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Ocular Manifestations in People Living with HIV/AIDS (PLWHA) at the Kerti Praja Foundation, Denpasar, Bali

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ABSTRACT

Background and purpose: People living with Human Immunodeficiency Virus - acquired immunodeficiency syndrome (PLWHA) could present various ocular manifestations according to the CD4+ lymphocyte count. This study aims to determine the socio-demographic characteristics and ocular manifestations of PLWHA.

Methods: This study is an observational study with a cross-sectional design and consecutive sampling, involving a total of 118 samples, conducted in August 2021 at Kerti Praja Foundation Denpasar. Data were collected through history taking and ocular examinations, which included the variables of gender, age, occupation, residence, working status, level of education, duration of ARV treatment, treatment compliance, visual acuity, anterior segment manifestation, posterior segment manifestation, and CD4 T-cell count. Data analysis was performed with a statistical software.

Results: A total of 118 samples were involved in this study, with 53 respondents (44.9%) experienced ocular manifestations and 55.1% did not experience ocular manifestations. The most frequent ocular manifestation identified was dry eye (68.5% found in right eye and 54.9% found in left eye), while only 2 patients have posterior-segment manifestation.

Conclusion: The most common ocular manifestation in HIV-infected people on anti-retroviral therapy was dry eye. Screening for dry eye is recommended in PLWHA.

Keywords: HIV-AIDS, PLWHA, Ocular Manifestations

INTRODUCTION

Human Immunodeficiency Virus (HIV) targets white blood cells in the human body (lymphocytes) and causes a decrease in immunity level that leads to the increased susceptibility to various diseases. Damage of the immunity system due to HIV can cause a group of clinical signs known as acquired immunodeficiency syndrome (AIDS).[1] People living with HIV-AIDS (PLWHA) have a high risk of various opportunistic infections which can cause death. At the end of 2021, there were an estimated of 38.4 million people living with HIV, where 650,000 people died in the same year.[1] The number of HIV cases in Indonesia tends to increase every year while the number of AIDS cases tends to be stable. While it is still debated, an estimated of 640,000 people are living with HIV in Indonesia or approximately accounted for 0,4% of adult population.[2]

Ocular involvement in HIV infection occurs most commonly due to opportunistic infections and neoplasms.[2] Opportunistic infections like CMV retinitis occur with a significantly reduced CD4 T-cell count and are one of the common causes of blindness in HIV patients. Unlike other diseases, ocular infection in these immunosuppressed patients is associated with minimal inflammatory signs. HIV has been isolated from tears, cornea, vitreous, and chorioretinal tissue in affected persons. The ocular structures affected by HIV include the adnexa, anterior segment, posterior segment, and orbit.[3]

Ocular manifestations in HIV-AIDS patients are all signs and complaints in the eyes due to the disease.[3] It is suggested up to 80% patients will exhibit at least one ocular manifestation at some point during the disease that correlates with the CD4 count or viral load. Past studies focused primarily on posterior segment manifestation, however at present, the introduction of Highly Active Antiretroviral Therapy (HAART) has dramatically changed the dynamics of HIV/AIDS clinical presentation. Study showed anterior segment was affected in about 25% of ocular manifestations associated with HIV. The most common anterior segment and adnexa manifestation of non-HAART PHWLA was caused by the opportunistic infection such as *Herpes zoster opthalmicus (HZO), blepharitis, Mulloscum Contagiosum, Sarcoma Kaposi*, and Conjunctivitis.[3]

Denpasar City is one of the areas with high number of HIV infection and AIDS cases which have increased from year to year.[4] HIV-infected people in Denpasar can access health services both at government and private health facilities. One of the institutions in Denpasar City engaging in the field of HIV/AIDS is the Kerti Praja Foundation, providing HIV and sexual transmitted infection (STI) testing services, counseling and anti-retroviral (ARV) treatment for the public and at-risk groups. This study aims to assess the ocular manifestations characteristics in HIV-infected people at the Kerti Praja Foundation, Denpasar. The study will give information about the distribution and common ocular manifestations in PLWHA who have been treated with ARV.

