OCULAR FINDINGS IN HIV POSITIVE PATIENTS IN KABGAYI HOSPITAL, RWANDA

A DISSERTATION SUBMITTED AS PART FULFILLMENT FOR THE DEGREE OF MASTER OF MEDICINE IN OPHTHALMOLOGY, UNIVERSITY OF NAIROBI.
DECLARATION

This dissertation is my original work and has not been presented for a degree in any other university.

Signed: ..........................  Date: ..........................

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This dissertation has been submitted with our approval as University supervisors

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DEDICATION

To my husband Charles Ndoli for his encouragement and for sacrificing his career to allow me to carry out this postgraduate study.

To my children Lionel and Lynn Ndoli for the sacrifice of precious moments.

To my mother Mukamwiza Josephine for all her support and encouragement.
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I would like to acknowledge my statistician Alex and all those who in various ways assisted in the preparation of this book.
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<tr>
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<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC</td>
<td>Abacavir</td>
</tr>
<tr>
<td>AIDS</td>
<td>Acquired immunodeficiency syndrome</td>
</tr>
<tr>
<td>ARV</td>
<td>Antiretroviral therapy</td>
</tr>
<tr>
<td>AZT</td>
<td>Zidovudine</td>
</tr>
<tr>
<td>CD4</td>
<td>Cluster of differentiation</td>
</tr>
<tr>
<td>CMV</td>
<td>Cytomegalovirus</td>
</tr>
<tr>
<td>CSW</td>
<td>Commercial sex workers</td>
</tr>
<tr>
<td>DDI</td>
<td>Didanosine</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribonucleic Acid</td>
</tr>
<tr>
<td>D4T</td>
<td>Stavudine</td>
</tr>
<tr>
<td>EFV</td>
<td>Efavirenz</td>
</tr>
<tr>
<td>ELISA</td>
<td>Enzyme linked essay</td>
</tr>
<tr>
<td>FBC</td>
<td>Full blood count</td>
</tr>
<tr>
<td>HAART</td>
<td>Highly Active anti-Retroviral Therapy</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>HZO</td>
<td>Herpes zoster Ophthalmicus</td>
</tr>
<tr>
<td>IDV/r</td>
<td>Indinavir/ritonavir</td>
</tr>
<tr>
<td>LFTs</td>
<td>Liver function tests</td>
</tr>
<tr>
<td>LOP/r</td>
<td>Lopinavir/ritonavir</td>
</tr>
<tr>
<td>NVP</td>
<td>Nevirapine</td>
</tr>
<tr>
<td>PHILA</td>
<td>People living with HIV/AIDS</td>
</tr>
<tr>
<td>RDHS</td>
<td>Rwanda Demographic and Health Survey</td>
</tr>
<tr>
<td>RNA</td>
<td>Ribonucleic Acid</td>
</tr>
</tbody>
</table>
ABSTRACT

Background
The eye is one of the commonly affected organs by HIV/AIDS. However, data on HIV/AIDS related ocular lesions among HIV positive patients is not available in Rwanda.

Objectives
The objective was to determine the prevalence and pattern of ocular findings in patients with HIV/AIDS on HAART and those not on HAART.

Method
This was a cross sectional descriptive study conducted on HIV positive patients attending the HIV clinic in Kabgayi Hospital, in which those aged 16 years and above were evaluated for ocular lesions. Their demographic data, history of CD4 cell count and use of HAART was taken.

Visual acuity was assessed with the use of a snellen’s chart. Both anterior and posterior segments were examined using a Haag Streit 900 slit lamp, direct and indirect ophthalmoscope. Data was recorded in a questionnaire and analyzed using SPSS version 12.0. A significance level of 95 % was used.

Result
A total number of 252 patients (169 females and 83 males) with a mean age of 40.4 years were examined. The current CD4 cell count was ranging from 72 to 2601 cells/μL with a mean of 501.3. The prevalence of HIV related ocular lesions was 23%. The most common ocular lesions were Herpes Zoster Ophthalmicus (1.5%) in the adnexa, dry eye syndrome (16.6%) in the anterior segment and both papilloedema and papillitis (0.4%) in the posterior segment.

There was no statistically significant association between the ocular manifestations and CD4 cell count, duration of being on HAART or the WHO HIV staging in this study.

Conclusion
The commonest ocular disease was dry eye syndrome. Majority of the patients were receiving HAART and had high CD4 cell count. This may explain the relatively low prevalence of HIV related eye disease.
1. INTRODUCTION AND LITERATURE REVIEW

Human Immunodeficiency Virus (HIV) infection is the first major pandemic of the 20th century. In 2007, almost 33 million people were known to be infected with this virus. There were 2.7 million new HIV infections, and 2 million HIV related deaths. Sub-Saharan Africa remains the region most heavily affected by the HIV, accounting for 67% of all people living with HIV and 75% of AIDS deaths in 2007.

