.00±14.95 years and the mean age of the non smoker group was 35.10±15.39 years. This study included more male smokers than female smokers, which aligns with broader smoking trends in the region. Bhutia P et al., also suggested a significant male preponderance among smokers (n=38, 95%) (p-value <0.001) [12].

This study also concluded that long-term smoking may have a more pronounced effect on overall ocular health. Out of 40 smokers, 21 (52.5%) had been smoking for less than 10 years, while 19 (47.5%) had been smoking for more than 10 years. Bhutia P et al., also supported this, suggesting that the duration of smoking for almost half of the smokers (50%) ranged from 1 to 10 years, and out of 40 smokers, four were heavy smokers [12].

In the present study, Schirmer's test results indicate that smokers have significantly lower tear production than non smokers, with a p-value of <0.001, suggesting a statistically significant difference in tear production between the two groups. Similar to this study, Bhutia P et al., also found that mean Schirmer's scores were lower in smokers compared with non smokers (p-value=0.0127) [12]. This consistency across studies strengthens the evidence for the association between smoking and dry eye syndrome. In contrast, Altinor DD et al., found no significant difference between the Schirmer I test results among the two groups [18]. Thomas J et al., also found no significant difference in mean Schirmer's II test values between the two groups (p-value=0.22), concluding no association between tobacco smoking and aqueous production [4]. To reduce this ambiguity, more research is required to establish a correlation between smoking and reduced tear production.

Tear film stability, as measured by the TBUT test, is significantly worse in smokers compared to non smokers. This implies that the tear film in smokers is more prone to rapid breakup, causing an unstable tear film that leads to dryness and discomfort. This study concluded that smokers showed a lower mean TBUT than non smokers, with a p-value of <0.001, demonstrating a statistically significant difference and indicating that tear film stability is significantly worse in smokers than in non smokers. In accordance with this study, Bhutia P et al., also found that the mean TBUT was lower in smokers than in non smokers (p-value <0.0001) [12]. Similarly, Mohidin N and Jaafar AB also observed a notable impact of smoking on tear film stability, with smokers exhibiting poorer tear film stability compared to non smokers. This consistency across studies strengthens the evidence for the association between smoking and dry eye syndrome [19].

The present study revealed that smokers have significantly thinner CCT compared to non smokers, with a statistically significant difference (p-value <0.001). These findings corroborate the results reported by Wang D et al., who suggested that smoking could be correlated with decreased CCT in primary open-angle glaucoma [20]. Bhutia P et al., also concluded that the mean CCT was lower among smokers than non smokers, with a p-value of 0.0606, indicating no statistically significant difference [12]. Similarly, Sayin N et al., reported mean CCT values of 540.91±38.79 µm and 535.19±31.07 µm, respectively, with a p-value of 0.154, concluding that smoking was not related to CCT [21]. However, it was noted that there was a significant difference in baseline ocular pachymetry readings between chronic smokers and non smokers, suggesting that smoking may have a detrimental effect on corneal health, potentially making the cornea more susceptible to damage or disease.

In this study, smokers had a significantly lower mean endothelial cell count compared to the higher mean endothelial cell count in non smokers, with a p-value of <0.001, indicating a statistically significant difference between the two groups. This suggests that smoking may reduce the number of cells responsible for maintaining corneal transparency and hydration, which could compromise corneal function and health. These results were in concordance with Ilhan N et al., who also concluded that smokers had a lower mean endothelial cell count, with p-value <0.001, indicating a statistically significant difference between the two groups [22]. In contrast, a study by Sayin N et al., concluded that smokers had a mean endothelial cell count of 2772.42±260.53 cells/mm^2, whereas non smokers had a mean of 2716.65±275.37 cells/mm^2, with p-value <0.441, indicating no statistically significant difference between the two groups [21].

Overall, these results provide compelling evidence of the negative impact of smoking on various aspects of ocular health. The findings underscore the importance of smoking cessation interventions to mitigate the risk of ocular diseases and emphasise the need for regular ophthalmic evaluations in smokers to detect and manage any ocular complications at an early stage. Additionally, further research may be warranted to elucidate the underlying mechanisms by which smoking affects ocular tissues and to explore potential therapeutic strategies for mitigating smoking-related ocular damage.

Limitation(s)

Despite all efforts, there are a few limitations in this study. The study's cross-sectional design limits the ability to establish causality between smoking and ocular health outcomes. Longitudinal studies would provide stronger evidence for a causal relationship. The study's sample may not represent the general population, as it included only individuals from a specific demographic or geographic area. Additionally, the study relied on self-reported smoking status and duration, which may be subject to recall bias or misreporting. Objective measures, such as biomarkers of tobacco exposure, could strengthen the validity of the smoking data.

CONCLUSION(S)

The findings concluded that smokers had significantly lower tear production, worse tear stability, thinner CCT and decreased endothelial cell density compared to non smokers. This study emphasises the adverse impact of smoking on ocular health and the importance of smoking cessation in preserving ocular health and reducing the risk of vision-related complications. Therefore, one should encourage an integrated approach between ophthalmologists and tobacco prevention centres with adequate referrals from the ophthalmologist's end. This strategy may not only improve ocular health but also the holistic health of patients in general.

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