CLINICALLY MANIFEST OCULAR LESIONS AMONG HIV INFECTED PATIENTS AT KAMENGE UNIVERSITY HOSPITAL, BURUNDI

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A dissertation presented in partial fulfilment of the requirements for the Degree of Masters of Medicine in Ophthalmology, Faculty of Medicine, Department of Ophthalmology, University of Nairobi

DECLARATION

I hereby declare that this is my original work and it has never been published or presented for a degree in any other university.

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DEDICATION

To my loving and caring life **ANNICK NTUNZWENAYO** for her patience, encouragement and sacrifice of good moments

To our beloved sons **MICHAEL** and **RAPHAEL** the ever inquisitive and source of great joy

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LIST OF ABBREVIATIONS AND ACRONYMS

3 TC	Lamivudine
ABC	Abacavir
AIDS	Acquired Immune Deficiency Syndrome
ARV	Anti-Retroviral drugs
ATZ / r	Atazanavir/ritonavir
AZT	Zidovudine
CD 4	Cluster of Differentiation
CMVR	CytoMegaloVirusRetinitis
CNLS	Conseil National de Lutte contre le SIDA
ddI	Didanosine
DNA	Deoxyribonucleic Acid
EFV	Efavirenz
FTC	Emtricitabine
HAART	High Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
HZO	Herpes ZosterOphthalmicus
INRT	Inhibiteur Nucléosidique de la Réverse Transcriptase
IOP	Intraocular Pressure
IP	Inhibiteur de la Protéase
KS	Kaposi's Sarcoma
LPV / r	Lopinavir /ritonavir
MS access	Microsoft Access
MSPLS	Ministère de la Santé Publique et de la Lutte contre le SIDA
NVP	Névirapine
PMLE	Progressive Multifocal Leuco Encephalopathy
RTI	Respiratory Tract Infection
SCC	Squamous Cell Carcinoma
SPSS	Statistical Package for Social Sciences
ТВ	Tuberculosis
TBUT	Tear Break Up Time
TDF	TénofovirDisoproxilFumarate
UNAIDS	Joint United Nations Program on HIV/AIDS
UNICEF	United Nations Children's Fund

USA	United States of America
VZV	Varicela Zoster Virus
WHO	World Health Organization
NASCOP	National AIDS and STI Control Program
РМТСТ	Prevention Mother to Child Transmission
PVD	Posterior Vitreous Detachment
RD	Retinal Detachment
SD	Standard Deviation

ABSTRACT

Background

Over 33 million people live with HIV/AIDS worldwide and around 22 million are located in Sub-Saharan Africa, where access to medical treatment and care is poor.

The disease is associated with a wide variety of ocular complications and blindness. The number of HIV infected individuals is increasing due to better access to treatment therefore eye diseases and complications will increase too.

Objective

This study determined the patterns of ocular lesions in patients with HIV and their correlation with CD4 cells count.

Methods

This was a cross- sectional study carried out among the HIV infected patients aged 18 years and older attending the HIV clinic at Kamenge University Hospital. Patients were recruited during counseling sessions. Demographic data was recorded and ophthalmic examination done using slit lamp and indirect ophthalmoscope. The information was collected using the questionnaire and was later analyzed using STATA and presented using proportions. Univariate logistic regression was used to test for the association.

Results

A total of 392 study participants were interviewed. 349 (89.03%) were on HAART and 43 (10.97%) were not. Ocular manifestations were found in 30.61%. The commonest ocular manifestations found were: dry eye syndrome 25.77%, microvasculopathy, CMVR and papilledema 0.51% each. Others are Allergic conjunctivitis 3.32%, cataract 1.79% and Glaucoma suspect 0.77%. There was a positive association with ocular manifestations among patients with CD4 count < 350.

Conclusion

In this study the prevalence of ocular manifestations was high compared to the previous study which could be explained by the effect of HAART as it has showed to prolong the life expectancy and hence increased the risk of getting ocular manifestations.

There was a positive association with ocular manifestations and lower CD4 count.

1.0 INTRODUCTION

1.1 Epidemiology of HIV and AIDS

Thirty years after AIDS was first reported, HIV continues to spread and exact enormous price to communities in their bid for health, social and economic development. Over 33 million people live with HIV/AIDS worldwide with about two-thirds of these living in Sub-Saharan Africa¹. Although 2010 estimates suggest that the annual number of people newly infected with HIV has declined by 20% from the global epidemic peak in 1998; an estimated 2.7 million people acquired the virus in 2010 alone². Sub-Saharan Africa continues to bear a disproportionate share of the global HIV burden. In mid-2010, about 68% of all people living with HIV resided in sub-Saharan Africa, a region with only 12% of the global population. The 1.9 million people who became newly infected with HIV in 2010 in sub-Saharan Africa represented 70% of all the people who acquired HIV infection globally. However, the number of people newly infected in this region is decreasing. About 16% fewer people acquired HIV infection in2010 than in 2001 when an estimated 2.2 million people were newly infected².

Burundi has a population of 8,038,618 with 50.8% being women and 49.2% men. The first HIV case in Burundi was reported in 1983. The HIV prevalence in Burundi is on the decrease, with the national prevalence reducing from 4% in 2002 to 2.97% in 2008(2.91% female and 2.81% male). Within the same years, the HIV prevalence reduced from 9.5% to 4.59% in towns and from 10.4% to 4.41% in cities respectively^{3,4}. One of the most seriously affected cities in Burundi is Bujumbura, with an estimated prevalence of 4.59%. According to the Secretariat *Executif Permanent/Conseil National de Lutte contre le SIDA au Burundi* in December 2012, a total 29,121 patients on were put on HAART and 24,793 reported by SIDA INFO. Almost one thirtieth are on second line (849 / 23944). The total number of HIV patients follow up in Burundi was 45 474 among them 16855 men and 28619 women.

