"ONE YEAR CROSS-SECTIONAL STUDY OF OCULAR MANIFESTATIONS IN HIV-POSITIVE/AIDS PATIENTS EVALUATED AT KLE'S DR. PRABHAKAR KORE HOSPITAL AND MRC, BELGAUM"

REGISTRATION NO: BK0108003

Dissertation

Submitted to the

KLE University, Belgaum, Karnataka

In partial fulfillment

of the requirements for the Degree of

MASTER OF SURGERY

In

OPHTHALMOLOGY

DEPARTMENT OF OPHTHALMOLOGY,

JAWAHARLAL NEHRU MEDICAL COLLEGE,

BELGAUM, KARNATAKA.

MAY 2011

KLE University, Belgaum, Karnataka

Endorsement By The Hod, Principal / Head Of The Institution

This is to certify that the dissertation entitled **"ONE YEAR CROSS-SECTIONAL STUDY OF OCULAR MANIFESTATIONS IN HIV-POSITIVE/AIDS PATIENTS EVALUATED AT KLE'S DR. PRABHAKAR KORE HOSPITAL AND MRC, BELGAUM."** is a bonafide research work done by **REG. NO: BK0108003.**

Dr. R. K. DANDUR MS,DOMS
Professor and Head,
Department of Ophthalmology
J. N. Medical College,
Nehru Nagar,
Belgaum-590 010

Date :
Place : **Belgaum**

Dr. V. D. PATIL MD, DCH
Principal,
J. N. Medical College,
Nehru Nagar,
Belgaum-590 010

Date :
Place : **Belgaum**

LIST OF ABBREVIATIONS USED

AIDS –Acquired immunodeficiency syndrome

ARN-Acute Retinal Necrosis

CD - Cluster of differentiation

CDC- Center for the disease control

CMV- Cytomegalovirus

CNS-Central nervous system

CWS - Cotton wool spots.

DM-Diabetes Mellitus

DNA- Deoxy ribose nucleic acid

FDA- Food and Drug Administration

HAART-Highly Active Anti-Retroviral Therapy.

HIV- Human immunodeficiency virus

HSV-Herpes simplex virus

HTN-Hyperetension.

HZO-Herpes zoster ophthalmicus

IRU-Immune recovery uveitis

KS- Kaposi's sarcoma

LTRs-Long terminal repeats

NHR- Necrotizing herpetic retinopathy

PCP- Pneumocystis carinii pneumonia

PORN- Progressive Outer Retinal Necrosis.

RNA-Ribose nucleic acid

RT-Reverse transcriptase

TB-Tuberculosis

UNAIDS- United Nations Programme on HIV/AIDS

VZV-Varicella zoster virus

WHO-World Health Organisiation

ABSTRACT

Background: Acquired Immuno-Deficiency Syndrome is a multisystem disorder which affects almost all organs. The prevalence of ocular manifestations of HIV/AIDS is 50%-75%. Although studies to record prevalence of ocular manifestations have been done in other countries, less data is available from India and their correlation with the CD4+ T cell count has not been studied adequately.

Objective: To estimate the prevalence of ocular manifestations in a group of patients with HIV/AIDS with the secondary objective to find the correlation of ocular findings with CD4+T cell count.

Method: A cross sectional ophthalmic evaluation of HIV positive patients attending the outpatient clinic or admitted in the inpatient department having done their CD4+T cell counts.

Results:

100 patients were enrolled in this study. There were 76 men (Mean Age-40.48year), and 24 women. (Mean age -37.66years). 51(51%) patients had normal eye examination. The finding in the other 49(49%) patients are HIV retinopathy in 22 (22%) patients, Papilledema in 7(7%) patients, Dry eyes in 6(6%) patients , CMV retinitis in 4(4%) patients, choroidal tubercles in 3(3%), Cranial nerve palsy in 3 (3%) patients and other findings being less common. Posterior segment findings were more common than the anterior segment manifestations. Visual acuity was 6/18 in the better eye in 83(93.2%) of patients.2 (2%) patients had vision of <3/60 in both eyes and 11 patients were too ill to co-operate fully with the examination. Respiratory System was the most commonly involved organ, i.e in 40(40%) patients with 23(23%) patients having tuberculosis.

44 (54.3%) patients belonging to stage 3 & 4 WHO clinical staging for HIV had abnormal eye findings in comparison with the 5 (26 %) patients belonging to WHO clinical stage 1&2 and the association being statistically significant($p<0.1$).We found no correlation between CD4+T cell count and the ocular manifestations of HIV/AIDS.

Conclusion: The study concludes that AIDS affects the eyes of significant proportion of the patients. The spectrum of ocular lesions associated with HIV infection in this region is different from that seen elsewhere in the world. The prevalence of CMV retinitis is lower than other studies. Majority of the patients have no ocular complaints. Screening for ocular complaints is not a reliable method to identify those with the ocular morbidity. Comprehensive ophthalmic examination of all HIV infected patients with AIDS at regular intervals will help in identifying ocular morbidity early.

Key Words: HIV/AIDS infection; Ocular manifestation; CD4 positive T lymphocytes

CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF GRAPHS

INTRODUCTION

AIDS –Acquired immunodeficiency syndrome is a potentially lethal multisystem disorder caused by a retrovirus, the Human immunodeficiency virus (HIV).[1]

The disease was first described in 1981 in Los Angles, USA, and in India in 1986.[2] In April 1982, Holland and associates published the historic first article describing ocular disorders associated with AIDS. [3]

An estimated 33.4 million [31.1 million–35.8 million] people are living with HIV infection worldwide, while about 25 million people have died already. In India adult (aged 15-49 years) HIV prevalence is 0.3%.[4]

The primary clinical problems associated with HIV infection are the opportunistic infections and neoplasms that occur as a result of progressively severe immunodeficiency that develop during the course of the disease. The clinical profile of HIV disease in India includes a wide range of conditions like tuberculosis, cryptococcal meningitis, pruritic eruptions, cytomegalovirus retinitis and etc. Infection with HIV results in selective loss of the Cluster of differentiation (CD) 4 positive T lymphocytes count and their function resulting in the progressive damage to immune system of the human host.[5]

This potentially lethal multisystem disorder can affect any part of the visual system, namely the ocular adnexa, the anterior segment, the posterior segment, the optic nerve and afferent pathways and can be the initial manifestation of the disease.[6] An anatomical approach is useful in understanding and assessment of the disease. The number and the severity of the ophthalmic sequelae of HIV infection increase as the

immunocompetence decreases. Cytomegalovirus (CMV) retinitis is reported to be the most common ocular opportunistic infection, and occurs commonly when CD4+T cell count falls below 100cells/µl.[7, 8]

Introduction of antiviral drugs and measures aimed at treating or preventing the development of opportunistic infections associated with HIV/AIDS, led to an increased life expectancy. The disease is continuing to spread in developing countries, and the poor cannot afford to spend on these drugs. Consideration of natural history of HIV/AIDS and the outcome of less than full treatment of its ocular manifestations led to a paradox: the epidemic of blindness which may hit hard in regions where HIV care progressively improves and life expectancy is prolonged.[9]

Most studies on the prevalence of ocular manifestation of HIV/AIDS have been carried out in industrialized countries; nevertheless, more than 90% of all the patients infected with HIV live in poor and middle income countries. Between 5% and 25% of all HIV infected patients in developing countries can be expected to develop blindness at some time during their illness.[10]

Therefore HIV/AIDS will be a major challenge for VISION 2020-The Right to Sight.

Data regarding ocular manifestations in HIV/AIDS patients and its correlation with CD4+ T cell count in India remain scarce. Therefore the focus of the current study is to find out the prevalence of ocular manifestations of HIV/AIDS with the secondary objective to study its correlation with CD4+ T cell count.

OBJECTIVE

The objectives of the present study are

Primary Objective: To estimate the prevalence of ocular manifestations in a group of patients with HIV/AIDS.

Secondary Objective: To determine the correlation between ophthalmic manifestations of HIV/AIDS and CD4+ T lymphocyte cell counts.

REVIEW OF LITERATURE

History: [8, 11]

Thirty years ago, the acquired immunodeficiency syndrome (AIDS) was unknown to medical science. Now, it is one of the leading causes of death among young adults and has a profound impact on the health of the people worldwide.

There have been many historical events in the evolution of AIDS and its treatment.

- 1981: AIDS was first reported in United States.
- 1982: The term AIDS (Acquired immune deficiency syndrome) was used for the first and the center for the disease control (CDC) defined AIDS.
- 1984: The causal agent of the AIDS was identified in France (Lymphadenopathy associated virus) and in United States (Human lymphotrophic virus type III) finally called Human immunodeficiency virus. Eminent HIV scientist Dr Robert Gallo (United States) is considered to be the one who discovered HIV.
- 1985: The serologic testing for HIV (Food and Drug Administration-FDA approved) became effective.
- 1986: HIV infection was first identified in India in Madras (now called Chennai).
- 1987: Zidovudine became the first anti HIV drug to be approved by FDA.
- 1993: CDC revises its definition of AIDS.

- In field of ophthalmology, the first report on ocular involvement in AIDS patients appeared in American journal of ophthalmology in 1982 and in India in 1995.

- 1995: The first Protease inhibitor was introduced and the combination of nucleoside along with Protease inhibitor generally known as Highly Active Anti Retroviral Therapy (HAART) came into wide use.

  These therapies have created a revolution in the treatment of HIV disease.

EPIDEMIOLOGY.

Global HIV/AIDS estimates: End of 2008.

The latest statistics of global HIV/AIDS were published by United Nations Programme on HIV/AIDS (UNAIDS) in November 2009, and refer to the end of 2008.

Statistics of global HIV/AIDS at end of 2008.	Estimate in millions.
Total number of people living with HIV/AIDS	33.4
Women	15.7
Children	2.1
People newly infected	2.7
AIDS death	2.0

More than 25 million people have died of AIDS since 1981.[4]

India HIV and AIDS Statistics

The spread of HIV in India has been uneven. HIV epidemics are more severe in the southern half of the country and the far north east.

The highest HIV prevalence rates are found in Andhra Pradesh, Maharashtra, Tamil Nadu, and Karnataka in the south, and Manipur and Nagaland in North east.

People living with HIV/AIDS at the end of 2007: 2.31 million. The estimated adult prevalence in the country is 0.34% and it is greater among males (0.44%) than among females (0.23%).[12]

Due to lack of efficient reporting system these figures significantly under represent the actual number of people living with AIDS. Many AIDS deaths go unreported in India, due to the stigmata and discrimination. In many situations, the cause of death is attributed to an opportunistic infection with Tuberculosis, without HIV having been diagnosed.

Perhaps 85% of HIV transmission in India is through sexual contact. Injection drug use is an important factor in the North East Myanmar, in North West near Afghanistan and Pakistan and in major cities. India still has many paid blood donors, and hence contaminated blood and blood products account for about 2% of HIV infection.[13]

ETIOLOGY: [14]

The Human immunodeficiency virus belongs to the family of retroviruses and subfamily of lentiviruses. The retrovirus has a unique manner of replication. An enzyme, reverse transcriptase (RT) carried by the virus reverses the usual flow of genetic information by causing the ribose nucleic acid (RNA) genetic information of the virus to be transcribed into DNA.

MORPHOLOGY

Electron microscopy shows that the HIV virions comprise icosahedral cores, containing the RNA genome, the RT enzyme and gag proteins, surrounded by an envelope. The complete sequence of HIV-1 contains a 9.2 kb genome. Long terminal repeats (LTRs) flank the genes for gag, pol and env and on either side of env gene additional frame for coding 6 protiens of which 5 are involved for regulation. These involve the products of following genes; *tat* (transcription gene), *rev* (regulator of virus gene), *nef* (negative factor gene), *vif* (viral infectivity factor gene), *vpu* and *vpx*. Viral protein R (VPR) imparts a rapid growth advantage to HIV-1.

Structural antigens:

Core antigens: The inner cone-shaped component of the nucleocapsid consists of a shell of the gag cleavage product p24. Its presence is a marker for viral replication.

Envelope antigens: In the envelope of the virion this protein is present as a 2 cleaved products, a transmembrane glycoprotein, gp41, and an external glycoprotein, gp120. These have the functions of attachment of the virus to the target cell (gp120) and fusion of virus envelope and cell membrane (gp41)

RT antigen: The reverse transcriptase enzyme is necessary for reverse transcription.

VIRUS CELL INTERACTION:

For the cell to be susceptible to the infection, 2 conditions have to be fulfilled. First, the envelope of the virus has to react with the cell surface and cell must be capable of supporting viral replication.

The initial function of the virus envelop is to bind to CD4 as receptor by use of recombinant HIV envelope gp 120. A second human receptor component mediated by gp41 is required for viral entry, and this second function of the viral envelope produces fusion between the adjacent membranes seen as the typical cytopathic effect of syncytium formation.

As the retrovirus is able to integrate into the host DNA, the hallmark of the infection by HIV is persistence and as a consequence of this, a person once infected will there after remain at risk of virus related disease and will remain infectious.

PATHOGENESIS OF HIV INFECTION:

Shortly after the infection and before any immune response to the virus is detectable, free virus and viral antigens circulate in the blood. As antibody titers increase, the amounts of free virus decrease, indicating a degree of immunological suppression of virus replication. Viruses are sequestrated in the lymph nodes after early viremic burst, but over time viral replication is continual and persistent. In healthy HIV seropositive individual, quantitative viral RNA analysis, estimate that 10^7 - 10^9 virions are produced each day and calculations based on CD4 T cell loss predict that 2 X 10^9 CD4 T cells are destroyed per day. Most patients maintain a reduced level of viral replication in the first few years of infection, but as the damage to immune system becomes more marked, viral replication increases.

In the disease process, the naive CD4 T cells (CD 45 Ra) are lost during disease progression at a higher rate than CD 45 Ro memory cells. Therefore an infected individuals immune response is first lost to specific recall antigens and then to allogenic antigens and finally to mitogen stimulation.

The mechanism of CD4+T cell loss has been speculated to be either due to direct effect of the virus followed by apoptosis or indirect mechanisms, such as gp120-CD4 antibody cross linking, viral protein – induced cellular dysregulation.

Finally, it should be mentioned that, as a prerequisite for HIV replication, cellular activation and proliferation are important factors and this is thought to be induced by antigens via specific T cell receptor or cytokines.

TRANSMISSION: [15, 16]

HIV infection spreads by three routes of transmission;

1. Sexual contact with an infected person (homosexual or heterosexual)
2. Blood and blood products
3. By infected mother to infant(intra partum, perinatally or via breast milk)

SEXUAL TRANSMISSION:

Worldwide, the most common mode of infection is heterosexual transmission. HIV appears to be concentrated in seminal fluid and also in vaginal fluid, particularly in situations as in genital inflammatory conditions. It is found that male to female transmission is more efficient than female to male transmission and presence of sexually transmitted disease has been strongly associated with HIV transmission.

India's AIDS case surveillance system attributes 86% of HIV infections to sexual risks.

TRANSMISSION BY BLOOD AND BLOOD PRODUCTS:

HIV can be transmitted to individuals who receive HIV-tainted blood transfusions, blood products, or transplanted tissue as well as to Injection drug users (IDUs) who are exposed to HIV while sharing injection paraphernalia. Parental transmission can occur during IV puncture, S.C or I.M injections. It is estimated that 90-100% of individuals who were exposed to HIV-contaminated products became infected. Current technology cannot detect HIV RNA for the first 1-2 weeks following infection due to low levels of viremia. Thus despite best efforts of science, one cannot completely eliminate the risk of transfusion-related transmission of HIV since.

India's AIDS case surveillance system attributes 2.4% to injection drug use, 2.0% to blood transfusions, of HIV infections.

OCCUPATIONAL TRANSMISSION OF HIV:

Health care workers and laboratory workers are potentially at risk of HIV infection while working with HIV containing materials with percutaneous injuries or contact of mucous membrane or non intact skin with blood, tissue or potentially infectious fluid. HIV transmission following skin puncture with sharp object contaminated with blood from a person with documented HIV infection is 0.3% and after a mucous membrane exposure it is 0.09%. Factors that might be associated with mucocutaneous transmission of HIV include exposure to a large amount of blood, prolonged contact, and a potential portal of entry and antiretroviral drugs as post exposure prophylaxis decreases the risk of infection. Therefore it is very important to use universal precaution when caring for all patients.

MATERNAL-INFANT FETAL / INFANT TRANSMISSION:

HIV infection is transmitted from infected mother to her fetus during pregnancy, during delivery, or by breast feeding. Relative proportions of transmission are 23-30% before birth, 50-65% during birth and 12-20% via breast feeding. Breast feeding in early months is an important modality of transmission of HIV infection in developing countries and factors that increase the likely hood of transmission include detectable levels of HIV in breast milk, presence of mastitis, low maternal CD4+T cell counts, and maternal vitamin A deficiency.

India's AIDS case surveillance system attributes 3.6% to perinatal transmission.

REVISED CDC CLASSIFICATION SYSTEM FOR HIV: [18]

The revised CDC classification system for HIV-infected adolescents and adults (greater than or equal to 13 years) categorizes persons on the basis of clinical conditions associated with HIV infection and CD4+ T- lymphocyte counts.

The three CD4+ T-lymphocyte categories are defined as follows:

- Category 1: greater than or equal to 500 cells/µl.
- Category 2: 200-499 cells/ul.
- Category 3: less than 200 cells/ul.

EXPANSION OF THE CDC SURVEILLANCE CASE DEFINITION FOR AIDS: [17]

AIDS surveillance case definition includes all HIV-infected persons with CD4+ T- lymphocyte counts of less than 200 cells/ul or a CD4+ percentage of less than 14. In addition to retaining the 23 clinical conditions in the previous AIDS

surveillance definition, the expanded definition includes pulmonary tuberculosis (TB), recurrent pneumonia, and invasive cervical cancer.

REVISED WHO CLINICAL STAGING OF HIV/AIDS FOR ADULTS AND ADOLESCENTS: [18]

Primary HIV infection

Asymptomatic

Acute retroviral syndrome

Clinical stage 1

Asymptomatic

Persistent generalized lymphadenopathy (PGL)

Clinical stage 2

Moderate unexplained weight loss (<10% of presumed or measured body weight)

Recurrent respiratory tract infections)

Herpes zoster

Angular cheilitis

Recurrent oral ulcerations

Papular pruritic eruptions

Seborrhoeic dermatitis

Fungal nail infections of fingers

Clinical 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

a. Unexplained anaemia (< 8 g/dl), and or neutropenia (<500/mm3) and or thrombocytopenia (<50 000/ mm3) for more than one month
b. All clinical events or conditions referred to are described in the Annexes in WHO

Clinical 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 (CNS) 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

DIAGNOSIS AND LABORATORY MONITORING OF HIV INFECTION: [19,20]

The diagnosis of HIV-1 infection is based on the detection of specific antibodies (ELISA, Western blot) and antigens. Serological tests are generally used for screening and provide results in as little time as 20 min. Rapid tests are important tools for surveillance, screening, and diagnosis, and can be readily be done on plasma, serum, whole blood, or saliva by health care providers. The two limitations of the serological tests are detection of infection when antibodies are absent, and in infants younger than 18 months who might bear maternal antibodies. In these instances direct viral detection is the only option (eg, quantification of viral RNA or p24 antigen).

For staging purpose and to monitor therapeutic success of HAART, measurement of CD4+T cells and plasma viral load is required. The viral load determines the rate of destruction of the immune system; the number of CD4+T cells reveals the degree of immunodeficiency. Flow cytometry analysis is the standard method for CD4+T cells quantification.

CLINICAL MANIFESTATIONS OF HIV DISEASES: [15]

The clinical course of human immunodeficiency virus (HIV) disease and pattern of opportunistic infections varies from patient to patient and from country to country. The clinical consequences of HIV infection encompass a spectrum ranging from an acute syndrome associated with primary infection to a prolonged asymptomatic state to advanced disease.

THE ACUTE HIV SYNDROME

It is estimated that 50–70% of individuals with HIV infection experience an acute clinical syndrome ~3–6 weeks after primary infection; they occur along with a burst of plasma viremia. The symptoms of the acute HIV syndrome include fever, skin rash, pharyngitis, and myalgia which persist for one to several weeks and gradually subside as an immune response to HIV develops. Opportunistic infections during this stage of infection reflect the immunodeficiency resulting from dysfunction and reduced numbers of CD4+ T cells. Lymphadenopathy occurs in ~70% of individuals with primary HIV infection. Most patients recover spontaneously from this syndrome.

THE ASYMPTOMATIC STAGE—CLINICAL LATENCY

In most patients, primary infection with or without the acute syndrome is followed by a prolonged period of clinical latency; the median time for untreated patients is ~10 years. HIV disease with active virus replication is ongoing and progressive during this asymptomatic period. The rate of disease progression is directly correlated with HIV RNA levels. Long-term non-progressors show little if any decline in CD4+ T cell counts over extended periods of time and have extremely low levels of HIV RNA (<50 copies per milliliter).

During this period of HIV infection, the average rate of CD4+ T cell decline is ~50/µl per year.

SYMPTOMATIC DISEASE

Symptoms of HIV disease can appear at any time during the course of HIV infection. When the CD4+ T cell count falls to <200/µl, the resulting state of immunodeficiency is severe enough to place the patient at high risk for opportunistic infection and neoplasms. The causative agents of the opportunistic infections are *P.* jiroveci, atypical mycobacteria, CMV, and other common bacterial and mycobacterial pathogens. Fewer than 50% of deaths among AIDS patients are as a direct result of an AIDS-defining illness, and the average CD4+ T cell count of an HIV-infected patient at the time of death is 300 cells/µl. Similarly, following the widespread use of combination ARV therapy and implementation of guidelines for the prevention of opportunistic infections, the incidence of secondary infections has decreased dramatically. Overall, the clinical spectrum of HIV disease is constantly changing as patients live longer with HAART treatment.

PULMONARY MANIFESTATIONS OF HIV

Pulmonary diseases associated with HIV infections are Tuberculosis (TB), Pneumocystis jerovecii pneumonia (PCP) and bacterial pneumonia.

Tuberculosis:

In India, the most common opportunistic infection among people with HIV infection is pulmonary tuberculosis ~60% [21]

Unlike other opportunistic infection TB is unique in that it can occur over a wide range of CD4 counts, although it is more frequent at CD4 counts <300 cells/µl

and present in an atypical pattern. Extra-pulmonary tubercular manifestations occur in 46 to 79 per cent of patients with pulmonary TB and HIV and are frequent in severely immunocompromised patients. Tuberculin positivity is less prevalent among HIV seropositive patients due to anergy resulting from immunosuppression. The risk of death in an HIV-infected patient with TB is 3.5 times greater than the risk in HIV infected patients without TB.

Pneumocystis carinii pneumonia (PCP):

Occurrence of PCP establishes the diagnosis of AIDS. PCP occurs in patients with CD4 counts of < 200 cells/ µl. PCP can simultaneously occur with other pulmonary infections, including TB, cryptococcosis, and cytomegalovirus. PCP responds to high dose cotrimoxazole.

Bacterial pneumonia:

The most common causes of acute community acquired pneumonia, are encapsulated bacteria, Streptococcus pneumonia and Haemophilus influenza. Rates of bacterial pneumonia are 25-fold higher among HIV infected adults than in the general community.

NEUROLOGICAL MANIFESTATIONS OF HIV:

Neurological complications of HIV disease can be categorized into opportunistic infections, malignancy, AIDS related dementia, and vasculitis/stroke.

Cryptococcal meningitis has been reported as the most common opportunistic infection (2-4.7 per cent of all opportunistic Infections) of the Central nervous system (CNS) among Indian patients with HIV infection. Toxoplasmosis, TB meningitis primary multifocal leukoencephalopathy are also common of the CNS.

CNS Non Hodgkins Lymphoma in Indian patients with AIDS are few as compared to western literature (2 %). Other neurological manifestations can be AIDS dementia complex, vasculitis/stroke secondary to a number of infections. Psychiatric illnesses like depression and anxiety are common in patients with HIV/AIDS.