In Rwanda, the Rwanda Demographic and Health survey (RDHS) in 2005 found that the national prevalence of HIV in the Rwanda population was 3%, with 7.3% in urban areas and 2.2% in rural areas. In that survey, HIV prevalence among women of age 15-49 (3.6%) was higher than that of men in the same age group (2.3%). The infection ratio between women and men was therefore equal to 1.6, which means that 160 women were infected for every 100 men. HIV prevalence increased with age. However, the highest prevalence among women was in the 35-39 age group (6.9%), whereas among men it was in the 40-44 age group (7.1%).

According to a report published by Treatment and Research AIDS Center (TRAC) in 2008 almost 56,653 adults living with HIV were receiving Highly Active anti-Retroviral therapy (HAART) first line, and 743 second line.

HIV affects the immune system, which can either directly inflict damage on organs of the body by itself and/or make the organs vulnerable to many opportunistic pathogens and diseases. There are wide arrays of diseases affecting the eyes of people living with HIV/AIDS (PLHA) that can occur at any time along the natural course of the disease.

Individuals infected with the virus pass through several predictor stages, with progressive decrease in circulating CD4 T cells. During the advanced stage, these patients develop various opportunistic infections or malignancies or both. CD4 T-lymphocyte counts have been used to predict the onset of certain ocular infections in patients who are HIV positive. CD4 T-cell counts of less than 500 cells/μL are associated with Kaposi sarcoma, lymphoma, and tuberculosis while CD4 T-cells count of less than 250 cells/μL are associated with pneumocytosis and toxoplasmosis and CD4 T cell count less than 100 cells/μL is associated
with retinal or conjunctival microvasculopathy, CMV retinitis, and Varicella-Zoster virus (VZV) retinitis, mycobacterium avium complex infection, cryptococcosis, microsporidias, HIV encephalopathy and progressive multifocal leukoencephalopathy.

1.1 NATURAL HISTORY AND CLASSIFICATION OF HIV-AIDS. 6

Infection by the Human Immunodeficiency Virus (HIV) may result in a spectrum of diseases ranging from asymptomatic seropositivity to the development of profound immunodeficiency.

Features of the HIV cycle may explain aspects of the pathogenesis of HIV-induced disease. The tropism of HIV for CD4 cell of both lymphocytic and monocytic origin is of considerable importance in immune deficiency. HIV is a member of the lentivirus subfamily of retrovirus. Two distinct groups of viruses are pathogenic to humans: HIV 1 and HIV 2. Both are transmitted sexually and known to cause immunodeficiency disease.

HIV 1 can be sub-classified into 3 groups:

a. The “Major” group M
b. The “Outlier” group O
c. The “New” group N

More than 90% of HIV 1 infections belong to group M. Within group M, there are at least 9 genetically distinct subtypes of HIV 1. There are subtypes A, B, C, D, F, G, H, J and K.

HIV 1 is a double stranded RNA virus, and its basic structure is typical for other retroviruses. The integrated form of HIV known as provirus is approximately 9.8 kilo bases in length.

The gene of HIV is located in the central region of the proviral DNA and encodes at least 9 proteins, divided into 3 classes:

a. The major structural proteins: Gag, Pol and Env
b. The regular proteins : Tat, Rev
c. The accessory proteins : Vpu, Vpr, Vif and Nef

The mature HIV virion is 100 to 150 nm icosahedrons, with an inner dense core of 2 single strands of RNA and associated proteins and enzymes including nucleocapsid p7, P6, P2, p1 and reverse transcriptase.
The central nucleic acid is surrounded by a capsid (P24) and matrix (P17) proteins. Forming the outermost surface is the viral envelope, which consists of a lipid bilayer including trimers of viral glycoprotein gp 120 and gp 41 and host cell proteins including major histocompatibility complex class I and class II antigens.

1.1.1 HUMAN IMMUNODEFICIENCY VIRUS (HIV-1) LIFE CYCLE.

The viral life cycle can be separated into viral entry, reverse transcription, integration, viral mRNA and protein expression, and viral assembly and budding.

Viral entry begins with the formation of a high affinity bond between the viral glycoprotein gp 120 and the CD4 receptor on the target cell, present on T lymphocytes and macrophages. CD4 binding results in a conformational change in the gp 120 molecule, exposing its chemokines receptor binding site: HIV is known to use two such chemokine receptors; CCR5 or CXCR4.

Following binding of the viral envelope protein to the CD4 molecule and chemokine receptors, fusion of the viral envelope with the host cell occurs, and viral RNA is released into the target cell.

Reverse transcriptase, a viral enzyme, then catalyzes the reverse transcription of viral RNA into double stranded DNA. The double stranded DNA translocate, to the nucleus the “pre-integration complex” and is inserted into the host genome by another viral enzyme called integrase.

After transcription and translocation, viral proteins undergo post-translational modification and are directed to the host plasmin membrane, where assembly of virions occurs.

Viral budding occurs at the cell plasma membrane when the viral core agues. The envelope containing gp 120 and gp 41 along with the host cell protein.