In Burundi, monotherapy (one molecule) was started in 1997, Bitherapy (combination of two molecules) in the year 2000 and tritherapy (combination of three or more molecules) in 2004. The number of patients on HAART has increased steadily in Burundi, from 600 persons in 2002, to 1,210 persons in 2003, to 8,234 persons in 2006, to 11,000 persons in 2007, to 18,129 persons in 2009 and 29,121 persons by the end of 2012. The numbers of

treatment sites have also increased from only three sites in 2003, 38 sites in 2006, 50 sites in 2007, 84 sites in 2009 and 135 sites by the close of 2012^4 .

WHO clinical stage	CD4 count no available	CD4 count available
1 and 2	NO TREATMENT	START Treatment IF CD ₄ count LESS than 350 cells per mm ³
3 and 4	Treatment	START Treatment Independent to CD4

Table 1.1: Criteria to Start HAART in Burundi

Table 1.2: Guidelines of HIV Treatment in Burundi

1 st line	Second line		
	INRT	IP	
AZT + 3TC/FTC + NVP/ EFV	ABC + TDF or ABC + DDI	ATZ/r or LPV/r	
TDF + FTC/3TC + NVP / EFV	ABC + AZT or ABC + DDI		

1.2 Ophthalmic Manifestations in HIV Patients

Ocular complications in HIV patients were first described by Holland and al. in 1982⁵. The frequency of ocular manifestations in asymptomatic HIV patients is estimated between 0 and 2%.

As immune competency decreases, ophthalmic complications in HIV infection increase in severity⁶. Some studies have shown that about 70% of all patients infected with HIV will develop ocular lesion after certain time of their illness and every part of the eyeball can be involved^{7 – 9}. A study conducted in the United States in 2012 showed that ocular findings in HIV infected patients was 50% and found Herpes zoster ophthalmicus (HZO) is the commonest in anterior segment, whereas HIV retinopathy was more frequently seen in posterior segment¹⁰. In India, some studies have almost the same incidence results where as others differ according to the methods used, study population and the sample size. Jabs

et al. in 1995, found it at 50%.¹¹Gharai S et al. in 2008 found $45\%^{12}$ and Nateshan C. R found 31.5 % in 2011.¹³

1.2.1 Adnexal Manifestations

A number of studies have shown that ocular complications occur as a result of HIV disease and they can lead to impairment of vision. Adnexal parts include eyelids, conjunctiva and lacrimal drainage system. Ocular adnexal complications are seen in about 25% of patients¹⁴.

Dugel PU, Tchach A.B concluded that the most common ocular neoplasm in HIV infected patients was Kaposi's sarcoma. The other tumors found were Lymphomas and squamous cells carcinoma. Kaposi's sarcoma and Squamous cells carcinoma develop in the conjunctiva and ocular adnexa whereas Lymphoma develop into the orbit and intraocularly^{15.} Copeland and al found four commonest ocular manifestations in patients infected by HIV such as Herpes Zoster Ophthalmicus, molluscum contagiosum, Kaposi's sarcoma and conjunctival microangiopathy in the adnexal region^{16.} Jeng and al.found that in African populations, anterior segment and adnexal ocular manifestations in HIV infected patients such as squamous cells carcinoma is seen to be predominant among ophthalmic problem^{17.}

Sonia K, in her Rwandan study found ocular manifestations in 23%, adnexal lesions in 1.9%, anterior segment manifestations in 18.6% whereas in posterior segment found 2.3% of lesions. There was no case of CMV retinitis⁻ Most common finding in adnexal was herpes zoster ophthalmicus (HZO) in 1.5%, in anterior segment, dry eye syndrome at 16.6% whereas in posterior segment was papilloedema, papillitis and optic atrophy for each $0.4\%^{18}$.

1.2.2 Anterior Segment Manifestations

The anterior segment is one of the regions to be affected during the course of HIV/AIDS illness. In Africa, combine with adnexal, it is the most part of the eye to be involved in patients with HIV infection especially with Squamous cells carcinoma^{19.} Common complications include dry eye, conjunctival microvasculopathy, keratitis and iridocyclitis. Depending on the population of the study and probably others factors, one of these

complications can be more common than others. Mehta and Gilada however, reported that ocular tuberculosis was a common finding in their study. Retinal hemorrhages, cotton-wool spots, HZO, CMV retinitis, and disc edema were other non-tubercular AIDS-related lesions. Chisi *et al.* in 2006 evaluated 409 patients infected by HIV and estimated at 7.8% the prevalence of conjunctival squamous cell carcinoma. 103 of them had suggested lesions whereas 32 shown histology report of squamous cell carcinoma²⁰. Verma et al. Studies 172 patients and find that all presented asymptomatic uveitis over 4 years period; 12 with symptomatic uveitis and they conclude that uveitis is not very symptomatic in HIV patients²¹

1.2.3 Posterior Segment Manifestations

Structures involving posterior segment in HIV patients include Retina, Choroid and optic nerve head.

It represents the most common presentation in ocular manifestations in HIV patients. More than 50% of all HIV patients develop disorders involving at least one of the above structures^{22-26.} Floaters, flashing light, visual field defects and reduced vision are usually the typical symptoms.

