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Original Research Article

# Effect of Smoking on Ocular Surface and Tear Film: A Clinico Pathological Study

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**Abstract:**

**Aim:** Smoking is an important risk factor for many chronic diseases; however its association with dry eyes is still unclear. The study was undertaken to evaluate the effect of smoking on ocular surface clinically and its correlation pathologically with the help of impression cytology.

**Methods:** The study was conducted on 100 elderly patients from 18 to 50 years. The study group on the basis of number of cigarettes consumed was further subdivided in mild (<10 cigarettes per day) moderate (11-20 cigarettes per day) and heavy smokers (>20 cigarettes per day). OSDI score, TBUT (tear film break up time), Basal tear secretion (Schirmer test 2), and conjunctival impression cytology have been performed.

**Results:** The study comprises of 100 patients, 50 smokers and 50 age matched non-smokers. The mean age of the smoker 38.40 ± 8.06 years and the mean age of nonsmokers in control group was 32.60 ± 6.54 years. Mean tear film break up time in non-smoker was 15.69 ± 4.34 sec as compared to 12.07 ± 2.29 seconds in smokers (p=0.0001). Mean score of Schirmer's test was 13.58 ± 2.79 seconds in non-smokers as compared to 11.40 ± 2.64 seconds in smokers with significant statistical difference (p=0.001). On Impression cytology, 20% of the subjects in smoker group showed grade 2 metaplasia and 8 % showed grade 3 metaplasia in comparison to 3% and 0 % in non-smoker group respectively (p=0.0001).

**Conclusion:** Smoking is a significant risk factor in the development of dry eyes and ocular surface disorder characterized by squamous metaplasia and loss of goblet cells. Furthermore, the severity of dry eyes has positive correlation with the amount of smoking.

**Keywords:** Ocular Surface Disorder, Dry Eyes, Impression Cytology.



## Introduction

Tobacco smoking is a serious public health problem which contains various heavy metals and toxic mineral elements that have been associated with cardiovascular and respiration disorders. Tobacco smoke contains greater than 4000 compounds and a puff of smoke contains 300 million to 3.5 billion particles existing both in gas and particulate form which on exposure are eventually toxic to the ocular tissue and affect the eye through ischemic and oxidative mechanism.[1]

Tobacco smoking is not only associated with cataract,[2] ARMD,[3] AION and toxic optic neuropathy but also with dry eye syndrome. Ocular surface is highly sensitive to air borne chemical fumes and irritative gas and its persistent exposure may lead to ocular surface damage and dry eye syndrome. Environment, lifestyle, age, sex, drug history, and systemic diseases are the main risk factors associated with dry eyes, amongst which the lifestyle factors may play an important role.[4] Smoking is already known as an important risk factor for many chronic diseases; however, it is still an uncertain risk factor for dry eye. The study was undertaken to evaluate the effect of smoking on ocular surface clinically and its correlation pathologically with the help of Impression Cytology.

## Materials and Methods

The study was conducted on 100 patients aged 18 to 50 years, subjects were divided in groups, smokers (study group) and non-smokers (control group). The study group on the basis of number of cigarettes consumed, was further subdivided in mild (<10 cigarettes per day) moderate (11-20 cigarettes per day) and heavy smokers (>20 cigarettes per day).

Patients with history of occupational exposure, contact lens use within 6 months of study, drug abuse, allergy, and systemic diseases were excluded from the study. Subjective and objective evaluation of patients was carried out for dry eyes which included OSDI score,[6] TBUT (tear film break up time), Basal tear secretion (Schirmer's test 2), and conjunctival impression cytology. Patients were given questionnaire and symptom scoring was done according to OSDI score.

Average score was calculated. It ranged from 0 to 100, with higher scores indicating more troubles or signs and symptoms. Conjunctival cytology was performed in each eye of the patients of the study group and the control subjects. The samples were collected from the temporal interpalpebral bulbar conjunctiva.

