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Original Research Article

Dry Eye Disease among the Staff of the Department of Radiology: A Cross-Sectional Study

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Abstract

Background: Dry eye disease is one of the common ocular surface disorders and is sometimes asymptomatic. Radiologists are one of the most vulnerable among medical professionals due to heavy computer work in the air-conditioning room. Different clinical and laboratory tests are there to evaluate dry eye disease and ocular surface abnormalities. Measurement of ocular surface disorder burden among the staff of the Radiology department and early intervention can reduce the morbidity.

Methodology: The staff (doctors and technicians) of the Radiology department and the same number of control population were taken from the refraction clinic of the Ophthalmology department after applying inclusion and exclusion criteria. After history taking and thorough general and ophthalmological evaluation, the Schirmer test (Schirmer's test I) has been done to measure basal plus reflex secretion. Tear film breaks up time (T-BUT) measurement and Rose Bengal Staining (RBS score) gradation have been done in each eye. After that Conjunctival Impression Cytology (CIC) specimen was collected using cellulose acetate paper. Then the cytology grading was done in the departmental laboratory. All the data collected before and after the investigational work-up are statistically evaluated and analysed.

Results and Analysis: In this cross-sectional study in a tertiary care hospital in West Bengal, the mean age of the Radiology staff group is 50.83 years (+/- 9.268) and the control group is 48.95 years (+/- 7.575). Both groups are comparable in respect to age and gender. Schirmer test in the right eye and RBS scoring in both eyes have shown statistically significant differences) between the groups. Though TBUT values and CIC grading have not shown statistically significant differences between the two groups (p>0.05), they are suggestive of dry eye disease in the Radiology staff group. Schirmer test values have shown a negative correlation with TBUT values a but negative correlation with RBS score, CIC grading in both the eyes in the Radiology staff group, which is also suggestive of dry eye disease.

Conclusion: The incidence of dry eye and abnormal ocular surface among the asymptomatic staff of the Radiology department is comparatively high compared to the age-gender matched controls. Early diagnosis and treatment are highly recommended.

Keywords: Radiology, Dry eye, Schirmer's test, TBUT, RBS score, CIC grading.

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Introduction

Dry eye is defined as a disorder of the tear film due to tear deficiency or excess tear evaporation resulting in interpalpebral ocular surface damage and is associated with symptoms of ocular discomfort. [1] Dry eye is a common condition seen with increased prevalence in patients with auto-immune disease, post-menopausal women, and the elderly. [2] As in many professions that require long-term computer monitor use, radiologists also work extensively with computers and monitors in daily practice, which leads to a diminished blinking reflex. In offices where radiologists work, air conditioners lead to increased tear vaporization. [3] It is known that all of the aforementioned conditions predispose individuals to dry eye syndrome. A Sievert (Sv) is a rather large amount of radiation, so a burst of 5 Sieverts of radiation will fairly reliably kill an individual in a few weeks. Older units of radiology are Roentgens, Rads and Rems. The biological effects of diagnostic radiation depend not only on the amount of radiation but also on the type of radiation being emitted, what tissue is being irradiated and how much radiation is being absorbed. e.g. the dose from a diagnostic chest computed tomography scan (CT Scan) is equivalent to about one hundred to two hundred fifty plain chest films. [4] The NCRP recommends an annual radiation dose limit for individual members of the public from all sources of radiation other than natural background and the individual's medical care as 1mSv(NCRP,2004). Infrequently, in that individual's lifetime, they permit a dose up to 5mSv. [5] The incidence of dry eye is found to be higher in radiologists than in non-radiologist controls. [6] Cytological changes in the conjunctiva corresponding to dry eye disease are also found in the profession compared to the non-radiologist group. [3] To describe and classify the dry eye among our study population, in a tertiary care centre in West Bengal, Schirmer's test (ST), Tear Film Break-Up time (T-BUT), Rose Bengal staining (RBS), and Conjunctival Impression Cytology (CIC) have been performed.

Aims and Objectives:

- To assess the tear function in Radiology departmental staff and age-gender matched subjects.
- To compare different tear-film parameters between the groups.