The most common complications in these structures are: retinal vasculopathy (noninfectious), opportunistic infections, and neuro ophthalmologic abnormalities. Jyotirmay Biswas and al. reported that HIV patients showed 45.7% of ocular lesions and the most common being cytomegalovirus retinitis 21.4%, whereas others less common were cotton wool spots 12.8%, chorioretinitis 5.7%, endogenous endophthalmitis8.5% anterior uveitis 4.2% and molluscum contagiosum 1.4% ²⁷. Cochereau et al. evaluated patients with HIV and find, 10.3% microangipathy, 3.2% retinal perivasculitis, 1.2% HZO, 1.2% viral retinitis and 0.64% oparescence of vitreous^{28.}

2.0 STUDY JUSTIFICATION

UNAIDS estimates that currently 34million people are HIV infected worldwide. Around 22.4million of them live in Sub-Saharan Africa, where access to medical treatment and care is poor. Ocular manifestations of HIV infection are common. Eye disease occurs in 50-75% of HIV infected individuals at some point during the course of their illness, which can lead to visual impairment and blindness if untreated. Visually impaired persons

as well as their families face social and economic challenges that affect their lives. The specific eye conditions associated with HIV are related to the state of the patient's immune system with more serious problems occurring in advanced HIV disease. Ocular diseases like KS and TB occur earlier with CD4 above 350cells/mm³, while Toxoplasmosis occurs at CD4 count below 200cells/mm³ and CMV at CD4 count less than 100cells/mm³. Screening for eye conditions should therefore be part of the initial evaluation of patients diagnosed with HIV.

The number of HIV infected individuals is increasing due to better access to treatment therefore eye diseases and complications will increase too. Early diagnosis and treatment of eye diseases is therefore of major importance.

Several studies on ocular manifestations in HIV patients have been done in many countries and have shown that ophthalmic complications occur in about 50 to 75% of HIV patients during the course of the disease. HIV/AIDS is the 4th cause of mortality in Burundi, after Malaria, Upper respiratory infections and diarrheic disease⁴⁻⁵. A number of studies on Systemic manifestations have been done in Burundi. However, there is a lack of information in ocular manifestations in HIV patients in Burundi, with only one study done in 1998 in patients hospitalized in Kamenge University Hospital. This (in 1998), was before the widespread roll out of highly active antiretroviral therapy (HAART) in Burundi, thus the need to undertake a new study on ocular findings in HIV patients in Burundi, in the context of the currently rolled out HAART programs. In addition, the management of HIV patients has been improved through changing care and treatment regimens, enhanced early start up to HAART and better adherence, thus increased survival among HIV patients. This study will establish the pattern of ocular manifestations among HIV patients in Burundi, information necessary for improved HIV programming in Burundi.

3.0 RESEARCH QUESTION AND OBJECTIVES

What are the ocular lesions among HIV patients in Burundi?

3.1 Broad objective

To determine the pattern of clinically manifest ocular lesions in patients with HIV in Kamenge University Hospital.

3.2 Specific objectives

- To determine the prevalence of ocular lesions among HIV patients at Kamenge University Hospital
- 2) To establish the association between ocular lesions and the severity of immune suppression.

4.0 METHODS

4.1 Study Design

A cross sectional descriptive study conducted in HIV infected patients who attending HIV clinic at Kamenge University Hospital.

4.2 Study Area

The Study area was the Kamenge University Hospital, a Public University Hospital in Burundi hosting a Medical School. It is located in west of the capital, Bujumbura. Kamenge Teaching Hospital is one of the most well equipped hospitals in Burundi and works as a referral hospital for the other health facilities. During this study, the hospital had a clinic for patients with HIV infection where approximately 20 patients were seen daily. This figure excludes patients who came directly to collect their medicine at the pharmacy. Including all these, clinic received daily about 50 patients. The total numbers of HIV infected patients on follow up at the Hospital were 4011, of which 2203 were on HAART²⁹.

4.3 Target Population

All the patients attending HIV clinic at Kamenge University Hospital were eligible to participate in the study.

4.4 Sampling

4.4.1 Sample Size Determination ³⁰⁻³¹

Sample size $n = t^2 p (1-p)/E^2$

Where:

n is the minimum sample size required (approximation)t standard normal deviation which set conventionally at 1.96 and

correspond to 95% confidence interval
p estimation prevalence of ocular manifestations in HIV/AIDS patients (50%)
E maximum random sampling error acceptable which is 0.05 degree of precision at 95% level of confidence (at expected prevalence of 50%)

Calculated sample size n = 385.

4.4.2 Sampling Procedures

Sampling techniques described in this section were used to identify participants to be interviewed (study population). The facility appointments register room was working as the central point for enumerating participants for purposes of inclusion in the study. All HIV clients coming to Kamenge University Hospital have to first register at the appointment service point before receiving further care within the clinic. First information was given every morning during counseling sessions whereas further was for those who accepted to participate in the study.

4.5 Eligibility Criteria:

4.5.1 Inclusion Criteria:

Known HIV positive patients with results of CD4 cell count

4.5.2 Exclusion criteria:

Age under 18 years

4.6 Data Collection

Data were collected using a structured questionnaire (Appendix I) in English and in Kirundi. The first section of the questionnaire captured demographics data and was administered through an interview with the participant. The second section captured the findings ophthalmic examination.

