



Ocular manifestations of HIV and AIDS patients on antiretroviral therapy in a tertiary hospital in South Africa



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Background: Human immunodeficiency virus and acquired immunodeficiency syndrome (HIV/AIDS) causes impairment to the immune system, which then leads to immunocompromised conditions, and allows for opportunistic infection to invade many organs of the human body. Ocular involvement is very common; the various ocular complications may be asymptomatic and they may be the initial manifestations of the underlying diseases.

Aim: This study aimed to determine the prevalence and the type of ocular manifestations that occur in HIV and AIDS patients.

Setting: The study was conducted on ART (antiretroviral treatment) clinic patients in the Department of Ophthalmology at the Steve Biko Academic Hospital, Pretoria.

Methods: This descriptive, cross-sectional study was conducted on HIV and AIDS patients referred from the ART clinic for complete ophthalmological evaluation, irrespective of the immune system status and presence or absence of symptoms. All the participants underwent an ophthalmologic evaluation, which included case history and ocular examinations of both anterior and posterior segments.

Results: Out of the 177 participants, 72.3% had visual acuity of between 6/3 to 6/18, 10% had poor vision, 7% had lost one eye to ocular complications and 5% were blind. The most common anterior segment manifestations were uveitis and dry eye, whilst HIV-related retinopathy and papilledema were the most prevalent conditions in the posterior segment. Only three participants had third cranial nerve palsy.

Conclusion: The prevalence of ocular manifestations was significantly higher with lower CD4+ cell counts, which could be regarded as predictors for the occurrence of ocular morbidity in HIV and AIDS patients.

Keywords: AIDS; HIV; CD4+ cell count; ocular manifestations; anterior segment; posterior segment.

Introduction

The human immunodeficiency virus (HIV) is a retrovirus which replicates in cluster of differentiation 4 (CD4+) lymphocytes.^{1,2} It causes impairment to the human immune system, which leads to immunocompromised conditions and allows for opportunistic infections to invade many organs. The multisystem disorders caused by HIV are grouped under the name acquired immunodeficiency syndrome (AIDS). Human immunodeficiency virus and acquired immunodeficiency syndrome are still a major public health problem in South Africa, even though there are many campaigns to publicise the importance of HIV treatment. The 2018 report on HIV/AIDS shows that the number of newly diagnosed HIV patients is still increasing. Since the first case of HIV in 1981, it has become a worldwide pandemic; ocular involvement has been a common finding and loss of vision is a serious problem in people living with HIV/AIDS.^{3,4,5,6,7,8,9,10,11,12,13,14}

It is estimated that approximately 50% to 80% of HIV-infected patients are expected to be treated for HIV-related eye disorders in the course of their illness.^{3,4,5,6,7,8,9,10,11,12,13,14} The ocular manifestations of HIV and AIDS can affect almost all the structures of the eye, from the adnexa and anterior segment to posterior segment of the eye and the optic nerve.

With the advent of highly active antiretroviral therapy (HAART), there is a reduction in the number of opportunistic infections and a general improvement in the length and quality of life, but the longer survival rate may lead to an increased prevalence of blindness because of immune recovery uveitis (IRU) and unknown disorders caused by antiretroviral drugs.

Knowledge of the effect of HIV and AIDS on the eye is important, as ocular manifestations may be the cause of visual impairment or blindness, which may compromise the quality of life for patients living with HIV and AIDS. Ophthalmic clinicians are faced with the challenge of recognising, identifying and treating unusual presentations of HIV and AIDS. If these ocular manifestations are detected at an early stage and treated promptly, it is possible to prevent or minimise the consequences of visual damage. This study was undertaken to identify and document ocular manifestation of HIV/AIDS in a tertiary referral hospital. Ocular manifestation may be the primary presentation of the diseases, so ophthalmologists and optometrists may make the initial diagnosis of HIV/AIDS.

Methods

This was a prospective cross-sectional descriptive study, conducted from April 2016 to December 2018 at the Department of Ophthalmology, Steve Biko Academic Hospital in Pretoria, South Africa, which is a tertiary healthcare centre and teaching hospital. The participants, who were all above the age of 18, signed informed consent document before participating in the study. They were informed about the purpose and details of the study and it was stressed that their participation was entirely voluntary. The study followed all the tenets of the Helsinki Declaration on human participants (subjects). The study was carried out on every consecutive HIV-positive patient receiving antiretroviral treatment (ART) at the hospital's ART clinic.