Materials & Methods

This cross-sectional study was conducted on the staff (doctors and technicians) of The departments and the controls were taken from patients attending the refraction clinic of the outpatient department of the Department of Ophthalmology, Burdwan Medical College and Hospital during the entire study period of 6 months.

Inclusion Criteria

- All staff (doctors and technicians) working in the Department of Radiology, Burdwan Medical College and Hospital.
- Control groups are taken from the patients attending Ophthalmology OPD (refraction clinic), Burdwan Medical College and Hospital.

Exclusion Criteria

 Already diagnosed with dry eye due to preexisting ocular surface disease or any other aetiology or having any ocular disease for which he/she has been treated with any topical or systemic medications within the last 1 month.

- Taking medications for any systemic disease or psychiatric disease.
- Previous intra-ocular or extra-ocular surgery or procedure.
- Known radiation exposed person from another source (in the control group).
- Contact lens wear.
- Recent history of trauma within 1 month
- Allergic to the chemical compounds which would be used.

Sample Size

At the beginning of the study, all the staff (doctors and technicians) of the Department of Radiology, were included by complete enumeration technique and the number comes to 40 (forty). Then, the same number (40) of controls have been taken. So, in each group, forty (40) subjects have been included. All are asymptomatic from an ophthalmological point of view and controls are taken randomly from the refraction clinic of the Dept. of Ophthalmology, Burdwan Medical College and Hospital, Kolkata.

Study Tools

Snellen's chart, Slit lamp (TRC-50X; TOPCON), Binocular indirect ophthalmoscope (HEINE OMEGA 500), Auto Refractometer (Topcon RM-8800), Goldmann Applanation Tonometer (GAT), 78D /90D lens (Volk double aspheric lens), 0.5% Proparacaine eye drop, Schirmer strip: No-41 Whatman filter paper (35 mm × 5mm), Fluorescein strip: 1 mg dye impregnated, Rose Bengal strip: 1.3 mg dye impregnated, cellulose acetate paper and staining solutions for conjunctival impression cytology.

Ocular Examination

After obtaining informed consent from each participant in each group, a detailed ocular examination has been carried out.

- Examination of the ocular adnexa: Lid margin, blinking, canthi, and patency of lacrimal passages were noted.
- Slit lamp examination:

Ocular surface cellular damage using vital stains such as Rose Bengal and fluorescein.

Debris contaminating the tears.

Meibomian openings and oil droplets at the lid margin Lashes for the general state of hygiene, health and signs of inflammation.

Schirmer test (Schirmer's test I) [7] using sterile No-41 Whatman filter paper (35 mm \times 5mm) has been done in unanaesthetised eye measuring basal plus reflex secretion. The extent of ocular surface damage was assessed by instilling a small amount

of Rose Bengal and fluorescein onto the ocular surface. Tear film break-up time (T-BUT) [8] measurements and Rose Bengal Staining gradation (RBS) [9] were done in each eye 30 minutes apart between tests. It is usually the area within the lid aperture that is most likely to stain in dry eye. Fundus examination and extraocular muscle function examination have been performed sequentially followed by Conjunctival Impression Cytology (CIC) [10] specimen collection using cellulose acetate paper.

Schirmer test (in mm) is done with a strip of filter paper measuring 5 by 35mm. It is kept at a junction of the outer 1/3rd and middle 1/3rd of the lower eyelid. The amount of wetting in 5 minutes is measured [11]. Measurement of tear stability and breakup time (T-BUT) (in seconds) gives an idea about the stability of tear film. After staining the conjunctival film with fluorescein, the patient is asked to blink and keep the eyes open. The time between the last blink and the first appearance of the dry spot is measured. Time less than 10 seconds suggests mucin deficiency. Normally it is 30 seconds to 1 minute [12-14]. The ocular surface Rose Bengal staining (RBS) method, stains damaged conjunctival and corneal epithelium as well as mucus threads and corneal filaments. Van Bijsterveld's scoring system [15] has been used to quantify the level of staining observed (with scores ranging from 0 to 9). It suggests a deficiency of tear components like mucin and albumin. [16] Conjunctival Impression Cytology (CIC) staging, depending upon staining characteristics and NC ratio, goblet cell density, squamous metaplasia, and mucin aggregates, has been performed in the departmental laboratory. This staging of CIC findings has been proposed by Nelson, Wittpenn, and Norn. [17] Conjunctival impression cytology is a minimally invasive technique allowing for the investigation of conjunctival changes at the cellular level. [18,19]

All the tests were performed maintaining a sterile technique and prophylactically broad-spectrum antibiotic drops (moxifloxacin eye drop 0.5%) 1 drop 4 times/day has been advised in each eye after the procedure.