Virally encoded protease catalyses the cleavage of Gag Pol precursor (P55) to yield the structural proteins that form the mature virion. HIV is essentially an infection of the immune system. While CD4 T lymphocytes are the primary targets of HIV, others cells such as the macrophages and dendrite cells can also harbor or transmit infection.
1.2 OPTHALMIC MANIFESTATIONS OF HIV

The AIDS epidemic has had a profound impact on ophthalmology since the ophthalmic manifestations of AIDS were first described in 1982. Since the earliest days of the AIDS epidemic, the ophthalmologist has played an important role in the care of people with HIV infection. This is reflected in the fact that thousands of research articles and reviews have been published on HIV related ophthalmic disorders during the past 25 years.

More than anything else, the introduction of highly active antiretroviral therapy (HAART) in the late 1990s changed the face of the AIDS epidemic. HAART resulted in a marked reduction in mortality and decrease incidence of associated opportunistic infections and neoplasms including those of the eye.

HAART has indeed decreased the incidence of some ophthalmic problems, such as CMV retinitis, but it seems not to have affected others, and it has brought with it new challenges such as immune recovery uveitis.

Copeland et al, in their review article on ocular manifestations of HIV, noted that the common adnexal manifestations include herpes zoster ophthalmicus (HZO), Kaposi sarcoma, molluscum contagiosum and conjunctival microvasculopathy. This review showed that more than 50% of HIV positive patients manifest anterior segment complications, including keratoconjunctivitis sicca, keratitis (viral, fungal), iridocyclitis and neuro ophthalmic manifestations including papilloedema, ocular motility disorders, cranial nerve palsy and visual fields defects. Orbital manifestations include orbital lymphoma and orbital cellulitis.

1.2.1 ADNEXAL AND ANTERIOR SEGMENT MANIFESTATIONS

The ocular adnexa include the eyelids, conjunctiva and lacrimal drainage system. The complications mostly affecting these structures are herpes zoster ophthalmicus, Kaposi’s sarcoma, molluscum contagiosum and conjunctival microvasculopathy.

Herpes Zoster ophthalmicus affects 5 to 15% of HIV positive patients; Kaposi’s sarcoma affect up to 25%, molluscum contagiosum of the eyelids occurs in up to 5%, conjunctival microvasculopathy occurs in 70% to 80% of HIV patients.
The most common anterior segment manifestations include keratoconjunctivitis sicca, keratitis and iridocyclitis. Keratoconjunctivitis sicca occurs in 10-20% of patients while infectious keratitis occurs in less than 5%.

In Cameroon, Mvogo et al found that the principal lesions of the anterior segment were herpetic keratitis (10.5%) and HZO (12.3%). Ndoye et al also studied ocular manifestations of HIV in Senegal and found a prevalence of 52.23%. In Ndoye’s study, patients with CD4 counts greater than 400 cells/μL had conjunctivitis (one case was Kaposi’s sarcoma-related conjunctivitis), HZO and dry eye syndrome. The only ocular lesion in patients with CD4 counts between 200 and 400 cells/μL was HZO.

1.2.2 POSTERIOR SEGMENT MANIFESTATIONS
The ocular posterior segment manifestations of AIDS may be divided into 4 categories: retinal vasculopathy, malignancies, neuro-ophthalmic abnormalities and opportunistic infections.

Retinal vasculopathy is the most common ocular manifestations of AIDS (40-60%), and the prevalence is inversely proportional to CD4 count. In Tamara’s study, malignancies such as non-Hodgkin’s lymphoma increased from 4.4% to 6.3% since the advent of HAART. Neuro-ophthalmic abnormalities were uncommon occurring in only 6%.

Ndoye et al in their study on ocular manifestations in Senegal noted that retinal pathology was by far the most frequently observed (63%). Patients with CD4 count between zero and 200 cells/μL had macular oedema, cotton-wool like nodules, retinal vasculitis and microangiopathy, while those with higher CD4 count had none of these ocular lesions.

In a study done by El Mansouri in Casablanca in 400 HIV patients, 127 had infection of the posterior segment and 44 had opportunistic retinal infection mainly CMV (18 cases). Cochereau et al, studied the ocular manifestations of HIV/AIDS in 154 HIV-I seropositive patients in Burundi and found that 99% of patients were seropositive for CMV and VZV. Eighty-six patients in that study had CD4 count more than 100 cells /μL. Ocular involvement comprised 16 cases of microangiopathy, 6 of opalescence of the anterior chamber, 5 of retinal perivasculitis, 2 of HZO, 2 of viral retinitis and 1 of opalescence of the vitreous.
2. RATIONALE OF THE STUDY

The burden of HIV disease is high in Rwanda. Studies elsewhere have shown that ophthalmic complications occur in up to 50% -75% of patients during the course of the disease. The management of patients with HIV/AIDS has improved in Rwanda with the creation of TRAC (Treatment and Research Aids Center) and effective antiretroviral therapy. Improved prophylaxis and treatment of opportunistic infections has led to an increase in the survival of individuals affected with AIDS. We therefore hypothesize that this has led to an increase in the prevalence of ocular manifestations of HIV/AIDS in Rwanda.

Also, HAART and good follow up may have changed the presentation of ocular manifestations in patients with HIV/AIDS.

