Original Article

DOI: 10.17354/ijss/2015/349

Correlation of CD4 Count and Severity of Dry Eye in Human Immunodeficiency Virus Positive Patients

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Abstract

Introduction: Ocular lesions occur in 70% of patients with human immunodeficiency virus (HIV)/AIDS. More than 50% of HIV infected patients have anterior segment manifestations. Keratoconjunctivitis sicca has been reported as one of the most common anterior segment manifestations in these patients.

Purpose: To evaluate the dry eye status in HIV-positive patients and correlate it with CD4 count.

Materials and Methods: Sample size: A total of 50 patients (100 eyes), patients attending the outpatient and inpatient department, Department of Ophthalmology, and the ART center at a tertiary care center diagnosed with HIV who fulfill the inclusion and exclusion criteria were selected randomly. All patients were investigated for dry eye with Schirmer's test (significant if <10 mm), tear film break up time (significant if <10 s), and slit lamp examination with Rose Bengal stain.

Results: Relative frequency of eyes with significantly decreased aqueous tear production (<10 mm Schirmer's test) 53.0%, decreased lipid layer (<10 s TBUT) 20%, decreased mucin layer (positive Rose Bengal) 20% in 100 eyes.

Conclusion: The aqueous tear production is affected in our study group, but increased frequency of decreased tear production is not associated with the level of CD4+ count.

Key words: CD4 lymphocyte count, Dry eye syndromes, Human immunodeficiency virus

INTRODUCTION

Dry eye is a clinical condition characterized by deficient tear production or excessive tear evaporation. It causes ocular irritation resulting from an alteration of the tear film. The effects can vary from minor inconvenience for most sufferers to rare sight-threatening complications in severe cases.[1]

The common feature of all dry eye syndromes is tear film instability, a result of disease or dysfunction of one or more component of lacrimal functional unit. Some of the many factors involved in the causation of dry eye include age, hormonal deficiencies, medications, surgery, and systemic autoimmune disease. All these can cause dysfunction of the lacrimal functional unit that is associated with ocular surface inflammation and eventually the signs and symptoms of dry eye. The symptoms that the patient complains of are heaviness of the lids, foreign body sensation, burning, stinging, itching, photophobia, dryness, soreness, and ocular fatigue.[2]

Human immunodeficiency virus (HIV) is a global pandemic causing morbidity and mortality at the rate of millions. India has the world's third-largest population suffering from HIV/AIDS. The NACO 2012-2013 annual report stated that in 2011, 20.9 lakh people are living with HIV/AIDS in India and about 1.16 lakh new cases of HIV infection are detected annually.[3]

Ocular manifestations of HIV infection typically occur late in the course of disease when there occurs profound

Access this article online

IJSS

www.ijss-sn.com

Month of Submission : 06-2015
Month of Peer Review : 07-2015
Month of Acceptance : 07-2015
Month of Publishing : 08-2015

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CD4+ T-lymphocyte depletion (<200 cells/mm^3), or the development of opportunistic infections or unusual neoplasms. Anterior segment is affected in up to 20% of the ocular complications associated with HIV infection, and yet remain unrecognized or undertreated in many patients. Keratoconjunctivitis sicca or dry eye occurs in later stages of the disease in 10-20% of the patients. An abnormal Rose Bengal staining and Schirmer's test is invariably detected in these patients. The cause of dry eye in HIV patients is complex. Combined effects of HIV-mediated inflammation and destruction of the lacrimal and salivary glands and direct HIV infection of the conjunctiva is the proposed mechanism.[4]

Dry eye by itself may be of a small consideration in view of the other more serious sequelae of HIV infection. However, when considering the importance of tear film in maintaining the ocular surface integrity, it becomes apparent that treatment of dry eye is important to prevent the sight-threatening complications such as secondary corneal ulcers or infections. Dry eye In HIV-positive patients can be managed by the usual methods of tear substitutes.[5]

With the increasing global burden of HIV, there is an increasing need to identify, treat and hence reduce the cause of morbidity and mortality. The causes of ocular morbidity are well documented in ophthalmic literature. Several studies have been done on the various ocular manifestations of HIV and their correlation with the level of CD4 count.[6,7]

According to the literature, dry eye is the most common anterior segment manifestation of HIV infection. But, no study has been done to correlate the severity of dry eye with the CD4 count.[8,9]

The present study has endeavored to correlate the level of CD4 count with the severity of dry eye in HIV seropositive patients.

MATERIALS AND METHODS

This explorative study was conducted at the Department of Ophthalmology, KR Hospital, Mysore between January 2014 and June 2014.