DISEASES OF THE HEMATOPOIETIC SYSTEM:

Disorders of the hematopoietic system including lymphadenopathy, anemia, leukopenia, and/or thrombocytopenia are common throughout the course of HIV infection due to various causes. HIV infected patients can develop persistent generalized lymphadenopathy as an early clinical manifestation of HIV infection. Approximately 4% of patients with HIV infection experience venous thrombotic events such as deep vein thrombosis or pulmonary embolism.

Immunologic and rheumatologic disorders are common in patients with HIV infection like excessive immediate-type hypersensitivity reactions, reactive arthritis, drug allergies, AIDS-associated arthropathy, septic arthritis and etc.

DISEASE OF THE OROPHARYNX AND GASTROINTESTINAL SYSTEM:

Oral candidiasis occurs in up to 70 per cent of individuals with HIV infection with median CD4 counts of patients with candida ranging between 107and 189 cells/µl. The presence of oral candidiasis indicates the need to start PCP prophylaxis.

Periodontal disease, Oral hairy leukoplakia , Oral ulcers, are other oral lesions found in HIV/AIDS patients.

Candidal esophagitis and other infectious pathogens, such as CMV or HSV causing dysphagia or odynophagia, are very common among patients with advanced HIV disease.

Chronic diarrhoea is a major problem in HIV infected persons, affecting up to 76 per cent of those with AIDS. Isospora belli and Cryptosporidium parvum were the two most common causes of chronic diarrhoeal disease in HIV infected persons in India. AIDS enteropathy or HIV enteropathy is most likely a direct result of HIV infection in the gastrointestinal tract.

Abdominal mass lesions in HIV patients can be caused by abdominal tuberculosis and abdominal lymphoma.

OTHER SYSTEMIC INVOLVEMENT

Diseases of the kidney or genitourinary tract may be a direct consequence of HIV infection, due to an opportunistic infection or neoplasm, or related to drug toxicity.

Patients with HIV infection can develop endocrinological abnormalities like lipodystrophy syndrome and hyponatremia due to the syndrome of inappropriate antidiuretic hormone (vasopressin) secretion (SIADH) and hypogonadism.

Cutaneous manifestations can occur in up to 90 per cent of HIV-infected individuals. Herpes zoster which occurs early in the course of HIV disease can last longer than the usual. Molluscum contagiosum, occurs in a disseminated fashion in severely immunocompromised individuals. Staphylococcal skin infection, Papular pruritic eruption (PPE), and Alopecia are common in HIV infected patients.

WOMEN AND CHILDREN

Among special concerns for women with HIV are its effects on pregnancy, and mother-to-child transmission of HIV.

Vertical transmission is responsible for between 67 and 87 per cent of paediatric HIV infection. In a study by Biswas et.al in south India found 5.5% of the children below 15 years are affected by HIV/AIDS.[22] The clinical features of HIV infection in children are different from those in adults presenting most commonly as failure to thrive. Pulmonary and extrapulmonary tuberculosis is the most frequent opportunistic infection. Severe malnutrition, serious pyogenic infections, chronic diarrhoea were also associated with increased risk of being HIV positive.[5]

OCULAR MANIFESTATIONS IN HIV POSITIVE AND AIDS PATIENTS.

HIV has various ocular manifestations and with the introduction of HAART, their pattern and prevalence has changed. Hodge et al have reported that the life time cumulative rate of at least one abnormal ocular lesion developing in an HIV positive patient ranges from 52-100%.[23] Shah SU et al have reported the prevalence of ocular manifestations of HIV/AIDS in 8% of patients on HAART and the manifestations were significantly higher in the patients with CD4+ T cell count of 0-100 cell/µl and WHO clinical stage 3 and 4 patients than other group.[21]

ADNEXAL AND ANTERIOR SEGMENT MANIFESTATIONS OF HIV/AIDS:

Opportunistic infections develop in when there is a deterioration of the immune status of the individual which can be measured with the help of CD4 cell counts. Corneal and anterior segment lesions affect more than 50% of all HIV patients. Ocular adnexal complications, seen in about 25% of patients, can be a sign of severe systemic immunosuppression.[24]

Herpes zoster ophthalmicus:

Herpes zoster ophthalmicus is vesicobullous dermatitis of the first division of the trigeminal nerve that can present as the first sign of AIDS / HIV infection. Its presence in a person younger than 45 years indicates depressed underlying immunity and warrants HIV testing.[24, 25]. Hodge et al in a study have reported a relative incident risk ratio of 6.6/1 for herpes zoster infection for HIV positive patients compared to HIV negative control subjects and a prevalence of 5-15 % of HIV-positive patients co infected with HZO.[23] The risk of Herpes zoster in HIV positive patients is found independent of the age, sex, type of protease inhibitor , CD4 counts and viral load at baseline 1 month.[26] Sellitti TP et al in a study have reported that the ocular involvement in HIV-positive patient is more severe with higher incidence of corneal involvement and sequelae range from zoster keratitis, uveitis and chronic infectious pseudo dendritic keratitis, the later being almost exclusively unique to AIDS patients which can be devastating and difficult to manage. The keratitis is associated with deep pain and photophobia and is characterized by chronic grey, elevated, dendriform epithelial lesions that typically stain poorly with flourescien but well with rose bengal staining. These lesions can also involve limbal and conjunctival epithelium and have favorable response to antiviral therapy.[26], [27]

A variant of HZO known as zoster sine herpete can present with conjunctivitis, uveitis, episcleritis, scleritis and corneal hypoesthesia without skin lesions. About 50% of patients with HZO develop anterior uveits. The uveitis can lead to elevated intra ocular pressure, heterochromia iridis, and sector iris atrophy. Necrotizing retinitis can be complication of HZO due to the chronic nature of disease in AIDS patients so also post herpetic neuralgia. The incidence of post herpetic neuralgia decreases with early treatment with IV Acyclovir. [28] The appropriate

treatment for HZO in HIV positive patients consists of IV acyclovir 10mg/kg body weight 3 times a day for 7 days followed by an oral maintainance regimen of 800 mg 3 to 5 times daily for at least 3 – 6 weeks. Other drugs include famcyclovir and IV foscarnet.

Molluscum contagiosum:

Molluscum contagiosum eye lid lesions associated with AIDS is considered as a marker of late-stage disease. Leahey et al have reported Molluscum contagiosum as initial manifestation of AIDS.[29] It is a contagious dermatitis affecting 5% of HIV infected patients. It can appear on skin or mucous membrane with central umbilicated pearly papules of 2-3mm in size. Peripherally located lesions may be associated follicular conjunctivitis and punctuate epithelial keratitis.[24] Robinson et al have reported in a study that the Molluscum contagiosum lesions are more confluent in patients with AIDS and local removal appears to be of limited value in these patients.[30,]

Kaposi's sarcoma

Kaposi's sarcoma (KS) is a highly vascularized, painless mesenchymal tumour, appears as multiple purple-to-red nodules affecting the eyelids or conjunctiva in up to 5% of HIV positive patients. It can mimic a chalazion in the lids and a subconjunctival hemorrhage or pyogenic granuloma in conjunctiva. Histologically, KS can resemble an angioma, hemangioma, lymphangioma or granulation tissue. Dugel and associates have classified adnexal KS lesions clinically and histopathologically into three stages. Stage I and II lesions are flat (less than 3 mm in height), patchy and of less than four months duration; Stage III lesions are nodular, greater than 3 mm in height and greater than four months in duration. This staging

may have prognostic value regarding the course of disease and response to therapy.[31] Kaposi's sarcoma of the eyelid and conjunctiva is rare in the Indian subcontinent possibly due to the rarity of the probable causative agent, human herpes virus 8. Complete and partial resolution of Kaposi's sarcoma has been observed with HAART. The clinical response correlates with an increase in CD4 cells and a decrease in plasma HIV-1 RNA levels. There are reports of decreased incidence of AIDS-related Kaposi's sarcoma with the widespread use of HAART.[32,33]

Non-Hodgkin's lymphoma (NHL) accounts for 3.5–5% of AIDS-defining illnesses, can affect eyelids and conjunctiva presenting as rapidly enlarging erythematous lesions. [26]

Squamous cell carcinoma of the conjunctiva is the third most common neoplasm associated with HIV presenting at a younger age and usually more aggressive. HIV testing should therefore be carried out in all cases of conjunctival tumors for patients living in high-risk areas as it may be the first sign of HIV-positivity. [26]

Infectious keratitis:

Varicella zoster virus (VZV) and herpes simplex virus (HSV) are the most common etiologic agents of infectious keratitis in HIV/AIDS patients. A study by Morgolis TP et al revealed 35% incidence of VZV stromal keratitis in patients with HZO.[28] Punctate corneal dendritic lesions which are larger and more peripherally situated, pathognomic bulb-tipped branching pattern, decreased corneal sensation and elevated intraocular pressure provide clues to the diagnosis. [24] Corneal stromal involvements have been reported infrequently in individuals with AIDS or other immunosuppressed states due to the T-lymphocyte dysfunction. Both VZV keratitis and HSV keratitis may recur more frequently and in some cases be more resistant to

treatment in HIV-positive patients than in other patients.[35] Treatment consists of debridement and antivirals such as topical trifluridine, topical acyclovir, or oral acyclovir(400 mg twice a day for 1 year) to prevent diseases recurrence.[24]

Spontaneous fungal keratitis, in the absence of corneal compromise and occasionally ocular microsporidiosis can develop in HIV/AIDS patients. [34]

Other manifestations

Keratoconjunctivitis sicca (KCS):

Dry eye occurs in 20–38.8% of HIV infected hosts in the later stages of AIDS. Etiology is multifactorial and is due to the combined effects of HIV-mediated inflammatory destruction of primary and accessory lacrimal glands and to the direct conjunctival damage due to the HIV virus itself. Autoimmune etiology has been attributed to kerato conjunctivitis sicca and tends to occur at higher CD4+T cells count. Afflicted individuals are more susceptible to bacterial keratitis and abnormalities in the composition of the tear film are typically present. Management options include artificial tears, long-acting lubricants and punctal occlusion in severe cases.[26,35]

Other anterior segment manifestations can be non-specific, culture-negative conjunctivitis (<1%), asymptomatic conjunctival microvascular changes and blepharitis.. [26]

Anterior and intermediate uveitis

Symptomatic anterior uveitis is uncommon in patients with HIV infection because the uveitis associated with CMV retinitis does not usually present with a painful red eye. In symptomatic uveitis with granulomatous features, the physician should suspect ocular tuberculosis and lymphoma, in cases of non-granulomatous uveitis, herpes zoster should be suspected, especially in patients with a history of systemic illness with herpes zoster. In addition, a CD 4+T cell count of less than 40 cells/mL is more commonly associated with nongranulomatous uveitis. Despite its low incidence, intraocular lymphoma should be suspected in patients whose uveitis is resistant to corticosteroid treatment.[32] Ocular syphilis, usually presents as granulomatous or non granulomatous anterior uveitis, pan uveitis with an incidence of 0.06% in the HIV positive population.

Rosenberger et al have reported case of uveitis in HIV positive patients not responding to conventional treatment with steroids whose aqueous paracentesis demonstrated HIV P^{24} core antigen. These patients respond to treatment with Zidovudine.[36]

Immune recovery uveitis:

This phenomenon occurring in patients on HAART on their path to immune recovery, involves mainly the anterior uvea and vitreous, and is often associated with a marked disturbance of visual function. Karavelles et al have reported the anterior segment complications of IRU, and include anterior and posterior sub capsular cataract, persistent post operative anterior chamber inflammation with development of posterior synechiae and large visually important inflammatory deposists on intra ocular lens.[37]

Other iatrogenic manifestations can be drug-induced uveitis and Stevens-Johnson syndrome (SJS). [24, 26]

POSTERIOR SEGMENT MANIFESTATIONS OF HIV/AIDS:

The posterior segment manifestations of AIDS can be divided into four categories: retinal vasculopathy, opportunistic infections, unusual malignancies and neuro-ophthalmologic abnormalities.[38].Since the introduction of HAART, the incidence of retinitis related to CMV, VZV, tuberculosis and toxoplasmosis has decreased significantly, with CMV retinitis incidence falling by around 80%.[32] Non-infectious posterior segment manifestations include HIV-retinopathy (most commonly), and optic disc atrophy.[39]

HIV-RETINOPATHY

Microvasculopathy is the most common ocular manifestation of AIDS, seen in about 40% to 60% of HIV-positive patients. Clinically manifests as cotton-wool spots (CWS), intraretinal haemorrhages and microaneurysms, particularly around the posterior pole. Most patients with retinal microvasculopathy are asymptomatic. [32,38] Various studies have shown that the likelihood of CWS formation in HIV patients was significantly higher in patients with low CD4 counts which suggest that retinal microinfarctions are related to HIV disease progression and immunosuppression.[40, 41] There seems to be a significant difference in the morphology of the cotton wool spots observed in diabetes mellitus compared with those observed in HIV infection. CWS in HIV positive patients are boomerang-shaped and are more eccentric. Therefore in the event of unexplained cotton wool spots prompt tests to rule out HIV infection is indicated.

Jaworski et al have postulated various theories for CWS genesis in HIV patients. They include Immune complex deposition in the vessel wall, direct infection of the blood vessel by the virus and increased fibrinogen in the blood causing small vessel occlusion and ischemia.[42]

Akduman L and associates have reported case of macular ischemia as a result of HIV retinopathy.[43]

CYTOMEGALOVIRUS RETINITIS:

According to the various reports CMV retinitis is the most important ocular opportunistic infection among patients who are HIV-positive. It can be an initial AIDS- related ocular opportunistic infection in 1.8-3% patients.[49] Hodge et al have reported that the relative risk of CMV retinitis is infinite in HIV-positive patients compared to HIV-negative control subjects. [23] The cross sectional prevalence of CMV retinitis is 20% in HIV positive patients with CD4+ T cells <200cells/µl, which increases to 30% with CD4+T cells <50 cells/ µl which suggest that there is increased risk of development of CMV retinitis with decline in CD4+ T cells count. Use of antiviral drugs can delay the onset of CMV retinitis in patients with lower CD4+T cell count. [41]

There are three clinical forms of CMV retinitis. The classical form (pizza pie retinopathy or cottage cheese with ketchup) is characterized by confluent retinal necrosis with hemorrhage that develops mostly in the posterior retina and over several weeks untreated lesions progress to full-thickness necrosis with resultant retinal gliosis and pigment epithelial atrophy. Patients often have loss of visual field or visual acuity and scotoma. The indolent form is recognized as a granular lesion in the peripheral retina, often with little or no hemorrhage. Patients may notice floaters, or

they may be asymptomatic. Neither form have much vitreous inflammatory reaction overlying the lesion, a third uncommon presentation is frosted branch angiitis. [38, 44]

In the HAART era, zone 1 involvement and retinal detachment remain the most common causes of visual acuity loss among patients with CMV retinitis. Cataract and CME also are common causes of loss of visual acuity, primarily in those patients with HAART-induced immune recovery.[45]

Currently available anti-CMV agents include ganciclovir and its prodrug valganciclovir, foscarnet, cidofovir, fomivirsen, ganciclovir implant and oral valganciclovir.[38]

OCULAR TUBERCULOSIS:

Ocular tuberculosis most commonly occurs after primary pulmonary infection attributable to direct hematogenous spread or by hypersensitive responses. Babu RB, et al has reported the incidence of ocular tuberculosis to be 1.95% in HIV/AIDS patients [46] and similar incidence of 2.8% of choroidal granuloma in HIV positive patient with tuberculosis has been reported by Beare NAV et al[47]. Lewallen S. and associates have reported abnormal eye findings in 22% of tuberculosis patients with HIV/AIDS. It can have varied presentations like choroidal granuloma (52%), subretinal abscess, panophthalmitis etc and almost all have associated pulmonary tuberculosis. Ocular tuberculosis can occur even at CD4+T cell counts greater than 200cells/µl. Diagnosis is based on clinical appearances and confirmed by histopathology and Polymerase Chain Reaction Test (PCR).[48]

RETINITIS

1. Necrotizing herpetic retinopathy:

Necrotizing herpetic retinopathy (NHR) is a continuous spectrum of posterior segment inflammation induced by herpes viruses, most commonly varicella zoster virus. Its two most recognizable clinical patterns are Acute Retinal Necrosis (ARN) and Progressive Outer Retinal Necrosis (PORN). Usually, the ARN occurs in healthy persons or AIDS patients with only mild immune dysfunction and elevated CD4+ counts, whereas the PORN usually develops in those who are severely immunocompromised. In addition to VZV, HSV and CMV have been isolated in patients with ARN, and HSV in eyes with PORN. Incidence of NHR in HIV-positive patients after HZO is reported to be 4%- 17%.[27,31]

Acute retinal necrosis is characterized by the clinical triad of peripheral retinitis, vitritis, and retinal arteritis associated with significant intraocular inflammatory response with anterior segment findings, including keratic precipitates and dendritic keratitis. Progressive outer retinal necrosis is characterized by a very rapidly progressive retinitis that begins as multifocal areas of deep whitening throughout the macula or periphery that coalesce within days to confluent sheets. Vitritis, retinal vasculitis, and anterior segment inflammation are absent. [49] Aggressive medical treatment with appropriate systemic antivirals may improve long-term visual outcome in patients with NHR. Treatment of ARN includes intravenous acyclovir. Following resolution of retinitis, prophylactic laser barrage is considered beneficial to prevent retinal detachment. However, visual loss due to progressive infection, optic nerve sheath effusion, or, in most cases, retinal detachment occurs in up to 70 to 85% of patients. [19, 38]

2. Toxoplasmosis

Ocular toxoplasmosis in AIDS is often bilateral, multifocal, and not associated with chorioretinal scars, suggesting that in most cases, it is a primary infection rather than a reactivation. There is associated inflammatory reaction in the form of iritis, vitritis, choroiditis, multifocal or diffuse necrotizing retinitis, papillitis or retrobulbar neuritis, or outer retinal toxoplasmosis. The intraocular inflammation is usually more severe and hemorrhages are fewer. Infection responds to the standard anti-parasitic drugs (pyrimethamine, clindamycin, sulfonamides) in most cases, but there are reactivations and progression of disease when therapy is stopped. Severe retinal necrosis can lead to retinal tears or detachment. Ocular toxoplasmosis can be the first manifestation of Toxoplasma gondii infection. [50]

3. HIV Retinitis

HIV may cause a peripheral chronic multifocal retinal infiltrates with associated low-grade vitritis and retinal vasculitis. Unlike CMV, the lesions are stationary or progress very slowly and are not associated with retinal hemorrhage. These lesions are grey white or yellow, irregular in shape, and < 200µm in dimension located in mid periphery or anterior retina. Retinitis in inflamed eyes usually occurs in patients with higher CD4 counts and is more commonly due to ARN, toxoplasmosis, syphilis, or late stages of cryptococcus. Retinitis in quiet eyes occurs in patients with lower CD4 counts and is more commonly due to CMV and PORN.[49] These patients usually present with floaters as most common symptom followed by blurred vision. Other symptoms include photopsia, photophobia, tearing, and foreign body sensation. The etiology is uncertain but HIV infection is presumed as treatment with anti-retroviral agents cause regression and vitreous cultures are negative for organisms

other than HIV. Patients must be evaluated for syphilis which may cause a similar clinical picture.[51]

CHOROIDITS:

Pneumocystis: Pneumocystis choroiditis is classically bilateral and multifocal yellowish, well-demarcated, choroidal lesions located in the posterior pole not associated with vitritis, iritis, or vasculitis. They are slowly progressive and often not associated with visual loss. Other manifestations include conjunctivitis, orbital mass and optic neuropathy. Ocular lesions respond in most cases to induction and subsequent maintenance treatment with systemic pentamidine, trimethoprim and sulfamethoxazole, or dapsone.[38, 49, 52.]

Cryptococcus: Cryptococcal meningitis is the most common cause of AIDS- related neuro-ophthalmolgic lesions. Cryptococcal choroiditis may be multifocal, solitary, or confluent and may be associated with eyelid nodule, conjunctival mass, granulomatous iritis, iris mass, vitritis, necrotizing retinitis, endophthalmitis. The most common ocular manifestations of Cryptococcus are papilledema and retrobulbar neuritis with or without intraocular extension, are directly related to central nervous system infection. Fluconazole maintenance therapy 200 mg/day is currently recommended in all patients even in the era of HAART and after one week of treatment Kestelyn P has reported resolution of the granuloma with scar formation 2 months later. [38, 49, 53]

Syphilis

It has been argued that syphilis is not an opportunistic infection in AIDS because of a similar prevalence among HIV positive and HIV negative patients.[23] Syphilis in AIDS may develop when CD4-counts are greater than 200 cells/µl. Failures of intramuscular and intravenous penicillin to prevent progression of primary or secondary syphilis or neurosyphilis, or to prevent recurrent ocular syphilis, have been reported in AIDS patients. Clinical findings of ocular syphilis in AIDS may include iritis, retrobulbar optic neuritis, perineuritis, papillitis, neuroretinitis, retinal vasculitis, a necrotizing retinitis which may be clinically indistinguishable from CMV and exudative retinal detachment. Vitritis can be present as a primary manifestation of ocular syphilis with HIV infection.[54] Diagnosis is by Rapid plasma reagin tests, Venereal Disease Research Laboratory (VDRL) tests, Fluorescent treponemal antibody absorption test (FTA-ABS), etc. Treatment of ocular syphilis includes 12–24 million units of intravenous aqueous penicillin be administered for 10 days in AIDS patients.[38, 49]

Immune recovery uveitis

Immune recovery is defined as an increase in CD4+ T cell count by 50 cells/µl or more to a level of 100 cells/µl or more.[55] Immune recovery uveitis (IRU) is a noninfectious intraocular inflammation which develops in patients with inactive CMV retinitis who have had a substantial elevation in CD4 count with HAART. [56] Kempen JH and associates have reported an incidence of 9.6% of IRU in patients with CMV retinitis who develop immune recovery in response to HAART. The same study reported the common posterior segment manifestation of IRU as cystoid macular edema in 45%, and epiretinal membrane in 48% of cases. The other clinical features

include anterior chamber or vitreous reaction, panuveitis with hypopon, cataract, optic disk edema, vitreomacular traction syndrome, and proliferative vitreoretinopathy, increased risk of moderate visual loss $\leq$ 20/50. Large CMV lesions involving >25% of retinal area and use of intravitreous cidofovir are risk factors for IRU. The risk of IRU increases with increasing CD4+T cells and declining HIV load.[37, 57]

The interval between the initiation of combination antiretroviral therapy and the onset of vitreous inflammation generally parallels the rise in CD4+T cell count with duration varying between 1 to 8 months. Retinal detachment can be the complication of IRU.[56]

Sendi P et al has reported a case of isolated toxoplasmic retinochoroiditis and immune recovery vitritis after initiating HAART. Treatment with corticosteroids (subtenon or systemic or intravitreal) is effective in controlling inflammation and improving vision in some cases. [58]

Ocular posterior segment opportunistic infections are manifestations of disseminated disease in AIDS patients. Therefore treatment of ocular disease must take into account the systemic nature of the infection.[49]

Neuro ophthalmological abnormalities

Neuro-ophthalmic manifestations account for 10-15% of all eye manifestation in patients with HIV in one of the Indian studies. [59] Neuro-ophthalmologic abnormalities usually are an indication of infection or lymphoma of the brain or meninges.[49]

Mawanza et al have reported neuro ophathalmological manifestations in 60% of neurologically symptomatic HIV infected patients. This study reported eye movement disorders in the form of abnormal saccades as most common in 51% of

cases followed by visual field defects in 39% cases, and papilledema in 27% of cases. Other findings include optic neuropathy that presents clinically as neuroretinitis, anterior or retro bulbar optic neuropathy, and ocular motor palasies involving abducens and oculomotor nerve, and cortical blindness. [60]

Goldsmith P et al in a study have reported optic neuropathy related to HIV infection itself which responded to HAART therapy with improvement in vision.[61.] Hong YJ has reported a case of complete binocular blindness as the first manifestation of HIV-related cryptococcal meningitis with unremarkable fundoscopic examination. The possible mechanisms for binocular blindness include direct fungal infiltration of the optic nerve, optic chaisma, or optic tracts, adhesive arachnoiditis, cerebral vasculitis and intra cranial hypertension.[62] Battu RR et al has reported a case of papilledema with peripapillary haemorrhages in an AIDS patient with cryptococcal meningitis which resolved with anti fungal treatment.[63]

Acquired Immunodeficiency syndrome- Related Intraocular B-Cell Lymphoma:

Rivero M E, et al has reported that the AIDS related Intra ocular B cell lymphoma can be clinically confused with CMV retinitis. Ocular involvement can be isolated or in association with CNS and/ or systemic disease. There are some significant differences between the ocular manifestations of NHL-CNS and systemic lymphoma. NHL-CNS usually manifests as lesions in the retina, the subretinal pigment epithelial space, and the optic nerve, whereas intraocular manifestations of systemic lymphoma typically involve the uveal tract owing to invasion through the choroidal circulation. Vitritis is common in both settings. Posterior segment manifestations of NHL include necrotizing retinitis, multifocal choroiditis, retinal

vasculitis, vitritis, subretinal mass, and pseudo-hypopyon uveitis. Treatment options include radiation and chemotherapy.64, 49

Drug related complications

Yoganathan K et al has reported a case of bilateral retinal hemorrhages and ischemic maculopathy in association with zidovudine-induced anemia in an HIV-positive man.[65] High-dose didanosine has been associated with retinal pigment epithelial abnormalities. These adverse effects are dose related and resolve following discontinuation of the drug, with the exception of the abnormal retinal pigment epithelial changes. [66]

METHODOLOGY

The present study titled 'ONE YEAR CROSS-SECTIONAL STUDY OF OCULAR MANIFESTATIONS IN HIV-POSITIVE/AIDS PATIENTS' was conducted in Department of ophthalmology, KLE'S Dr Prabhakar Kore Hospital and Medical Research Centre, Belgaum.

