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Original Research Article

Evaluation of tear function and ocular surface changes in patients with pseudoexfoliation

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ABSTRACT

Aims and Objectives: This study intends to evaluate the Tear function and ocular surface changes in patients with pseudoexfoliation.**Materials and Methods:** This cross-sectional study will be conducted on a minimum of 45 patients fulfilling the inclusion criteria in the department of Ophthalmology, at tertiary care institute. Tear meniscus height (TMH), Schirmer's test, tear breakup time (TBUT), fluorescein staining, conjunctival impression cytology were used to assess dry eye disease in pseudoexfoliation (PEX) patients.**Results:** In our study the majority of patients with PEX were >70 years and females (23) are more than males (22). According to Grading of dry eye, 41(45.5%) were moderate grade, 24(26.7%) were mild grade, 13(14.5%) were severe grade and 12 (13.3%) were normal grade. Conjunctival impression cytology, fluorescein staining, TBUT, Schirmer's tests, and TMH, all showed a statistically significant results with dry eye in the current study.**Conclusion:** The patients with pseudoexfoliation syndrome are more prone to develop dry eye, as it causes tear film irregularities and a reduction in the number of goblet cells which is evident with conjunctival impression cytology and Tear film tests.This is an Open Access (OA) journal, and articles are distributed under the terms of the [Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License](https://creativecommons.org/licenses/by-nc-sa/4.0/), which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.For reprints contact: reprint@ipinnovative.com

1. Introduction

Pseudoexfoliation syndrome is clinically a generalized fibrilopathy characterized by accumulation of abnormal elastic fibrillar material in intraocular and extraocular tissue.¹ Pseudoexfoliation syndrome is a common age related condition present in 10% population over 60 years of age, is characterized by accumulation and deposition of white fluffy amyloid like proteinaceous material.²

In the eye it is present in the anterior chamber and its angle, corneal endothelium, trabecular meshwork, ciliary body epithelium, iris, lens and conjunctiva. The extraocular deposition is seen in skin, lungs, myocardium, liver, kidney and cerebral meninges.^{3,4}

Ocular manifestations of pseudoexfoliation syndrome include dry eye disease, open angle glaucoma, and cataract. It also affects the dilation of pupil, and causes intraoperative complications such as vitreous loss and subluxation of lens.⁵

The cause of dry eye in pseudoexfoliation is due to accumulation of the PEX material at the conjunctiva which consists of accessory lacrimal glands and goblet cells, resulting in instability of tear film.⁴

"International dry eye workshops classification" defines Dry eye syndromes (DES) as 'Multifactorial disease of tears and ocular surface that results in symptoms of discomfort, visual disturbance and tear film instability with potential damage to the ocular surface'.⁶

Dry eye is a common eye disorder characterized by inadequate synthesis of tear film to moisturise the ocular

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surface. The prevalence of dry eye increases as the age advances and it varies from 5 to 50% globally.^{7,8}

Thus, we intend to take up this study in our setup to determine the association between tear function and ocular surface changes in patients with pseudoexfoliation syndrome in Kolar district.

2. Materials and Methods

This prospective cross-sectional observational study was conducted on minimum of 45 patients fulfilling the inclusion criteria in the department of Ophthalmology, tertiary care institute in Karnataka from January 2020 to June 2022, after obtaining ethical clearance from Institutional Ethical Committee and written informed consent from the subjects.

All patients of either sex above 40 years of age with pseudoexfoliation were included in this study and patients on any topical anti-glaucoma medications, lacrimal gland drainage disorder, history of previous ocular surface surgery or ocular trauma and diabetes mellitus were excluded.

2.1. Methods of collection of data

Each patient was assessed by detailed history and ocular examination by slit lamp bio-microscopy, indirect ophthalmoscopy, and evaluation of tear film abnormalities by the following tests:

1. **Tear Meniscus Height:** After normal blinking, the lower meniscus height was read off the scale on the reticule of the slit lamp. A value of <0.25 mm was considered abnormal.
2. **Schirmer's Test:** About 5mm of the Schirmer strip was bent and placed in the lower fornix at the junction of middle and lateral thirds of the lower fornix and after 5 min a reading of <10mm was considered abnormal.
3. **Tear Breakup Time:** After staining the ocular surface with a fluorescein -impregnated strip the interval between the last blink and appearance of the first random corneal dry spot was measured. A value <10 sec was regarded as abnormal.
4. **Corneal Fluorescein Staining:** After staining the ocular surface with a fluorescein strip the corneal staining pattern is graded for the superior, central and inferior areas, in a score ranging from 0 (no staining) to 3 (continuous epithelial defect). The total score is the sum of the three areas, with a maximum score of 9. A score >3 was considered abnormal.
5. **Conjunctival Impression Cytology:** a 5x5 mm cellulose acetate filter is applied to the bulbar conjunctiva near the limbus for 3-5 seconds to remove the superficial layers of the ocular surface epithelium in a peeling motion. The tissue is transferred to glass slide and then in to coplin jar containing fixative solution (70% ethyl alcohol, 37% formaldehyde, and

glacial acetic acid in a 20: 1: 1 volume ratio) for 10 minutes. Papanicolaou or haematoxylin stains are the commonly used for routine histological staining of impression cytology specimens that is examined under microscope and graded as below.