Materials: Questionnaire; Pens, pencil, colours, note books; Torches, penlight, batteries, bulbs; Snellen's chart, literate and illiterate; Slit lamp, spirit, gauze; Fluorescein

strips; Indirect ophthalmoscope; Loupe 20 D and 90 D; Mydriatics: tropicamide and cocktail; Tetracaine eye drops/Amethocaine; Flash disc for data transport.

Ocular examination: Snellen's Visual Acuity chart was used to take Visual Acuity. Inspection and slit lamp examination for ocular adnexal were done. Tear Break Up Time method was used and less than 10 seconds was considered to indicate dry eye. Dilatation of the pupil was done using Tropicamide. Indirect ophthalmoscope and or slit lamp with 20D or 90D where it was necessary helped to examine the fundus.

4.7 Management and Analysis

The data collected, at the end of each day were cleaned and handed over to the investigator for review to enter into MS excel. The filled questionnaires were kept under lock and key.

Data later were exported in STATA base for analysis. Univariate logistic regression was used to test for the association. The findings are presented using tables, frequencies, pies, figures and histograms.

4.8 Ethical Consideration

Informed Consent: All study participants were taken through the informed consent process (see appendix II) and they willingly agreed to participate.

Ethical approval: The Kenyatta National Hospital/University of Nairobi Ethics & Research Committee as well as the Kamenge University hospital has approved this study.

Beneficence: Study participants were educated on the benefits of ophthalmic screening after undertaking the survey.

5.0 RESULTS

A total of 392 patients were recruited into this study

Characteristic, n =392	Number of patients	Percentage
MARITAL STATUS		
Married	337	85.97
Separated	13	3.32
Single	13	3.32
Widow	29	7.40
PROFESSION		
Business	77	19.64
Public sector	38	9.69
Agriculture	32	8.16
Student	3	0.77
Drivers	6	1.53
Not employed	236	60.20

Table 5.1	:	Demographic	data
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The majority of the respondents were married (85.97%) and were not employed (60.20%)

Age groups	Male patients		Female patients	
	Number	Percentage	Number	Percentage
20-29	0	0	37	9.43
30 - 39	17	4.33	87	22.19
40-49	42	10.71	126	32.14
>50	30	7.65	53	13.52
Total	89	22.70	303	77.30

 Table 5.2: Distribution by Age and Sex

The majority of the respondents were female (77.30%). There was a statistically significant difference in the gender proportion (p-value <0.001)

The majority of the respondents were aged between 40-49 years (42.86%) and the least age –group respondents was between 20-29 years of age (9.44%) The mean age of the respondents was 41.61, SD=9.87, median=42 and range 21 - 71 years

Visual Acuity	Right eye		Left eye		Both eyes	
	Number of	%	Number of	%	Number of	%
	patients		patients		patients	
<u>>6/18</u>	385	98.21	377	95.92	388	98.98
> 6/18 - 6/60	5	1.28	13	3.32	4	1.02
< 6/60 - 3/60	0	-	1	0.26	0	-
< 3/60	2	0.51	1	0.26	0	-

Table 5.3: Distribution of Visual Acuity in Each Eye

Most of our patients did not have visual impairment and none was totally blind.

Variable	Number of	%
	patients	
Duration since diagnosis, n=392		
<1 year	0	0
1-5 years	154	39.29
>5 years	238	60.71
On ARV, n =392		
Yes	349	89.03
No	43	10.97
Types HAART, n=349		
Emtriva+Tenofovir+ Efavirenz	47	13.47
Zidovudine+Lamivudine+Efavirenz	51	14.61
Zidovudine+Lamivudine+Nevirapine	238	68.19
Emtriva+Tenofovir+Nevirapine	12	3.44
Emtriva+Tenofovir+ Kaletra	1	0.29

Majority of the patients had been diagnosed HIV more than 5 years prior this study. None of participant had less than one year of HIV diagnosis.

89.03% of the patients were on HAART and the common type of HAART was

Zidovudine+Lamivudine+Nevirapine (68.19%). Only one patient was on second line.





The mean duration on ARV was 4.30, SD=1.95, median = 4, and range 1 - 10

Table 5.5: Frequency	of Ocular	Complaints
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Ocular complaints	Number of patients	%
Burn	1	0.26
Foreign body sensation	2	0.51
Itchiness	8	2.02
Poor Vision	30	7.65
Pain + photophobia	1	0.26
Tearing	1	0.26
Itchiness + Poor Vision	1	0.26
Itch + Foreign body sensation	1	0.26
None	347	88.52
Total	392	100

Majority (88.52%) of participants did not have ocular complaints.

Opportunistic disease	Number of patients	%
Chronic diarrhea	2	0.51
Meningitis	1	0.26
Tuberculosis	23	5.87
Tuberculosis + Meningitis	1	0.26
None	365	93.11
Total	392	100

Table 5.6: Frequency of Opportunistic Diseases

Of a hundred, 93.11% of patients did not have opportunistic diseases while the most featuring opportunistic disease was tuberculosis (5.87%)

CD4 count,	Lowest		Current	
	Number of %		Number of	%
	patients		patients	
< 50	22	5.61	0	-
50 - 100	18	4.59	1	0.26
101 – 200	70	17.86	10	2.55
201 - 350	159	40.56	59	15.05
>350	123	31.38	322	82.14
Total	392	100	392	100

Table 5.7: Pattern of Lowest and Current CD4 Count

The majority of patients had their current CD4 count cells being at a higher level > 350 (82.14%). 68.62% patients had the lowest CD4 count cells < 350.