METHODS

This study used a quantitative approach with a cross-sectional study design and consecutive sampling to describe the ocular manifestations in HIV patients at the Kerti Praja Foundation, Denpasar. All HIV patients who visited Kerti Praja Foundation were the population of this study. Patients aged 20-60 years old, had sufficient data in their medical records, in an adequate general health to be able to follow instructions during ocular examinations and willing to be examined were included in the study, while patients with incomplete medical records and those who refused to sign the consent form were excluded. Consecutive sampling

technique was used for the study with the minimum sample size needed was 75 patients. A total of 118 patients were finally included for the study.

Primary data was obtained through eye examination and interviews with HIV-infected people regarding their characteristics. The information obtained regarding the characteristics of the respondents included name, age, gender, address, level of education, working status, time of the HIV infection diagnosis, types and duration of ARV treatment, treatment compliance, and the latest CD4 count. Secondary data was collected through medical records of the patients at Kerti Praja Foundation. The eye examination of HIV-infected people was begun with an anamnesis regarding eye complaints and then continued with examination of visual acuity using the Snellen Chart. Furthermore, the eye examinations conducted were examination of eye pressure using a portable tonometer, Schirmer test, examination of the anterior segment with a portable slit lamp, and examination of the posterior segment with indirect fundoscopy.

After the data was collected, a univariate and bivariate analysis using Chi-square test was performed. This research was approved by the Research Ethics Committee of Faculty of Medicine, Udayana University with an ethical clearance number: 948/UN14.2.2.VII.14/LT/2021.

RESULT

Table 1. Socio-demographic characteristics and treatment history of PLWHA

Variables	Frequency (n)	Percentage (%)
Gender		
Male	88	74.6
Female	28	23.7
Transgender	2	1.7
Age (years)		
20–29	36	30.5
30–39	43	36.4
≥ 40	39	33.1
Residence		
Denpasar	78	66.1
Outside Denpasar	40	33.9
Working status		
Working	103	87.3
Not working	15	12.7
Level of education		
Low (Not attending school, primary, junior high)	42	35.6
High (High school and university)	76	64.4
Duration of ARV treatment		
<1 year	20	16.9
1-5 years	62	52.5
>5 years	36	30.5
Treatment compliance		
Comply	112	94.9
Not comply	6	5.1
CD4 count		
<200	18	15.3
200-499	57	48.3
>499	43	36.4

Of the 118 respondents, 74.6% were male, 23.7% female and 1.7% transgender. The age of respondents was almost equally distributed in the three ages bracket of 20-29, 30-39 and 40 years or above, and approximately two third of respondents (66.1%) reside in Denpasar City. Respondents who was working during the time of study was 103 people (87.3%), and the majority (64.4%) of them have high education level. Regarding the treatment history, a total of 62 respondents (52.5%) had consumed anti-retroviral therapy for 1-5 years, most of the respondents (94.9%) reported that they had good compliance to the treatments, while the rest had experienced drug withdrawal before. Almost half of the respondents (48.3%) have CD4 level ranging from 200-499 cells (Table 1).

Table 2. Distribution of the ocular examination results among PLWHA

Variable	Frequency (n)	Percentage (%)
Reported Eye Complaints		
Yes	71	60.2
No	47	39.8
Visual Acuity (OD)		
<0.5	111	94
0.5-1.0	7	6
1.0-1.3	0	0
>1.3	0	0
Visual Acuity (OS)		
<0.5	112	94.9
0.5-1.0	6	5.1
1.0-1.3	0	0
>1.3	0	0
Anterior Segment Examination (OD)		
Abnormality	54	45.7
No Abnormality	64	54.3
Anterior Segment (OS) Examination		
Abnormality	49	41.5
No Abnormality	69	58.5
Posterior Segment Examination (OD)		
Abnormality	0	0
No Abnormality	118	100
Posterior Segment (OS) Examination		
Abnormality	2	1.7
No Abnormality	116	98.3
Ocular Manifestation		
Yes	53	44.9
No	65	55.1

OD=ocular *dextra*/right eye; OS=ocular *sinistra*/left eye

Based on interviews related to eye complaints, 71 respondents (60.2%) reported having eye complaints. The distribution of respondents based on Best Corrected Visual Acuity (BCVA) both right and left eye shows that 94% was included in the mild visual impairment category (<0.5). Based on anterior segment examination, 12 respondents had abnormalities in the right eye and 13 respondents had abnormalities in the left eye. Furthermore, the examination of the posterior segment shows that 1 respondent had abnormalities in both eyes, while the other 117 respondents did not experience abnormalities in both eyes. Respondents who experienced ocular manifestations were 53 people (44.9%) and those who did not experience ocular manifestations were 55.1% (Table 2).