Systemic manifestations of HIV have been extensively studied in Rwanda, but not ocular manifestations, and there is no systematic ophthalmic screening of HIV/AIDS patients.
3. OBJECTIVES

3.1 BROAD OBJECTIVE

1. To determine the prevalence and pattern of ocular findings in patients with HIV/AIDS.

3.2 SPECIFIC OBJECTIVE

1. To describe the ocular findings in patients with HIV/AIDS on follow up without antiretroviral therapy.

2. To describe the ocular findings in patients with HIV/AIDS on antiretroviral therapy.

3. To determine if there is an association between ocular findings and CD4 count, WHO clinical stage of HIV and duration of the disease.
4. METHODOLOGY

4.1 STUDY DESIGN
This was a cross-sectional descriptive study in which HIV infected patient attending HIV clinic were evaluated for ophthalmic disorders.

4.2 STUDY LOCATION AND DURATION
The study period was 8 weeks (November to December) in Kabgayi District Hospital, Rwanda.

4.3 STUDY POPULATION
The study population was comprised of HIV patients attending the HIV clinic in Kabgayi District Hospital.

4.4 SAMPLE SIZE

\[ N = \frac{t^2 pq}{E^2} \]

\( N \) = the minimum sample size required (approximation)
\( t \) = standard normal deviation set at 1.96 which correspond to 95% confidence interval.
\( p \) = Prevalence estimate of ocular findings in HIV patients (50%).
\( E \) = the maximum random sampling error acceptable. \( E = 0.05 \) degrees of precision at 95% level of confidence (at expected prevalence of 50%)
\( n = (1.96)^2 \times 0.5 \times 0.3 / (0.05)^2 = 230 \)
4.5 **CASE DEFINITION**

All HIV positive patients attending the HIV clinic in Kabgayi District Hospital.

The algorithm that was used to determine the positivity of the patient consisted of testing the specimens with Determine for screening and Sd Bioline for confirmation and Uni-Gold for tie-breaker.

4.6 **INCLUSION CRITERIA**

1. Patient diagnosed to have HIV.
2. CD$_4$ cell count data available.
3. Consented to participate in the study.
4. Age above 16 years.

4.7 **EXCLUSION CRITERIA**

1. Patient who refused to give consent
2. Patient without CD$_4$ cell count
3. Persons under 16 years.

4.8 **MATERIALS**

- A formulated questionnaire
- Pens and note books
- Torches/spotlights with batteries and spare bulbs
- Snellen’s chart, literate and illiterate
- Slit lamp, spirit, dry gauze
- Direct and indirect ophthalmoscope, retinoscope
- Loupes +20D, +90 D
- Mydriatics: Tropicamide, mydriatic cocktail.
4.9 PROCEDURE

The patients were recruited daily for the HIV outpatient clinic. The investigator was introduced to the patients by the counselor during the counseling sessions which took place every morning before the medical review of the patients. Patients were explained to the aim of the study. Those who consented to participate in the study were explained to the study procedure, and interviewed using a structured questionnaire before commencement of the ocular examination.

4.9.1 IN THE EYE CLINIC

Visual acuity was assessed using Snellen’s chart. Ocular adnexa and anterior segment were assessed using a slit-lamp (Haag Streit). Examination for dry eye was done using tear break up time (TBUT) method and and break up time less than 10 seconds was considered as dry eye. Dilated fundus examination was carried out using a direct, an indirect ophthalmoscope and +90D loupe where appropriate.

Findings were recorded in a detailed questionnaire together with the patient’s demographic data and details of ocular complaints. The patients past medical history and treatment were retrieved from their medical records and recorded in the questionnaire. The protocol for HAART therapy and monitoring regimen is as in appendix V and VI.

4.9.2 DATA ANALYSIS

The data was collected using a structured questionnaire in English, administered by the principal investigator, and translated to Kinyarwanda. The data collected was cleaned, stored and analyzed using SPSS version 12.0.1. Comparisons were done using appropriate statistical tests.

The proportions of various ocular findings were described, giving standard deviation and confidence intervals. A 95% level of significance was used.

The findings were presented in histograms, pie chart, tables and frequency tables and frequency tables.
4.10 ETHICAL CONSIDERATIONS

Informed written consent was obtained from all the patients who were willing to be enrolled in this study. Ethical approval was obtained from the Rwanda National Ethics Committee (ERC).
5. RESULTS

Two hundred and fifty two participants were recruited into the study.

Table 1: Demographic factors (n = 252)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Frequency, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>83 (32.9)</td>
</tr>
<tr>
<td>Female</td>
<td>169 (67.1)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>252 (100.0)</td>
</tr>
<tr>
<td><strong>Age (Years)</strong></td>
<td></td>
</tr>
<tr>
<td>Mean (sd)</td>
<td>40.5 (34-47)</td>
</tr>
<tr>
<td>Median (IQR)Range</td>
<td>17 - 79</td>
</tr>
<tr>
<td><strong>Age group (years)</strong></td>
<td></td>
</tr>
<tr>
<td>&lt; 20</td>
<td>9 (3.6)</td>
</tr>
<tr>
<td>20 to 29</td>
<td>28 (11.1)</td>
</tr>
<tr>
<td>30 to 39</td>
<td>77 (30.6)</td>
</tr>
<tr>
<td>40 to 49</td>
<td>85 (33.7)</td>
</tr>
<tr>
<td>50 +</td>
<td>53 (21.0)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>252 (100.0)</td>
</tr>
</tbody>
</table>

The mean age of the study participants was 40.4 years with a standard deviation of 10.7. The median was 40.5 years and the interquantile range was 17 - 79 years.