For each participant, a detailed ocular history including demographic information was recorded, such as age, gender, duration of HIV infection, recent CD4+ cell count and associated systemic symptoms. A detailed ocular examination was carried out which included slit lamp biomicroscopy, visual acuity, ocular motility, colour vision, pupillary reflexes and dry eye. The dry eye diagnosis criteria included both of subjective discomfort symptoms (if one or more symptoms were noted as severe from the questionnaire) and clinical sign of ocular surface disorder using the Schirmer 1 test. The posterior segment was evaluated using the fundus imaging technology. Those participants who needed relevant treatment or surgical interventions for systemic conditions were treated in consultation with the physician. Those who needed further refraction were assisted by optometrists.

Participants were HIV-positive patients of both genders, registered at the ART clinic and referred to the Department of Ophthalmology for treatment of ocular complaints. Patients were excluded as participants if referred directly from other clinics and hospitals and were not originally known to be HIV-

positive. They were referred to the ART clinic and subsequently tested for HIV because of suspicious ocular disorders. Patients with additional medical conditions such as diabetes mellitus, hypertension and ocular trauma (which can have manifestations overlapping with the HIV and AIDS), and those who were not willing to give informed consent or who were younger than 18, were excluded. Participants' anonymity was guaranteed and their medical records and personal information were kept confidential.

Statistical analysis

Statistical Package for Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, United States [US]) was used to perform statistical analyses. Descriptive statistics was utilised to determine the percentages of the ocular manifestation of HIV and AIDS of the total participants examined. Relevant variables were age, gender, visual acuity and ocular findings. The association between ocular manifestations of HIV/AIDS and CD4+ cell counts was analysed using the chi-square test.

Ethical considerations

Ethical approval was obtained from the Ethics Committee of the University of Pretoria, Faculty of Health Sciences (ethical clearance number 253-2016). Permission to conduct the study was granted by the hospital administration. Informed and written consents were obtained from every participant in the study. Privacy and confidentiality were maintained throughout the study period.

Results

A total of 177 HIV and AIDS participants were assessed during the study period: 118 (67.2%) females and 57 (32.8%) males. The female-to-male ratio was 1:0.5. Their ages ranged from 18 to 73 years, with a mean age of 42.78 ± 12.4 years (see Table 1). The most common age group was 31–40 years in 28.8% of the participants. The youngest participant was 18 years old and the oldest was 73 years of age. The total number of affected participants was 128 (72.3%).

The participants were divided into groups according to their visual acuities, which ranged from 6/3 to 6/18, and 6/48 to 6/90, counting fingers, hand movement, light perception and no light perception (Table 2). About 69.3% of the participants were found to have normal visual acuity. About 25.0% of the participants had a history of eye problems. Pain, blurring of vision and photophobia were the most reported symptoms.

TABLE 1: Age distribution of participants studied in groups (years).

Age range (years)	Frequency	Percentage
18–30	35	19.8
31–40	51	28.8
41–50	38	21.5
51–60	36	20.3
61–70	14	7.9
> 71	1	0.6

N = 177.

Those who reported to have a history of eye problems (11.3, 95% confidence interval [CI]: 7.85–18.62) were 11 times more likely to develop ocular manifestations compared to those who did not report history of eye problems. Participants with reduced visual acuity (3.62, 95% CI: 1.46–8.33) were 3.6 times more likely to have HIV and AIDS manifestations than those who had normal visual acuity.

The CD4+ cell count was obtained in all the participants (Table 3). The mean CD4+ cell count was 382.59 cells/ μ L \pm 235.4 cells/ μ L (cells/ mm^3) with a range from 50 cells/ μ L to 1308 cells/ μ L (Table 3). Other clinical tests done are shown in Table 4. The mean CD4+ cell count for those with anterior and posterior segment ocular manifestations was significantly different at 453.8 cells/ μ L \pm 402.8 cells/ μ L and 187.50 cells/ μ L \pm 101.6 cells/ μ L ($p < 0.05$). The average duration of HIV infection was 6.75 \pm 2.3 years.

Other variables investigated are presented in Table 4. Colour vision defects were observed in 53 (29.9%) whilst pupillary abnormalities were seen in 42 (63.3%). Twenty-two (23.7%) participants had unresponsive pupils whilst abnormal ocular motility was seen in 48 (27.1%).