Study design

One year cross sectional study.

Study period

The present study was conducted during January 2009 to December 2009.

Method of collection of data

Source of Data

Patients known to be positive for HIV infection with or without AIDS on treatment/without treatment, and have determined their CD4+T lymphocyte cell count, attending outpatient clinics and admitted in inpatient wards at Medical/Ophthalmic departments, belonging to any age and of either gender at KLE'S Dr.Prabhakar Kore Hospital and Medical Research Centre, Belgaum, were enrolled in this study.

Sample size

A sample size of 100 cases.

Sampling procedure

In this study taking 50% as reference value[10], sample size is calculated using formula.

$$n = \frac{4pq}{d^2}$$

where p = Prevalence = 50%

q = 100-p = 50%

d = absolute error = 10%

$$n = \frac{4 \times 50 \times 50}{100} = 100$$

Selection criteria

Inclusion Criteria

- All patients who are seropositive to HIV
- Seropositive HIV patients with or without AIDS
- Seropositive HIV patients in whom CD4+T cell count has been determined

Exclusion Criteria

- Seropositive HIV patients with Diabetes mellitus (DM)
- Seropositive HIV patients with Hypertension (HTN)
- Patient not given the consent

Methodology

After obtaining the informed consent, patients were enrolled in the study. Detailed evaluation of the patient including the detailed history by personal interrogation either with the patient or their relative in case patient is unconscious was noted. Emphasis was given to elicit history of high risk behaviour, blood transfusion, intravenous drug abuse, and other habits. Family history, status of the spouse if

married and children if present, weather dead or alive and the cause of death noted. History regarding ocular complaints was enquired in detail.

General physical examination and systemic examination by an internist and relevant investigations to rule out Hypertension and Diabetes mellitus were obtained and recorded. The clinical stage of the diseases was defined using World Health Organisiation (WHO) clinical staging criteria. The HIV status of all the patients verified and the CD4+ T cell count was obtained.

The CD4+T cell subset analysis was performed by using a standard technique for dual-colour immunofluorescence staining of the peripheral whole blood. The percentage of CD4+ T lymphocyte count was calculated by multiplying the percentage of CD4+ T lymphocytes obtained from single platform flow cytometry using Guava PCA system by the absolute lymphocyte count obtained from complete blood cell count with differential. All flow cytometric analysis of the CD4+T cell count was done by the laboratory which is certified and monitored for quality assurance by College of American Pathologists

The ophthalmic evaluation was done in Ophthalmic OPD in all the patients except for those who were too ill to be moved to the OPD in whom the evaluation was done at bed side.

Detailed ocular examination in all patients was carried out, including visual acuity, anterior segment examination with torch light while examining bed side, Slit lamp bio microscopy in ambulatory patients examined in OPD, and fundus examination with direct and/or indirect ophthalmoscope.

Visual acuity was recorded by Snellen's test chart. In few patients where visual acuity by Snellen's test chart could not be recorded due to poor general

condition and hence clinically recorded bed side by finger counting. Ability to count fingers at 6 meters was considered clinically good. Visual acuity in unconscious or comatose patients, and with dementia or disoriented could not be tested.

Anterior segment examination was performed in all conscious and cooperative patients with diffuse illumination on the Slit lamp. The pupils were dilated with Phenylephrine 5% and Tropicamide 0.8% combination eye drops. Direct and indirect ophthalmoscopy was performed in all patients. Documentation of relevant findings of the ocular adnexa and eye were made in the form of external photography, fundus diagrams and fundus photography.

The relevant treatment for ocular complaints was instituted along with the consultation with the physician for systemic condition when required.

Main parameters Studied

1. **Prevalence rate** of ocular manifestations in HIV/AIDS patients.
2. **Association** between CD4+T lymphocyte cell count and ocular manifestations of HIV/AIDS.

STATISTICAL ANALYSIS:

- Prevalence rate of ocular manifestations of HIV/AIDS as the percentage of the total patients examined having ocular manifestation of HIV/AIDS.
- Association between ocular manifestations of HIV/AIDS & CD4+T cell count is analysed using Chi-square (χ^2) test.

RESULTS

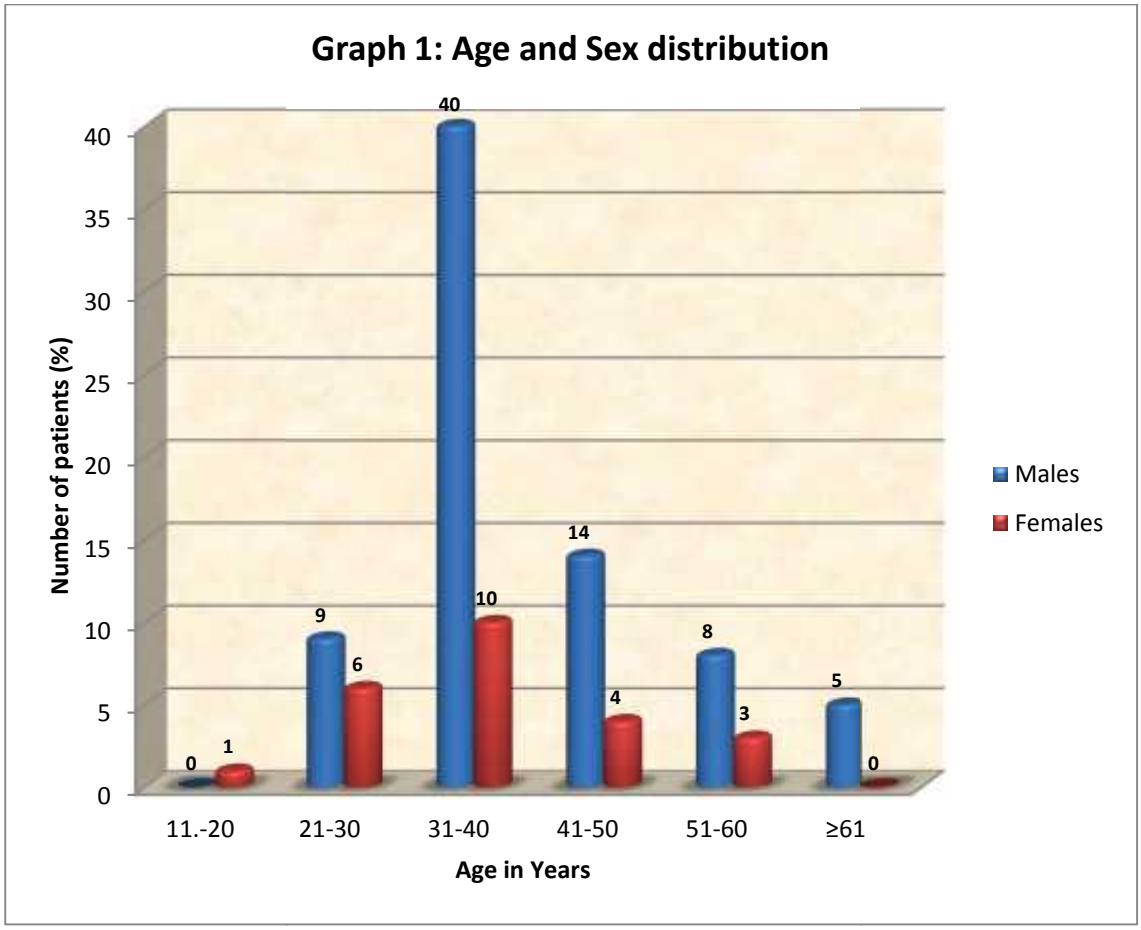
The present study was conducted on 100 patients who are known to be positive for HIV infection with or without AIDS on treatment / without treatment, and have determined their CD4+T lymphocyte cell count at Department of Ophthalmology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum during study period. Prevalence rate of ocular manifestations in HIV/AIDS patients and association between CD4+T lymphocyte cell count & ocular manifestations of HIV/AIDS were studied.

The data obtained was tabulated as below.

TABLE 01 - Age and Sex distribution:

n=100

Age (Years)	Males		Females no		Total no	
	Nos.	Percentage	Nos.	Percentage	Nos.	Percentage
11-20	00	0	01	1	01	01
21-30	09	09	06	06	15	15
31-40	40	40	10	10	50	50
41-50	14	14	04	04	18	18
51-60	08	08	03	03	11	11
≥61	05	05	00	00	05	05
TOTAL	76	76	24	24	100	100

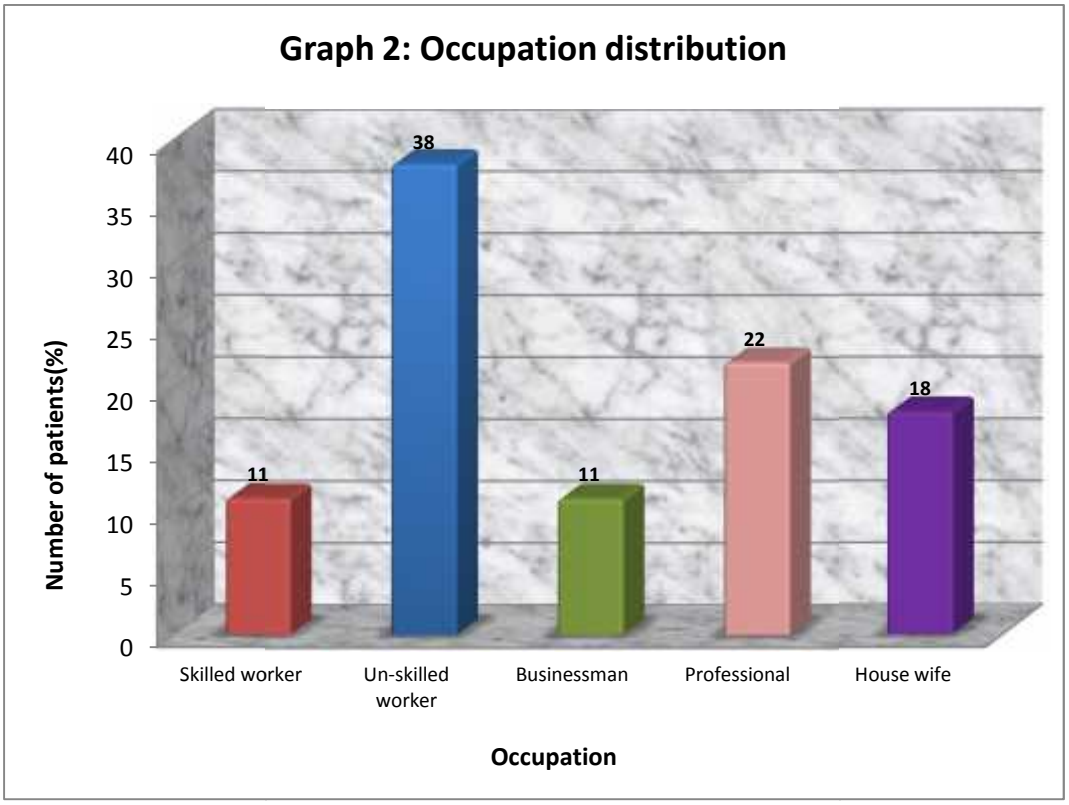


In the present study the mean age of the patients was 39.81years with standard deviation (SD) 10.87 years. The age of the patient ranged between 14 years to 76 years. The mean age was 40.48 years in males and 37.66 years in females. There were 76 (76%) males and 24 (24%) females. Both among males and females most of the patients were in the range of 31-40 years that is 52(52%) males and 41(41%) females.

TABLE -02: Occupation distribution:

n=100

Occupation	No. of cases	%
Skilled worker	11	11
Un-skilled worker	38	38
Businessman	11	11
Professional	22	22
House wife	18	18
TOTAL	100	100

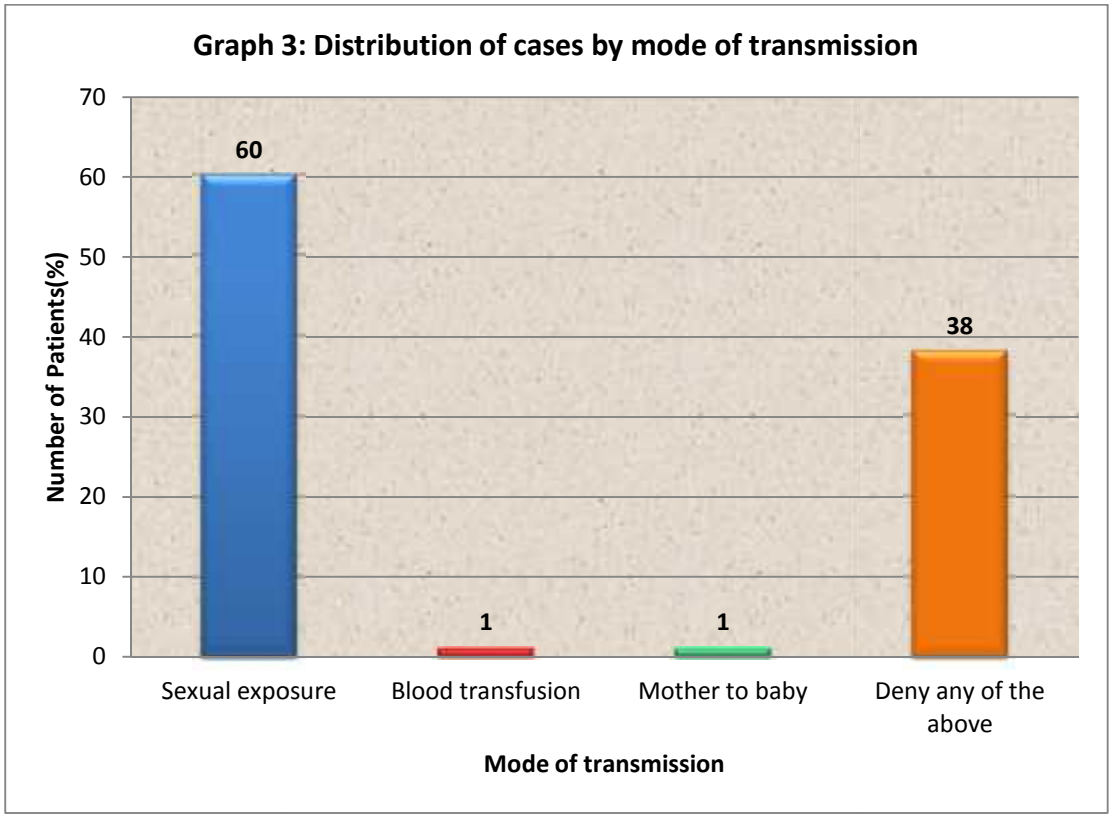


In this study majority of the patients that is 38 (38%) were unskilled workers and among them most of the males were farmers (28 patients, 28%), followed by drivers & porters i.e 9 (9%) patients each. Among females most of them were house wives (18 patients, 18%). 22 (22%) patients were professional workers.

TABLE -03: Distribution of cases by mode of transmission:

n=100

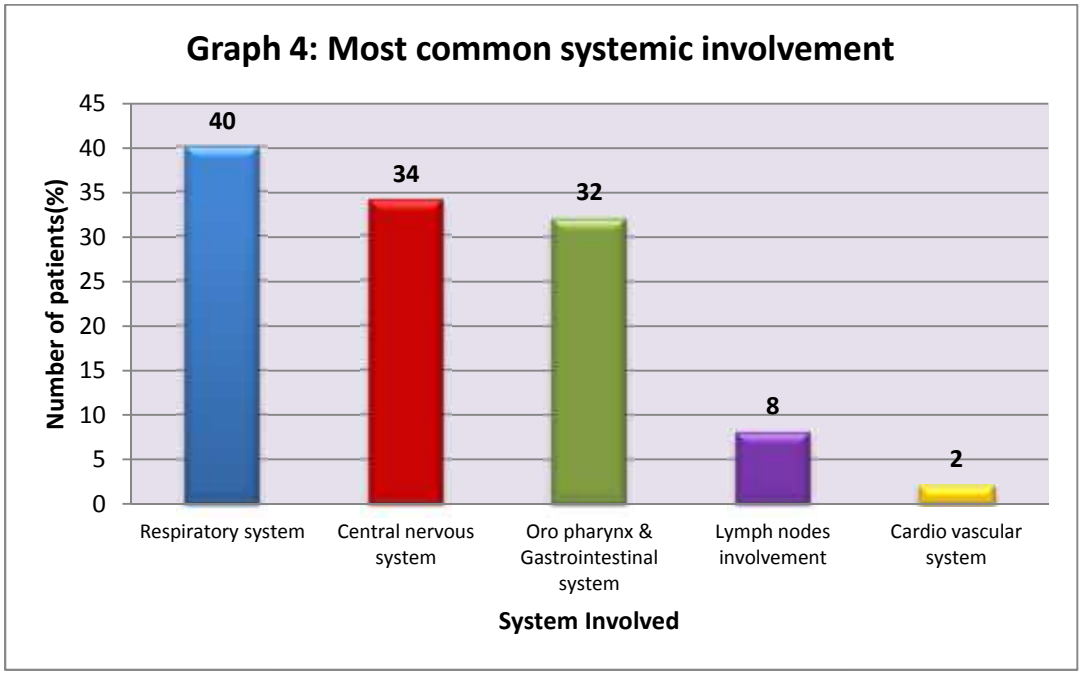
Mode of transmission	No. of Cases	%
Sexual exposure	60	60
Blood transfusion	01	01
Mother to baby	01	01
Deny any of the above	38	38
TOTAL	100	100



Of the total 100 patients majority i.e.60 (60 %) patients had acquired HIV infection by sexual transmission. One child aged 14 years had acquired infection perinatally and in one patient the mode of acquiring infection could be traced to blood transfusion. 38 (38%) of patients denied any of the above routes of transmission of infection.

TABLE -04: Most common systemic involvement

System involved	%
Respiratory system	40
Central nervous system	34
Oro pharynx & Gastrointestinal system	32
Lymph nodes involvement	08
Cardio vascular system	02

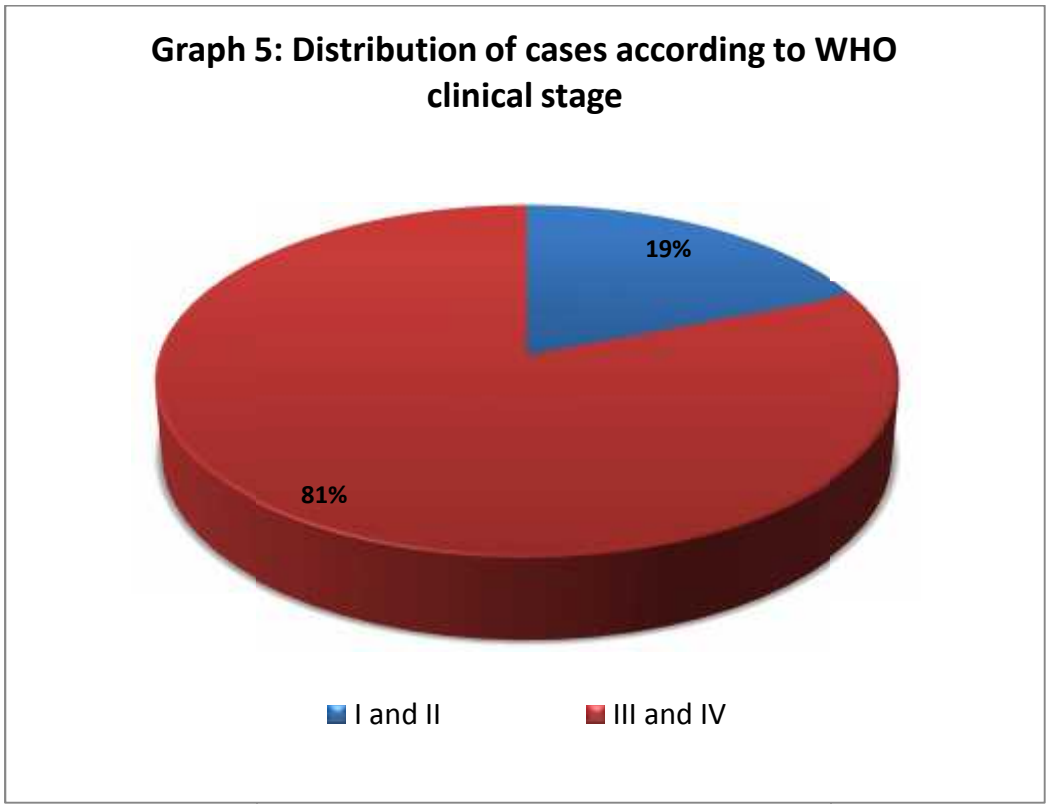


In the present study majority of the patients i.e. 40 (40%) patients had respiratory system involvement mainly in the form of pulmonary tuberculosis and its related complications in 23(23%) patients. 34 (34%) patients had CNS involvement and among them majority that is 26 (76.4%) patients had manifestations mainly in form of meningitis, meningo-encephalitis and encephalitis and 3 (8.8%) patients had cerebro vascular accident. 32(32%) patients had Oro pharynx and gastrointestinal system involvement in the form of oral and esophageal candidiasis in14 (14%) patients, and 11 (11%) had Acute gastro enteritis.