Table 3. Ocular Manifestations among PLWHA

Ocular Manifestations	f (%)	
	OD (n=54)	OS (n=51)
Anterior-segment manifestations		
- Conjunctivitis	1 (1.8)	5 (4.2)
- Pterygium	7 (12.9)	7 (13.7)
- Corneal cicatrix	1 (1.8)	3 (5.8)
- Microphthalmia	1 (1.8)	0 (0.0)
- Senile immature cataract	7 (12.9)	5 (4.2)
- Dry eye disease	37 (68.5)	28 (54.9)
- Conjunctival nevus	0 (0.0)	1 (1.9)
Posterior segment manifestations		
- Retrobulbar mass	0 (0.0)	1 (1.9)
- Optic atrophy	0 (0.0)	1 (1.9)

f= frequency, OD=right eye, OS=left eye

Table 4. Distribution of patients with ocular manifestations according to sociodemographic characteristic, treatment history and CD4 count

Variables	Ocular Manifestation		p-value
	Yes (n=53) f (%)	No (n=65) f (%)	
Gender			
Male	39 (44.3)	49 (55.7)	
Female	14 (50.0)	14 (50.0)	0.380*
Transgender	0 (0.0)	2 (100.0)	
Age (years)			
20–29	10 (27.8)	26 (72.2)	
30–39	20 (46.5)	23 (53.5)	**0.024**
≥40	23 (59.0)	16 (41.0)	
Residence			
Denpasar	36 (46.2)	42 (53.8)	0.845
Outside Denpasar	17 (42.5)	23 (57.5)	
Working status			
Not working	8 (53.3)	7 (46.7)	0.483
Working	45 (43.7)	58 (56.3)	
Level of education			
Low (Not attending school, primary, junior high)	23 (54.8)	19 (45.2)	0.110
High (High school and university)	30 (39.5)	46 (60.5)	
Duration of ARV treatment			
<1 year	5 (25.0)	15 (75.0)	
1-5 years	26 (41.9)	36 (58.1)	**0.027**
>5 Years	22 (61.1)	14 (38.9)	
Treatment compliance			
Comply	51 (45.5)	61 (54.5)	0.689*
Not comply	2 (33.3)	4 (66.7)	
CD4 count			
<200	9 (50.0)	9 (50.0)	
200-499	23 (40.4)	34 (59.6)	0.626
>499	21 (48.8)	22 (51.2)	

* Fisher Exact Test

Table 3 describes the ocular manifestations among PLWHA in this study which consist of anterior and posterior segment manifestation. The major ocular manifestations in anterior segment were dry eye disease (OD 68.5%; OS 54.9%), followed by pterygium (13.7% in both eyes), senile immature cataract (OD 12.9%; OS 4.2%), conjunctivitis (OD 1.8%; OS 4.2%), corneal cicatrix (OD 1.8%; OS 5.8%), microphthalmia (OD 1.8%), and conjunctival nevus (OS 1.9%). We found only 2 patients with posterior-segment manifestations.

Table 4 describes the distribution of ocular manifestation related to different variables in the study. Older age (≥40 years) tends to have higher proportion of ocular manifestation than the younger age (p=0.024). Other sociodemographic variables such as gender, residence, working status and level of education were found to be not statistically correlated to ocular manifestations in PLWHA. Regarding to treatment, duration of ARV treatment was associated with ocular manifestation, with those who have been treated longer show higher proportion of ocular manifestation (p=0.027). Treatment compliance also did not correlate significantly with the incidence of ocular manifestation, although patients with shorter treatment duration and less compliant to treatment shows more ocular manifestation than those who had treatment for more than 5 years. Lastly, patients who develop ocular manifestation tend to have lower CD4 count (<100), although the result was not statistically significant (p=0.626).