M: F ratio was 1:2.
Most of the participants were diagnosed between 2004 and 2006 (109).

Majority of the patients (39.3%) were in stage I at diagnosis.
Table 2: Profile of CD₄ cell count (n=252)

<table>
<thead>
<tr>
<th>Statistics</th>
<th>At Diagnosis (cells/ml)</th>
<th>Lowest (cells/ml)</th>
<th>Current (cells/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>314.3</td>
<td>254.3</td>
<td>501.3</td>
</tr>
<tr>
<td>Median</td>
<td>249.0</td>
<td>225.0</td>
<td>465.0</td>
</tr>
<tr>
<td>Range</td>
<td>1 - 1.233</td>
<td>1 - 976</td>
<td>72 - 2601</td>
</tr>
<tr>
<td>IQR</td>
<td>153.3 - 430.8</td>
<td>143.5 - 322.5</td>
<td>317.0 - 623.0</td>
</tr>
</tbody>
</table>

Most patients were not immunosuppressed.

Figure 3: Participants HAART status (n=252)

Seventy eight percent of participants were on HAART.
Most of the participants were on the first line regimen: AZT/3TC/NVP (41.8%).

Majority of the patients were on HAART for one year, 45 for 2 years and another 45 for more than 4 years.
Table 4: Frequency of systemic features from medical record

<table>
<thead>
<tr>
<th>Systemic features</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herpes Zoster</td>
<td>24 (9.5)</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>19 (7.5)</td>
</tr>
<tr>
<td>Oral Thrush</td>
<td>19 (7.5)</td>
</tr>
<tr>
<td>Cryptococcal meningitis</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Weight Loss &gt; 10%</td>
<td>27 (10.7)</td>
</tr>
<tr>
<td>Weight Loss &lt; 10%</td>
<td>28 (11.1)</td>
</tr>
<tr>
<td>Chronic Diarrhea</td>
<td>21 (8.3)</td>
</tr>
<tr>
<td>Severe Infection (septicemia)</td>
<td>3 (1.1)</td>
</tr>
<tr>
<td>Minor respiratory tract infection</td>
<td>18 (7.1)</td>
</tr>
<tr>
<td>Minor mucocutaneous manifestations</td>
<td>27 (10.7)</td>
</tr>
<tr>
<td>Unexplained Fever &gt;1 month</td>
<td>8 (3.1)</td>
</tr>
<tr>
<td>No history of infections</td>
<td>55 (21.8)</td>
</tr>
</tbody>
</table>

Minor mucocutaneous manifestations and weight loss < 10% were the commonest systemic findings in the study participants as recorded in the medical record.
168 patients had ocular complaints.

The main complaint was itchiness with 29.4%
Most patients did not have visual impairment. None were blind.

Table 5: Ocular adnexal manifestations

<table>
<thead>
<tr>
<th>Findings</th>
<th>Mean Age</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herpes zoster ophthalmicus</td>
<td>46</td>
<td>4 (1.5)</td>
</tr>
<tr>
<td>Molluscum contagiosum</td>
<td>18</td>
<td>1(0.4)</td>
</tr>
</tbody>
</table>

The predominant finding in the ocular adnexa was HZO (healed scar).
Table 6: Anterior segment findings

<table>
<thead>
<tr>
<th>Condition</th>
<th>Mean age (years)</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry eye syndrome</td>
<td>41</td>
<td>42 (16.6)</td>
</tr>
<tr>
<td>Uveitis</td>
<td>28.8</td>
<td>4 (1.5)</td>
</tr>
<tr>
<td>Conjunctival microvasculopathy</td>
<td>52</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Cataract</td>
<td>48.7</td>
<td>18 (7.1)</td>
</tr>
<tr>
<td>Allergic Conjunctivitis.</td>
<td>38.5</td>
<td>33 (13.1)</td>
</tr>
<tr>
<td>Remnant of pupillary membrane</td>
<td>36</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Pterygium</td>
<td>34</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Corneal foreign body</td>
<td>59</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Blepharitis</td>
<td>50</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Chalazion</td>
<td>29</td>
<td>1 (0.4)</td>
</tr>
</tbody>
</table>

Dry eye syndrome (DES) was the commonest anterior segment finding.
### Table 7: Posterior segment findings (n=35 eyes)