TABLE -05: Distribution of cases according to WHO clinical stage

n=100

WHO clinical stage	No. of Cases	Percentage
I and II	19	19%
III and IV	81	81%
TOTAL	100	100%



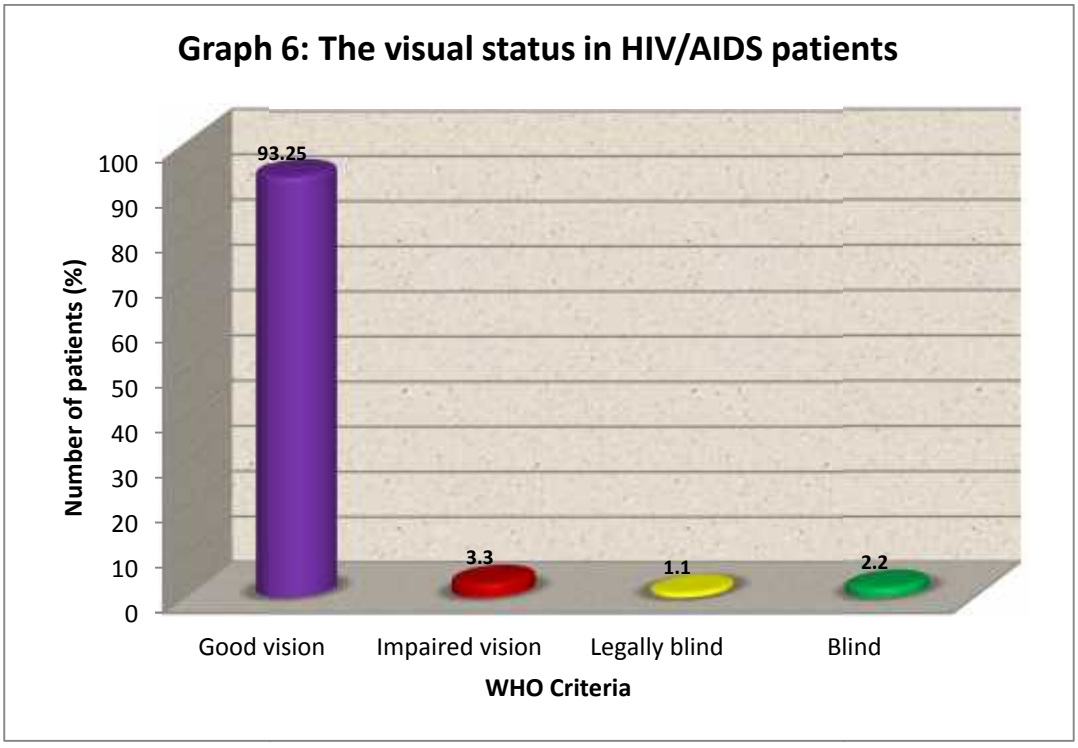
In the present study majority of the patients belonged to WHO clinical stage III and IV that is 81 (81%) patients. 19 (19%) patients belonged to WHO clinical stage I and II.

TABLE-06: The visual status in HIV/AIDS patients:

n = 89

WHO criteria	BCVA	Total number of patients (%)
Good vision	6/6-6/18	83(93.25%)
Impaired vision	6/24-6/60	03(3.3%)
Legally blind	6/60-3/60	01(1.1%)
Blind	<3/60	02(2.2%)

*In 11 patients vision could not be assessed as the patients were unconscious. Hence for this table n=89

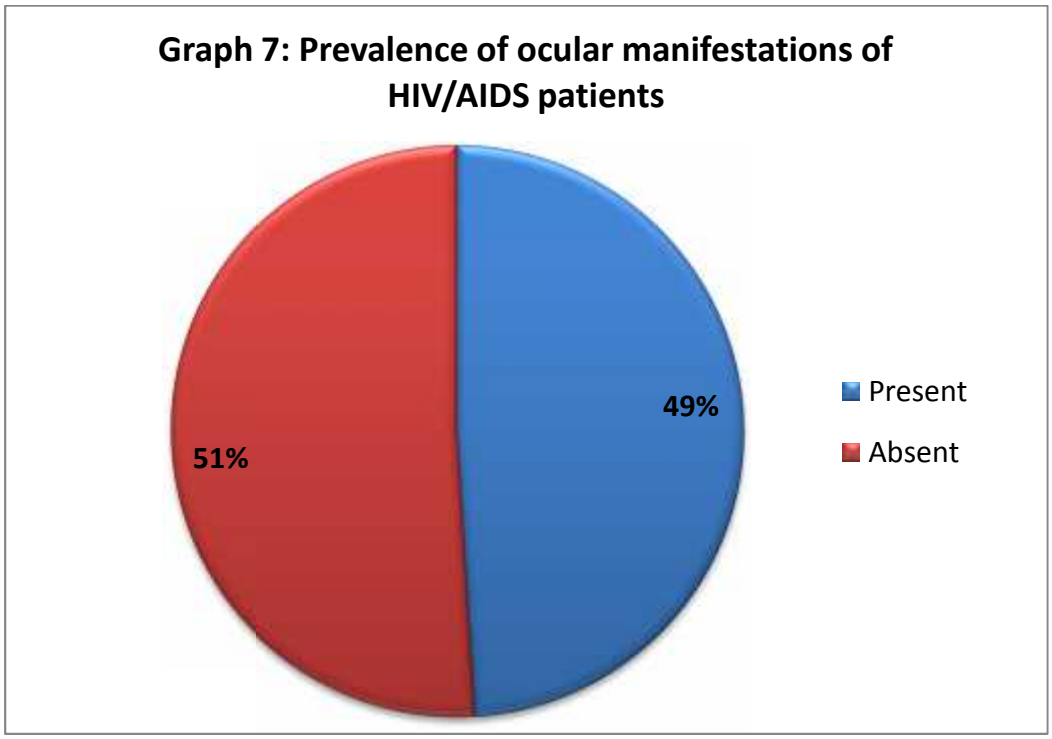


Of the 89 patients, 83 (93.2 %) patients had good vision, 3 (3.3%) patients had impaired vision and 2 (2.2%) patients were blind. 38 (42.6%) patients had uncorrected refractive error, 37(41.5%) patients had normal vision, and 4 patients had cataract.

TABLE -07: Prevalence of ocular manifestations of HIV/AIDS patients:

n=100

Present	Absent	Total
49	51	100



In the present study, the ocular manifestations of HIV infection/AIDS were found in 49 (49%) of the patients. 51 (51%) patients with HIV infection/AIDS had no ocular abnormality.

TABLE-08: Ocular manifestations in HIV/AIDS patients:

Ocular Manifestation	No
I. A) Adnexal lesions	
1) Molluscum contagiosum of the eye lids.	02
2) Herpes zoster ophthalmicus (HZO)	01
3) Multiple chalazion	01
4) Lid erosions bacterial infection	01
II. Anterior segment lesions in HIV/AIDS	
1) Dry eye	06
2) Anterior uveitis(HZO & CMV)	02
3) Conjunctival microvasculopathy	01
4) Infective Keratitis (Herpes simplex)	01
5) Exposure keratitis	01
6) Necrotizing Scleritis	01
III. Posterior segment lesions in HIV/AIDS	
1) HIV retinopathy	22
2) CMV retinitis	04
3) Choroidal tubercles	03
4) Toxoplasmic retinochoroiditis	01
5) ARN (HSV)	01
IV. Neuro Ophthalmic lesions in HIV/AIDS	
1) Papilloedema	07
2) Cranial nerve palsies	03
TOTAL	57*

* The total number of ocular manifestation is greater than the prevalence that is 49% because more than one finding was present in few of the patients.

This table shows the various ocular manifestations of HIV infection and AIDS. In this study the most common ocular manifestation was HIV retinopathy found in 22 (22%) patients followed by papilledema in 7 (7%) patients and dry eyes in 6 (6 %) patients. Posterior segment manifestations constituted 31% of the findings.

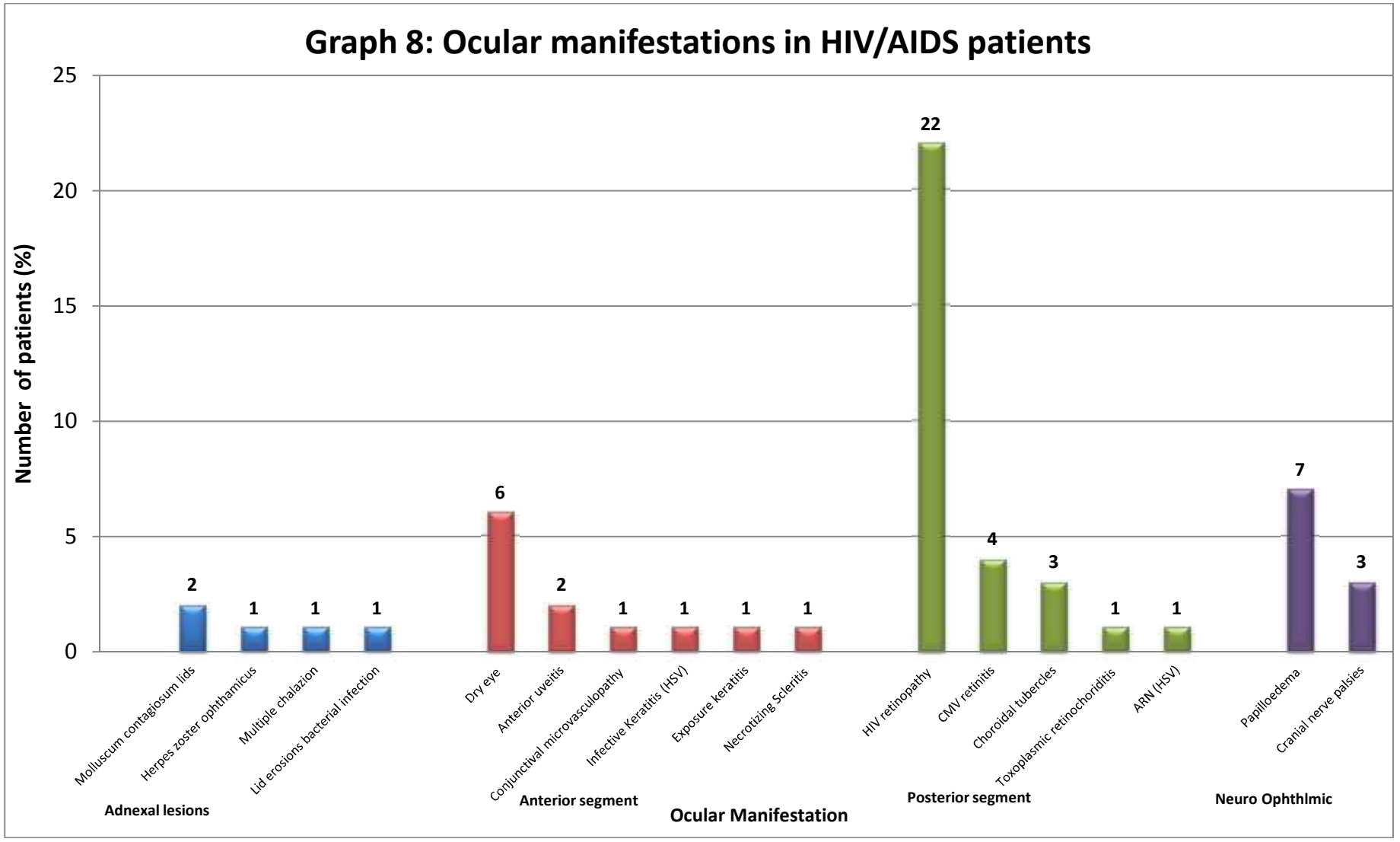
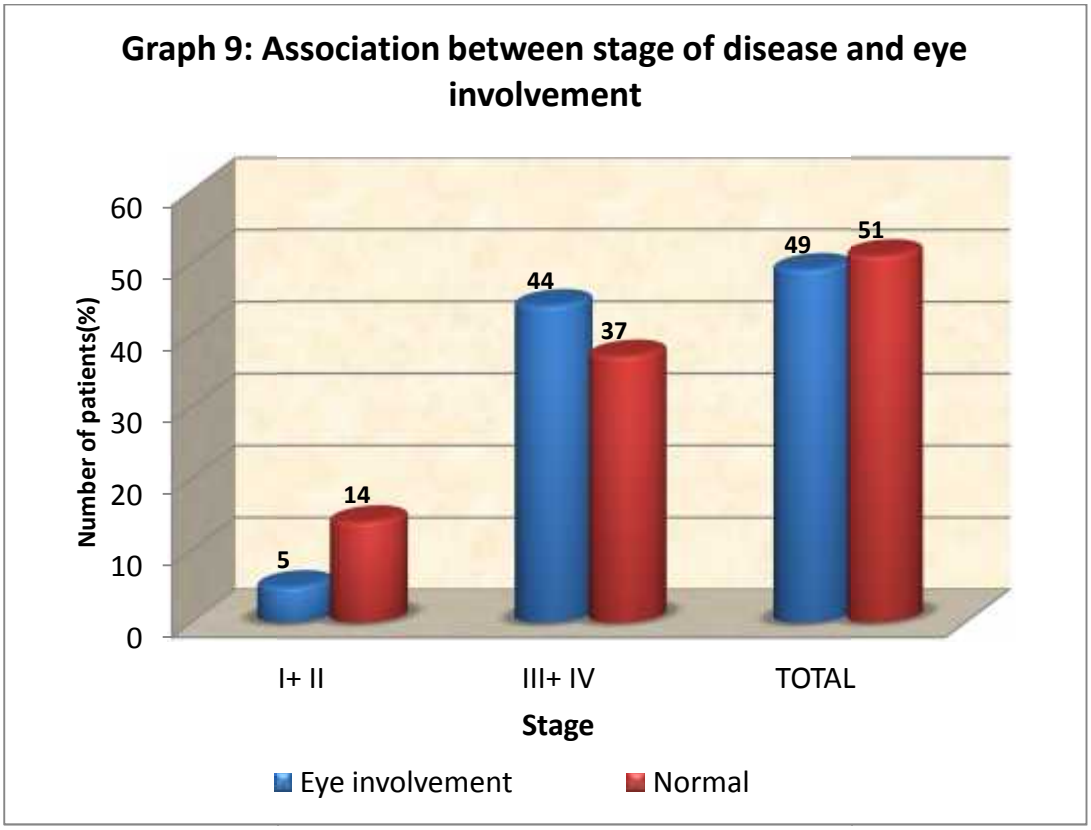

Graph 8: Ocular manifestations in HIV/AIDS patients
Number of patients (%)
25
20
15
10
5
0
2
1
1
1
6
2
1
1
1
1
22
4
3
1
1
7
3
Molluscum contagiosum lids
Herpes zoster ophthamicus
Multiple chalazion
Lid erosions bacterial infection
Dry eye
Anterior uveitis
Conjunctival microvasculopathy
Infective Keratitis (HSV)
Exposure keratitis
Necrotizing Scleritis
HIV retinopathy
CMV retinitis
Choroidal tubercles
Toxoplasmic retinochoriditis
ARN (HSV)
Papilloedema
Cranial nerve palsies
Adnexal lesions
Anterior segment
Posterior segment
Neuro Ophthlmic
Ocular Manifestation

TABLE -09: Association between stage of disease and eye involvement:

n=100

Stage	No. of Cases	Eye involvement	Normal
I+ II	19	05	14
III+ IV	81	44	37
TOTAL	49	49	51
Chi-square= 4.84 p =0.02 , p<0.05			



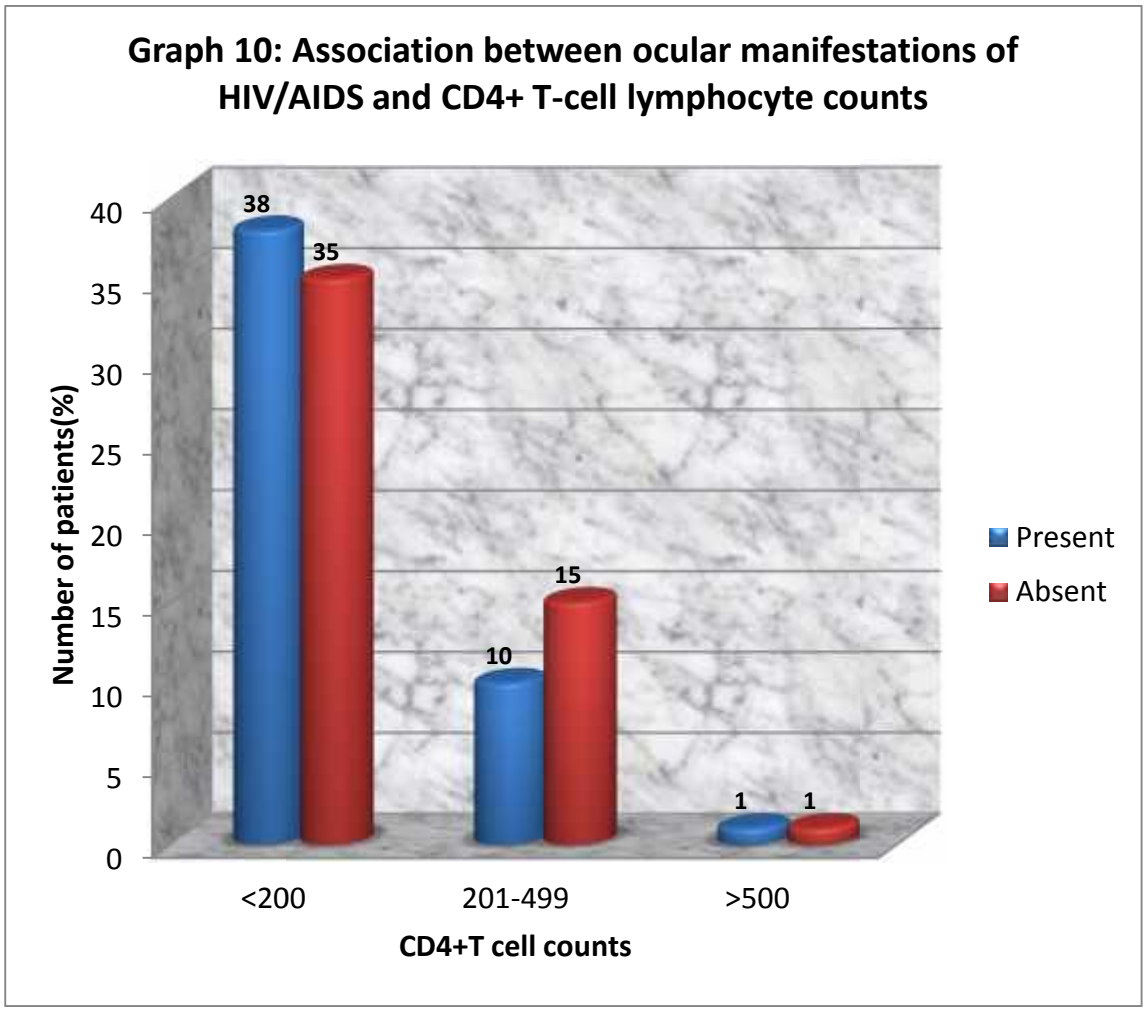
In the present study majority of the patients belonged to WHO clinical stage III and IV that is 81 (81%) patients. Among those 81 patients, 44 (54.3%) patients had ocular manifestations of HIV/AIDS.

Chi-square analysis showed that the prevalence of ophthalmic lesions associated with HIV infection was significantly higher in those with WHO clinical stages 3 & 4. (p value<0.05)

TABLE: 10: Association between ocular manifestations of HIV/AIDS and CD4+ T-cell lymphocyte counts

n=100

CD4+T cell counts (/µl)	Present		Absent		Total	
	No. of cases	Percentage	No. of cases	Percentage	No. of cases	Percentage
≤200	38	38	35	35	73	73
201-499	10	10	15	15	25	25
≥500	01	01	01	01	02	02
Total	49	49	51	51	100	100
Chi-square- 1.443 p =0.486 (p<0.05)						



In the present study 73 (73%) patients had CD4+T cell lymphocyte counts of ≤200 cells/µl with an average cell count of 151cells/µl and the geometric mean of 89.4cells/µl. 25 (25%) patients had CD4+T cell lymphocyte counts in the range of 201-499 cells/µl and only 2% with CD4+T cell lymphocyte counts ≥ 500 cells/µl.

Of the 49 patients with ocular manifestations, 38 (77.7%) patients had CD4+ T cell counts ≤200 cells/µl, 10 (20.4 %) patients with CD4+T counts of 200 cells/µl and 1 (2.04%) patient had CD4+T cell count of >500cells/ µl. Chi square analysis of the data revealed p value of 0.486 which is not clinically significant.

DISCUSSION

The present cross sectional study was conducted on 100 patients who were known to be positive for HIV infection with or without AIDS on treatment / without treatment, and have determined their CD4+T lymphocyte cell count, at Department of Ophthalmology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum during study period of January 2009- December 2009.

HIV/AIDS affects multiple organs of which ocular involvement is common. It affects all the parts of eye leading to blindness. Estimates of 2.47 million people infected by HIV infection are living in India. Therefore the role of ophthalmologist in the management of HIV infected patient is increasingly becoming important in preserving vision by early diagnosis and treatment.

I: SOCIO DEMOGRAPHIC CHARACTERISTICS OF STUDY PARTICIPANTS:

Age and sex distribution:-

In the present study the mean age of the participants was 39.81 years, standard deviation (SD) 10.87 years, ranging from 14 years–76 years. Majority i.e. 50 (50%) participants were in the age group of 31-40 years. 76 (76%) patients were males and 24 (24 %) patients were females. The male: female ratio was 3.2:1. 40 (52%) males and 10 (41%) females were in the age group of 30-40 years followed by 09 (11.8%) males and 6 (25 %) females were in the age group of 21-30 years age group.

Cochereau I et al in a study in Africa in 1999 has found the mean age of 37 years and the male: female sex ratio was 1.85.[67] In a similar study in India in 2000, Biswas et al found the median age of the participants being 31 years and most patients

(76%) belonged to age group of 20 years – 40 years. Among the study population 77% was constituted by males and 23% by females. [68] In a study in Northern India, Attili V S have reported the mean age of the patients of 37.6 years and a higher ratio of HIV infected males of 3.7: 1 as compared to females in 2006.[69]

Serial no	Authors	Year	Mean age	Ratio M:F
1	Cochereau I [67]	1999	37	1.85
2	Biswas J [68]	2000	31(Median)	3.3
3	Atilli V S [69]	2006	37.6	3.7
4	Present study	2010	39.81	3.2:1

In this series the highest prevalence is in the 3rd and 4th decade with the mean age of 39.81 years. The present study in accordance with the previous studies has a similar pattern of age and sex distribution. In India, the incidence of HIV infections in men greater than in women can be attributed to the low educational status and delay in seeking medical attention by the female population.

Occupation distribution:-

More than one third of the participants in this study were unskilled workers i.e. 38 (38%) participants; majority of them were constituted by farmers 28 (28%) participants, drivers 9 (9%) participants, porters 7 (7 %) participants and others (3%). 11 (11 %) participants had business as their main occupation, and rest 22 (22 %) participants were in various other services. Among 24 (24%) females majority were house wives i.e. 18 (75%) females, 4 (16%) were skilled workers 2 (8%) were unskilled workers. None in our study were commercial sex workers; probably those females addressed themselves as house wives because of social issues.

A data published in 2006 by United Nations development programme on socio economic impact of HIV and AIDS in India, showed similar results in which 21 % were farmers and cultivation labours, 9% were businessmen, 6.5% were transport workers and 22% were professionals [70]. A study by Sharma S K et al reported similar results in which majority of the participants were unskilled laborer (29%) followed by businessmen (17.9%), drivers (10.4%), and others 18%.[71] The higher prevalence among unskilled workers is due to the lack of education and awareness regarding the modes of transmission.

Distribution of cases by mode of transmission:-

The present study shows the most common risk of exposure is sexual route which is observed in 60 (60 %) participants, of which one person acquired the infection by homosexual route and was found to be exploited by his friends as he seemed to be of low IQ and innocent. A 14 year old female child with CMV retinitis had acquired infection perinatally and in 1 (1%) patient the mode of acquiring infection could be traced to blood transfusion. Rest of the 38% denied revealing the route of infection.

Biswas J et al have similarly reported that 70% of the patients had acquired HIV infection by heterosexual route and 5% by homosexual route.[68] A similar study has reported relatively higher percentage of transmission through heterosexual route in 94% of the patients, homosexual contact in 2.7% of the patients, blood transfusion and intravenous drug abuse in 1.3% of the patients. [72] A study conducted in Thaiwan showed different figures as compared to Indian studies. In this study 46% of the participants were heterosexual, 41% were homosexual or bisexual, 7.8 % were

homosexual, 7.8% were hemophiliacs and 4.5% were both drug abusers and were heterosexual.[73]

Serial no	Author	Year	Route of transmission (%)		Blood transfusion (%)	Perinatally (%)
			Hetero sexual	Homo sexual		
1	Biswas J [68]	2000	70	05	12	6
2	Chiou S H[73]	2000	46	41	7.8	-
3	Pathai S [72]	2009	94	02.7	1.3	-
4	Present study	2010	59	01	1	1

This series shows heterosexual route of transmission is the major route of transmission in India as compared to other countries. This could mean that in India homosexual population is less due to cultural difference as compared to other countries or they are not revealing the history. In the present study 38 % patients denied any history suggestive of mode of transmission. This could be due to hesitancy of revealing the history for social reasons.