	Number of	CD4 Counts			
	patients	<200	200 - 350	351 - 499	>500
Disorders	n=392	n=11	n=59	n=148	n=174
LIDS Blepharitis	1	0	0	0	1 (0.57)
CONJUNCTIVA					
Micro vasculopathy	1	1(1.69)	0	0	0
Allergic conjunctivitis	13	0	3 (5.08)	5 (3.38)	5 (2.87)
Growth	35	0	4 (6.77)	18 (12.17)	13 (7.47)
DRY EYE SYNDROME	66	2 (18 18)	16 (27 12)	20 (10 50)	10
Yes	00	2 (10.10)	10 (27.12)	29 (19.39)	(10.92)
ANTERIOR CHAMBER	1	0	0	0	
Anterior uveitis					1 (0.57)
LENS	7	0	1 (1.69)	3 (2.03)	3 (1 72)
Cataract					5 (1.72)
VITREOUS	1	0	0	0	1 (0 57)
CHOROID					1 (0.57)
Toxoplasma chorioretinitis	1	0	1 (1.69)	0	0
RETINA		1 (0.00)	1 (1 (0))	0	
CMV R	2	1 (9.09)	1 (1.69)	0	0
RD	1	1(9.09)	0	0	0
Macula scar		-()	~	-	0
OPTIC NERVE	3	0	2 (3.39)	0	
Glaucoma suspect	0	0	1 (1.69)	0	1 (0.57)
Papilloedema	2	1 (9.09	0	1 (0.68)	0

Table 5.8: Pattern of Ocular Findings and CD4 Count

Almost all patients (99.74%) did not have adnexal ocular findings The most featuring findings at the anterior segment were dry eye syndrome at 25.77% and conjunctiva growth 8.93%.

In posterior segment Glaucoma suspect was (0.77%), followed by CMVR and Papilledema at 0.51% each.



Figure 2: Ocular findings

The prevalence of ocular findings was 30.61%

Table 5.9: Association Between Current CD4 Count and Ocular Findings

Variable	Ocular finding present	Ocular finding	OR (95% CI)	p-value
		absent		
CD4 count				
<200 (11)	4	7	1.00	
200-350 (59)	23	36	1.12 (0.29 –	0.870
351-499	51	97	4.25)	0.898
(148)	42	132	0.92 (0.26 –	0.369
>500 (174)	120	272	3.29)	
Total			0.56 (0.16- 2.00)	

There is a positive association with ocular findings in patients with CD4 count less than 350. The difference is clinically significant but not statistically significant. (OR: More than 1 for less than 350 CD4 count and less than 1 for more than 350 CD4 count) P value more than 0.05.

6.0 DISCUSSION

Demographic Data

The Mean age in this study was 41.61standard deviation (SD) 9.87, median 42 and range 21 to71. Majority of participants were in age group 40 to 49 (42.86%).Our finding is consistent with the results of national survey which showed a prevalence of HIV patients much higher in age group 15-49 than others ⁵. Other studies find majority of patients in age group between 30 to 40 ^{18,32,33}. This can be explained by the fact that HIV is mainly transmitted sexually and some people also delay to test their serologic status, so most patients HIV positive fall in that age group.

Majority of the patients examined were females (77.30%), male consisted of 22.70% giving a female to male ratio of 3.5: 1. The sex ratio Female/male was high. There was statistically significant difference between the two group (p<0.001) which is consistent to the national survey results showing that, in general population, Female are more affected by HIV than Male.

Also, female are at high risk of acquiring HIV infection and they accept easily their status hence they seek healthcare often than male. Studies done in Ethiopia by Bekele et al and Sonia in Rwanda found similar results.^{34, 18}. Some studies however found a lower female to male ratio. ^{11,12,13,35}

Most of our patients had lowest CD4 count less than 350(68.62%) at the diagnosis whereas the current CD4 count greater than 350 was higher for 82.14% of our participants. The current CD4 showed that majority was not immune suppressed. This is due to the effect of HAART and better follows up: 89.03% of participants were on HAART and the rest were not.

Visual Acuity Status of Our Participants

According to the WHO classification, majority of our patients 98.98% had vision better than 6/18 in both eyes. One patient (0.26%) had left eye blind due to CMVR, 2 patients with right eye blind one due to CMV and another to retinal detachment. No case of bilateral blindness noted in our study. Most of ocular findings affect one eye and because of better vision in another eye, those patients complaint rarely for vision. The prevalence of blindness due to HIV infection may be underestimated in a study like ours as many of those people spend their last days home hence, are not going to visit eye care. To detect ophthalmic manifestations in routine screening and visual acuity should not be taken as an indicator of ophthalmic manifestation in HIV patients.

Prevalence

A prevalence of 30.61% was found in this study. This is comparable to previous studies, which showed a prevalence range of 19 - 60.5%. This variation has been as a result of a number of reasons.

The findings of this study is much lower than Balo et al ³⁶Yared et al³⁷, Ndoye et al³⁸ and Jabs et al ¹¹ respectively at 60.5%, 60%, 52.23% and 50%. This is possibly from the effect of HAART as majority of our participants (89.03%) were on HAART and the use of this treatment has shown a reduction of ocular problems especially intraocular infections and inflammation in patients with HIV³⁹.

In Yared study, the highest prevalence was due to the nature of the study which was conducted in patients admitted to hospital with medical problem and came to eye clinic with ocular complaint, in addition majority of those patients was in stage III and IV WHO classification, which was different to the current study (out patients, with or without ocular complaint). Other studies found less prevalence than the present mostly because of their small sample size. It has been postulated that in Africa, the lower prevalence was possibly because patients died before the opportunistic infections occur².