DISCUSSION

Ocular manifestations in HIV-AIDS patients are all signs and complaints in the eyes due to the disease.[3] The ocular manifestations can be an indicator of systemic infection in asymptomatic HIV-positive person. HIV has been isolated from tears, cornea, vitreous, and *chorioretinal* tissue in affected persons. The ocular structures affected by HIV include the adnexa, anterior segment, posterior segment, and orbit. It is suggested up to 80% patients will exhibit at least one ocular manifestation at some point during the disease that correlates with CD4 count or viral load.

Of the 118 patients involved in the study, 71 patients reported to have eye complaints in which complete ocular examinations were carried out and we confirmed 51 patients with ocular manifestations. Most of the manifestations were related to anterior segment of the eye, while there were only 2 patients having posterior segment manifestation. Dry eye disease was the most common ocular manifestation in PLWHA observed in this study. Other manifestations that are also reported, including: conjunctivitis, pterygium, corneal cicatrix, microphthalmia, senile immature cataract, conjunctival nevus, retrobulbar mass and optic atrophy. Variables that are found to be statistically significant with the incidence of ocular manifestation are level of education, treatment duration, and CD4 count.

This study revealed sociodemographic patterns that are quite similar to previous studies. Health-seeking behaviors are heavily influenced by gender, education, and socio-economic status. In developing world such as Indonesia, male tend to predominate in seeking health facilities rather than female. Level of education and working status also affected people knowledge of HIV/AIDS. Higher level of education increased the chances of people to be more proactive of their own health and to seek out information regarding the HIV/AIDS. This can also explain the higher number of patients with active working status who come to Kerti Praja Foundation. Age group also play an important role in knowledge of HIV/AIDS. Although the participants in this study were almost equally distributed among three age groups, previous study suggested that there were discrepancies in knowledge of HIV/AIDS between young age (<20 years old) and older age (>50 years old). Urban residence such as Denpasar will increase likelihood of health-seeking behavior as life in larger cities provides greater access to complete health facilities such as Kerti Praja Foundation. All

respondents are frequent patients who have been on treatments with ARV. Highly Active Anti-Retroviral Therapy (HAART) was developed approximately almost 25 years ago and until now successfully displayed prolonged HIV/AIDS patients survival, resulting in improvement of PLWHA's general health status due to higher CD4 count trend. This could also explain the new emerging ocular manifestations nowadays seen on HIV patients due to increased life expectancy.

The most common type of ocular manifestation found in this study was dry eye disease. The etiology of dry eye disease in HIV patients is usually thought to be due to HIV-mediated lymphocytic infiltration of the lacrimal gland. This leads to the destruction of the lacrimal acini and the ductal system, as well as direct conjunctival damage.[5] Dry eye can also be due to blepharitis in these patients, the pathogenesis could be explained as reduced ability to control normal flora and more complex changes in the cutaneous glands of the eyelids. Meibomitis has been the causative factor in lipid layer dysfunction in these patients. The resulting keratoconjunctivitis contributes to a chronic inflammatory state, further promoting cytokine secretion, destruction and dysfunction of the lacrimal gland, and loss of tear production. Anterior segment disorders can lead to ocular morbidity and so affect the quality of life of patients. Reduced quality of life is reported in many patients with dry eye disease. Moreover, anterior segment abnormality such as dry eye disease could predispose to more severe ocular manifestation due to impaired ocular immune system in anterior segment.[6]

Lucca JA et al reported 21.4% prevalence of dry eye in HIV and AIDS patients. However, their study was based on individual symptoms of dry eye and the clinical examination used a non-standardized test.[7] De Carlo DK et al also reported prevalence of dry eye as 38% in HIV positive patients which matched our results with TBUT.[8] Another study by Geier SA et al showed that decreased tear production occurred in approximately 20%–25% of patients with HIV infection, but decreased tear production was not found to be associated with the severity of HIV disease.[9]