The prevalence of ocular manifestations of HIV and AIDS was 72.3% with 95% CI: 65.4% – 81.2%. Table 5 shows the anterior segment manifestation of the HIV and AIDS. A total of 42 (23.7%) had anterior segment lesions. The most common were uveitis, dry eye, conjunctival growth and molluscum contagiosum. There was a wide range of severity of dry eye with deposit on the ocular surface.

The frequency of participants with posterior segment disorders is shown in Table 6. The posterior ocular manifestations were seen in 56 (31.6%) participants. Human immunodeficiency virus-related retinopathy was seen in 25 (44.6%) participants, followed by papilledema and

TABLE 2: Distribution of visual acuity measurements of participants.

Visual acuity	OD		OS	
	<i>n</i>	%	<i>n</i>	%
6/3–6/18	121	68.4	124	70.1
6/24–6/36	10	5.7	14	8.0
6/48–6/90	5	2.8	9	6.0
Counting fingers	6	3.4	8	4.5
Hand movement	8	4.5	8	4.5
Light perception	7	4.0	3	1.7
No light perception	20	11.3	11	6.2

OD, right eye; OS, left eye.

TABLE 3: Distribution of CD4+ cell count range and number of lesions.

Range (cells/ μ L)	Frequency	Percentage
0–100	20	11.3
101–200	23	13.0
201–300	22	12.4
301–400	30	16.9
401–500	21	11.9
501–600	21	11.9
> 600	4	5.6

cytomegalovirus (CMV) retinitis at 19.6%. The incidence of posterior segment ocular manifestations was higher than the anterior segment manifestations.

Table 7 lists 30 neuro-ophthalmologic lesions found in the study participants. Papilloedema was the most common finding followed by optic atrophy. Third cranial nerve palsies were seen in three participants. However, no significant association was found between cranial nerve palsies and CD4+ cell count of participants, $p > 0.05$.

Table 8 shows the association between ocular lesions and level of CD4+ cell counts. There were 49 participants who had CD4+ cell counts below 100 cells/ μ L, 51 had CD4+ cell count between 100 and 200 whilst 28 had CD4+ cell counts above 200 cells/ μ L. The results of this study showed that 128 (72.3%) of the participants had various ocular manifestations of HIV and AIDS. The mean CD4+ cell count was higher for those having anterior segment lesions (453.8 cells/ μ L \pm 4 cells/ μ L) than those having posterior segment lesions (187.5 cells/ μ L \pm 1 cells/ μ L).

Ocular manifestations of HIV and AIDS were present in 128 participants (72.3%, 95% CI: 65.4% – 81.2%). Anterior segment

TABLE 4: Clinical characteristics of human immunodeficiency virus and acquired immunodeficiency syndrome participants.

Variables	Frequency	Percentage
Visual acuity each eye		
Normal	124	71.8
Impaired	53	29.9
Blind	31	17.5
Colour vision		
Normal	124	70.1
Abnormal	53	29.9
Pupillary reflexes		
React normal	112	12.4
React abnormal	42	63.3
Does not react	22	23.7
Ocular motility		
Smooth	129	72.9
Abnormal	48	27.1
Anterior segment		
Normal	133	75.1
Abnormal	44	24.9
Posterior segment		
Normal	91	51.4
Abnormal	86	48.6

TABLE 5: Ophthalmic manifestations in the anterior segment of human immunodeficiency virus and acquired immunodeficiency syndrome participants in this study ($n = 42$).

Anterior lesions	Unilateral	Bilateral	Total frequency	
			<i>n</i>	%
Uveitis	0	9	9	21.4
Dry eye	0	8	8	19.1
Conjunctival growth	5	2	7	16.7
Herpes zoster ophthalmicus	4	3	7	16.7
Molluscum contagiosum	2	4	6	14.3
Subconjunctival haemorrhage	1	2	3	7.8
Vernal conjunctivitis	0	2	2	4.4

TABLE 6: Ophthalmic manifestations in posterior segment of human immunodeficiency virus and acquired immunodeficiency syndrome participants in this study ($n = 56$).

Posterior	Unilateral	Bilateral	Total	
			<i>n</i>	%
HIV-related retinopathy	0	25	25	44.6
Retinal microvasculopathy	2	10	12	21.4
CMV retinitis	0	11	11	19.6
Retinal vein occlusion	2	6	8	14.3

HIV, human immunodeficiency virus; CMV, cytomegalovirus.