Statistical Analysis: All the collected data are compiled in Microsoft Excel and Statistical Package of Social Sciences version 20(SPSS version 20) has been used for statistical analysis. Required parametric and non-parametric data analysis test has been used to test the significance and a p-value <0.05 has been considered to be significant.

Result and Analysis

In this cross-sectional study in a tertiary care hospital in West Bengal, the mean age of the staff is 50.83 years (+/- 9.268) and the control group is 48.95 years (+/- 7.575). Both follow the normal distribution. In the staff group, 32 were male (80%) and 30 were male (75%) in the control group. Comparison between the two groups has shown that no statistically significant difference exists between the two groups (p>0.05) i.e. the groups are comparable.

Schirmer test, TBUT measurement, Rose Bengal Staining (RBS) score, and CIC grading have been done in each eye of every staff and control. Values from each eye have been taken into consideration separately for statistical calculation.

The collected values from different dry eye tests were compared between the two groups, along with the correlation coefficient calculated. Comparison between the two groups concerning the Schirmer test and RBS score are statistically significant (p<0.05). Though 'decreased Schirmer 1 test value' signifies aqueous layer involvement and 'increased RBS score' signifies mucin layer involvement, we have noted the significant and simultaneous presence of both factors in the radiology staff group.

	Group (Staff=1,	Ν	Mean	Std. De-	Std. Error	Sig (p)
	Control=2)			viation	Mean	
Age(in years)	1	40	50.83	9.268	1.465	0.325
	2	40	48.95	7.575	1.198	

Table 1: Com	parison	of age	between	the two	groups	(p=0.325)	
	0	G , ,					

Table 2: Comparison of gender between the two groups (p=0.598)

Group Statistics							
	Group (Staff=1, Control=2)	Ν	Mean	Std. De- viation	Std. Error Mean	Sig (p)	
Gender (M=1, F=2)	1	40	1.20	0.405	0.064	0.598	
	2	40	1.25	0.439	0.069		

The mean TBUT value in the radiology staff group was found to be 13.20 seconds (right eye) and 14.23 seconds (left eye). In the control group, the values are higher (16.15 seconds in the right eye and 116.7 the8 in the left eye) though it was found to be statistically insignificant (p>0.05). CIC grading of the eyes when compared between the two groups, has not been found statistically

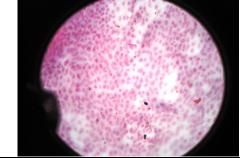
International Journal of Pharmaceutical and Clinical Research

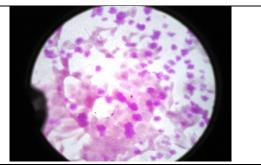
significant (p>0.05)An increase in Schirmer 1 value and TBUT value is suggestive of a less dry ocular surface. The Schirmer 1 test value in both eyes maintains a strong significant (P<0.05) positive correlation with TBUT values which suggests a commensurate involvement of the aqueous and mucin layer in the tear film of the

radiology staff group. An increase in grading signifies ocular surface epithelial and goblet cell changes while an increase in RBS score signifies more damaged surface epithelium. RBS scoring and CIC grading maintain a strong significant (p<0.05) negative correlation with the Schirmer 1 value and TBUT value in both eyes.