This study included 50 patients (100 eyes) who were diagnosed with HIV infection in the ART center at K.R Hospital, Mysore irrespective of whether they were on ART or not at the time of our evaluation. Data was collected using a piloted proforma meeting the objectives of the study after an informed consent. A detailed history of each patient was obtained regarding the age, gender, address, occupation, duration of the disease, duration since start of ART, history of any other illness. All patients were investigated for dry eye with Schirmer's test, Tear film break up time and slit lamp examination with Rose Bengal stain. Patients with history of certain systemic illnesses such as primary Sjogrens's syndrome, autoimmune diseases like rheumatoid arthritis and systemic lupus erythematosus, sarcoidosis, neuroparalytic keratitis, anterior and posterior blepharitis and contact lens wearers were excluded from the study as these could independently cause dry eye.[1]

Schirmer's test was performed using Schirmer's strips (5 mm × 35 mm filter paper), which was placed in the inferior fornix at the junction of medial two-third and lateral one-third of the lid. The amount of wetting of the strip was noted. It was considered to be negative if the value was >10 mm, mild dry eye between 5 and 10 mm and severe when <5 mm. Tear film break up time was assessed by staining the eye with 2% fluorescein strips and the eye was examined under cobalt blue filter with the slit lamp. The time taken for the first random dark spot to appear was noted and considered positive when <10 s. Rose Bengal stains healthy epithelial cells if a normal amount of mucin does not overlie the cell surface. Hence, in patients with dry eye Rose Bengal stains the conjunctiva and/or cornea.[1,10]

Statistics

Chi-square test and contingency coefficient analysis were used for statistical analysis of the data collected.

RESULTS

The Schirmer's Test was significantly less in 53% of all patients. However, in patients with CD4 count of 101-500 cells/mm^3 it was <10 mm in 25 out of 44 eyes (56.82 %). In patients with 0-100 cells/mm^3 and >500 cells/mm^3 20 out of 34 eyes (58.81%) and 8 out of 22 (36.36%) eyes had dry eye. This however was not found to be statistically significant (P = 0.2) (Table 1 and Figure 1).

Tear film break up time <10 s only in 20% of all eyes. In patients with CD4 count of 101-500 cells/mm^3 the tear film break up time was <10 s only in 12 eyes (27.27%). In patients with 0-100 cells/mm^3 and >500 cells/mm^3 only 20.59% and 4.5% of the eyes had dry eye. This was not found to be statistically significant (P = 0.09) (Table 2 and Figure 2).

In Rose Bengal test in the count of 0-100 cells/mm^3, only 7 eyes were positive for Rose Bengal staining which constitutes 20.59% and in 101-500 cells/mm^3 only 29.55% eyes were positive. But, with count of >500 cells/mm^3 100% were negative (P = 0.018) (Table 3).

Table 1: Results of Schirmer's test

CD4 count (cells/mm^3)	Schirmer's strip wetting			Total
	<5 mm	5-10 mm	>10 mm	
0-100				
Count (%)	4 (11.77)	16 (47.07)	14 (41.19)	34 (100)
101-500				
Count (%)	7 (15.90)	18 (40.90)	19 (43.20)	44 (100)
>500				
Count (%)	0 (0.0)	8 (36.36)	14 (63.64)	22 (100)
Total				
Count (%)	11 (11.0)	42 (42.0)	47 (47.0)	100 (100.0)

Table 2: Tear film break up time results

CD4 count (cells/mm^3)	Time		Total
	<10 sec	>10 sec	
0-100			
Count (%)	7 (20.59)	27 (79.41)	34 (100)
101-500			
Count (%)	12 (27.27)	32 (72.73)	44 (100)
>500			
Count (%)	1 (4.5)	21 (95.5)	22 (100)
Total			
Count (%)	20 (20)	80 (80)	100 (100)

Table 3: Results of Rose Bengal stain

CD4 count (cells/mm^3)	Rose Bengal staining		Total
	Negative	Positive	
0-100			
Count (%)	27 (79.41)	7 (20.59)	34 (100)
101-500			
Count (%)	31 (70.45)	13 (29.55)	44 (100)
>500			
Count (%)	22 (100)	0 (0.0)	22 (100)
Total			
Count (%)	80 (80)	20 (20)	100 (100.0)

There was no significant difference in dry eye between those on ART and those who were not on ART.

No significant difference was found between males and females in our study.