II. CLINICAL PROFILE OF THE PARTICIPANTS

Systemic illness:-

In the present study 40 (40 %) patients had pulmonary affection of which Tuberculosis in 28 (70%) participants constituted the most common systemic association with HIV/AIDS. 34 (34 %) participants had Central nervous system abnormality; majority of them had meningitis (23 participants), 7(7%) participants had tubercular meningitis and encephalitis, 6 (6%) participants had cryptococcal meningitis, and 4(4%) participants had toxoplasmic meningitis. Oral and esophageal

Candidiasis was found in 14 (14 %) patients and lymph node involvement in 8 (8%) of patients. 31(31%) patients had tuberculosis (pulmonary and extra pulmonary) .A study conducted in Chennai in 1999 reported tuberculosis as the most frequently associated systemic illness in 50% of the patients and oral candidiasis in 29% of the patients.[59] Pathai et al in a study have reported similar findings in which 53% of the patients had either current or a previous history of tuberculosis .[72]

Our findings are consistent with other studies in which tuberculosis is the most common systemic infection associated with HIV/AIDS, which is not unexpected because pulmonary tuberculosis is widely prevalent in India.

Clinical stage:-

In our study, 81(81%) patients belonged to WHO clinical stage 3 and 4 and 19 (19 %) patients belonged to stage 4.

A study conducted in Chennai showed majority (72%) of the patients belonged to CDC criteria group 4.[59] Pathai et al have reported similar finding in a study where 59.7% had symptomatic diseases belonging to WHO clinical stage 3 and 4.[72]

Our study in comparison to the previous studies has similar results. Due to social stigma most people do not seek medical advice until the diseases progresses to an advanced stage. Therefore those with early HIV infection were under represented in this study.

III. OCULAR MANIFESTATIONS:

The visual status in HIV/AIDS patients:

In our study of the 89 patients in whom vision could be recorded, 83 (93.2 %) patients had good vision, 3 (3.3%) patients had impaired vision and 2 (2.2%) patients were blind. 38 (42.6%) patients had uncorrected refractive error, 37(41.5%) patients had normal vision, and 4 (4.4%) patients had cataract.

Shah SU et al has reported that HIV/AIDS is a significant cause of visual impairment (6%) including blindness.[22] Biswas J et al have reported that in due course of the disease process visual acuity worsened in 9 eyes of the 163 eyes due to various ocular lesions.[68]

In our study majority i.e. 83 (93.2%) had good vision. This shows that diminution of vision is rarely complained of by the patients suffering from HIV infection because of the good vision in the better eye. It is important to note that 38 (42.6%) of the patients had uncorrected refractive error. HIV /AIDS may be an important factor for the patients not seeking treatment which could be attributed to the stigmata of the disease as well as the disabling illness associated with HIV/AIDS.[69] The prevalence of the blindness due to HIV/AIDS may be under estimated in a cross sectional study like ours as many of them spend last days of their lives in their homes. So visual acuity cannot be taken as the indicator of the ophthalmic manifestation. Routine screening is the only way to detect the ophthalmic manifestations of HIV infection.

Prevalence of ocular manifestations:-

In our study the ocular manifestations of HIV/AIDS was found in 49 (49%) patients. Lewallen S in a study of 99 patients with AIDS reported that 26% of the patients had abnormal ocular findings and rest 73 % had normal ocular examination.[48] A study done in Africa by Cochereau I et al reported the prevalence of AIDS related eye diseases in 21 % of the patients.[67] Biswas J et al in 1999 reported ocular lesions in 45.7% of the HIV infected patients examined at a referral eye center in Chennai.[59] A recent study by Attili V S et al have reported 19% of prevalence of eye manifestation in patients with AIDS.[69]

Serial no	Authors	year	Prevalence (%)
1	Lewallen S [48]	1994	26
2	Cochereau I [67]	1999	21
3	Biswas J [59]	1999	45.7
4	Attili V S [69]	2006	19
5	Present study	2010	49

This series represent higher prevalence of ocular manifestations as compared to African study that attribute it to early death of the patients in Africa due to the diseases process.[67] Our study has comparable results to the study in Chennai. The higher prevalence in our study as compared to other studies can be attributed to the examination of all HIV infected patients including those with no visual complaints but had ocular findings and higher number of patients in WHO clinical stage 3 and 4 with various complications, for which patients were being referred to our tertiary center. The prevalence is well within the range of 50-100% life time cumulative risk as quoted by Kestenyl PG et al.[10]

Ocular manifestations in HIV/AIDS patients:-

Posterior segment manifestations:-

HIV Retinopathy:

In the present study, 22 (22%) patients had HIV retinopathy as the most common ocular finding. Of these 22 patients, 17 (77.2%) had cotton wool spots. 6 (27.2%) patients had retinal hemorrhages in the form of flame shaped hemorrhages, blot hemorrhages and white centered ('Roth spots') hemorrhages. Among 17 patients with cotton wool spots, 16 had cotton wool spots only, 1 patient had associated blot hemorrhage. In 1 patient, single CWS was found in both eyes.

Kupperman et al, found HIV related non infectious retinal vasculopathy in 35 % patients.[41] Lewallen S et al in a study of retinal findings in Malawian patients with AIDS reported 13 % of patients had cotton wool spots.[48] Biswas J et al in a study have reported 15 % prevalence of the HIV retinopathy as the second most common findings.[68]

Serial no	Authors	year	Prevalence (%)
1	Kupperman [41]	1993	35
2	Lewallen [48]	1994	13
3	Biswas J [68]	2000	15
4	Present study	2010	22%

Our findings are consistent with the other studies in which HIV retinopathy is the most common ocular manifestation of HIV/AIDS. The reason for the higher prevalence of HIV retinopathy can be due to screening of the patients who do not have visual complaints as CWS rarely cause symptoms and relatively higher number of patients in WHO clinical staging 3 and 4. In our study one patient had single CWS in both eyes. This highlights the fact that in absence of DM and HTN presence of even a single CWS in an otherwise normal fundus is suggestive of HIV infection.[74]

CMV Retinitis:

In the present study Cytomegalovirus retinitis was found in 4 patients (4%).

Biswas et al in a study have reported CMV retinitis in 17 % of the patients.[68] Jabs DA et al in 2007 observed CMV retinitis as the most frequent ocular finding in 22.7% of the study participants. The same study also reported that the patients with CMV retinitis at the time of enrollment during their study had a significantly greater mortality than those without CMV retinitis with relative risk of 2.3.[75, 76] In a similar study by Pathai S et al, CMV retinitis was found in 8.7% of the patients with HIV infection enrolling for HAART therapy in India.[72]

Holland et al observed that the introduction of HAART has markedly reduced the incidence of CMV retinitis, but has not eliminated new cases all together.[77]

Serial no	Authors	year	Prevalence (%)
1	Biswas J [68]	2000	17
2	Jabs D A [75]	2007	22.7
3	Pathai S [72]	2009	8.7
4	Present study	2010	04

The proportion of patients who had CMV retinitis in our series (4%) was lower than the rate reported by other studies. The reason can be the peripheral lesions which do not cause the visual impairment go undiagnosed. In western countries majority of the patients are put on anti-retro viral therapy following which the subclinical CMV becomes manifest in the form of IRU. In our study less number of patients were newly started on HAART therapy. So no case with IRU due to CMV infection was found resulting in over all less prevalence of CMV retinitis.

Ocular Tuberculosis:

In the present study 3 (3%) out of the 23 patients with active tuberculosis patients had choroidal tubercles. Of these 3 patients, 2 patients had miliary tuberculosis. Another patient was referred for ophthalmic examination with diagnosis of HIV infection with pyrexia of unknown origin who was found to have choroidal tubercles. Later chest X- ray proved the diagnosis of pulmonary tuberculosis.

Beare N A V et al in a study have reported choroidal granulomas in 2.8 % of HIV positive patients with Tuberculosis.[47]

Babu R et al in a study reported ocular TB in 1.95% of the HIV/AIDS patients. Most common presentation was choroidal granulomas in 53% of patients with ocular TB.[46]

Serial no	Authors	Year	Prevalence (%)
1	Beare N A [47]	2002	2.8
2	Babu R[46]	2006	1.95
3	Present study	2010	3

The prevalence of choroidal tubercles in HIV infected patients with tuberculosis is comparable with the previous studies. However we did not find large choroidal granuloma in our study.

Neuro- ophthalmic manifestations:

In our study 34 (34%) patients had neurological abnormalities. Of the 34 patients 10 (29.4%) patients had neuro ophthalmic abnormality. They included papilledema in 7 (70%) patients, cranial nerve palsy in 3(30%) patients.

Hong Y J et al reported complete binocular blindness as the first manifestation of HIV related cryptococcal meningitis.[62] Karna et al reported a case of multiple cranial nerves (sixth, ninth, tenth and twelfth nerve) palsy in a HIV positive patient.[78] Mawanza J C et al reported 60 % abnormal neuro-ophthalmological disorder in HIV infected subjects with neurological manifestion.[60] Mansour A M in a study on Neuro ophthalmic findings in acquired immunodeficiency syndrome reported abnormalities in the form of perineurits, papilledema, papillits, retro bulbar neuritis, and optic atrophy in about 6% of the patients.[79] Biswas et al reported optic atrophy in 7% and gaze palsy in 1 % patient in a study on ocular lesions in HIV-positive cases.[68] In a study, Attili V S has reported papilledema in 29.5% of patients with ocular manifestations of AIDS as the common neuro-ophthalmic manifestation.[69]

Our study had majority of the findings as papilledema and the prevalence of neuro ophthalmic findings is similar to other Indian studies.[68]

Other posterior segment manifestations:

Other posterior segment manifestations in our study included ARN in 1(1%) patient and Toxoplasmic retino choroidits in 1(1%) patient.

Cochereau et al has reported viral retinitis in 1% of the patients in a study in Africa. [67] Morgalis T P et al observed 4% patients developing necrotizing retinitis following herpes zoster ophthalmicus in patients with HIV infection.[28] Gharai S et al has reported Isolated Unilateral ARN syndrome as the initial manifestation of HIV.[80] Shah S U et al reported immune recovery vitrits in 3 % of the patients of HIV/AIDS.[21] Biswas J et al has reported chorioretinits in 5 % of the patients and relatively higher incidence of retinal detachment in 5 % of patients .[68] These other findings have been relatively less common in other studies and are comparable with the present study.

Anterior segment manifestions:-

In the present study adnexal and anterior segment findings were less common as compared to the posterior segment findings.

Most of the patients had dry eyes (6 cases, 6%) ranging from mild to moderate dryness with main complaints of foreign body sensation and grittiness.

Dry eye has been reported to be present in 20-38.8% of the patients reported in a review literature on anterior segment manifestation in HIV by Biswas J.[26]

Though in the present study it is most common anterior segment manifestation relative prevalence is low compared to previous studies.

In the present study Molluscum contagiousm of the eye lids was found in 2 (2%) patients. Herpes zoster ophthalmicus with associated anterior uveitis, herpes simplex keratitis, multiple chalazion and lid erosion secondary to bacterial infection were less common and noted in 1(1%) patient each. An unconscious patient had exposure keratitis. Conjunctival microvasculopathy (aneurysum) and necrotizing scleritis were other findings in this study. There was no ocular lesion of kaposis sarcoma in this study which is in agreement with the similar study in India.[72]

In a study by Biswas et al, Molluscum contagiosum was observed in 1.4 % of the patients. The same study also reported 3 cases of isolated anterior uveitis for which no specific cause could be found. Also one patient with herpes zoster ophthalmicus had non granulomatous anterior uveitis.[59] In one of the largest study on ophthalmic manifestations of HIV infection in 781 patients Jabs DA et al observed herpes zoster ophthalmicus infection in 3% of the patients and 49% of these patients developed ocular complication of which most common was keratitis in 26 % followed by uveitis in 23%. The same study reported kaposis sarcoma in 2% of the patient.[81]

Similarly Couchereau I et al have found lesser frequency of anterior segment manifestation as compared to posterior segment manifestations with 6% of patients having anterior segment inflammation.[67]

In a study of 460 patients with HIV in North India, authors found molluscum contagiosum of lids in 6 patients, conjunctivitis in 3 patients and blepharitis in 34 patients. This study similar to our study reported HIV retinopathy as the commonest eye manifestation in patients with HIV infection.[69]

Thus in our series anterior segment findings were less frequent. This is in agreement with other studies from India which report such manifestations to be relatively less frequent than the posterior segment findings.

Association between stage of disease and eye involvement:-

In the present study majority of the patients i.e. 81 (81%) patients belonged to WHO clinical stage III and IV. None of the patients in stage I had ocular lesions and 44 (54.3%) patients belonging to stage III and IV had ocular lesions. Chi-square analysis showed that the prevalence of ophthalmic lesions associated with HIV was significantly higher in those with WHO clinical stages III or IV (p value < 0.05).

In a study by Pathai et al the prevalence of ophthalmic lesions associated with HIV was significantly higher in those with WHO clinical stages 3 or 4. They also found that those with advanced HIV as defined by WHO clinical stage were nine times more likely to be at risk of developing ocular manifestations of the disease.[72]

Similarly Jabs et al have reported that the HIV patients with eye diseases had more advanced immunodeficiency reflected by advanced WHO stage of diseases.[75]

Our study showed that prevalence of ophthalmic lesions associated with HIV was significantly higher in patients belonging to WHO clinical stages 3 or 4 and is comparable with other previous studies. Thus WHO clinical stage may be important predictors of the presence of HIV related eye disease.

Association between CD 4 + T cell counts and eye involvement:

In the present study, of the 49 patients with ocular manifestations, 38 (77.7%) patients had CD4+ T cell counts ≤200 cells/µl, 10 (20.4 %) patients with CD4+T counts of 200 cells/µl and 1 (2.04%) patient had CD4+T cell count of >500cells/ µl. Chi square analysis of the data revealed p value of 0.486 which is not clinically significant.

Shah SU et al in a study have found the prevalence of the ocular manifestations due to HIV/AIDS to be maximum in patients with CD4+T cell counts 0-50 cells/µl than 51-100 cells/µl. But the difference was statistically not significant.[21] Attili VS et al studied the correlation between CD4+ T cell counts, CRP and ocular manifestations and found a similar result. However there was a clinically significant association between CD+T cell counts and CNS lesions.[69]

In our study we found no association between ocular manifestations and lower CD4+T cell count. This can be due to the generalization of the finding without defining the particular disease. The diagnosis of the patient is based entirely on clinical appearance without laboratory diagnosis as a proof. The distribution of CD4+T cell count used was based on CDC criteria.[18] Also the sample size is low so that to draw a definite conclusion further research needs to be done. Therefore it is important to refer all patients with HIV infection irrespective of the CD4+T cell counts for ophthalmological examination.

Strengths of the study:

All the patients had CD4+T cell counts done by a standard method single platform flow cytometry using Guava PCA system.

All the patients were examined irrespective of the visual complaints.

The studies published till date lacked the objective of the present study to find a definite association between ocular manifestations and the CD4+T cell counts.

Limitations of the study:

Being a cross sectional study we were unable to establish the cause and effect relationship in relation to CD 4+T cell count.

In addition, limited sample size of the study could not give statistical significance for the stated objective.

CONCLUSION

The present study is a hospital based cross sectional study representing the patients with advanced diseases due to HIV infection.

The study concluded that HIV/AIDS is a significant cause of ocular disease with 49 (49%) patients having ocular manifestations of HIV/AIDS. The commonest ocular lesions observed were the posterior segment manifestations such as HIV retinopathy, Papilledema, and CMV retinitis. The less common ocular manifestations seen were the adnexal and the anterior segment manifestations such as Dry eyes and Molluscum contagiosum.

The study shows that the spectrum of the ocular lesions associated with HIV infection in this region is different from elsewhere in the world. The prevalence of CMV retinitis is lower and there have been no cases of Kaposis sarcoma.

The prevalence of ocular manifestations correlated significantly with HIV/AIDS WHO clinical stage 3 and 4. The association between the prevalence of the ocular manifestations and the WHO clinical stages suggest that ocular manifestations are related to HIV diseases progression.

We found no correlation with ocular manifestations of HIV/AIDS and CD4+T cell lymphocyte counts. Additional data and longer follow up are necessary to identify contributing factors and come to a definite conclusion as regards the correlation with CD4+Tcell counts.

HIV/ AIDS may be an important cause limiting the patients from seeking medical care for visual impairment. Screening for ocular complaints is not a reliable method to identify those with the ocular morbidity. Comprehensive ophthalmic

examination of all HIV infected patients with AIDS at regular intervals will help in identifying ocular morbidity early.

There is still a great need for the definitive diagnosis of the ocular lesions in HIV positive patients. The cases of atypical ophthalmic manifestations as an initial presentation of HIV infection highlights the need for increased index of suspicion for HIV infection in young patients. Therefore ophthalmologist need to recognize ocular lesions in HIV infection along with careful and pertinent systemic evaluation with timely referral as it may help in earlier diagnosis and prompt treatment of these cases which otherwise may be missed with serious consequence on the visual function.

SUMMARY

The present study titled 'One year cross-sectional study of ocular manifestations in HIV-positive/AIDS patients evaluated at KLE'S Dr Prabhakar Kore Hospital and Medical Research Centre, Belgaum**"** was carried out to estimate the prevalence of ocular manifestations in a group of patients with HIV/AIDS with the secondary objective to determine the correlation between ophthalmic manifestations of HIV/AIDS and CD4+T lymphocyte cell counts.

100 patients were included in this study, during the period of January 2009 to December 2009. Detailed systemic and ophthalmic evaluation of all the patients was done and CD4+T cell count determined.

The result showed that the majority of the patients belonged to the age group of 31-40 years with mean age of 39.81 years and a higher ratio of HIV infected males of 3.2:1 as compared to females.

More than one third of the participants (38%) were unskilled workers of which majority were farmers (28%) and drivers (10.4%).Among females majority of them were housewives(75%). 60% of the patients had acquired infection by sexual route and 38% denied to reveal the route of acquiring the infection. 81% of the patients belonged to HIV/AIDS WHO clinical staging 3 and 4.

Respiratory system was the most commonly involved system among the patients followed by the central nervous system affection. Tuberculosis (pulmonary and extra pulmonary) was the most common opportunistic infection among the patients.

Of the 89 patients in whom vision was recorded, 93.2% had good vision (BCVA > 6/18). Diminution of vision is rarely complained of by the patients suffering from HIV infection because of the good vision in the better eye.

In our study 49% of the patients had ocular manifestations with posterior segment being more commonly involved than the anterior segment. The commonest ocular lesion was HIV retinopathy, found in 22% of the patients. CMV retinitis (4%) was less common. Common neuro-ophtahlmic manifestation was Papilledema (7%).

The prevalence of ocular manifestations correlated significantly with HIV/AIDS WHO clinical stage 3 and 4. No correlation was found between ocular manifestations of HIV/AIDS and CD4+T cell lymphocyte counts.

In conclusion, AIDS affects the eyes of significant proportion of the patients with HIV/AIDS. We found no association between ocular manifestations of HIV/AIDS and CD4+T cell count. The association between the prevalence of the ocular manifestations and the WHO clinical stages suggest that ocular manifestations are related to HIV diseases progression. Comprehensive ophthalmic examination of all HIV infected patients with AIDS at regular intervals will help in identifying ocular morbidity early.

BIBLIOGRAPHY

1. Rao N A. Acquired immunodeficiency syndrome and its ocular complications. Indian J Ophthalmol 1994; 42:51-63.

2. Simoes EAF, Babu PG, John TJ, Nirmala R, Soloman S, Narayanan L, et al. Evidence of HTLV III infection in prostitutes in India. Indian J Med Res 1987; 87:335-38.

3. Holland GN, Gotlieb MS, Yee RD. Ocular disorders associated with a new severe acquired cellular immunodeficiency syndrome. Am J Ophthalmol 1982; 93:393-402.

4. UNAIDS. 2009 AIDS Epidemic update .Available from: URL:

   http://data.unaids.org/pub/Report/2009/JC1700_Epi_Update_2009_en.pdf

   (Access date - October 03, 2010).

5. Kumarasamy N, Vallabhaneni S, Flanigan TP, Mayer KH and Solomon S. Indian J Med Res 2005 April; 121: 377-394.

6. Ah-Fat FG, Batterbury M. Ophthalmic complications of HIV/AIDS Postgrad Med J 1996; 72:725-730.

7. Jabs DA. Ocular manifestations of HIV infection. Trans Am Ophthal Soc 1995; 93:623-83.

8. Sudharshan S, Biswas J. Introduction and immunopathogenesis of acquired immune deficiency syndrome. Indian J Ophthalmol 2008; 56:357-62.

9. Belfort R. The ophthalmologist and the Global Impact of the AIDS Epidemic LV Edward Jackson Memorial Lecture. Am J Ophthalmol 2000; 129(1):1-9.

10. Kestelyn PG,Cunnigham ET .HIV/AIDS and blindness. Bull World Health Organ 2001; 79:208-13. Available from www.scielosp.org/scielop.php? (Access date 30/06/2008).

11. Biswas J, Madhavan HN, Badrinath SS. Ocular lesions in AIDS: A report of the first two cases in India. Indian J Ophthalmol 1995; 43:69-72.

12. Current Epidemiological Situation of HIV/AIDS - Department of AIDS Control Ministry of Health and Family Welfare Government of India ANNUAL REPORT 2008-2009. Available from: URL: http://www.nacoonline.org/upload/Publication/Annual_Report_NACO_2008-09.pdf. (Access date 06/09/2010*).*

13. Steinbrook R. HIV in India - A Complex Epidemic. Perspective. N Engl J Med 2007 March 15; 356(11):1089-1093 Available from; URL: www.nejm.org/doi/pdf/10.1056/NEJMp078009. (Access date 06/09/2010).

14. Folks TM, Khabbaz RF. Retroviruses and associated diseases in humans, Chapter 38. Topley and Wilson's Microbiology and microbial infection, Virology, Vol 1, 9thedi, London: Arnold publishers; 1998:781-809.

15. Fauci AS, Lane CH. Human Immunodeficiency Virus Disease: AIDS and Related Disorders, Chapter 182. Harrison's Principles of Internal Medicine, 17th edi, New York: The McGraw-Hill Companies; 2008: 1137-1204.

16. National AIDS Control Program National AIDS Control Program Phase III (2006-201): Strategy and Implementation Plan: Ministry of Health and Family Welfare, Government of India. 2006. Available from: URL: http://www.nacoonline.org/upload/Publication/Strategy%20and%20Implementati

on%20Plan%20-%20NACO%20Programme%20Phase%20III%20(2006-2011)%202006.pdf. (Access date 06/09/2010).

17. The 1993 Revised Classification System for HIV Infection and Expanded Surveillance Case Definition for AIDS Among Adolescents and Adults In MMWR 1992 December 18, / 41(RR-17) Available from URL: www.cdc.gov/mmwr/preview/mmwrhtml/00018871.htm. (Access date 14/08/2010).

18. World Health Organisation: Interim WHO clinical staging of HIV/AIDS and HIV/AIDS case definitions for surveillance; African region. Geneva, Switzerland: WHO; 2005:2-8. Available from www.who.int/hiv/pub/guidelines/clinicalstaging.pdf . (Access date 20/07/2010).

19. Biswas J, Fogla R, Gopal L, Narayana KM, Banker AS, Kumarasamy N, Madhavan HN. Current approaches to diagnosis and management of ocular lesions in human immunodeficiency virus positive patients. Indian J Ophthalmol 2002; 50:83-96.

20. Simon V, Ho DD, Karim QA. HIV/AIDS epidemiology, pathogenesis, prevention, and treatment. The Lancet 2006 Aug 5;368(9534): 489 – 504.