Table 3: Comparison betw	en the groups as per	r the assessment of Dry	Eye with different methods
(Schirmer test, TBUT, Rose	Bengal Staining, Conju	Inctival Impression Cyto	logy). (Significant if p<0.05)

	Group (Staff=1,		Mean	Std. De-	Std. Er-	Sig (p)
	Control=2)			viation	ror Mean	
schirmer1 right eye	1	40	13.30	5.464	0.864	0.032
(in mm)	2	40	15.95	5.406	0.855	
schirmer1 left eye	1	40	14.35	5.586	0.883	0.245
(in mm)	2	40	15.80	5.488	0.868	
TBUT right eye (in	1	40	13.20	6.157	0.973	0.056
seconds)	2	40	16.15	7.396	1.169	
TBUT left eye (in	1	40	14.23	6.742	1.066	0.121
seconds)	2	40	16.78	7.781	1.230	
RBS right eye	1	40	4.40	2.951	0.467	0.017
(scoring points)	2	40	2.93	2.411	0.381	
RBS Left eye (scor-	1	40	4.60	3.011	0.476	0.008
ing points)	2	40	2.95	2.396	0.379	
CIC right eye	1	40	1.40	1.081	0.171	0.465
(Grading)	2	40	1.23	1.050	0.166	
CIC left eye (Grad-	1	40	1.48	1.062	0.168	0.188
ing)	2	40	1.18	0.958	0.151	





Slide 1: Microphotograph showing sheets of Slide 2: Microphotograph showing the presence of squamous epithelial cells and absence of gob-squamous epithelia cells with fair number of goblet let cells found in normal cytology.

 Table 4: Correlation between different dry-eye diagnostic test values observed in the right eye of the radiology staff group

Correlations					
		schirmer1	TBUT right	RBS right	CIC right
		right eye	eye (in sec-	eye (scor-	eye (point
		(in mm)	onds)	ing points)	scoring)
schirmer1	Pearson Correlation	1	0.858**	-0.634**	-0.485**
right eye (in	Sig. (2-tailed)		0.000	0.000	0.002
mm)	Ν	40	40	40	40
TBUT right	Pearson Correlation	0.858^{**}	1	-0.572**	-0.374*
eye (in sec-	Sig. (2-tailed)	0.000		0.000	0.017
onds)	Ν	40	40	40	40
RBS right	Pearson Correlation	-0.634**	-0.572**	1	0.792**
eye (scoring	Sig. (2-tailed)	0.000	0.000		0.000
points)	Ν	40	40	40	40
CIC right	Pearson Correlation	-0.485**	-0.374*	0.792^{**}	1

International Journal of Pharmaceutical and Clinical Research

eye (point	Sig. (2-tailed)	0.002	0.017	0.000			
scoring)	Ν	40	40	40	40		
**. Correlation is significant at the 0.01 level (2-tailed).							
*. Correlation is significant at the 0.05 level (2-tailed).							

 Table 5: Correlation between different dry-eye diagnostic test values or scores in the left eye of the radiology staff group

 Correlations

Correlations					
		schirmer1	TBUT left	RBS Left	CIC left eye
		left eye (in	eye (in sec-	eye (scoring	(point scor-
		mm)	onds)	points)	ing)
schirmer1 left eye	Pearson Correlation	1	0.896**	-0.731**	-0.647**
(in mm)	Sig. (2-tailed)		0.000	0.000	0.000
	Ν	40	40	40	40
TBUT left eye (in	Pearson Correlation	0.896**	1	-0.732**	-0.621**
seconds)	Sig. (2-tailed)	0.000		0.000	0.000
	Ν	40	40	40	40
RBS Left eye	Pearson Correlation	-0.731**	-0.732**	1	0.839**
(scoring points)	Sig. (2-tailed)	0.000	0.000		0.000
	Ν	40	40	40	40
CIC left eye	Pearson Correlation	-0.647**	-0.621**	0.839**	1
(point scoring)	Sig. (2-tailed)	0.000	0.000	0.000	
	Ν	40	40	40	40
**. Correlation is s	significant at the 0.01 leve	el (2-tailed).			

No adverse reaction or ocular surface inflammation was reported after the tests in any of the groups. Temporary redness which appeared just after the tests, reduced within half an hour to one hour. Though it was a cross-sectional study, diagnosed dry eye disease cases have been treated according to the standard management protocol and followed up regularly.