Other reasons which can explain those variations are: difference in characteristics of study population and difference in sample size.

Adnexal Manifestations

In our study, blepharitis was found in 1(0.26%) patient. This was similar to the study done by Shivayogi K. et al ⁴⁰ who found it in 1 patient (1%). Study done by Bekele in Ethiopia ³⁴ found blepharitis at 3.2%. This difference can be related to the study population which in this study was majority on HAART compare to the late.

Unlike to other studies, no case of HZO and molluscum contagiusum found in our patients. Sonia in Rwanda found 1.5% HZO and 0.4% Molluscum contagiusum, Yassefa in Ethiopia 5.6% HZO, Ndoye et al 8.5% HZO and Nwosu et al with 48% HZO. This can be due to the fact that 89.03% are on HAART and majority of participants have CD4 count more than 350.

It has postulated that reconstitution immune system due to HAART can limit expression of molluscum contagiosum infection. There was also no case of eyelids malignancies which was found in others studies.

Anterior Segment Findings

The most common anterior segment findings were dry eye syndrome with 25.77%. Other studies find it at lower level, Sonia in Rwanda found it at 16.6% and Bekele et al find 11.3%. This difference can be due to their small sample size. The etiology was thought to be related to HIV mediated inflammation and damage of accessory and major lachrymal glands.

Uveitis was found in 1 patient (0.26%). This is comparable to others studies Sonia 1.5% and Indian study 2.5%. Uveitis was possibly due to immune reconstitution syndrome as the patient started HAART one year later.

Other study done by Jyotimay Biswas and al. find anterior uveitis at 4.2%. Verma et al. Studies 172 patients and find that all presented asymptomatic uveitis over 4 years period; 12 with symptomatic uveitis and the conclusion was that uveitis is not very symptomatic in HIV patients^{23.}

In this study, microvasculopathy was found in 2 patients being 0.51%. The etiology of this manifestation is not well known, but it has been believed that there is involvement of increase plasma viscosity and immune complex deposition; direct infection of

conjunctival epithelium by HIV virus could be one of the causes¹⁴. A study done in Ethiopia by Bekele et al. shows a rate of 2.3% which is consistent with our findings. The previous study done in Burundi by Cocheau found 10.3%. This difference was due to the fact that the study population was patients admitted at the hospital, hence possibly were in advanced stage of immune suppression.

Allergic conjunctivitis is reported in some literature as not specifically related to HIV but dermatologists associate it to HIV manifestations^{46.} This study reports it at 3.32%. Thirty five patients (8.93%) in our study had conjunctiva growths. There was no histology done to exclude any malignancy.

Seven cataracts (1.79%) were reported in this study. Sonia found 7%. A study done by Accorinti et al found that HAART therapy had induced occurrence of new lesions related both to metabolic alterations induced by HAART and to immune reconstitution^{41.}

Posterior Segment Manifestations of HIV

Comparatively, this study showed less occurrence of posterior segment as compare to anterior segment findings in HIV patients. The commonest finding was CMVR in 2(0.51%) patients.

Sonia in Rwanda did not found any case of CMVR and this difference is possibly due to her small sample size. The lower level can be attributed to the high number of patients on HAART more than 5 years with CD4 count more than 350. One patient had macular scar following CMVR. Other studies found high number than ours mostly the difference is due to the characteristics of study population (on HAART or not) and sample size. Other studies found CMVR at high level Nateshan 5%, Jyotimay Biswas et al 21.4%. Chorioretinitis was found in one (0.26) patient following toxoplasmosis infection. This is consistent with other study such as Sonia 1 (0.4%), Bekele et al. 1 (0.9%), JABS 1% and Nateshan1.5%. Two cases (0.51%) of papilledema were found in this study which is consistent with Sonia study (0.4%).

Our study found only one (0.26%) patient with Optic neuritis. This finding is comparable to other studies, Nateshan 1.3% and JABS 2%. Others are much higher Biswas J. et al with 7% and Gharai S. et al with 12%. Other findings are, PVD in 1 patient, 1 retinal

detachment following CMVR and 3 patients with glaucoma suspect based on Cup Disc Ratio which was greater than 7.

Association Between Ocular Findings and CD4 Count

In our study, 120 (30.61%) patients had ocular findings. Patients with lower CD4 count were more likely to have ocular findings compared to those with high CD4 count (WHO classification). This is consistent with the study done by Bekele et al who found the association between ocular manifestations with low CD4 count.

7.0 CONCLUSION

In this study, the prevalence of ocular findings was 30.61%. Anterior segment was more affected follow by posterior segment and adnexa. Majority of our study population had CD4 count greater than 200 and also was on HAART which can explain the low prevalence of ocular findings in this study. Some ocular findings are not well known to be related directly to HIV. There was a positive association with ocular findings in patients with lower CD4 count compared to those with high CD4 count.

8.0 RECOMMANDATIONS

HAART treatment with better follow up may be reduced the prevalence of ocular manifestations in HIV patients.

Other studies are needed to elucidate which ocular finding is typical for HIV.

9.0 LIMITATION

The number of patients not on HAART was small for comparison.

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APPENDICES

APPENDIX I: STUDY QUESTIONNARE

SOCIO DEMOGRAPHIC DATA

• Number of partners and they HIV status

OPHTHALMIC EXAMINATION

• Symptoms

Poor vision
Pain
Red eye
Tearing
Photophobia

Others of	nacify			
Oulors s	peeny	 	 	

VA	<u>RE</u>	SC	N	F
		CC	N	F
	<u>LE</u>	SC	N	F
		CC	N	F

Dry eyes RE LE.....