TABLE 7: Neuro-ophthalmologic lesions of human immunodeficiency virus and acquired immunodeficiency syndrome participants in this study ($n = 30$).

Lesion	Unilateral	Bilateral	Total	
			<i>n</i>	%
Papilloedema	0	16	16	53.3
Optic atrophy	6	5	11	19.6
Third cranial nerve palsy	2	1	3	10.0

TABLE 8: Association between ocular lesion and CD4+ cell count.

Ocular lesion	CD4+ cell count			Total	
	< 100	100–200	> 200	<i>n</i>	%
Anterior segment					
Uveitis	2	4	3	9	21.4
Dry eye	3	5	0	8	19.1
Conjunctival growth	6	1	0	7	16.7
Herpes zoster ophthalmicus	3	4	0	7	16.7
Molluscum contagiosum	1	4	1	6	14.3
Subconjunctival haemorrhage	0	2	1	3	7.1
Vernal conjunctivitis	0	0	2	2	4.7
Total	15	20	7	42	23.7
Posterior segment					
HIV-related retinopathy	9	6	10	25	44.6
Retinal microvasculopathy	4	6	2	12	21.4
CMV retinitis	5	4	2	11	19.6
Retinal vein occlusion	4	3	1	8	14.3
Total	22	19	15	56	31.6
Neuro-ophthalmology					
Papilloedema	8	4	4	16	53.3
Optic atrophy	4	5	2	11	19.6
Third cranial nerve palsy	0	3	0	3	10.0
Total	12	12	6	30	16.9
Overall total	49	51	28	128	72.3

HIV, human immunodeficiency virus; CMV, cytomegalovirus; CD4+, cluster of differentiation 4+.

manifestations were present in 42 participants (23.7%, 95% CI: 15.6% – 31.2%). The most common ocular lesions were uveitis, dry eye, conjunctival growth and herpes zoster ophthalmicus. The posterior segment manifestations of the HIV and AIDS were present in 56 participants (31.6%, 95% CI: 21.7% – 36.4%). Thirty (16.9%) participants had neuro-ophthalmologic manifestations that included papilloedema, optic atrophy and third cranial nerve palsies.

Applying the chi-square test, there was no significant difference between the anterior segment ocular lesions and the low CD4+ cell count, $p > 0.05$. Out of 56 posterior segment lesions, 22 participants had CD4+ cell count below 100 and 19

between 100 cells/ μ L and 200 cells/ μ L. There was a significant difference between posterior segment lesions and the level of CD4+ cell count, $p < 0.05$. No significant difference was observed between neuro-ophthalmologic lesions and the level of the CD4+ cell count, $p < 0.05$.

Discussion

Human immunodeficiency virus and acquired immunodeficiency syndrome causes a wide spectrum of diseases, and ocular manifestations are amongst the most common clinical features manifesting in HIV and AIDS individuals. These manifestations are varied, can affect almost all the structures of the eye, and can occur throughout the illness, with an increasing HIV virulence and a progressive loss of CD4+ cell numbers. Various studies have shown that the prevalence of the ocular manifestations in HIV/AIDS individuals can range from 50% to 80%.^{3,4,5,6,7,8,9,10,11,12,13,14,15,16,17} These ocular manifestations can be the presenting sign of a systemic infection of an otherwise asymptomatic individual. The lifetime risk of having at least one abnormal ocular lesion amongst HIV and AIDS individuals ranges from 52% to 100%.^{15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30}

The results of this study showed that 72.3% of HIV and AIDS participants seen at Steve Biko Academic Hospital had ocular lesions or disorders. In this study, 89 (50.3%) belonged to the economically productive age group of 31–50 years. This needs to be emphasised as the morbidity of these individuals has a considerable impact on the economy of their families. The prevalence found in this study is higher than the studies done elsewhere in Africa. Assefa et al.¹² found a prevalence of 60% in a study done in Ethiopia. Martin-Odoom et al.¹⁴ found a prevalence of 48% of ocular complications in HIV patients on antiretroviral therapy in Ghana.