Other study by Burtin T et al reported that 70%–80% of HIV positive patients presented dry eye symptoms and signs which much higher than this study.[10] A recent study by Gowda et al. showed decreased tear production in 50% of the HIV patients by using the Schirmer test.[11] However, in Mathebula SD et al study results from Schirmer test showed prevalence of dry eye in around 80% of HIV patients which was also higher compared to this study.[12]

In the same study, it is stated that 50.3% cases of dry eye disease in HIV patients belonged to the economically productive age group of 31-50 years. This finding is similar to our study where most ocular manifestations were experienced by patients aged more than 30 years. This needs to be emphasized as the morbidity of these individuals has a considerable impact on the economy of their families. In normal population studies, females have more prevalence of dry eye disease than males mainly due to the estrogen effect after menopause. However, in our study, males had a higher prevalence than females, which is similar to USA, India, and Brazil. We have not found a clear explanation for this contradictory finding and may require further investigations out scope of our current study.

This study, however, only showed significant statistical correlation of ocular manifestation to age group, but not with level of education, working status, and residential area. Several previous studies had observed the relationship between demographic and socioeconomic status with HIV. One study by Pradnyani et al revealed that education level significantly correlated with knowledge level of HIV/AIDS. Education can indirectly elaborate the reason behind increasing ocular manifestation due to higher knowledge and health-seeking behavior tendencies among patients with higher level of education and active working background.[13] The result that shows more ocular manifestation identified in Denpasar could be the basis for improvement in expanding mobile health services through community services to cover more case-findings in rural areas.

Most of the ocular manifestation in this study found in HIV-infected people with CD4 count >200 cell/µl and it is somehow related to the severity of the diseases to some extent. In this study, most of the HIV-infected people who came to Kerti Praja Foundation was people with well controlled disease by ARV. Previous studies showed contradictory findings, some stated that ocular manifestation was common in patients with a CD4+ T cell count of <200 cells/µl. This study, however, showed insignificant statistical correlation of dry eye disease and low CD4 count. There was significant correlation between the CD4 count and Schirmer's results (r=0.7) and between the CD4 count and TBUT (r=0.48) based on the study by Mathebula.[12] A similar study by Sharma et al showed a significant correlation between CD4 count with Schirmer test without anesthesia and TBUT in 90 eyes. Patients with low CD4 counts showed a trend of severe dry eye, although this relationship was said to be not significant, just like in our study.[14]

Generally, patients who were on highly active anti-retroviral therapy (HAART) had a high prevalence of ocular manifestation compared to those who were not on HAART. This could be due to the low CD4+ T cells count during the initiation of HAART as patients with a CD4+ T cell count of <250 are put on HAART. This low CD4 count is associated with higher prevalence of ocular manifestation as shown in this study and patients might have already developed the manifestation before initiation of HAART. Even though patients are on HAART and their CD+T cells count increases, the newly formed population of lymphocytes are not associated with functional maturity of the immune system and patients are not protected. This clearly explained the finding in our study where length or duration of ARV treatment significantly correlated with ocular manifestation reported.

The compliance of ARV medication will support the immune reconstitution which showed by increasing the number of CD4+T cell count. In this study, compliance of medication correlates with ocular manifestation significantly. Mathebula et al showed that the risk of opportunistic infections in the eye and other organs increases significantly in CD4<100 cell/µl.[12] The ocular manifestations of presenting opportunistic infection in posterior segment such as CMV retinitis infection, Toxoplasmosis, and Syphilis become the leading cause of blindness in HIV-infected person. Other pathologic lesion such as ocular surface squamous neoplasia (OSSN) also found in HIV-infected patient, but we did not find this kind of anterior segment disorder.

This study explored limited variables, hence in the future more variables such as type of ARV treatment, viral load, comorbidities, or history of transmission could be considered and contribute more to the collectivity of study regarding ocular manifestation in PLWHA. Also, treatment compliance was self-reported and could be a subject of social desirability bias.

CONCLUSION

Almost half of PLWHA experienced ocular manifestations with the most common was dry eye. Variables that are related to the presence of ocular manifestation were older age and longer duration of ARV treatment. Screening for ocular manifestation is recommended in HIV-infected people to prevent serious ocular morbidity.

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CONFLICT OF INTEREST

All authors declared that they have no conflict of interests.

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