After instillation of a single drop of propacaine 0.5%, the cellulose acetate filter paper was applied over the temporal interpalpebral bulbar conjunctiva at distance of 3 mm from the limbus. Following 95% of alcohol fixation for at least 10 min, the specimen was stained with periodic acid Schiff and hematoxylin, the cytologic changes were graded according to the Nelson' s grading system.

Grade 0: Small and round epithelial cells with eosiniphilic staining cytoplasm. Nucleocytoplasmic ratio 1:2, abundant, plump, oval goblet cells with intensely PAS-positive cytoplasm.

Grade 1: Slightly larger and more polygonal epithelial cells with eosinophilic staining cytoplasm and nucleo-cytoplasmic ratio 1:3. There was decrease in goblet cell number.

Grade 2: Larger and polygonal, occasionally multinucleated epithelial cells with variably staining cytoplasm. Nucleocytoplasmic ratio 1:4-1:5. Smaller and less intensely PAS positive goblet cells with poorly defined cellular borders and marked decrease in number.

Grade 3: Large and polygonal epithelial cells with basophilic staining cytoplasm. Nucleo-cytoplasmic ratio greater than 1:6 and absence of goblet cells.

The findings of grades 2 and 3 on the interpalpebral conjunctiva suggest the diagnosis of dry eye. Parameters between the groups have been analyzed by the student t-test and analysis of variance with SPSS software program.

The Mann-Whitney U test and Kruskal-Wallis test were used for the analysis of non-parametric values such as grade of conjunctival squamous metaplasia. A P-value of less than 0 was considered statistically significant.

**Results**

The study comprised of 100 patients, 50 smokers and 50 age matched non-smokers. The mean age of the smokers was 38.40 ± 8.06 years and the mean age of non-smokers in control group was 32.60 ± 6.54 years with insignificant statistical difference. In our study, 42% of the subjects within the smoker group had history of smoking for 5-10 years and 28% had history of smoking for 10-15 years.

Among 50 smokers, 53% (n=24/50) were mild smokers, 30% (n=15/50) were mild smokers and 18% (n=9/50) were heavy smokers. Redness (34%) was the most common symptom in smokers followed by ocular tiredness (27%), burning sensation (23%), itching (23%) and foreign body sensation (15%), however most of the smokers were asymptomatic at the time of presentation (37%). OSDI score was 35.85 ± 20.79 units in smokers as compared to 22 ± 8.4 in non-smokers with significant statistical difference ($p<0.001$) (table 1).

Moreover, Symptom score became highest among heavy smokers 45 ± 6.8 and lower 26 ± 7.2 among mild smokers, but the difference was not statically significant (p=0.65) (table 2). Mean tear film break up time in non-smoker was 15.69 ± 4.34 mm as compared to 12.07 ± 2.29 seconds in smokers with statistically significant difference (p=0.0001) (Table 1).

TBUT was lower in patients with heavy smokers (8.54 seconds) as compared to 11.80 seconds in mild smokers, however the difference among the three group was not significant (p=0.03) (Table 2). Mean score of Schirmer's test was 13.58 ± 2.79 mm in non-smokers as compared to 11.40 ± 2.64 mm in smokers with significant statistical difference (p=0.001).

In subgroup analysis, mean Schirmer's test was 9.77 mm in heavy smokers as compared to 12.5mm in mild smokers (p=0.002). On impression cytology, 21% of the subjects in smoker group showed grade 2 metaplasia and 8 % showed grade 3 metaplasia in comparison to 3% and 0% in non-smoker group respectively (p=0.0001). In sub group analysis, 23.2% (n=2/9) of the subjects showed grade 3 metaplasia as compared to 6.9% (n=1/15) and 3.9% (n=1/26) in moderate and mild smokers respectively.