SC: without correction (if patient use or not spectacle)

CC: with own correction (if patient have spectacle)

F: far vision or distant vision

N: near vision

ADNEXAL MANIFESTATIONS

• LIDS

• Orbit

ANTERIOR SEGMENT MANIFESTATIONS

• Conjunctiva

		• •	•••	• •	•••	•••	• •	•••	• •	•••	•••	• •	• •	•	•••	• •	• •	•	• •	• •	••	• •	••	• •	•	
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•	Cornea	l																								
																		_								 _

..... Sclera • Anterior chamber ٠ Iris ٠ Pupil • Lens ٠

POSTERIOR SEGMENT MANIFESTATIONS

• Vitreous
• Choroid
• Retina :
• Optic nerve

KIRUNDI

Ibibazo

•	Nomeroy'icirwa
•	Nomero ya dosiye
•	Imyaka
•	Igitsina
•	Urubatse
•	Akazi
Ibijan	ye n'umugera wa SIDA
•	Igihe umaze kuva bayitoye
•	Niwaba uri ku miti
•	Igihe umaze ku miti
	Ko woba warigeze kuyihagarika
Ko bo	ba bamaze kuguhindurira
•	Ubwoko bw'imiti
•	Igitigiri c'abasoda bake umaze kugira
	Abasoda ufise ubu

Indwaraz'ivyuririzi

.....

.....

.....

-
- Kowoba waragiye mu bitaro kubera umugera
- Iyindi miti uriko urafata
- Igitigiri c'abana n'ibipimo vy'umugera wa sida
- Igitigiri c'abo muhuza ibitsina n'ibipimo vy'umugera wa sida

APPENDIX II: CONSENT FORM

You are invited to participate in a research study on the *clinically manifest ocular lesions and HIV infected patients at Kamenge University hospital, Burundi,* being done by a researcher from the University of Nairobi, Kenya. Findings from this study shall be analyzed and compiled into a thesis for presentation and defense for the degree of Master of Medicine, Ophthalmology of the University of Nairobi. The final report form this study shall also be shared with Burundi health authorities as well as the Kamenge University Hospital and with organizations working on HIV treatment, care and support in Burundi.

Procedures of the Study: If you agree to participate in this study, you will be requested to respond to a questionnaire. We will pose questions for your response. Some of the questions may be sensitive. The questions you will be askew will basically be to draw your demographic information. You are free not to answer any question which you are uncomfortable with. We will then conduct an eye assessment on you. No invasive methods will be used. We will apply some medicine so that the eye can dilate - to be able to see in the back of your eye. This can give you mild irritation and transient blurring of vision for about 4 to 6 hours after application. We will record observations made through this examination by use of a questionnaire. The questionnaire you complete will be analyzed together with others to generate a report.

Benefits associated with participating in this study: There will be no direct monetary benefits to the individual study participants. However, individual participants will be sensitized on basic eye care after participating in the study. Information generated from this study will help improve the ophthalmic care given to patients with HIV/AIDS.

Participants Consent: I have read the foregoing information (or it has been read to me). I have had the opportunity to ask questions about it and any questions I have asked have been answered to my satisfaction. By signing below, I consent to participate in the study described above, with knowledge that I can withdraw from the study at any time.

Participants

Name	
Participants Signature/Thumb Print	Date
Name of Person Consenting	
Signature:	
Date	

Ubutumire

Uratumiwe kuba umwe mubandi bazofasha muri iki cirwa kijanye nokuraba indwara z'amaso zifata umuntu agendana umugera wa SIDA kizobera mubitaro Roi Khaled mu kamenge. Ico cirwa kiriko kigirwa numushakashatsi avuye muri Kaminuza ya Nairobi muri Kenya. Ibizovamwo azovyegeraniriza mu gitabo co guheza amashure yokuvura amaso aho muri Kaminuza ya Nairobi muri Kenya. Icegeranyo kizoshikirizwa abarongoye ibitaro vya Roi Khaled, ubushikiranganji bw'amagara y'abantu n'ukurwanya ikiza ruhonyanganda SIDA hamwe n'amashirahamwe mpuzamakungu afasha uburundi mukurwanya ico kiza.

Ubushake bwo kwinjira muri iki cirwa

Kuja muri iki cirwa nikubushake bwawe. Ushatse kutajamwo, ntankurikizi n'imwe ijanye no gukumirwa muri iri vuriro kandi iyongingo yawe itegerezwa gukurikizwa.

Uzobandanya wivuriza muri iri vuriro.Ushobora nokuvamwo igihe cose ubishakiye kandi ntagihano na kimwe ushobora kuronka

Ivyo wemeye mu kwinjira muri iki cirwa

Kwishura kubibazo birashobora kutakurwa neza. Kugira tukorohereze, ikibazo kitakuguye neza urashobora kureka kucishura. Turiko turagupima amaso, hari umuti tugushira mumaso kugira amaso afunguke dushobore kubona inyuma yayo.

Ivyo bishobora kugutuma wummva hari nkutuntu mumaso kandi no kubona ntubone neza ivyo bitwara hagati y'amasaha ane n'atandatu inyuma yo kuwushira mumaso.