21. Shah SU, Kerkar SP, Pazare AR. Evaluation of ocular manifestations and blindness in HIV/AIDS patients on HAART in a tertiary care hospital in western India.Br J Ophthalmol 2009;93:88-90.

22. Biswas J, Kumar AA, George AE, Madhavan HN, Kumarasamy N, Mothi SN and Solomon S. Ocular and systemic lesions in children with HIV .Indian Journal of Pediatrics 2000*;* 67(10*):* 721-724.

23. Hodge WG, Seiff SR, Margolis TP. Ocular opportunistic infection incidences among patients who are HIV positive compared to patients who are HIV negative. Ophthalmology 1998; 105:895-900.

24. Ali R, Kim JY, Henderson BA. Adnexal and anterior segment manifestations of HIV-AIDS. Int Ophthalmol Clin 2007; 47:15-32.

25. Sandor EV, Millman A, Croxson TS, Mildvan D. Herpes zoster ophthalmicus in patients at risk for the acquired immune deficiency syndrome (AIDS). Am J Ophthalmol 1986; 101:153-5.

26. Biswas J, Sudharshan S. Anterior segment manifestations of human immunodeficiency virus/acquired immune deficiency syndrome. Indian J Ophthalmol 2008; 56:363-75.

27. Sellitti TP, Huang AJ, Schiffman J, Davis JL. Association of herpes zoster ophthalmicus with acquired immunodeficiency syndrome and acute retinal necrosis. Am J Ophthalmol 1993; 116:297-301.

28. Margolis TP, Milner MS, Shama A, Hodge W, Seiff S. Herpes zoster ophthalmicus in patients with human immunodeficiency virus infection. Am J Ophthalmol Mar 1998;125(3):285-91.

29. Leahey AB, Shane JJ, Listhaus A, Trachtman M. Molluscum contagiosum eyelid lesions as the initial manifestation of acquired immunodeficiency syndrome. Am J Ophthalmol Aug 1997; 124(2):240-1.

30. Robinson MR, Udell IJ, Garber PF, Perry HD, Streeten BW. Molluscum contagiosum of the eyelids in patients with acquired immune deficiency syndrome. Ophthalmology Nov 1992; 99(11):1745-7.

31. Dugel PU, Gill PS, Frangieh GT, Rao NA. Ocular adnexal Kaposi's sarcoma in acquired immunodeficiency syndrome. Am J Ophthalmol Nov 15 1990; 110(5):500-3.

32. Ng WT, Versace P. Ocular association of HIV infection in the era of highly active antiretroviral therapy and the global perspective. Clin Experiment Ophthalmol Jun 2005; 33(3):317-29.

33. Basic and clinical science course. Intraocular inflammation and uveitis.USA American Academy of Ophthalmology; 2005-2006. p. 241-62.

34. Cunningham ET, Margolis TP. Ocular manifestations of HIV infection. N Eng J Med 1998; 339:236-44.

35. Geier SA, Sicca syndrome in patients with HIV. Ophthalmology, 1995 ;102: 1319-1324.

36. Rosberger DF, Heinemann MH, Friedberg DN, Holland GN. Uveitis associated with human immunodeficiency virus infection. Am J Ophthalmol 1998; 125: 301–5.

37. Karavellas MP, Song M, Macdonald JC, Freeman W. Long-term Posterior and Anterior Segment Complications of Immune Recovery Uveitis Associated with Cytomegaovirus Retinitis . Am J Ophthalmol 2000; 130: 57-64.

38. Banker AS. Posterior segment manifestations of human immunodeficiency virus/ acquired immune deficiency syndrome. Indian J Ophthalmol 2008 Sep–Oct; 56(5): 377–383.

39. Soman R, Purandare B. Human immunodeficiency virus and the ophthalmologist, Guest Editorial. Indian J Ophthalmol 2008 Sep–Oct; 56(5): 355–356.

40. Freeman WR, McCutchan JA , Arevlo JF, Wolfson T, Marcotte TD, Heaton RK et al. The relationship between AIDS retinal cotton wool spots and neuropsychological impairment in HIV-positive individuals in the pre-highly active antiretroviral therapy era. Ocul Immunol Inflamm 2004 March; 12(1): 25–33.Available from: URL: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1378132/pdf/nihms6043.pdf. (Access date 15/07/2010).

41. Kupperman BD, Petty JG, Richman DD, Mathews WC, Fullerton S, Rickman ST, et al. Correlation between CD4+ counts and prevalence of cytomegalovirus retinitis and human immunodeficiency and human immunodeficiency virus related non-infectious retinal vasculopathy in patients with acquired immunodeficiency syndrome. Am J Ophthlamol 1993; 115:575-82.

42. Jaworski, Charles OD, Faoo. Morphology of the HIV Versus the Diabetic Cotton Wool Spot. Optometry & Vision Science: November 2000; 77(11); 600-604. Available from: URL: http://journals.lww.com/optvissci/Abstract/2000/11000/Morphology_of_the_HIV_Versus_the_Diabetic_Cotton.10.aspx. (Access date 15/07/2010).

43. Akduman L, Feiner MA, Olk RJ, et al. Macular ischemia as a cause of decreased vision in a patient with acquired immunodeficiency syndrome. Am J Ophthalmol 1997; 124: 699-702.

44. Dunn JP, Holland GN. AIDS and the Eye: New concepts and Emerging Problems. In Current practices in ophthalmology, 1st edi, St Louis: Mosby; 1992. 1-32.

45. Thorne JE, Jabs DA, Kempen JH, Holbrook JT, Nichols C, Meinert CL.Incidence of and Risk Factors for Visual Acuity Loss among Patients with AIDS and Cytomegalovirus Retinitis in the Era of Highly Active Antiretroviral Therapy. Ophthalmology 2006; 113:1432–1440.

46. Babu RB, Sudharshan S, Kumarasamy N, Therese L, Biswas J. Ocular tuberculosis in acquired immunodeficiency syndrome. Am J Ophthalmol. 2006; 142: 413–418.

47. *Beare NAV,* Kublin JG, Lewis, DK, Schijffelen, MJ, Peters RPH, Joaki *G* et al. Ocular disease in patients with tuberculosis *an* HIV presenting with fever in Africa, Br J Ophthalmol 2002*;*86; 1076-1079.

48. *Lewallen* S, Kumwenda J, Maher D, Harries AD. Retinal findings *in* Malawian patients with AIDS. Br J Ophthalmol 1994*;* 78:757-759.

49. Vrabec TR. Posterior segment manifestations of HIV/AIDS. Survey of Ophthalmology 2004 March-April; 49(2): 131-157.

50. Holland GN, Engstrom RE , Glasgow BJ, Berger BB, Daniels SA, Sidikaro Y, et al. Ocular toxoplasmosis in patients with the acquired immunodeficiency syndrome. Am J Ophthalmol 1988 Dec 15; 106(6):653-67.

51. Levinson RD, Vann R, Davis JL, Friedberg DN, Tufail A, Terry BT etal Chronic Multifocal Retinal Infiltrates in Patients Infected With Human Immunodeficiency Virus. Am J Ophthalmol 1998 125(3): 314-324.

52. Rosenblatt MA, Cunningham C, Teich S, Friedman AH. Choroidal lesions in patients with AIDS. Br Ophthalmol 1990; 74: 610-614.

53. Kestelyn P, Taleman H, Bogartes J, Kagame A, Aziz MA, Batugwanyo J et al. Ophthalmic manifestations due to infections with cryptococcus neoformans in patients with acquired immune deficiency syndrome. Am J Ophthalmol 1993;116:721-27.

54. Kuo IC, Kapusta MA,Rao NA.Vitritis as the Primary Manifestation of Ocular Syphilis in Patients With HIV Infection, Am J Ophthalmol 1998;125(3):306-311.

55. Nguyen QD, Kempen JH, Bolton SG, et al: Immune recovery uveitis in patients with AIDS and cytomegalovirus retinitis after highly active antiretroviral therapy. Am J Ophthalmol 2000; 129:634–639.

56. Zegans ME, Walton RC, Holland GN, et al: Transient vitreous inflammatory reactions associated with combination antiretroviral therapy in patients with AIDS and cytomegalovirus retinitis. Am J Ophthalmol 1998; 125:292–300.

57. Kempen J, Min YI, Freeman WR, Holland GN, Friedberg DN, Dieterich DT, et al. Risk of immune recovery uveitis in patients with AIDS and cytomegalovirus retinitis. Am J Ophthalmol 2006; 113:684-94.

58. Sendi P, Sachers F, Drechsler H and Graber P. Immune recovery vitritis in an HIV patient with isolated toxoplasmic retinochoroiditis. AIDS 2006; 20(17):2237-2238.

59. Biswas J, Joseph A, Raizada S, Kumamsamy N, Solomon S. Ophthalmic manifestations of human immunodeficiency virus (HIV) infection in India. Indian J Ophthalmol 1999; 47:87-93.

60. Mwanza JC, Nyamabo LK, Tylleskär T, Plant GT. Neuro-ophthalmological disorders in HIV infected subjects with neurological manifestations. Br J Ophthalmol 2004; 88:1455-1459.

61. Goldsmith P, Jones RE, Ozuzu GE, Richardson J, Ong EL. Optic neuropathy as the presenting feature of HIV infection: Recovery of vision with highly active antiretroviral therapy. Br J Ophthalmol 2000; 84:551-553.

62. Hong YJ, Jung S, Kim JY, Kwon SB, Song KB, Hwang SH et al. Complete binocular blindness as the first manifestation of HIV- related cryptococcal meningitis. Journal of clinical neurology 2007 Dec; 3: 212-214.

63. Battu RR, Biswas J, Jayakumar N, Madhavan HN, Kumarsamy N, Solomon S. Papilloedema with peripapillary retinal haemorrhages in an acquired immunodeficiency syndrome (AIDS) patient with cryptococcal meningitis. Indian J Ophthalmol 2000; 48:47.

64. Rivero ME, Kuppermann BD, Wiely CA, Garcia CR, Smith MD, Dreilinger A, et al. Acquired Immunodeficiency Syndrome-Related Intraocular B cell Lymphoma, Arch ophthalmol 1999 May;117:616-622.

65. Yoganathan K, Austin M. Ischemic maculopathy in zidovudine-induced anemia in an HIV-positive man. Clinical Ophthalmology 2008:2(1) 237–239.

66. Copeland R, phillpotts BA. Ophthalmology for the general practitioner-Ocular manifestations of HIV 2006 June 22, Available from URL:http://www.emedicine.com/oph/TOPIC26/HTM (Access date 30/06/2008).

67. Cochereau I, Malika-Cabanne N, Godinaud P, Niyongabo T, Poste B, Ngayiragije A, et al. AIDS related eye disease in Burundi, Africa. Br J Ophthalmol 1999; 83:339-342.

68. Biswas J, Madhavan HN, George AE, Kumarswamy N, Solomon S. Ocular lesions associated with HIV Infection in India: A series of 100 consecutive patients evaluated at a referral centre. Am J Ophthalmol 2000 Jan; 129(1):9-15.

69. Attil VS, Singh VP, Reddy B, Varma D, Rai M, Gulati KA, et al. Ocular manifestations and Human immunodeficiency virus retinopathy in patients with Acquired immunodeficiency syndrome in North India. Asian J Ophthalmol 2006 Aug;8(4):139-142.

70. Pradhan BK, Sundar R, Singh SK. Impact of HIV status on ncome and employment.In Socio-Economic Impact of HIV and AIDS in India. Chapter 4. New Delhi:United Nations Development Programme,2006: 37-55 Available from URL: http://data.undp.org.in/hivreport/India_Report.pdf. (Access date-20/09/2010).

71. Sharma SK, Kadhiravan T, Banga A, Goyal T, Bhatia I and Saha PK. Spectrum of clinical disease in a series of 135 hospitalised HIV-infected patients from north India. BMC Infectious Diseases 2004; 4:52 Available from: URL: http://www.biomedcental.com/1471-2334/4/52. (Access date 20/09/2010).

72. Pathai S, Deshpande A, Gilbert C, Lawn SD. Prevalence of HIV-associated ophthalmic disease among patients enrolling for antiretroviral treatment in India: A cross-sectional study. BMC Infectious Diseases 2009, **9**:158. Available from: URL: http://www.biomedcental.com/1471-2334/9/158. (Access date 20/09/2010).

73. Chiou SH, Liu CY, Hsu WM, Chan YJ, Chou CK, Chug YM, et al. Ophthalmic findings in patients with acquired immunodeficiency syndrome. J Microbiol Immunol Infect 2000; 33:45-48.

74. Brown GC, Brown MM, Hiller T, David F, Benson W, Magargal LE. Cotton-wool spots. Retina 1985; 5:206-214.

75. Jabs DA, Holbrook JT, Mark L, Van Natta ML, Clark R, Jacobson MA et al. Risk Factors for Mortality in Patients with AIDS in the Era of Highly Active Antiretroviral Therapy .Ophthalmology 2005; 112:771–779.

76. Jabs DA, Van Natta ML, Holbrook JT, Kempen JH, Meinert CL, Davis MD. Longitudinal Study of the Ocular Complications of AIDS. 2. Ocular Examination Results at Enrollment. Ophthalmology 2007; 114:787–793.

77. Holland GN.AIDS and ophthalmology: the first quarter century. Am J Ophthalmol 2008; 145(3):397-408.

78. Karna S, Biswas J, Kumaraswamy N, Sharma P, Solomon S. Multiple Cranial Nerve Palsy in an HIV-positive Patient. Indian J Ophthalmol 2001; 49:118-120.

79. Mansour AM. Neuro-ophthalmic findings in Acquired immunodeficiency syndrome. J Clin Neuro-ophthalmol 1990; 10:167-74.

80. Gharai S, Venkatesh P, Garg S, Sharma SK, Gharai PG, Vohra R. Isolated Unilateral Acute Retinal Necrosis Syndrome as the Initial Manifestation of HIV Infection. The AIDS Reader 2009 June; 19 (6):231-234. Available from:URL: http://www.theaidsreader.com/display/article/1145619/1420071. (Access Date-15/08/2009).

81. Jabs DA. Ocular manifestations of HIV infection. Trans Am Ophthalmol soc 1995; 93:623-683. Available from: URL: http://www.ncbi.nml.gov/pmc/articles/PMC1312074/ (Access date-15/08/2009).

ANNEXURE- I

INFORMED CONSENT FORM

I.D. No ☐ ☐ ☐

TITLE: "ONE YEAR CROSS-SECTIONAL STUDY OF OCULAR MANIFESTATIONS IN HIV-POSITIVE/AIDS PATIENTS EVALUATED AT KLE'S DR. PRABHAKAR KORE HOSPITAL AND MRC, BELGAUM."

INVESTIGATORS: Dr. _____, Post-Graduate in M.S. Ophthalmology under the guidance of Dr. _____, M.S., D.O.M.S. Professor, Department of Ophthalmology, J N Medical College, Belgaum.

Mr. /Mrs./Ms_____

you are invited to participate in our above research study.

Respected sir/ madam,

We request you to enroll yourself to participate in our study as, you are eligible for this study. Your participation in research is voluntary, your decision whether or not to participate in the study will not affect your relationship with J N Medical College.

Purpose of the Study:

The main purpose of research is to study the eye manifestation in HIV/AIDS and secondly to determine their correlation with certain cells in the body i.e. CD4+T lymphocyte count.

Procedure Involved:

In this study, you will be asked to give detailed history of the disease you have and undergo necessary investigations. You will then be examined and findings will documented, and if necessary photographed.

Risks and Benefits:

As such there are no major risks involved, however some discomfort may occur during the process of examination and investigation for which all precautions will be taken. The investigator does not promise or guarantee that you will receive direct benefit being in the study.

Your participation may benefit you and others suffering from same ailment in future, by helping us learn more about the disease process and better treatment modalities. No financial incentives are promised to you for being a part of study.

Alternatives:

Your decision whether or not to participate in this study will not affect the quality of treatment you receive and if you are not willing to participate, further you may withdraw from the study at any time.

Privacy and Confidentiality:

The only people to know that you are a research subject are members of the research team. No information about you or information provided by you during the research will be disclosed to others without your written permission, except:

1. In emergency to protect your rights and welfare.
2. If required by law

Compensation:

In the event of injury related to the study, treatment will be made available through KLE's Dr Prabhakar Kore Hospital and M R C, Belgaum. There is no compensation or payment for such medical treatment by law. The doctors and the staff will provide facilities and medical attention to you.

Costs for participating in this research:

There will not be any extra cost incurred by you except for the investigations which are the part of the existing management protocol for this ailment. There is no commitment for any reimbursement or any other compensation for the participant.

Authorization to Publish Results:

The results of the research may be published or discussed in a conference, or used for teaching purpose. However the participant's identity will be kept confidential.

Questions:

If you have any questions about the research you may please contact:

1) Chief investigator, Dr. _____ P.G. Department of Ophthalmology, J N Medical College, Belgaum . Contact No: _____.
2) Guide, Dr. _____, Professor, Department of Ophthalmology, J N Medical College, Belgaum . Ph: _____.
3) Dr. _____, Principal, J N Medical College Belgaum and Chairman of Institutional Ethics Committee. Ph: _____.

Consent Statement:

I voluntarily agree for the participation as a subject of study. By signing this consent form I am not giving up any of my legal rights. I am signing the consent form after having read or been read for me in vernacular language, including the risks and the benefits and having all my questions answered.

Subject name: _____

Signature or the Left Thumb Print of Subject: _____

Witness Name: _____

Signature or the Left Thumb Print of Witness: _____

Investigators Name: _____

Signature of Investigator: _____

Date: _____

Place: _____

ANNEXURE – II: SCREENING FORM

Sl.No:

ID No

IP/OP No:

Name:

(First Name) (Middle Name) (Surname)

Age: Years

Sex: 1 – Male; 2 – Female

Address: _____

Phone No if any;

Occupation:

Religion: 1- Hindu 2 – Muslim 3 – Christian 4 – Sikh 5 Others (Specify)

Date of Examination:

HIV Status: 1.Positive 2. Negative

AIDS: Clinical Stage 1. Stage-I 2. Stage-II 3. Stage – III 4. Stage – IV

Diagnosis: Ocular Diagnosis _____

Systemic Diagnosis _____

Is the patient eligible for Study? 1 – Yes 2 – No

Has informed consent been taken? 1 – Yes 2 – No

Final Result Information :

1. Ineligible
2. Eligible, Refusal
3. Eligible, Participating

Doctor's Name: _____

Doctor's Signature: _____

Date:

ANNEXURE – II: PROFORMA

I.D. No:- ☐ ☐ ☐

Chief complaints: **If yes Duration**

Cough: ☐ 1 Yes 2. No

Fever: ☐ 1 Yes 2. No

Loss of appetite: ☐ 1 Yes 2. No

Loose motions: ☐ 1 Yes 2. No

Generalized weakness: ☐ 1 Yes 2. No

Loss of weight: ☐ 1 Yes 2. No

Ocular complaints: ☐ **1 Yes 2. No**

History of present illness:

I. Systemic

II.Ocular:

1. Diminution of vision
   - ☐ Gradual ☐ Sudden
   - ☐ Progressive ☐ Static
   - ☐ Painless ☐ Painful
   - ☐ (1-Distance; 2 Near; 3 Both)

2. History of Redness/ watering / Discharge ☐ 1 - Yes 2 - No

3. H/O Pain ☐ 1 - Yes 2 - No

4. History of Coloured halos ☐ 1 - Yes 2 - No

5. H/o wearing spectacles: ☐ 1 - Yes 2 - No

Any other complaints (if present, specify): ☐ 1 - Yes 2 - No

Past history

Diabetes: ☐ 1-Present 2-Absent Duration: _____months / years

Hypertension : ☐ 1-Present 2-Absent Duration: _____months / Years

Asthma ☐ 1-Present 2-Absent

Tuberculosis: ☐ 1-Present 2-Absent

Skin disorders: ☐ 1-Present 2-Absent

Genital lesions: ☐ 1-Present 2-Absent

Any other medical disorders: _____

Personal history:

H/o Bowel and Bladder habits: ☐ 1-Regular 2-Irregular

H/o sexual Exposure: ☐ 1-Present 2-Absent 3-Deny

H/o Blood transfusion: ☐ 1-Present 2-Absent

H/o I.V drug Abuse (Addiction): ☐ 1-Present 2-Absent

Family History:

☐ 1- Married 2-Unmarried

If married

Married life: Duration in years

Health status of spouse: ☐ 1- Healthy 2- Diseased 3-Dead

If dead specify the cause: _____

No of Childrens: ☐

Health status of childrens: ☐ 1- Healthy 2- Diseased 3-Dead

If dead specify the cause: _____

General physical examination

Pallor: ☐ 1-Present 2-Absent

Icterus ☐ 1-Present 2-Absent

Edema: ☐ 1-Present 2-Absent

Lymphadenopathy: ☐ 1-Present 2-Absent

Cyanosis: ☐ 1-Present 2-Absent

Clubbing: ☐ 1-Present 2-Absent

Vital signs:

Pulse rate (Per minute): ☐☐☐

Blood Pressure: (Mm of Hg) ☐☐☐ / ☐☐☐

Temperature: ☐ ^{0}C

Cardiovascular system: ☐ 1-Normal; 2-Abnormal; if abnormal specify: _____

Respiratory system: ☐ 1-Normal; 2-Abnormal; if abnormal specify: _____

Nervous System: ☐ 1-Normal; 2-Abnormal; if abnormal specify: _____

Per abdomen/Genital: Examination ☐ 1-Normal; 2-Abnormal; if abnormal specify: _____

Ocular Examination:

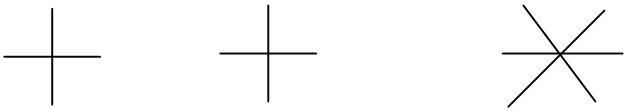
Head Posture: ☐ (1- Errect; 2 Tilted)

Facial Symmetry: ☐ (1-Symmetrical; 2-Asymmetrical)

Visual Axes: ☐ (1-Parallel; 2-Deviated)

Visual Acuity:	Right Eye	Left Eye
Distant:		
Pinhole:		
Near:		
With spectacles:		

Extra Ocular Movements: Right Eye Left Eye Binocular



	(RIGHT EYE)	(LEFT EYE)
Adnexa		
Conjunctiva		
Cornea		
Sclera		
Anterior chamber		
Iris		
Pupil		
Lens		

Direct

Indirect

FUNDUS: **Right Eye** **Left Eye** **Right Eye** **Left Eye**

Glow:

Media

Optic disc:

Cup: Disc ratio:

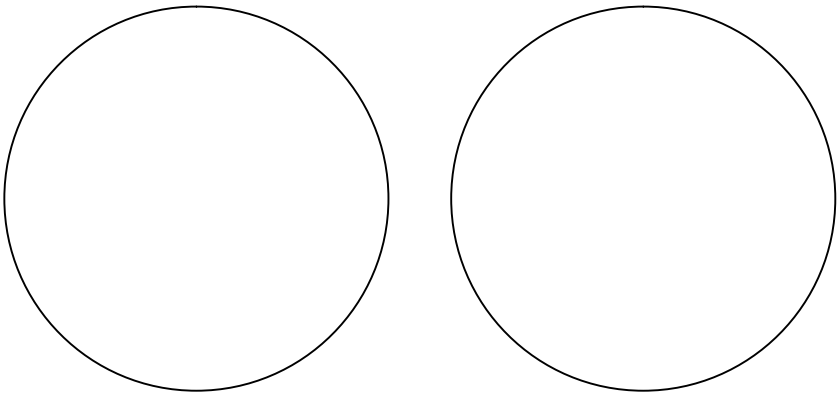
Vessels:

Background:

Foveal reflex:

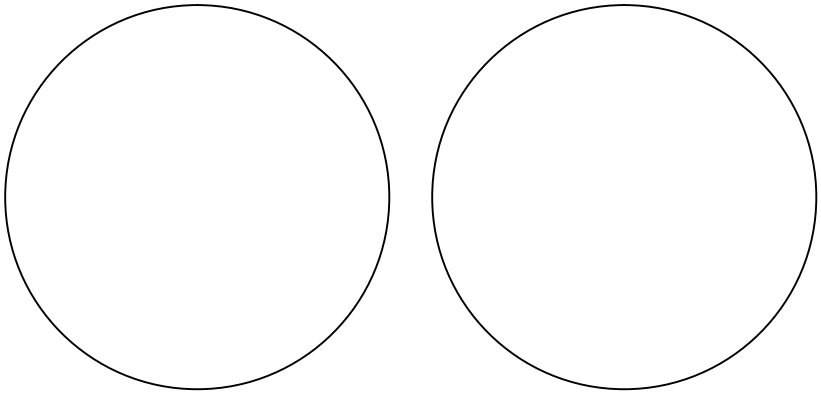
Direct

FUNDUS: **Right Eye** **Left Eye**



In Direct

FUNDUS: **Right Eye** **Left Eye**



Impression:

Investigation:

Group-1

VDRL:

HIV Elisa:

CD4 + T cell counts:

Group-2

Sputum for AFB:

Chest X-ray:

Group-3

Hb %:

TC/DC:

ESR:

Group-4

RBS:

LP:

Others if available:

Treatment history:

1. AKT	☐	1- On treatment	2- Not on treatment
2. HAART.	☐	1- On treatment	2- Not on treatment
3. Any other.	☐	1 – Yes	2 - No
		If yes specify	

Final Diagnosis: _____

(Ocular & Systemic)

ANNEXURE –III: PHOTOGRAPHS

POSTERIOR SEGMENT MANIFESTSTIONS

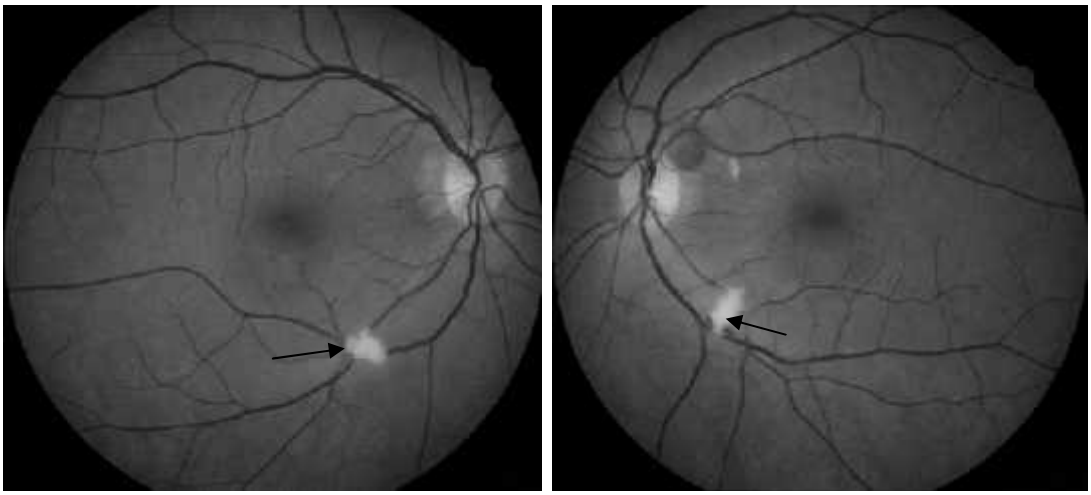


Figure 1: Case 97.Red free fundus photograph showing single cotton wool spot (HIV retinopathy), adjacent to the vascular arcade in both the eyes of a 35 year old male patient admitted with the diagnosis of HIV infection with PCP pneumonia and oral candidiasis. BCVA 6/6 in both eyes. CD 4+T cell count-5cells/µl.

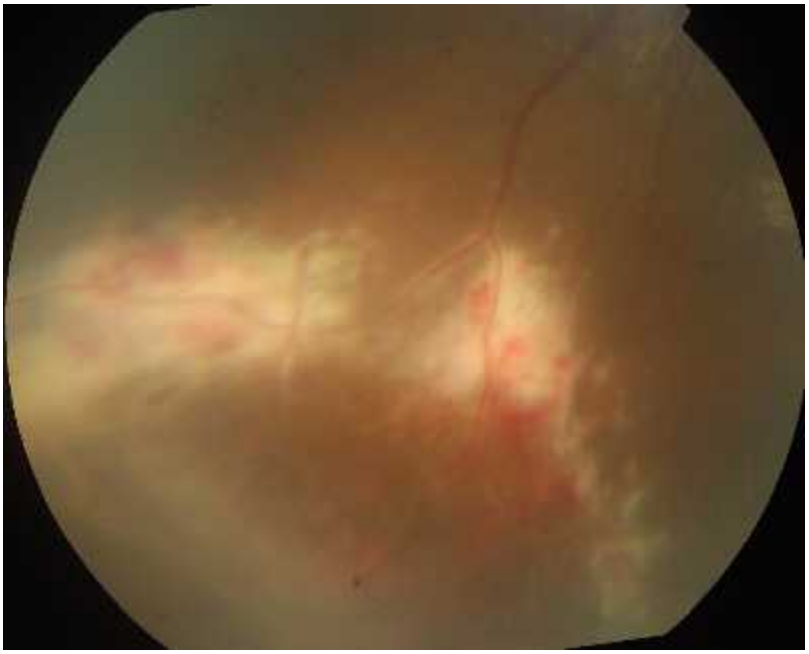
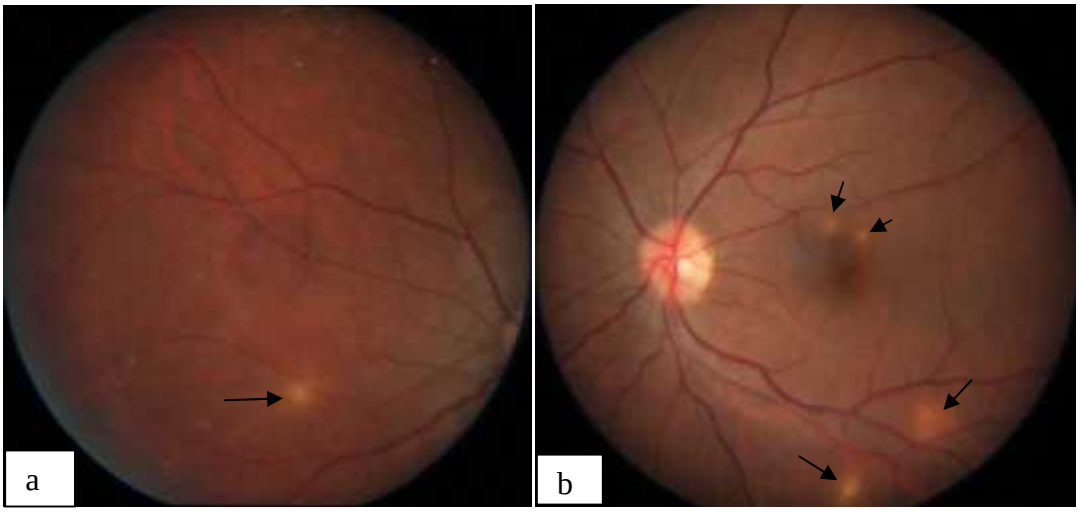


Figure 2: Case 45.Fundus photograph showing CMV retinitis in the peripheral infero nasal area of the left eye showing 'Brush fire' appearance with retinitis spreading along the veins, causing confluent areas of necrosis with intra retinal hemorrhages in a 14 year old female on HAART therapy. BCVA in LE was 6/9. CD4+T cell count-71 cells/µl and serum CMV IgG was >20 IU/L and IgM- 0.5 (ratio).

POSTERIOR SEGMENT MANIFESTSTIONS



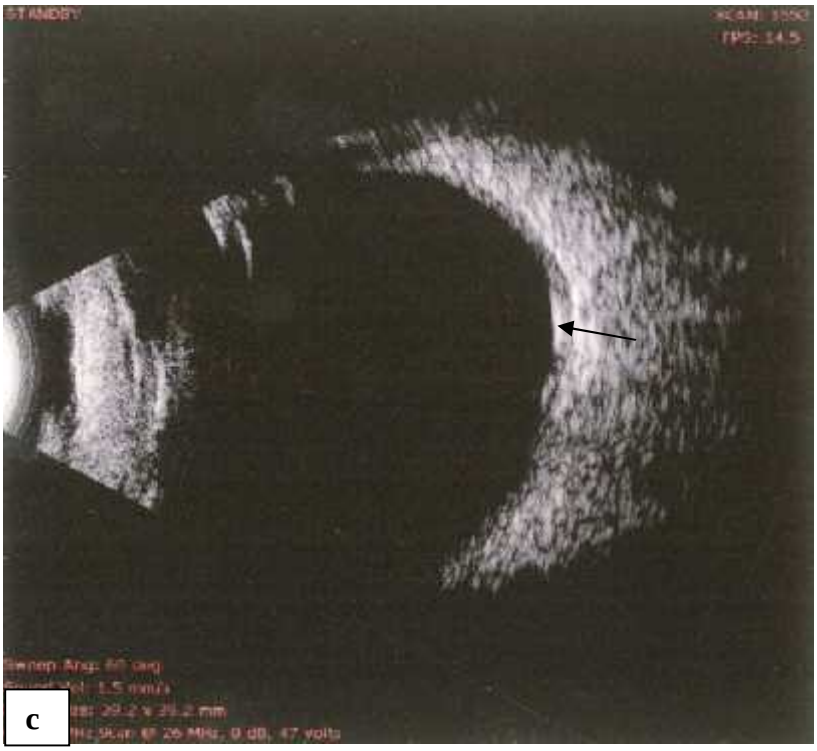


Figure3: Case 38:Fundus photograph showing multiple choroidal tubercles in both the eyes (fig a and b- black arrows) in a patient with pulmonary tuberculosis with systemic dissemination. BCVA in both the eyes were 6/6. B- Scan confirming the presence of choroidal tubercles seen in fig c. (Black arrow)

NEURO OPHTHALMIC MANIFESTATION

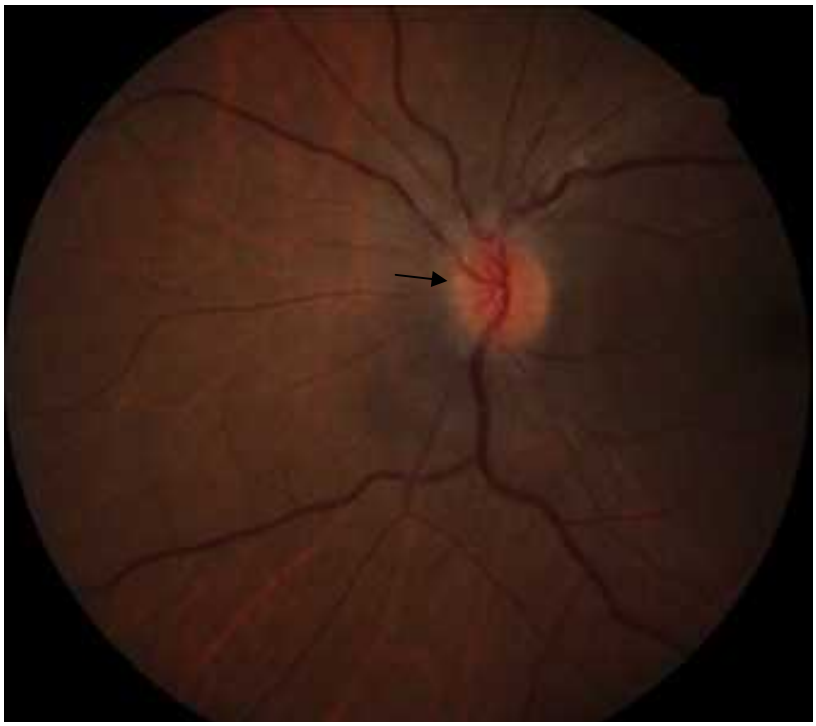


Figure 4: Case 83. Fundus photograph showing early papilledema in a 35 year old male patient, seropositive for HIV with Tubercular meningitis. Figure (arrow) shows hyperemic disc with blurring of nasal margin of the disc. Cd4+T cell count -31 cells/µl.

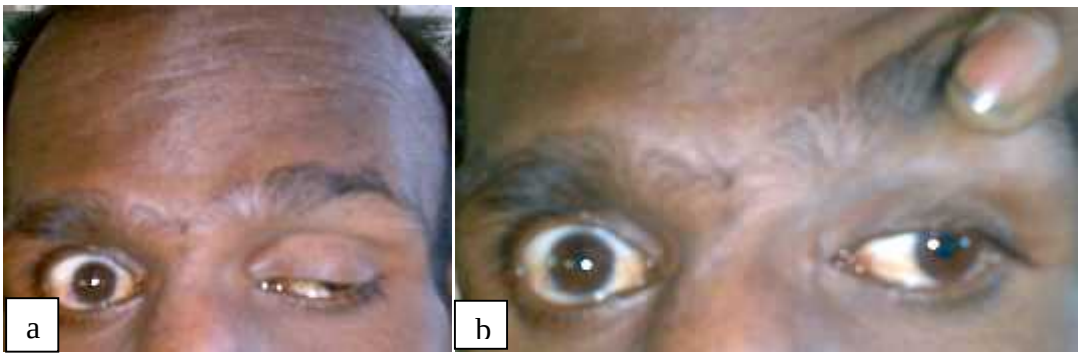


Figure 5: Case 5.Clinical photograph showing left sided complete III Cranial nerve Palsy (Fig:a-ptosis, Fig b-down and outward direction of the globe) with crossed hemiplegia (Weber syndrome) secondary to vasculitis in a 35 years old male patient. He was started on anti tubercular treatment. CD4+T cell count-281cells/µl

ANTERIOR SEGMENT MANIFESTATIONS

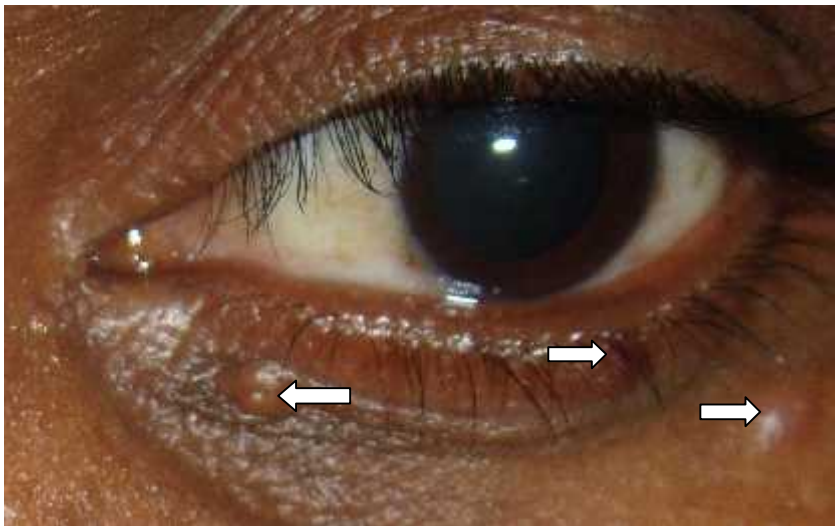


Figure 6: Case 50: Clinical photograph showing Molluscum contagiousum of the eye lid .Arrows pointing the typical umbilicated lesion in a 30 year old male patient on HAART with CD4+Tcell count 49cells/µl.

Figure 7: Case 52: Clinical photograph showing Herpes zoster ophthalmicus (arrows showing lesions in the stage of healing on forehead & eyelids) in a 38 year old HIV positive patient with CD4+T cell count of 61 cells /µl.

ANTERIOR SEGMENT MANIFESTATIONS

Figure 8: Case 49.Clinical photograph showing Necrotizing scleritis.(White arrow – Scleral necrosis, Black arrow- Iris prolapsed). An Atypical Presentation in a 35 year old female, with history of diminution of vision since 6 months, BCVA in both eyes Counting Fingers 1 meter. On Investigating she was found seropositive for HIV 1 & II infection. CD4 T cell count 101 cell /µl.

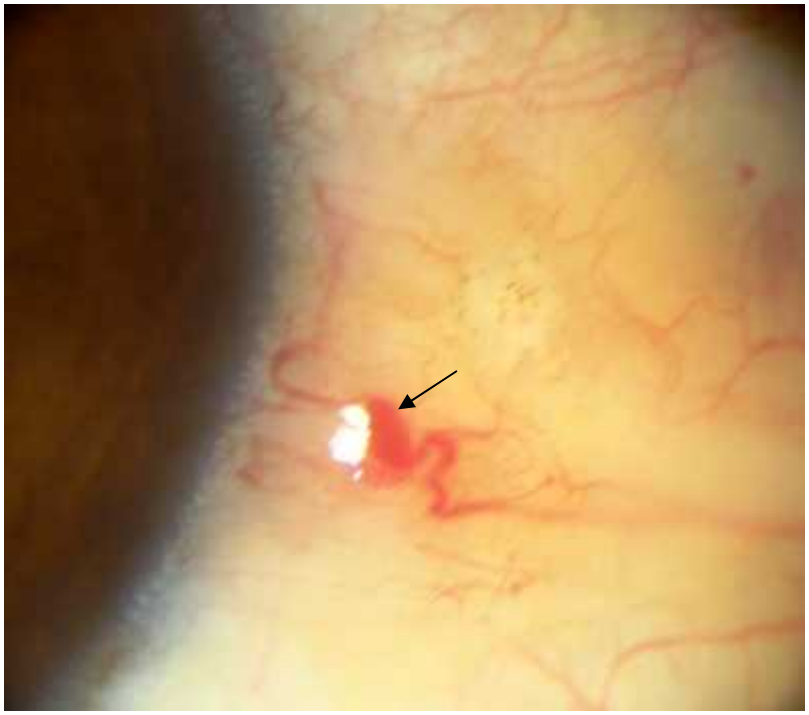


Figure 9: Case 55. Clinical photograph showing Conjunctival Microaneurysm (arrow pointing microaneurysm) in a 35 years male patient seropositive for HIV admitted with the diagnosis of pulmonary tuberculosis CD4 T cell count 21 cell /µl.

ANNEXURE-IV: MASTER CHART

SL NO	NAME	AGE	SEX	OCCUPATION	MODE OF TRANSMISSION	SYSTEMIC FINDINGS					CLINICAL STAGING	SYSTEMIC DIAGNOSIS	EYE	BCVA	EOM	ANTERIOR SEGMENT	POATERIOR SEGMENT	OCULAR DIAGNOSIS	CD4+T cells/µl
						LN	CNS	CVS	RS	OP & GI									
1	LRB	36	M	BUS	D	-	MENINGITIS	N	N	N	3	MENINGITIS	R	NA	NA	N	CWS	HIV RETINOPATHY	103
													L	NA	NA	N	CWS		
2	RMC	53	M	POL	D	-	N	N	TB	N	4	PUL TB	R	NA	NA	N	N	N	132
													L	NA	NA	N	N		
3	MNB	37	M	FAR	D	-	N	N	TB	N	3	PUL TB	R	6/18.	N	HZK,LID EROSION	N	HZK+ BACTERIAL LID EROSIONS	320
													L	6/6.	N	N	N		
4	PAK	28	M	FAR	S	-	MENINGITIS	N	N	N	3	MENINGITIS	R	NA	NA	N	PRE RETINAL HEMORRHAGE	HIV RETINOPATHY	312
													L	NA	NA	N	PRE RETINAL HEMORRHAGE		
5	KGK	35	M	DRI	S	-	WEBERS SYNDROME	N	N	N	4	CVA	R	6/6.	N	N	N	III N PALSY	281
													L	6/9.	III CN P	N	N		
6	IBH	46	F	TEA	S	-	N	N	PUL TB	N	2	PUL TB	R	6/6.	N	N	N	N	440
													L	6/6.	N	N	N		
7	BNP	34	M	FAR	D	-	N	N	N	GE	3	ACUTE GE	R	6/6.	N	N	N	N	111
													L	6/6.	N	N	N		
8	VRP	52	M	FAR	D	-	N	N	N	HPM	2	RVD+ALD	R	6/6.	N	N	N	N	280
													L	6/6.	N	N	N		
9	RSN	40	M	FAR	D	-	N	N	OLD TB	N	2	OLD TB	R	6/6.	N	CHALAZION	N	MULTIPLE CHALAZION	465
													L	6/6.	N	CHALAZION	N		
10	KGT	32	M	BUS	S	-	N	N	PNEU	N	3	PNEU	R	6/6.	N	N	N	N	39
													L	6/6.	N	N	N		

SL NO	NAME	AGE	SEX	OCCUPATION	MODE OF TRANSMISSION	SYSTEMIC FINDINGS					CLINICAL STAGING	SYSTEMIC DIAGNOSIS	EYE	BCVA	EOM	ANTERIOR SEGMENT	POATERIOR SEGMENT	OCULAR DIAGNOSIS	CD4+T cells/µl
						LN	CNS	CVS	RS	OP & GI									
11	SCB	26	M	FAR	D	-	MENINGITIS	N	N	N	4	MENINGITIS (CRYPTO)	R	6/6.	N	N	PAPILLEDEMA	PAPILLEDEMA (RESOLVING)	213
													L	6/6.	N	N	PAPILLEDEMA		
12	KTG	34	M	SER	S	+	MENINGITIS	N	N	N	4	MENINGO ENCPHALITIS+CER LN	R	6/6.	N	N	N	N	114
													L	6/6.	N	N	N		
13	PPS	42	M	BUS	D	-	N	N	N	N	4	NHL (IN ILLIAC FOSSA)-POST OP	R	6/9.	N	N	N	N	101
													L	6/9.	N	N	N		
14	SNP	35	M	CAR	S	-	PML, CEREBELLAR SIGNS	N	N	N	4	PML	R	NA	NA	N	PAPILLEDEMA	PAPPILEDEMA (EARLY)	160
													L	NA	NA	N	PAPILLEDEMA		
15	SBH	60	F	HW	S	-	AIDS dementia	N	N	N	4	AIDS	R	NO PL	N	N	FROSTED ANGITIS LIKE LESIONS INFEROTEMPORALLY	CMV RETINITIS	71
													L	6/6.	N	N	INFEROTEMPORALLY RETINITIS,		
16	SMR	47	M	FAR	S	-	N	N	TB	N	3	PULM TB	R	6/6.	N	N	N	N	186
													L	6/6.	N	N	N		
17	GNS	42	M	SER	D	-	TB MENINGITIS	N	TB	N	4	TB MENINGITIS +ALD	R	6/6.	N	N	N	N	88
													L	6/6.	N	N	N		
18	INK	32	M	DRI	S	-	MENINGO ENC	N	N	N	4	MENINGO ENC	R	6/6.	N	N	N	N	38
													L	6/6.	N	N	N		
19	CDB	36	M	POL	D	-	LYMPHOMA	N	N	N	4	LYMPHOMA (CNS)	R	6/6.	N	N	CWS	HIV RETINOPATHY	61
													L	6/6.	N	N	CWS		