<table>
<thead>
<tr>
<th>Feature</th>
<th>Mean age</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Optic Nerve Head</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Optic Atrophy</td>
<td>67</td>
<td>1(0.4)</td>
</tr>
<tr>
<td>Papilloedema</td>
<td>29</td>
<td>1(0.4)</td>
</tr>
<tr>
<td>Papillitis</td>
<td>50</td>
<td>1(0.4)</td>
</tr>
<tr>
<td>Glaucoma suspect</td>
<td>44.2</td>
<td>11(4.3)</td>
</tr>
<tr>
<td><strong>Retina</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chorioretinitis</td>
<td>36</td>
<td>1(0.4)</td>
</tr>
<tr>
<td>Drusen</td>
<td>32</td>
<td>3(1.1)</td>
</tr>
<tr>
<td><strong>Macula</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scar</td>
<td>52</td>
<td>1(0.4)</td>
</tr>
</tbody>
</table>

### Table 8: Other ocular findings

<table>
<thead>
<tr>
<th>Finding</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refractive errors</td>
<td>16(6.3)</td>
</tr>
<tr>
<td>Phthisical eye</td>
<td>2(0.7)</td>
</tr>
<tr>
<td>Nystagmus</td>
<td>1(0.4)</td>
</tr>
<tr>
<td>Old vitreous hemorrhage</td>
<td>1(0.4)</td>
</tr>
</tbody>
</table>
6. DISCUSSION

STUDY POPULATION

The male: female ratio of this study population (1:2 shown in table 1) is similar to the result of the national survey done in Rwanda in 2005. In terms of gender, females are more (52%) than males (48%) in the general population in Rwanda. The higher prevalence may be attributed to the fact that females are more at risk of acquiring the HIV infection and also accept their status more easily than males hence they seek health care more often.

The most affected group was between 30 and 40 years. This finding is consistent with the result of the national survey which showed a peak HIV infection between 30 and 40 years.

Agre et al studied 397 participants in Cote d’ Ivoire and found a similar pattern. Ndoye et al, who studied 67 participants reported the same pattern.

The current mean CD4 count (501.4 cells/µL) was higher than the mean CD4 count at diagnosis showing the effect of HAART. Most of the participants were effectively not immunosuppressed.

PREVALENCE

The prevalence of HIV related eye disease was 23%. This is much lower than Ndoye et al in Senegal (52.23%) and Balo et al in Togo (60.5%). This low prevalence is due to the fact that 78% of the population in this study was on HAART. Rodriguez et al in Brazil found that with the use of HAART, there is reduction in the frequency of ocular problem in HIV patient, especially intraocular infections and inflammations.

ADNEXAL FINDINGS

The prevalence of herpes zoster ophthalmicus (1.5%) noted in this study is lower than that noted by Ndoye et al who found that HZO affects about 8.5% of patients who are infected with HIV. Different studies have reported wide prevalence range of HZO. Nwosu et al in Nigeria studied 100 HIV positive patients and found HZO prevalence of 48%. In Ethiopia, Yassefa et al studied 120 patients and reported a prevalence of 5.6% in Gondar University Hospital.
HZO was not associated with significant ocular complications and visual disability. This is probably because most (78%) of these patients were on HAART and only 15 patients had CD4 count below 200 cells/µL.

Molluscum contagiosum of the lids was found in one (0.4 %) participant. This is in contrast to an earlier study by Husak et al which showed a high prevalence of 8.6%.\textsuperscript{23}

The reason for low prevalence of this infection in this study could be due to the fact that majority of the patients were on HAART and their CD4 cell count was above 200 cells /µL.

A case report by Albin and Rao found the patient’s reconstituted immune system from HAART can limit molluscum contagiosum infection. Such limited expression of molluscum contagiosum could be from a competent T cell response as noted in individuals with normal immune function or those with reconstituted immune response from HAART.\textsuperscript{24}

**ANTERIOR SEGMENT FINDINGS**

The commonest anterior segment findings were keratoconjunctivitis sicca(16.6%) and uveitis (1.5%) (Table 6).

The highest prevalence of dry eye syndrome was reported by DeCarlo et al in the USA.\textsuperscript{25} They noted a prevalence of 38.8% % in HIV infected male patients. The cause was thought to be related to HIV-mediated inflammation and destruction of primary and secondary lacrimal glands.

Uveitis was seen in 1.5 % of our patients. This was mainly anterior uveitis. Uveitis was observed more in patients on HAART as compared to patients not on HAART. This is possibly due to immune reconstitution syndrome or tuberculosis because 2 patients with uveitis had suffered from tuberculosis earlier.

Mean age of patients with cataract was 48.7 years. On examination of these patients, no signs of inflammation were found. Agre et al also found rather young HIV-infected participants with cataract.\textsuperscript{19} A study done by Accorinty et al, showed that HAART therapy had induced occurrence of new lesions related both to the metabolic alterations induced by HAART and to immune reconstitution.\textsuperscript{26} Even though allergic conjunctivitis is not specific to HIV /AIDS as reported in some literature, the dermatologists associate allergic conjunctivitis with HIV manifestations.\textsuperscript{27}

No case of conjunctival and eyelids malignancies was found unlike in other studies.\textsuperscript{30}
POSTERIOR SEGMENT FINDINGS

Posterior segment findings were papilloedema, papillitis, optic atrophy and chorioretinitis in 0.4% on each. A study done by Accorinty et al showed that HAART induced a dramatic decrease in the incidence of HIV-related microangiopathy and opportunistic retinal infection. The current study documented one case of papilloedema following cryptococcus meningitis.