Kugira utekane kuvyerekeye ivyo bijanye no gupimwa, uzotegerezwa gupimwa n'umuganga abizi neza

Icemezo :

Mpejeje gusoma (canke bahejeje kunsomera) ivyo biri hejuru . Naronse akanya ko kubaza ikibazo cose nshatse kandi naronse inyishu ihagije. Gushira umukono kuri uru rwandiko niyemeje kuja muri iki cirwa gisiguye aha hejuru nzineza ko nshobora kuvamwo umwanya uwariwo wose

Izina ryanje
Umukono wanje
Italiki
Izina ry'uwubikurikirana
Umukono w'uwubikurikirana
Italiki

APPENDIX III: WHO CLINICAL CLASSIFICATION OF HIV (2005)

Primary HIV infection:

Asymptomatic Acute retroviral syndrome

Stage I:

Asymptomatic Persistent generalized lymphadenopathy

Stage II:

Moderate unexplained weight loss (<10% of presumed or measured body weight) Recurrent respiratory tract infections (RTIs, sinusitis, bronchitis, otitis media, pharyngitis)

Herpes Zoster, angular cheilitis, recurrent oral ulcerations, popular pruritic eruptions, Seborrhoeic dermatitis, fungal nails infections of fingers.

Stage III:

Conditions where a presumptive diagnosis can be made on the basis of clinical signs or simple investigations

Severe weight loss (>10% of presumed or measured body weight) Unexplained chronic diarrhea for longer than one month Unexplained persistent fever (intermittent or constant for more than one month) Oral candidiasis, Oral hairy leukoplakia Pulmonary tuberculosis (TB) diagnosed in last two year Severe presumed bacterial infections (e.g. pneumonia, empyema, pyomyositis, Bone or joint infection, meningitis, bacteraemia) Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis

Conditions where confirmatory testing is necessary

Unexplained anemia (< 8 g/dl) and or neutropenia (< 500/ mm3 and or Thrombocytopenia (< 50 000/ mm3) for more than one month

Stage IV:

Conditions where a presumptive diagnosis can be made on basis of clinical signs or simple investigations HIV wasting syndrome Pneumocystis pneumonia Recurrent severe or radiological bacterial pneumonia Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration) Oesophageal candidiasis, extrapulmonary TB, Kaposi's sarcoma, Central nervous system toxoplasmosis, HIV encephalopathy

Conditions where confirmatory diagnostic testing is necessary:

Extrapulmonary cryptococcosis including meningitis Disseminated non tuberculous mycobacteria infection Progressive multifocal leukoencephalopathy (PML) Candida of trachea, bronchi or lung, Cryptosporidiosis, isosporiasis Visceral herpes simplex infection Cytomegalovirus (CMV) infection(Retinitis or of an organ other than liver, spleen or lymph nodes) Any disseminated mycosis (e.g. Histoplasmosis, coccidiomycosis; penicilliosis) Recurrent non typhoid salmonella septicaemia Lymphoma (cerebral or B cell Non Hodgkin) Invasive cervical carcinoma Visceral leishmanisis candidacies (esophageal, bronchi, tracheal)



CENTRE HOSPITALO-UNIVERSITAIRE DE KAMENGE

Bujumbura, le

V/Réf.: N/Réf.: 2013 DOHUK, 12857115

> Au Docteur REMEZO Philbert Université de Nairobi Département d'Ophtalmologie Tél. : 79 983 949

Objet : Accès aux données

Docteur,

En réponse à votre correspondance du 26/12/2013, je voudrais vous informer que je marque mon accord à votre demande d'accès aux données en rapport avec votre travail de fin d'études intitulé : « Clinically manifest ocular lesions and HIV infected patients at Kamenge University hospital, BURUNDI ».

Je tiens à vous informer également qu'il vous est demandé de déposer un exemplaire de votre travail à la Direction du CHUK.

Veuillez agréer, Docteur, l'assurance de ma considération distinguée.



COPIE POUR INFORMATION A :

- Monsieur le Directeur-Adjoint Chargé des Soins
- Madame le Directeur-Adjoint Chargé des Finances
- Madame le Médecin Coordinateur du Service CPAMP
- Madame le Chef de Service de Nursing

B.P.2210 Bujumbura, Tél: (257)-22236062; (257) 22236060; Fax; (257) 22232267; Mail: chukamenge@Yahoo.fr





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February 2014

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Link:www.uonbi.ac.ke/activities/KNH00NAT/O

Ref: KNH-ERC/A/30

Dr. Remezo Philbert Dept.of Ophthalmology School of Medicine <u>University of Nairobi</u>

Dear Dr. Remezo

RESEARCH PROPOSAL: CLINICALLY MANIFEST OCULAR LESONS AND HIV INFECTED PATIENTS AT KAMENGE UNIVERSITY HOSPITAL, BURUNDI (P509/10/2013)

This is to inform you that the KNH/UoN-Ethics & Research Committee (KNH/UoN-ERC) has reviewed and <u>approved</u> your above proposal. The approval periods are 12th February 2014 to 11th February 2015.

This approval is subject to compliance with the following requirements:

- a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
- b) All changes (amendments, devi
- c) ations, violations etc) are submitted for review and approval by KNH/UoN ERC before implementation.
- d) Death and life threatening problems and severe adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH/UoN ERC within 72 hours of notification.
- e) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH/UoN ERC within 72 hours.
- f) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (<u>Attach a comprehensive progress report to support the renewal</u>).
- g) Clearance for export of biological specimens must be obtained from KNH/UoN-Ethics & Research Committee for each batch of shipment.
- h) Submission of an <u>executive summary</u> report within 90 days upon completion of the study This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

For more details consult the KNH/UoN ERC website www.uonbi.ac.ke/activities/KNHUoN.

Protect to Discover