The study showed that 42 (23.7%) had anterior segment manifestations of HIV/AIDS. The most frequent disorders were anterior uveitis, dry eye, conjunctival growth, herpes zoster ophthalmicus and molluscum contagiosum. The anterior uveitis (21.4%) was the most common anterior segment finding. Gogri et al.¹⁹ and Sahoo et al.⁸ found anterior uveitis in 21.5% and 16.1% of participants in their recent works of ocular lesions in HIV and AIDS patients. The anterior uveitis could have been caused by the low immune status of participants, which resulted in opportunistic infections invading the body and causing inflammatory reactions.^{17,18,21} The more viral antigen in the eye could lead to IRU. Immune recovery uveitis is believed to be a result of a partially restored immune system after the initiation of HAART, which mounted an exuberant inflammatory response called immune reconstitution syndrome (IRS).²²¹

Dry eyes were found in eight (19.1%) of the study participants. Dry eye or keratoconjunctivitis sicca in HIV and AIDS participants may result from an autoimmune pathogenesis of disorders of tear production, which may infiltrate and damage the lacrimal gland acini and ducts.¹⁶ The dry eye diseases

were commonly seen with blepharitis. Dry eye in HIV and AIDS patients may be related to the possibility of an auto-immune-like pathogenesis of abnormal tear production, which is associated with lymphocytic infiltration, and eventual destruction of the lacrimal gland acini and ducts. Extensive molluscum contagiosum lesions were also found (14.3%). The possible cause of these lesions is unknown but could result from disorders or dysfunction of the T-lymphocyte-mediated immune response.^{10,11,12,13,14} Sharma et al.¹⁸ in their study found that the anterior segment manifestations of HIV and AIDS were present in 13.3% of their study participants.

The percentage of posterior segment manifestations of this study was 31.6% (56 participants). The most common was HIV-related retinopathy which was seen in 25 participants (44.6%). Of the 25 participants, 19 had cotton wool spots and haemorrhages. This finding correlates with the study of Kempen et al.²¹ who found 45% of HIV-related retinopathy in their study. Retinal macrovasculopathy was seen in this study at 21.4%. It manifested as cotton wool spots, intraretinal haemorrhages and microaneurysms around posterior pole. This suggests that in patients without diabetes and hypertension, the presence of cotton wool spots in an otherwise healthy individual with normal fundus could be suggestive of HIV infection. Generally, individuals with retinal microvasculopathy are asymptomatic. Retinal vein occlusion was seen in eight participants (14.3%), however, it had been rarely documented in previous studies.

Before the introduction of HAART, CMV retinitis affected 30% – 40% of HIV-infected individuals, with visual loss because of involvement of the posterior retina and retinal detachments.^{10,21} In the era of HAART, there has been an estimated 80% decrease in the incidence of CMV retinitis. In this study, the prevalence of CMV retinitis was lower. All the participants in the study were on HAART treatment, which had reduced the risk of opportunistic infection.

This study also found that participants with CD4+ cell count below 200 cells/ μ L were more likely to have ocular manifestation than those whose CD4+ count was greater than 200 cells/ μ L. This finding is consistent with the general facts of immunosuppression where a CD4+ count less than 200 is a predictor of ocular disorders in HIV and AIDS patients.^{19,20,21,22,23,24,25,26,27,28,29,30} Participants who had a low duration on HAART showed higher occurrence of ocular disorders compared to those with more than five years. This could be as a result of the longer use of ART drugs increasing the CD4+ cell counts, boosting the immune system and reducing the occurrence of opportunistic infections.^{21,23}

Neuro-ophthalmic manifestations such as papilloedema, optic neuritis and optic atrophy are some known disorders to occur in HIV and AIDS patients.^{19,20,21,22,23,24,25,26,27,28,29,30} In this study, 30 (16.9%) of the participant had neuro-ophthalmic lesions. The findings of this study were higher than those reported by Sudharshan et al. (8.9%), Biswas et al.²² (9.3%), Assefa et al.¹² (9.6%) and Gogri et al.¹⁹ (10%).

Conclusion

In this study, the prevalence of ocular complications in HIV and AIDS participants on antiretroviral drugs was high. Most ocular complications were seen in participants with less than 200 cells/ μ L, low visual acuities and less than 5 years of ART. Clinicians should be aware of the possible clinical presentation of ocular signs of HIV and AIDS. It is recommended that all HIV and AIDS patients with CD4+ cell counts below 200 cells/ μ L and low duration on ART be subjected to screening for visual loss and routine ocular examination. Furthermore, the findings of this study recommend that the eye examination be integrated in ART clinics to ensure early identification and treatment of ocular complications.

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Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

Both authors contributed equally to this work. P.S.M. collected data, S.D.M. analysed the data and both were involved in the writing of the manuscript.

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Data availability

Data sharing is not applicable to this article.

Disclaimer

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