No case of CMV retinitis was reported in this study, unlike Golberg who reported a prevalence of 20 to 40% in the pre-HAART era. This difference could be because of better immunocompetence following increase in the availability and use of HAART in recent years and because this study included many patients on treatment.

There was one patient with chorioretinal scar from presumed toxoplasmosis. This could have been acquired in childhood or resolved with rise in CD4 cell count when patient was started on HAART. In Ethiopia, Abeba et al noted chorioretinal scars in 3.1% of HIV/AIDS patients.

Other studies found retinal microangiopathy to be the commonest posterior segment ocular finding in HIV positive patients, but none was found in this study.

Some limitations of the study include the inability to address the cause–effect relationship because the sample size was small, and lack of an HIV-uninfected participant for comparison.
7. CONCLUSION

- The prevalence of ocular findings in this study population was 23%.
- There were more anterior segment HIV related eye diseases (18.6%), than adnexal manifestations (1.9%) and posterior segment (2.3%).
- The most common anterior segment finding was dry eye syndrome (16.6%).
- The commonest adnexal finding was Herpes Zoster Ophthalmicus (1.5%).
- Posterior segment findings were papilloedema, papillitis and optic atrophy (0.4% for each).
- The high level of CD4 count in this cohort may explain the low prevalence of HIV related ocular findings.
8. RECOMMENDATIONS

1. Early institution of HAART may be associated with low ocular disease in HIV infected persons.

2. Ophthalmologists should be involved in the follow up of HIV positive patients.
9. REFERENCES


3. Annual report Treatment and Research AIDS Center (TRAC), Rwanda. 2008.


10. Copeland, R., Philipots, B. Ocular manifestations of HIV. *e medicine,* 2006; available at www.emedecine.com... accessed on 20/05/2010


10. APPENDICES

10.1 APPENDIX I: QUESTIONNAIRE

SECTION A: Socio demographic Data

1) File Number ................................................
2) Date of birth ................................................
3) Age of the patient ..........................................
4) Gender   a) male    b) female
5) Weight   (kg)..............................................
6) Nationality............................................... 
7) Have you ever attended school   a) Yes □    b) No □
8) If yes, how many years of school have you completed? ....... years

SECTION B: ocular Complaints

SECTION C: Medical History

9) Date of initial HIV diagnosis (month/yr) ...........................................
10) Type of HIV (1or 2).............................................................................
11) CD4 count (at diagnosis) ........................................Date ......................... (Month/yr)....
12) CD4 Count (lowest) ..................................................Date .........................(month/yr)....
13) Current WHO stage 1.......2.......3.........4.................
14) Occurrence of opportunistic infections

   a) Kaposi Sarcoma
       Yes □  No □

   b) HZ0
       Yes □  No □
c) Tuberculosis

d) Oral trush

e) Squamous cell carcinoma

f) Meningitis

g) Toxoplasmosis

15) If the patient currently taking, or has the patient ever taken, any of the following antiretroviral medications

Yes

No

16) If yes fill the box next to each medication:

Zidovudine (azt) .......

Lamivudine (3tc).....

Stavudine (d4t).....

Tenovofir (tnf)........

Didanosine (ddi).....

Abacavir (abc)......

Nevirapine (nvp).....

Efavirenz (efv).....

Nelfinavir (nvp).....

Others.....................

17) Date of initial ARV (mm/yy).............................................................

18) Duration of ARV..................................................................................

19) Others chronic illness (DM,HTN).......................................................
SECTION D: OCULAR EXAMINATION

23) Presenting vision:

RE: F SC
    CC

LE: F SC
    CC

SECTION E: ADNEXA MANIFESTATIONS

Herpes zoster ophthalmicus
Squamous cell carcinoma
Kaposi Sarcoma
Molluscum
Conjunctival microvasculopathy
Conjunctival growth

IMPRESSION ..................
### SECTION F; ANTERIOR SEGMENTS FINDINGS

<table>
<thead>
<tr>
<th>Condition</th>
<th>RE TBU</th>
<th>LE TBU</th>
<th>Yes</th>
<th>No</th>
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</thead>
<tbody>
<tr>
<td>Dry eyes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Keratitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presumed bacterial</td>
<td>□</td>
<td>□</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presumed fungal</td>
<td>□</td>
<td>□</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presumed HZO</td>
<td>□</td>
<td>□</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presumed HSV</td>
<td>□</td>
<td>□</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uveitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KPS</td>
<td>□</td>
<td>□</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cellules</td>
<td>□</td>
<td>□</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flare</td>
<td>□</td>
<td>□</td>
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<tr>
<td>Hypopion</td>
<td>□</td>
<td>□</td>
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</table>

**IMPRESSION**

### SECTION G; POSTERIOR SEGMENT MANIFESTATIONS

<table>
<thead>
<tr>
<th>Condition</th>
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<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retinal microvasculopathy</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Cytomegalovirus retinitis</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Perivasculitis</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Chorioretinitis</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Endophthalmitis</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Vitreous haemorrhage</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Macular oedema</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