Discussion

Madhury Reddy et al [20] conducted a study to evaluate cytological changes in dry eye states and reported in 1991 that the main features of impression cytology were squamous metaplasia of epithelial cells and altered goblet cell density in the conjunctiva. Mavek J, Podhorska M [21] et al in the year 1995, found that specimens from dry eye showed morphological changes of the epithelial cells, different nuclear alteration, a decrease in goblet cell density and degree of cytological changes related to the severity of dry eye syndrome. A study conducted by S C Pflugfelder et al [22] in the year 1997, suggested that decreased goblet cell density and mucin expression by epithelial cells are associated with rose bengal staining.

A study conducted by Ozkurt H et al. [23] in 2010 found a higher incidence of dry eye syndrome in radiologists than in non-radiologists and the difference was statistically significant. The working conditions and circumstances, including airconditioned rooms and exposure to diagnostic radiation, may be possible causative factors of this outcome. Though the radiologist group in their study had comparatively less mean Schirmer's 1 test score (9.1)and tear-film break-up time (8.4) the control group had similar values compared to our study.

A study conducted by Gürdal C, Aydin S, Onmuş H, Sand engörT, and Ozarar M. in Turkey in 2002 evaluated the clinical and cytological changes in the ocular surface of radiology technicians (radiographers) exposed to diagnostic doses of radiation³. The cytological evaluation was made using the mapping technique. Significantly increased dry eye was detected in group radiology technician group compared to the control. In the impression cytology investigation, squamous and intraepithelial lymphocytic metaplasia infiltration were noted in all the cases. In our study, though we have found a statistically insignificant difference between the two groups, the mean CIC score is high in both eyes in the radiology-staff group compared to the control. Routine ophthalmic evaluation of radiology technicians would be beneficial in detecting early cytological changes and dry eye.

In this study conducted in a tertiary care hospital in West Bengal, all the persons of both groups are asymptomatic without any history of any kind of medication. The participants in b h the groups are matched for age and gender. Then the conventional tests for the diagnosis of dry eye have been performed. Schirmer 1 test was performed with sterile No-41 Whatman filter paper to test the aqueous tear deficiency dry eye and compared between the groups. We have found that the Schirmer 1 test value is significantly less in the radiology-staff group. The T-BUT test, to detect the mucin layer [24] deficiency in cases of dry eye, has shown significantly decreased values in the radiology staff group. The RBS score in both the eyes of the radiology-staff group is significantly higher than the control group. This corroborating finding of the T-BUT test and Rose Bengal Staining (RBS) score indicates the mucin deficiency in the tear film among the radiology staff group. Conjunctival Impression cytology (CIC) grading in this study, though not significant, is in the high range in the radiology staff group suggesting a correlation

with the other tests. The three layers of the tear film i.e. lipid layer, aqueous layer, and mucin layer have their function. A minimum change in any layer of the tear film can lead to instability of the tear film as a whole. [25] The staff of the radiology department are regularly exposed to various forms of radiation and constant work in front of monitors makes their eyes more vulnerable. Tests done to detect different forms of dry eye and ocular surface disorder in symptomatic cases and controls clearly showed their inter-relationship.

Conclusion

The results of the Schirmer 1 test and Rose Bengal Staining score were found to be significantly different (p<0.05) in the radiology staff group than in the controls. The TBUT value, though insignificant, is less in the radiology staff group. CIC grading is higher in the radiology staff group suggesting changes in the ocular surface which needs further long-term study with larger co-hort. The correlation coefficient analysis suggests that inter-relationship between the tested parameters. Thus, the Schirmer 1 test and Rose Bengal Staining score can be performed for screening patients suspected to have Dry eye and ocular surface disorders.

Limitation

A larger sample size with a long-term prospective study may have a conclusive result regarding the effect of radiation on the ocular surface and tear film status in the staff of the radiology department.

References

- 1. Lemp MA. Report of the National Eye Institute Industry workshop on clinical trials in dry eyes. CLAO Journal 1995; 21:221-32.
- 2. Fox RI, Howell FV, Bone RC, et al: Primary Sjogren's syndrome: Clinical and immunopathologic features. Semin Arthritis Rheumatol 1984;14:77-10.
- Gürdal C, Aydın S, Onmuş H, Şengör T, Özarar M. Change in the ocular surface: initial observations from a pilot study of diagnostic radiology technicians (radiographers). Eur Radiol 2002; 12:1589-93.