DISCUSSION

Ocular lesions occur in 70% of patients with HIV/AIDS[6] and affect almost all the structures of the eye.[11] In addition to the posterior segment lesions such as cytomegalovirus retinitis, the anterior segment, and ocular surface lesions can be vision threatening.[12] More than 50% of HIV infected patients have anterior segment manifestations. Kerato-conjunctivitis sicca has been reported as one of the most common anterior segment manifestations.[13] Various studies conducted on normal population show that the prevalence of dry eye ranges between 10% and 20%.[14,15]

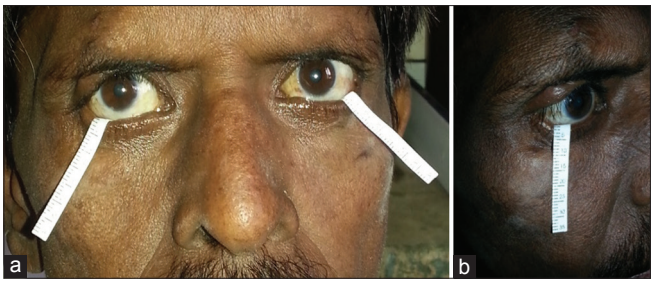

Figure 1: (a and b): Schirmer's test being performed in a patient whose CD4 count was 98 and Scirmer's test was OD - 5 mm, OS - 8 mm at the end of 5 min

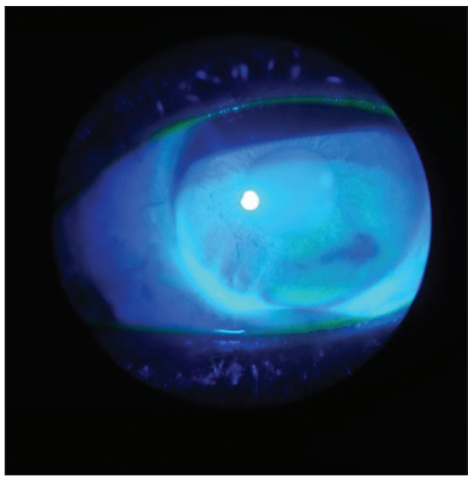

Figure 2: Tear film break up time (7 s) in a patient

The prevalence of dry eye is HIV seropositive patients is found to be higher than in normal population. However, there is a paucity of studies to determine the correlation between CD4 count and dry eye.

The demographic pattern in our study is similar to the Indian statistics, higher prevalence in males (64%) than females (36%) and in the age group of 20-50 years.[3] There was a significant decrease in the aqueous layer of the tear film assessed by Schirmer's test in more than half the eyes examined (53 out of the 100). This however was not statistically significant.

The Schirmer's test was positive 58.8% of eyes in patients with CD4 count of 0-100 cells/mm^3 and significantly lower in count of 101-500 cells/mm^3 (18.16%). This shows that the aqueous layer was deficient in the lower CD4 count. The tear film break up time showed dry eye in 29.1% of eyes (7 out of 34) in patients with CD4 count of 0-100 cells/mm^3, which was slightly higher than in a count of 101-500 cells/mm^3 (27.2%, 12 out of 44) and a lesser prevalence was noted among the higher count (4.5% in patients with >500 cells/mm^3). The Rose Bengal stain test was negative in 100% cases of CD4 count over 500 cells/mm^3, which could indicate that higher CD4 count may have a lesser prevalence of dry eye.

In all the three tests conducted for dry eye, we observe that the higher CD4 count had a lesser prevalence of dry eye than the lower CD4 count. This indicates that as the disease progresses dry eye prevalence increases. Whether the use of ART can halt this or not is inconclusive. The Schirmer's test was positive in 53% of the study population whereas tear film break up time and Rose Bengal staining was positive in 20% each. This signifies that the aqueous layer of the tear film is affected more than lipid and mucin in our study. The lacrimal gland may be affected due to the disease leading to a decrease in its secretion.[16]

Although, the results of the tests are statistically insignificant in our study, the fact that more than half the patients were positive for dry eye cannot be looked down upon. Further studies are needed with higher sample size to evaluate a relationship between CD4 count and dry eye.

The ocular involvement may often precede systemic manifestations in HIV infection,[14] hence the role of an ophthalmologist in the management of HIV-positive patients is becoming increasingly important.[6,12,17]

In a study, Sicca syndrome in patients infected with HIV conducted by Geier *et al.* data show that decreased tear production occurs in approximately 20-25% of patients with HIV infection. This increased frequency of decreased tear production is not associated with the CD4+ count or related to the severity of HIV disease, respectively.[18]

However, our study shows decreased tear production in around 50% patients. Although the association with CD4 count is inconclusive.

The limitations of our study was the small sample size. The role of ART on dry eye was not assessed in our study. But, a subset of literature has shown no such association between dry eye and ART. However, further studies with larger sample size may be needed to overcome these limitations.

CONCLUSION

In all the three tests that we conducted we found that there is decreased tear production. The aqueous tear production as evaluated by Schirmer's test is affected in our study group in 50% of patients. Tear film break up time and Rose Bengal staining is positive in only 20% each. However, increased frequency of decreased tear production is not associated with the level of CD4+ count.

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How to cite this article: Gowda HT, Krishnamurthy H, Tanushree V, Nayak S. Correlation of CD4 Count and Severity of Dry Eye in Human Immunodeficiency Virus Positive Patients. Int J Sci Stud 2015;3(5):68-71.

Source of Support: Nil, **Conflict of Interest:** None declared.