2.2. Nelson's grading⁹

1. **Grade 0:** The epithelial cells are small and round with eosinophilic-staining cytoplasm. The nuclei are large and basophilic, with a nucleus-to-cytoplasm ratio of 1:2. The goblet cells are abundant, plump, and oval and have an intensely PAS-positive cytoplasm.
2. **Grade 1:** The epithelial cells are slightly larger and more polygonal and have eosinophilic-staining cytoplasm. The nuclei are smaller, with a nucleus-to-cytoplasm ratio of 1:3. There are fewer goblet cells but they maintain their plump, oval shape with an intensely PAS-positive cytoplasm.
3. **Grade 2:** The epithelial cells are larger and polygonal, occasionally multinucleated, with variably staining cytoplasm. The nuclei are small, with a nucleus to-cytoplasm ratio of 1:4 to 1:5. The goblet cells are markedly decreased in number and are smaller and less intensely PAS positive, with poorly defined edges.
4. **Grade 3:** The epithelial cells are large and polygonal with basophilic-staining cytoplasm. The nuclei are small, pyknotic and, in many cells, absent. The nucleus- to-cytoplasm ratio is greater than 1:6. Goblet cells are absent.

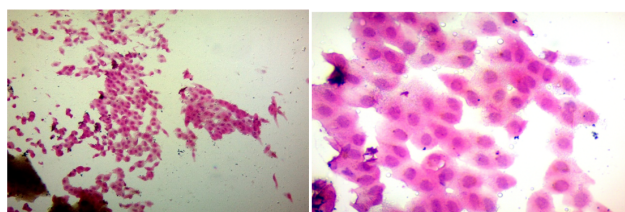


Fig. 1: Conjunctival impression cytology pas staining (10 X and 40 X)

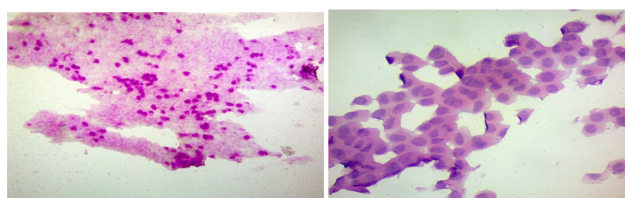


Fig. 2: Conjunctival impression cytology pas staining and H & E staining (10 X and 40 X)

2.3. Statistical methods

Data that was collected entered in Microsoft Excel 2019 Spreadsheet and analysed using IBM SPSS 21.0 version. The data on categorical variables was presented as frequency and percentages. The comparison of distribution of categorical variables was done using chi square test or Fisher exact test. P value less than 0.05 was considered statistically significant. Correlation between grading of dry eye and tear film stability markers was assessed by Pearson correlation.

3. Result

Among study participants of 22 male and 23 females, 22(48.9%) were aged >70 years, 13(28.9%) were aged 61-70 years and 10 (22.2%) were aged 51-60 years.

Table 1: Characteristics of patients with Pseudoexfoliation

Characteristics		Frequency	Percentage
Tear Meniscus height (mm)	Abnormal	51	56.7
	Normal	39	43.3
Schirmer's test	Normal	16	17.8
	Mild	17	18.9
	Moderate	47	52.2
	Severe	10	11.1
Tear Break Up Time (sec)	Mild	15	16.7
	Moderate	41	45.5
	Severe	34	37.8
Fluorescein staining	Abnormal	17	18.9
	Normal	73	81.1
Conjunctival impression cytology	Grade 0	9	10
	Grade 1	25	27.8
	Grade 2	39	43.3
	Grade 3	17	18.9
Grading of dry eye	Normal	12	13.3
	Mild	24	26.7
	Moderate	41	45.5
	Severe	13	14.5

Table 1 shows dry eye evaluation by tear Meniscus height to be normal in 39(43.3%) and abnormal in 51(56.7%). Schirmer's test showed 47(52.2%) patients with moderate grade, 17(18.9%) with mild grade, 16 (17.8%) with normal grade and 10 (11.1%) with severe grade. Tear Break up time was moderate in 41(45.5%) patients, severe grade in 34 (37.8%) and mild grade in 15 (16.7%) patients. Fluorescein staining of the ocular surface showed abnormality in 17 (18.9%) patients. Conjunctival impression cytology revealed grade 2 changes in 39 (43.3%), grade 1 in 25(27.8%), grade 3 in 17 (18.9%) and normal in 9 (10%)

patients. According to Grading of dry eye, 41(45.5%) were moderate grade, 24(26.7%) were mild grade, 13(14.5%) were severe grade and 12 (13.3%) were normal grade.

Fisher exact test applied, p value <0.05 is statistically significant.