**Table 1: Clinical and pathological profile of smoker's vs non smokers**

| | Smokers | Non smokers | P-value |
|---|---|---|---|
| Mean Age | 38.40 ± 8.06 | 32.60 ± 6.54 | 0.06 |
| Tear film break Up Time (TBUT) in seconds | 12.07 ± 2.29 | 15.69 ± 4.34 | 0.001 |
| Basal tear secretion(mm) | 11.40 ± 2.64 | 13.58 ± 2.79 | 0.001 |
| OSDI score | 35.85±20.79 units | 22 ± 8.4 | <0.001 |
| Conjunctival squamous metaplasia | 3.35 ± 1.02 | 2.02±0.54 | <0.001 |

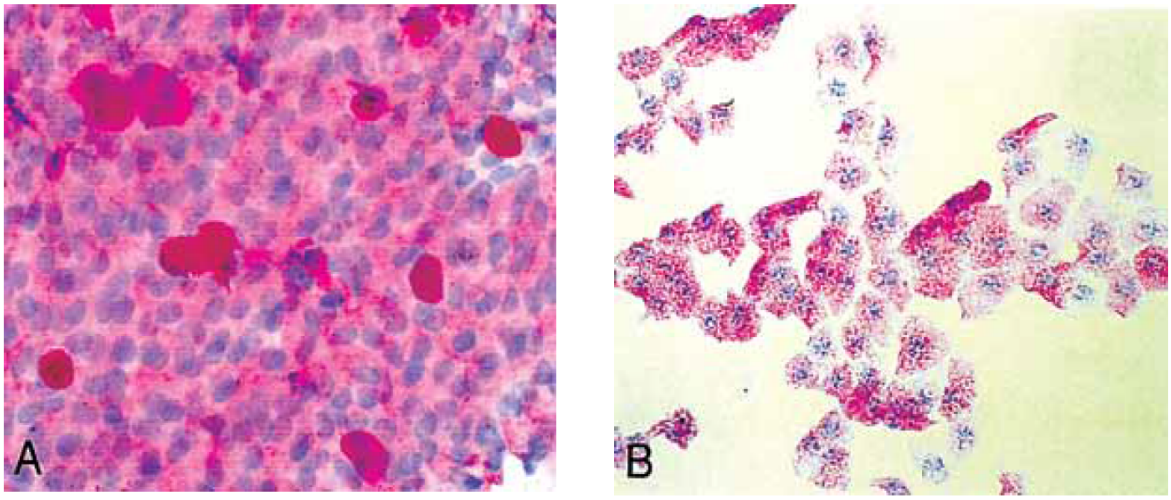


**Figure 1: Impression cytology (PAS, X400). (A) Specimen from a non-smoker shows PAS positive goblet cells and small, round epithelial cells with a nucleo-cytoplasmic ratio of 1:2. (B) Specimen from a heavy smoker shows loss of goblet cells and presence of large, polygonal epithelial cells with a nucleocytoplasmic ratio of 1:6.**

**Table 2: Clinical and pathological finding in mild, moderate and heavy smokers**

| | Mild (<10 cigarettes/day) | Moderate (11-20 cigarettes/day) | Severe (>20 cigarettes/day) | p value |
|---|---|---|---|---|
| Symptoms scored (OSDI) | 26 ± 7.2 | 39 ± 5.6 | 45 ± 6.8 | 0.67 |
| Mean basal tear secretion (mm) | 12.5 | 8.4 | 9.77 | 0.002 |
| Mean TBUT (sec) | 11.80 | 10.30 | 8.54 | 0.03 |
| Squamous metaplasia | 0.73 | 1.44 | 1.60 | 0.002 |

**Table 3: Impression cytology grading in smoker's vs non-smokers**

| Grading | Smokers (%) | Non-Smokers (%) |
|---|---|---|
| Grade 0 | 40(78%) | 13(28%) |
| Grade1 | 21(45%) | 10(17%) |
| Grade 2 | 11(21%) | 01(3%) |
| Grade 3 | 04(08%) | 0(0%) |