- 4. Lee CI, Haims AH, Monico EP, Brink JA, Forman HP. Radiology. Diagnostic CT scans: assessment of patient, physician, and radiologist awareness of radiation dose and possible risks 2004;231,393-8.
- 5. Kase S KR. Radiation protection principles of NCRP. Health Phys 2004; 87:273-81.
- Halpenny D, O'Driscoll D, Torreggiani WC. Ocular health among radiologists in the age of PACS: is it time for our profession to open its eyes to this issue in the light of existing European legislation? The British Journal of Radiology .2012;10:1259.
- Schirmer O. Studien zur Physiologie and Pathologie der Tranenabsonderung and Tranenabfuhr. Albrecht von Graefes Arch Ophthalmol. 1903; 56:197-291.
- Lemp MA, Holly FJ. Recent advances in ocular surface chemistry. Am J Optom Arch Am Acad Optom. 1970; 47:669-72.
- Paschides CA, Kitsios G, Karakostas KX, Psillas C, Moutsopoulos HM. Evaluation of tear break-up time, Schirmer's-I test and rose Bengal staining as confirmatory tests for keratoconjunctivitis sicca. Clinical and experimental rheumatology. 1989;7(2):155-57.
- Singh R, Joseph A, Umapathy T, Tint NL, Dua HS.Impression cytology of the ocular surface. British Journal of Ophthalmology. 2005;89 (12):1655-59.
- 11. Cho P, Yap M. Schirmer test I. A review. Optom Vis Sci 1993; 70:152-6.
- Feenstra RP, Tseng SC. Comparison of fluorescein and rose bengal staining. Ophthalmology. 1992; 99:605-17.
- 13. Lemp MA, Holly FJ. Recent advances in ocular surface chemistry. Am J Optom Arch Am Acad Optom. 1970; 47:669-72.
- 14. Van Bijsterveld O: Diagnostic tests in the sicca syndrome. Arch Ophthalmol 1969; 82:10-4.
- Lemp M A. Report of the National Eye Institute/ Industry Workshop on Clinical Trials in Dry Eyes. CLAO J. 1995; 21:221-32.
- 16. Mukerji N, Vajpayee RB, Sharma N. Technique of area measurement of epithelial defects. Cornea 2003; 22:549-51.
- 17. Wittpenn JR, Gadomski AM, K-johede et al. Conjunctival Impression cytology: Feasibility of field trial to detect subclinical vitamin A deficiency. Am J Clin Nutr. 1989;49: 490 –94.
- 18. Mc. Kelvie P. Ocular surface impression cytology. Adv Anat Pathol. 2003, 10(6): 328-37.
- 19. Egbert P.R; Lauber S. and Maurice D.M. (1977). A simple conjunctival biopsy. Am J Ophthalmol, 84: 798-801.
- 20. Reddy M, Reddy PR, Reddy SC. Conjunctival impression cytology in dry eye states. Indian journal of ophthalmology. 1991;39(1):22.
- 21. Mavek J, Podhorska M. Evaluation of changes in cells of conjunctival epithelium in dry eye

syndrome by impression cytology. Klin Oczna, 1995, 97 (6):176–88.

- 22. S C Pflugfelder, S C Tseng, K Yoshino, D Monroy, C Felix. Correlation of goblet cell density and mucosal epithelial membrane mucin expression with rose Bengal staining in patients with ocular irritation. Ophthalmology, 1997,104(2):223-35.
- Ozkurt H, Ozkurt YB, Basak M. Is dry eye syndrome a work-related disease among radiologists? Diagn Interv Radiol 2006; 12:163-5.
- 24. Acosta MC, Gallar J, Belmonte C. The influence of eye solutions on blinking and ocular comfort at rest and during work at video display terminals. Exp Eye Res 1999; 68:663-69.
- 25. Bron AJ, de Paiva CS, Chauhan SK, et al. TFOS DEWS II pathophysiology report. Ocul Surf 2017; 15:438-510.