### SECTION H: NEURO OPHTHALMOLOGIC MANIFESTATION:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optic atrophy</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Papilloedema</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Papillitis</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>
**SECTION I: ORBITAL MANIFESTATION:**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orbital cellulitis</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Orbital tumor</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Others (specify)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**SECTION J: SYSTEMIC MANIFESTATIONS**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary tuberculosis</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Oro pharyngeal candidasis</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>HIV enteropathy</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Cryptococcal meningitis</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Extrapulmonary tuberculosis</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Persistent generalized lymphadenopathy</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Recurrent Zoster dermatitis</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Kaposi sarcoma</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

**IMPRESSION**

**SECTION K: GENERAL IMPRESSION**
10.2 APPENDIX II: CONSENT

I am kindly requesting you to read and carefully fill in the questionnaire. Participation in this study is purely voluntary and the interview can be stopped at any time without giving reason. All information obtained will be treated with confidentiality at anytime.

Thank you.

I ____________________________ of __________________ do hereby consent to participate in this study. The details of the study have been explained to me and I understand well.

Date: ___________________________ signed: _________________________

I confirm that I have explained the nature of my study and I guarantee the confidentiality of the information provided by the above mentioned participant.
Primary HIV infection

Asymptomatic
Acute retroviral syndrome.

Stage 1:

Asymptomatic
Persistent generalized lymphadenopathy.

Stage 2:

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,
Papular pruritic eruptions, seborrhoeic dermatitis, fungal nail infections of fingers.

Stage 3:

**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 diarrhoea for longer than one month
Unexplained persistent fever (intermittent or constant for longer than one month)
Oral candidiasis, oral hairy leukoplakia
Pulmonary tuberculosis (TB) diagnosed in last two years
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 diagnostic testing is necessary**

Unexplained anaemia (< 8 g/dl), and or neutropenia (<500/mm3) and or thrombocytopenia (<50 000/mm3) for more than one month
Stage 4:

**Conditions where a presumptive diagnosis can be made on the 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 lungs

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-typhoidal salmonella septicaemia

Lymphoma (cerebral or B cell non-Hodgkin)

Invasive cervical carcinoma

Visceral leishmaniasis Candidacies (oesophageal, bronchi, tracheal)
10.4 APPENDIX IV: ELIGIBILITY CRITERIA AND HAART THERAPY

Criteria:

HIV positive and one of the 2 criteria:

- Stage 4
- Stage 1, 2, 3 and CD4 less than 350/mm³

Protocol for HAART therapy:

First line:
AZT + 3TC + NVP: avoid AZT if Hb < 9 g/dl
D4T + 3TC + NVP: Recommended in patient with anaemia
TDF + 3TC + NVP or TDF + FTC + NVP: Recommended in patient with anaemia and presenting sides effect of D4T.

Second line

<table>
<thead>
<tr>
<th>First line</th>
<th>Reverse transcriptase Inhibitors</th>
<th>Protease inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZT or D4T/3TC/NVP or EFV</td>
<td>DDI/ABC or TDF/3TC (±AZT)</td>
<td>Lop/r or IDV/r</td>
</tr>
<tr>
<td>TDF/3TC/NVP or EFV</td>
<td>DDI/ABC or DDI/3TC (±AZT)</td>
<td></td>
</tr>
<tr>
<td>ABC/3TC/NVP or EFV</td>
<td>DDI/3TC (±AZT) or TDF/3TC (±AZT)</td>
<td></td>
</tr>
<tr>
<td>AZT or D4T/3TC/TDF or ABC</td>
<td>EFV or NVP (±DDI)</td>
<td></td>
</tr>
</tbody>
</table>
### 10.5 APPENDIX V: MONITORING OF PATIENTS ON HAART

<table>
<thead>
<tr>
<th>Date</th>
<th>Clinic</th>
<th>Laboratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-HAART</td>
<td></td>
<td>CD₄,FBC,U/E/Cs, Chest Xray</td>
</tr>
<tr>
<td>Day 15</td>
<td>Adherence</td>
<td></td>
</tr>
<tr>
<td>Month 1</td>
<td>Adherence</td>
<td>FBC if AZT,LFTs</td>
</tr>
<tr>
<td>Month 2</td>
<td>Adherence</td>
<td></td>
</tr>
<tr>
<td>Month 3</td>
<td>Adherence</td>
<td>FBC if AZT,LFTs if NVP</td>
</tr>
<tr>
<td>Month 4</td>
<td>Adherence</td>
<td></td>
</tr>
<tr>
<td>Month 5</td>
<td>Adherence</td>
<td></td>
</tr>
<tr>
<td>Month 6</td>
<td>Adherence</td>
<td>CD₄,FBC,LFTs</td>
</tr>
<tr>
<td>After 6 month</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monthly during one year</td>
<td>Adherence</td>
<td>CD₄ every 6 month</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LFTs : month 12, and stopped after 12 month</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Viral load every 12 month</td>
</tr>
</tbody>
</table>