## Discussion

The ocular surface is covered by a tear film for lubrication which plays a major role of nutritional route for corneal epithelium. Cigarette smoke is a significant source of poisonous minerals and heavy metals, including more than 4000 poisonous chemical substances. Epidemiological studies [7,8] have shown that cigarette smoking can be of high-risk for several ophthalmological disorders, including cataract, age related macular degeneration and dry eye disease. In our study, there was increased prevalence of smoking in subjects of rural background and maximum number of smokers lies in the age group of 30 to 40 years (mean age of 38.40 ± 8.06 years). Xu et al[5] in meta-analysis have recommended several pathogenesis of dry eye including chronic inflammation of the ocular ourface, decreased sensitivity of cornea and conjunctiva, reduced production and/or stability of tears, and epithelial damage. Similarly, Kjaergard et al.[9] reported a higher degree of ocular irritation amongst tobacco workers who came in contact with a high concentration of the substance. In the present study, the eye irritation scores and indices of smokers were statistically higher than those of non-smokers. The indices of symptom score was dependent on rate of smoking and was higher in heavy smokers as compared to mild to moderate but the difference was not statistically significant.

Even though, TBUT was lower in heavy smokers compared to mild and moderate smokers but the

difference was no longer significant. In our study, basal tear secretion (Schirmer's 2) test value was lower in smokers (11.40 mm) as compared to non-smokers (13.58 mm). Our results were in contrast with the study conducted by Statistical. Of their study, Schirmer's test value was higher in smokers as compared to non-smokers which were attributed to reflex tear secretion. But, the Yoon et al.[10] reported that basal tear secretion became extensively lower in the smoking group. It is believed that tear film lipid layer minimise the evaporation of aqueous aspect of the tear film in physiologic state, however the negative impact of cigarette smoking in lipid layer is the main cause of deterioration. Our study found that there is a decrease in basal tear secretions (Schirmer's 2) similar to earlier studies conducted in the past, but there is an increase in reflex tear secretion thus resulting in increase in total secretion is seen amongst smokers.

Altinors et al. [11] found an increase in polymorphonuclear leucocytes and squamous epithelium cell counts both before and after work shift among tobacco workers, when compared to their referents. Conjunctiva exposed to cigarette smoke exhibit certain changes similar to those in eyes exposed to chronic irritation. Avunduk et al. [12] determined that tobacco smoke altered the conjunctival structure in rats by causing squamous metaplasia in the epithelial layer of conjunctival surface.

Several studies have reported a significant correlation among eye irritation and reduced TBUT and/or epithelial damage in smokers in comparison to the ones of non-smokers. Avunduk et al [12] determined a deterioration of projections and loss of microvilli, which are important for stabilizing the tear film in conjunctiva exposed to tobacco smoke. In our study, TBUT became lower among smokers as compared to non-smokers with significant statistical difference. This was attributed to deficiencies in lipid layer of tear film due to tobacco smoke.

Statistical 13] also reported that the degree of squamous metaplasia amongst smokers was higher than that of control group. Uchino et al [8] in their study also concluded that smoking is associated with ocular surface inflammation which leads to decreased tear secretion, goblet cell density and tear MUC5AC concentration. Our study has found a higher grade of squamous metaplasia in smokers compared to non-smokers. Grading of Sqaumous metaplasia became significantly higher in smokers as compared to non-smokers. Moreover, metaplasia was associated with the amount of smoking. Heavy smoking was related to significant higher grade of ocular surface damage as compared to mild to moderate smokers. Our study further strengthens the establishment of tremendous correlation with the amount of smoking. This is attributed to the inflammation associated with irritative and toxic agents associated with cigarette smoking. Thus, from the above finding it may be inferred that smoking has a deleterious impact on ocular surface mainly to the tear film abnormality and conjunctival squamous metaplasia.

## Conclusion

In our study we conclude that Smoking is a significant risk factor in the development of dry eyes and ocular surface disorder characterized by squamous metaplasia and loss of goblet cells. Furthermore, the severity of dry eyes has positive correlation with the amount of smoking.

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