SL NO	NAME	AGE	SEX	OCCUPATION	MODE OF TRANSMISSION	SYSTEMIC FINDINGS					CLINICAL STAGING	SYSTEMIC DIAGNOSIS	EYE	BCVA	EOM	ANTERIOR SEGMENT	POATERIOR SEGMENT	OCULAR DIAGNOSIS	CD4+T cells/µl
						LN	CNS	CVS	RS	OP & GI									
20	ASS	45	M	FAR	D	-	N	N	OLD TB	N	4	PCP+KOCH(OLD)+ HERPES LABIALIS	R	6/6.	N	N	CWS	HIV RETINOPATHY	26
													L	6/6.	N	N	CWS		
21	SSK	39	M	FAC	D	-	N	N	N	ALD	4	ALD	R	6/6.	N	N	N	N	186
													L	6/6.	N	N	N		
22	KRT	25	F	HW	S	-	N	N	TB PL EFFU	N	3	TB PL EFFUSION	R	6/6.	N	N	N	N	470
													L	6/6.	N	N	N		
23	SSG	33	M	FAR	D	-	MENINGITIS	N	N	N	3	MENINGITIS	R	6/12.	N	N	MULTIPLE WHITE CENTERED HEMORRHAGE	HIV RETINOPATHY	462
													L	6/12.	N	N	MULTIPLE WHITE CENTERED HEMORRHAGE		
24	NBC	40	M	BUS	D	-	N	N	TB PL EFFU	OC	3	TB PL EFFUSION + CANDIDIASI S(ORAL)	R	6/6.	N	N	N	N	83
													L	6/6.	N	N	N		
25	KBH	30	F	SER	S	-	N	N	N	GE	3	ACUTE GE	R	6/6.	N	N	N	N	526
													L	6/6.	N	N	N		
26	BRB	36	M	SER	S	-	N	N	N	N	2	RVD	R	6/6.	N	DRY EYE	N	DRY EYE(MILD)	181
													L	6/6.	N	DRY EYE	N		
27	YBH	76	M	TEA	D	-	N	N	N	OC	2	RVD	R	6/60.	N	N	N	N	286
													L	6/60.	N	N	N		
28	BSG	43	M	FAR	S	-	N	N	PCP PNEU	N	4	PCP	R	6/6.	N	N	N	N	315
													L	6/6.	N	N	N		

SL NO	NAME	AGE	SEX	OCCUPATION	MODE OF TRANSMISSION	SYSTEMIC FINDINGS					CLINICAL STAGING	SYSTEMIC DIAGNOSIS	EYE	BCVA	EOM	ANTERIOR SEGMENT	POATERIOR SEGMENT	OCULAR DIAGNOSIS	CD4+T cells/µl
						LN	CNS	CVS	RS	OP & GI									
29	ARK	46	M	FAR	D	-	MENINGITIS	N	N	N	4	MENINGITIS TOXO/CRYPTO	R	NA	NA	N	PAPILLEDEMA+ MULTIPLE SUPERFICIAL HEMORRHAGE	PAPPILEDEMA+ HIV RETINOPATHY	41
													L	NA	NA	N	PAPILLEDEMA + MULTIPLE SUPERFICIALHEMORRHAGE		
30	RLA	56	M	FAR	B	-	MENINGITIS(Crpto)	N	N	N	4	MENINGITIS (CRYPTO)	R	NA	NA	N	N	N	33
													L	NA	NA	N	N		
31	PCG	31	M	TEA	S	-	N	N	N	N	2	RVD	R	6/6.	N	N	N	N	68
													L	6/6.	N	N	N		
32	BRB	30	M	FAR	S	-	N	N	TB	N	3	TB PULM	R	6/6.	N	N	CWS	HIV RETINOPATHY	117
													L	6/6.	N	N	CWS		
33	DPT	52	M	FAR	D	-	MENINGITIS+ ADEM	N	N	EC	4	CANDIDIASIS(ESO)+MENINGITIS+ADEM	R	6/6.	N	N	N	N	20
													L	6/6.	N	N	N		
34	RBS	35	M	FAR	S	-	N	N	TB	N	4	TB PULM	R	6/6.	N	N	N	N	256
													L	6/6.	N	N	N		
35	KBD	50	M	FAR	D	-	TB MENINGITIS	N	N	OC	3	TB MENINGITIS	R	6/6.	N	N	N	HIV RETINOPATHY	182
													L	6/6.	N	N	CWS		
36	MDH	29	M	BUS	S	+	N	N	N	N	2	DRUG REACTION	R	6/6.	N	N	N	N	141
													L	6/6.	N	N	N		
37	DGM	60	M	SER	D	+	N	N	PNEU	OC	3	CANDIDISIS (ORAL)+PNEU	R	6/6.	N	N	N	HIV RETINOPATHY	56
													L	6/6.	N	N	CWS		

SL NO	NAME	AGE	SEX	OCCUPATION	MODE OF TRANSMISSION	SYSTEMIC FINDINGS					CLINICAL STAGING	SYSTEMIC DIAGNOSIS	EYE	BCVA	EOM	ANTERIOR SEGMENT	POATERIOR SEGMENT	OCULAR DIAGNOSIS	CD4+T cells/µl
						LN	CNS	CVS	RS	OP & GI									
38	ANA	32	M	FAR	S	-	N	N	TB	N	4	TB PULM	R	6/6.	N	N	CHOROIDAL TUBERCLES	CHOROIDAL TUBERCLES	35
													L	6/6.	N	N	CHOROIDAL TUBERCLES		
39	RVA	38	M	SER	D	-	N	N	TB	N	3	TB PULM	R	6/6.	N	N	N	DENDRITIC ULCER (HERPTIC)	36
													L	6/9.	N	DENDRITIC ULCER	N		
40	RRN	33	F	HW	S	-	N	N	PCP PNEU	N	4	PCP PNEU	R	NA	NA	N	N	DRY EYE (MILD)	5
													L	NA	NA	N	N		
41	SBT	50	F	HW	S	-	1	N	N	GE	2	ACUTE GE	R	6/9.	N	N	N	N	44
													L	6/9.	N	N	N		
42	SBP	30	F	HW	S	+	MENINGITIS CRYPTO	N	N	OC	3	CANDIDIASIS)+ GASTRITIS+ MEMINIGITIS	R	6/18.	N	N	PAPILLEDEMA EARLY	PAPPILEDEMA (EARLY)	60
													L	6/18.	N	N	PAPPILEDEMA EARLY		
43	YKT	49	M	POL	S	-	MENINGITIS (Chronic)	N	N	N	4	MENINGITIS CRYPTO(Chronic)	R	6/6.	N	N	N	N	32
													L	6/6.	N	N	N		
44	MSJ	40	M	FAR	S	-	MENININGITIS TOXO	N	TB	GE	3	TB PULM+MENINGITIS TOXO+HERPIS GENITALIS	R	6/6.	N	N	CWS	HIV RETINOPATHY	76
													L	6/6.	N	N	CWS		
45	PMG	14	F	STU	P	-	1	N	N	N	4	AIDS	R	CF-1MT	N	congestion,KP,NVI,.hyphema,RAPD,mid dilated pupil ,iris pigon lens	Vitreous clear,retinitis and hemorrhage along veins	CMV RETINITIS(BE)	71
													L	6/6.	N	N	Vitreous clear, in periphery retinitis and hemorrhage along veins .		

SL NO	NAME	AGE	SEX	OCCUPATION	MODE OF TRANSMISSION	SYSTEMIC FINDINGS					CLINICAL STAGING	SYSTEMIC DIAGNOSIS	EYE	BCVA	EOM	ANTERIOR SEGMENT	POATERIOR SEGMENT	OCULAR DIAGNOSIS	CD4+T cells/µl
						LN	CNS	CVS	RS	OP & GI									
46	VDS	38	M	WEL	S	-	1	N	PNUM	N	3	PNUM	R	6/12.	N	N	CWS	HIV RETINOPATHY	29
													L	6/9.	N		CWS		
47	PSK	47	M	BUS	S	-	1	N	N	GE	2	RVD	R	6/9.	N	N	BRVO,RD,Vitreous floaters,Pre retinal hemorrhage	CMV RETINITIS(LE)	96
													L	6/9.	N	RAPD, IRIS PIG ON LENS	BRVO+PVD+RD		
48	PSH	60	F	RET	S	-	1	N	OLD TB	OC	3	CANDIDIASIS+ OLD TB	R	6/9.	N	CONCRETION LOWER FORNIX	N	DRY EYE (MODERATE)	153
													L	6/9.	N	CONCRETIONS	N		
49	GSG	40	F	HW	S	-	1	N	N	N	3	RVD	R	CF-1MT	N	scleral melt,pupil irregular,sluggish reaction of pupil,PS,iris pig on lens of pupil	NA	NECROTIZING SCLERITIS	101
													L	CF-1MT	N	nasal cornea thin,scleral melt,bussaca nodules,PS,sluggish of reaction of pupil,iris pig on lens	NA		
50	GRK	30	M	POR	S	-	1	N	N	GE	3	RVD	R	PL+,PR Acc	N	Keratic precipitates	Toxoplasma retinochoroiditis+moll cont	TOXOPLASMA RETINOCHOROIDITIS + MOLL CONT	49
													L	PL+,PR Acc	N	Keratic precipitates	Toxoplasma retinochoroiditis,+moll cont		
51	CSC	65	M	BUS	D	-	1	N	N	N	3	RVD	R	CF-2MT	N	CATARACT	N	N	18
													L	CF-2MT	N	CATARACT	N		
52	MSP	38	M	FAR	D	-	1	N	N	N	2	RVD	R	6/6.	N	N	N	HERPES ZOSTER	61
													L	6/6.	N		N		
53	ABT	34	F	HW	D	+	1	N	TB MILIARY	N	3	TB PULM MILIARY	R	6/6.	N	N	N	N	311
													L	6/6.	N	N	N		
54	AGS	45	M	DRI	S	-	1	N	N	OC	3	CANDIDIASIS	R	6/9.	N	N	N	N	105
													L	6/9.	N	N	N		

SL NO	NAME	AGE	SEX	OCCUPATION	MODE OF TRANSMISSION	SYSTEMIC FINDINGS					CLINICAL STAGING	SYSTEMIC DIAGNOSIS	EYE	BCVA	EOM	ANTERIOR SEGMENT	POATERIOR SEGMENT	OCULAR DIAGNOSIS	CD4+T cells/µl
						L N	CNS	CVS	RS	OP & GI									
55	FCM	35	M	DRI	D	-	1	N	TB +PCP	N	4	TB PULM+PCP	R	6/6.	N	CONJUNCTIVAL VESSEL ANEURYSM NASALLY	N	CONJUNCTIVAL ANEURYSM	21
													L	6/6.	N	N	N		
56	MBK	32	F	HW	S	-	1	N	OLD TB	N	2	TB OLD	R	6/6.	N	N	N	N	397
													L	6/6.	N	N	N		
57	PIM	34	M	QU A	D	+	1	N	Up RTI	N	2	UpRTI	R	6/6.	N	N	CWS + MULTIPLE HEMORRHAGES	HIV RETINOPATHY	8
													L	6/6.	N	N	CWS		
58	VTB	45	M	SER	D	-	1	N	TB PL EFFU	N	3	TB PL EFFUSION	R	6/6.	N	N	N	N	87
													L	6/6.	N	N	N		
59	BST	22	F	HW	S	-	1	N	TB	N	3	TP PULM	R	6/6.	N	N	CWS	HIV RETINOPATHY	109
													L	6/6.	N	N	CWS		
60	SSS	32	M	BUS	S	-	1	N	TB	N	3	TB PULM	R	6/6.	N	MOLLUSCUM CONTGIOSUM LIDS	N	MOLLUSCUM CONTAGIOSUM	3
													L	6/6.	N	MOLLUSCUM CONTGIOSUM LIDS	N		
61	SSP	61	M	FAR	S	-	1	N	OLD TB	HPM	3	TB PULM OLD	R	6/36.	N	N	N	N	259
													L	6/36.	N	N	N		
62	JSM	25	F	HW	S	-	ENCEPHALOPATHY	N	N	ABD TB	4	TB(abd)+HIV ENCEPHALOPATHY+CVA	R	6/6.	N	N	N	N	128
													L	6/6.	N	N	N		
63	DVP	37	M	FAR	S	-	1	DVT	N	N	1	DVT	R	6/6.	N	N	N	N	268
													L	6/6.	N	N	N		

SL NO	NAME	AGE	SEX	OCCUPATION	MODE OF TRANSMISSION	SYSTEMIC FINDINGS					CLINICAL STAGING	SYSTEMIC DIAGNOSIS	EYE	BCVA	EOM	ANTERIOR SEGMENT	POATERIOR SEGMENT	OCULAR DIAGNOSIS	CD4+T cells/µl
						LN	CNS	CVS	RS	OP & GI									
64	PPK	32	F	HW	S	-	TB MENINGOENCHEPHALITIS	N	N	N	4	TB MENINGOENCHEPHALITIS	R	NA	N	N	N	LE MR PALSY + NYSTAGMUS	41
													L	NA	LE MR PALSY + NYSTAGMUS	N	N		
65	SSJ	34	M	DRI	S	-	MENINGITIS (CRYPTO)	N	N	N	4	MENINGITIS (CRYPTO)	R	NA	NA	N	N	N	76
													L	NA	NA	N	N		
66	SCK	45	F	POR	D	+	1	N	N	N	3	RVD	R	6/9.	N	CONCRETION LOWER FORNIX	N	DRY EYE (MODERATE)	82
													L	6/9.	N	CHEMOSIS INFERO TEMPORALLY	N		
67	MSM	38	M	MEC	D	-	1	N	TB	N	3	TB BRONCHIEACTISIS	R	6/6.	N	N	N	N	64
													L	6/6.	N	N	N		
68	MKL	55	F	HW	S	-	1	N	N	N	3	RVD	R	6/9.	N	N	CWS	HIV RETINOPATHY	5
													L	6/9.	N	N	CWS		
69	BLG	38	F	HW	S	-	ACUTE CONFUSIONAL STATE	N	N	N	4	ACUTE CONFUSIONAL STATE	R	NO PL	N	RAPD, IRIS PIG ON LENS	Media hazy, vitritis+,optic d pale, attenuated vessels, retinal necrosis	RE ARN	31
													L	6/6.	N	N	N		
70	LKT	56	M	POL	S	-	LT HEMIPLEGIA	N	TB	N	3	TB PULM	R	6/6.	N	N	N	N	448
													L	6/6.	N	N	N		
71	RHK	30	M	DRI	S	-	1	N	N	N	3	RVD	R	6/6.	N	CONJUNCTIVAL XEROSIS	CWS+ENGORGED VEINS	HIV RETINOPATHY + DRY EYE (MILD)	19
													L	6/6.	N	CONJUNCTIVAL XEROSIS	CWS+ENGORGED VEINS		
72	FMA	33	M	POR	S	-	TB MENINGITIS	N	TB PL EFFU	N	2	TB PULM-PL EFFUSION+ MENINGITIS	R	6/9.	N	N	N	N	84
													L	6/9.	N	N	N		

SL NO	NAME	AGE	SEX	OCCUPATION	MODE OF TRANSMISSION	SYSTEMIC FINDINGS					CLINICAL STAGING	SYSTEMIC DIAGNOSIS	EYE	BCVA	EOM	ANTERIOR SEGMENT	POATERIOR SEGMENT	OCULAR DIAGNOSIS	CD4+T cells/µl
						LN	CNS	CVS	RS	OP & GI									
73	YCP	65	M	FAR	D	-	1	N	N	GE	4	ANAEMIA+ PERIAMPULLARY DIVERTICULA	R	6/36.	N	N	N	N	163
													L	6/36.	N	N	N		
74	JRS	31	M	BUS	S	-	1	N	TB+PCP PNEU	N	4	TB PULM + PCP PNEUM	R	6/9.	N	N	N	CMV RETINITIS(LE)	11
													L	CF-1/2MTS	N	N	Optic disc covered by exudate, brush fire appearance, ChorioRetinal scar.		
75	SBK	48	F	POR	S	-	1	N	TB	N	3	TB PULM	R	6/6.	N	N	N	N	121
													L	6/6.	N	N	N		
76	NRD	22	M	DRI	S	-	1	N	N	N	2	PUO	R	6/6.	N	N	N	N	76
													L	6/6.	N	N	N		
77	HHH	40	M	POR	S	-	MENINGITIS	N	N	N	4	MENINGITIS	R	NA	NA	CCC,Inferior cornea epithelial defect	N	EXPOSURE KERATITIS	54
													L	NA	NA	CCC.Inferior cornea epithelial defect	N		
78	SBB	40	F	HW	D	-	TOXO ENCHEPHALITIS	N	N	N	4	TOXO ENCHEPHALITIS	R	NA	LATERAL GAZE PALSY+ NYSTAGMUS	N	N	LATERAL GAZE PALSY+ NYSTAGMUS	141
													L	NA	N	N	N		
79	SYK	36	M	FAR	S	-	1	N	N	GE	3	ACUTE GE	R	6/6.	N	N	CWS	HIV RETINOPATHY	211
													L	6/6.	N	N	CWS		
80	VPP	36	M	BUS	S	-	DISORIENTED	N	N	OC	4	HIV ENCEPHALOPATHY+ ALD+ORAL CANDIDIASIS	R	6/6.	N	N	N	CHOROIDAL TUBERCLES	106
													L	6/6.	N	N	CHOROIDAL TUBERCLES		

SL NO	NAME	AGE	SEX	OCCUPATION	MODE OF TRANSMISSION	SYSTEMIC FINDINGS					CLINICAL STAGING	SYSTEMIC DIAGNOSIS	EYE	BCVA	EOM	ANTERIOR SEGMENT	POATERIOR SEGMENT	OCULAR DIAGNOSIS	CD4+T cells/µl
						LN	CNS	CVS	RS	OP & GI									
81	HBK	45	M	FAR	D	-	1	N	TB	N	3	TB PULM	R	6/9.	N	N	N	N	15
													L	6/9.	N	N	N		
82	ASP	32	M	DRI	S	-	1	N	N	EC	4	CANDIDIASIS(ESO)	R	6/6.	N	N	N	HIV RETINOPATHY	7
													L	6/6.	N	N	CWS		
83	SPW	34	M	FAR	S	-	TB MENINGITIS	N	N	N	3	TB MENINGITIS	R	6/6.	N	CONJUNCTIVA DRY	PAPILLEDEMA+ ROTH SPOT+CHOROIDAL TUBERCLE	PAPILLEDEMA+ CHOROIDAL TUBERCLE+HIV RETINOPATHY	31
													L	6/6.	N	N	PAPILLEDEMA+ HEMORRHAGE		
84	SKB	28	F	HW	S	-	MENINGITIS(CRYPTO)	N	N	OC	4	MENINGITIS (CRYPTO)	R	6/6.	N	N	N	N	30
													L	6/6.	N	N	N		
85	BST	35	M	SER	D	-	HEMIPLEGIA	N	N	N	3	CVA+IHD	R	6/6.	N	N	PAPILLEDEMA	N	179
													L	6/6.	N	N	PAPILLEDEMA		
86	BNH	50	M	FAR	S	-	1	N	TB	N	3	TB PULM + HERPES ZOSTER THORAX	R	6/9.	N	N	N	N	179
													L	6/9.	N	N	N		
87	ASA	32	M	FAR	D	-	1	N	TB	N	3	TB PULM	R	6/6.	N	N	N	N	93
													L	6/6.	N	N	N		
88	PMC	66	M	SER	S	-	MENINGITIS	N	N	EC	4	CANDIDIASIS(ESO)	R	6/24.	N	N	CWS	HIV RETINOPATHY	225
													L	6/24.	N	N	CWS		
89	AKP	35	M	POR	D	-	MENINGITIS	N	N	N	3	MENINGITIS	R	6/9.	N	N	PEPILLEDEMA EARLY	PAPILLEDEMA (EARLY)	261
													L	6/12.	N	N	PAPILLEDEMA EARLY		
90	ULP	28	M	BUS	S	-	MENINGITIS	N	N	HPM	3	MENINGITIS	R	6/6.	N	N	N	N	58
													L	6/6.	N	N	N		

SL NO	NAME	AGE	SEX	OCCUPATION	MODE OF TRANSMISSION	SYSTEMIC FINDINGS					CLINICAL STAGING	SYSTEMIC DIAGNOSIS	EYE	BCVA	EOM	ANTERIOR SEGMENT	POATERIOR SEGMENT	OCULAR DIAGNOSIS	CD4+T cells/µl
						LN	CNS	CVS	RS	OP & GI									
91	VSU	36	M	SER	S	+	1	N	TB	HPM+A	3	TB PULM+ HEMORROIDS	R	6/6.	N	N	N	N	329
													L	6/6.	N	N	N		
92	KAM	55	M	ARM	S	-	1	N	TB	N	3	TB PULM	R	6/6.	N	N	SUPERFICIAL HEMORRHAGES	HIV RETINOPATHY	147
													L	6/6.	N	N	N		
93	BSD	53	M	POR	D	-	1	N	TB	N	3	TB PULM	R	6/9.	N	N	N	N	460
													L	6/9.	N	N	N		
94	TVH	30	M	FAR	D	-	1	N	N	N	2	RVD	R	6/6.	N	N	N	N	417
													L	6/6.	N	N	N		
95	BMD	37	M	DRI	S	-	1	N	N	GE	2	ACUTE GE	R	6/6.	N	N	N	N	286
													L	6/6.	N	N	N		
96	BVT	37	F	HW	S	-	1	A+D	N	HPM	3	ANEMIA + DCM	R	6/24.	N	N	CWS +ROTH SPOTS+HARD EXUDATES	HIV RETINOPATHY	294
													L	6/24.		N	CWS +ROTH SPOTS+HARD EXUDATES		
97	GDK	35	M	SER	S	-	1	N	PCP PNEU	OC	4	PCP+ CANDIDIASIS(ORAL)	R	6/6.	N	N	CWS	HIV RETINOPATHY	5
													L	6/6.	N	N	CWS		
98	ACK	40	F	HW	S	-	1	N	N	N	4	RVD	R	6/6.		TEAR MINISCUS LESS	N	DRY EYES (MILD)	663
													L	6/6.		TEAR MENISCUS LESS	N		
99	YCS	45	M	TEA	D	-	ACUTE PSYCHOSIS	N	N	GE+OC	2	ACUTE GE+ PSYCHOSIS +CANDIDIASIS	R	6/9.		N	N	N	113
													L	6/9.		N	N		
100	MJ	40	F	HW	D	-	1	N	N	GE	2	ACUTE GE	R	6/6.		N	N	N	40
													L	6/6.		N	N		

KEY TO THE MASTER CHART

Sex-

M-Male

F-Female

Occupation-

BUS- Business	POL-Police	FAR-Farmer
DRI- Driver	TEA-Teacher	SER-Service
CAR-Carpenter	HW-House wife	FAC-Factory worker
STU-Student	WEL-Welder	RET-Retired from service
MEC-Mechanic	POR-Porter	QUA-Quack
ARM-Army		

Mode of transmission:

S-Sexual route	B-Blood transfusion
P-Perinatal transmission	D-Deny any route

LN-Lymphadenopathy

+ Present	- Absent

N-Normal

CNS-Central Nervous System

PML-Progressive multifocal leukoencephalopathy

MENINGOENC-Meningo encephalitis

ADEM-Acute disseminated encephalomyelitis

CVS-Cardio Vascular System

DVT-Deep vein thrombosis in right mid thigh region

A+D-Anemia with Dialated Cardiomyopathy

RS-Respiratory system

TB –Tuberculosis

PNEU-Pneumonia

PCP-Pneumocystis carini pneumonis

OLD TB-Old case of tuberculosis treated with secondary infection.

PL EFFU-Pleural Effusion

Up RTI-Upper respiratory tract infection.

OP & GI-Oro pharnyx and Gastro intestinal system:

N-Normal

GE-Acute gastroenteritis

HPM-Hepatomegaly

A- Ascities

ABD TB-Abdominal Tuberculosis

OC-Oral candidiasis

EC-Esophageal Candidiasis

Systemic Diagnosis:

PUL TB-Pulmonary tuberculosis

CVA- Cerebro vascular accident

RVD-Retro viral disease

ALD-Alcoholic liver disease

CRYPT-Cryptococcus

CER LN-cervical lymphadenopathy

NHL-Non Hodgkins lymphoma

POST OP-Post operative

EYE-

R-Right eye

L-Left eye

BCVA-Best corrected visual acuity

NA-Not assessed as patient was un conscious /not cooperative

PL- perception of light

CF-1MT-Counting finger at 1 meter

PR Accu- Projection of rays is accurate.

EOM-Extra ocular movements

MR-Medial Rectus

Anterior segment:

MOLL CONT-Molluscum contagiosum

PS- Posterior synechiae

CCC-Circum corneal congestion

NS-Nuclear Sclerosis

PSC-Posterior sub capsular cataract

Ocular Diagnosis:

HZK- Herpes zoster keratitis

III N- III cranial nerve palsy