Table 2 shows the statistically significant correlation of Conjunctival impression cytology with the severity of dry eye among the PXF patients. Grade 0 was observed in 9 (75%), grade 1 had mild dry eye in 22(91.7%), grade 2 had mild 2 (8.3%) and moderate 37 (90.2%) dry eyes and grade 3 had moderate and severe dry eyes in 4 (9.81%) and 13 (100%) patients respectively.

4. Discussion

This study assessed the tear function and ocular surface changes in patients with pseudoexfoliation using five clinical tests (tear meniscus height, tear breakup time and Schirmer's test, fluorescein staining and conjunctival impression cytology).

Pseudoexfoliation syndrome is generalized fibrilopathy, characterized by abnormal production and accumulation of the pseudo exfoliative material in the whole body.¹⁰

The tear film is an essential part of the lacrimal functioning unit. Holly et al. published the traditional tear film structure in 1977, which had an anterior lipid, middle aqueous, and deeper mucin layer.¹¹

In our study the majority of patients with pseudoexfoliation were of >70 years followed by 61-70 years and 51-60 years. In research by Kaliaperumal et al., individuals with pseudoexfoliation had an average age of 66.27 years, and a range of 55 to 80 years.¹²

In our present study males were 22(48.9%) and females were 23(51.1%). In a study done by Pujar et al., males were 20(66.7%) and females were 23(33.3%).¹³ The findings in our study were consistent with study findings of other studies.

In our study Schirmer's test showed 47(52.2%) patients with moderate grade, 17(18.9%) with mild grade, 16 (17.8%) with normal grade and 10 (11.1%) with severe grade. These results were compared with study done by Noori et al, in the pseudo exfoliation group, Schirmer I value ≤ 5.5 mm was in 12 (6.06%), 163 (82.3%) eyes had Schirmer I value >10 mm and Schirmer I value between 6 and 10 mm were in 23 (11.6%) patients.¹⁴ In our study, the results of Schirmer's test in the pseudoexfoliation patients were considerably lower, which we attribute to partial deposition of pseudo exfoliation material in the primary lacrimal gland and its ducts.

Tear Meniscus height was measured, Normal height was present among 39(43.3%) and Abnormal height was present among 51(56.7%). The results were compared with study done by Noori et al., 100 (50.5%) eyes had Tear Meniscus height <0.35 mm whereas it was ≥ 0.35 mm in 98 (49.49%) eyes. The findings in our study were consistent with study

Table 2: Correlation of conjunctival impression cytology with the severity of dry eye

Conjunctival impression cytology		Grading of dry eye				P value
		Normal	Mild	Moderate	Severe	
Both eyes	Grade 0	9 (75%)	0	0	0	0.0001
	Grade 1	3 (25%)	22 (91.7%)	0	0	
	Grade 2	0	2 (8.3%)	37 (90.2%)	0	
	Grade 3	0	0	4 (9.81%)	13 (100%)	

findings of other studies. Tear Break up time was moderate in 41(45.5%) patients, severe grade in 34 (37.8%) and mild grade in 15 (16.7%) patients. The results were compared with study done by Gowthaman et al., according to Tear Break Up Time, 147(98%) were Normal grade, 3(2%) were mild grade.² TBUT evaluates the sufficiency of the tear film's mucin layer, which is decreased in patients with pseudoexfoliation. This deficiency, we hypothesise, is due to the deposition of pseudoexfoliation material at the mouths of the goblet cells, which reduces mucin production.

Fluorescein staining of the ocular surface showed abnormality in 17 (18.9%) patients. Conjunctival impression cytology revealed grade 2 changes in 39 (43.3%), grade 1 in 25(27.8%), grade 3 in 17(18.9%) and normal in 9 (10%) patients. According to Grading of dry eye, 41(45.5%) were moderate grade, 24(26.7%) were mild grade, 13(14.5%) were severe grade and 12 (13.3%) were normal grade. The results were compared with study done by Erdogan et al., among pseudoexfoliation groups, 21(43.8%) were grade 2, 9(18.7%) were grade 1, 15(31.2%) were grade 3 and 3(6.3%) were grade 0. In a study done by Kaliaperumal et al, Stage 1 was among 66.7%, Stage 2 was among 33.3%, which was significantly lower when compared to the pseudoexfoliation group.¹²

In our present study there was a statistically significant correlation of conjunctival impression cytology, fluorescein staining, Tear break up time, Schirmer's test, and tear meniscus height with Dry eye. It should be noted that, although aqueous layer tests in patients with PEXS may be normal, they tend to be lower than those in healthy persons, and this should be considered when choosing medicine to treat PEX glaucoma. Oncel et al. established that tear film osmolarity was higher in patients with PEX, which can be explained by the dysfunction of the goblet conjunctival cells.¹⁵

These findings supports that, because of the deleterious influence of PEX on the conjunctival goblet cells, PEX is the primary cause of tear film instability.

5. Conclusion

Observations from this study using conjunctival impression cytology and tear film tests, shows that patients with pseudoexfoliation syndrome are more likely to develop dry eye because of abnormal tear film and decrease in the number of goblet cells. More research is required to

ascertain the precise intricacies of how PEX modifies the morphology of goblet cells.

6. Source of Funding

None.

7. Conflict of Interest


None.

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