CLINICAL PROFILE OF ANORECTAL DISEASES IN HIV SEROPOSITIVE PATIENTS AND ITS CORRELATION WITH CD4+ COUNTS - A CROSS SECTIONAL STUDY

By

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I, **DR. HARSHAVARDHAN P BIRADAR** hereby declare that this dissertation entitled "**CLINICAL PROFILE OF ANORECTAL DISEASES IN HIV SEROPOSITIVE PATIENTS AND ITS CORRELATION WITH CD4+ COUNTS**", is a bonafide and genuine research work carried out by me under the guidance of **DR. TEJASWINI VALLABHA**$_{M.S.}$, Professor and HOD, Department of Surgery, B.L.D.E.U's Shri B. M. Patil Medical College Hospital and Research Centre,Bijapur.

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DR. HARSHAVARDHAN P BIRADAR

LIST OF ABBREVIATIONS USED

AIDS	–	Acquired Immunodeficiency Syndrome
APC	–	Antigen Presenting Cell
CD	–	Cluster of Differentiation
CDC	–	Centre for Disease Control
CMV	–	Cytomegalo virus
CTL	–	Cutaneous T Lymphocyte
DD	–	Differential Diagnosis
DLC	–	Differential Leucocyte count
EBV	–	Ebstein Barr Virus
EIA	–	Enzyme Immune Assay
ESR	–	Erythrocyte Sedimentation Rate
FDA	–	Food And Drug Administration
Hb%	–	Haemoglobin percentage
HAART	–	Highly Active AntiRetroviral Therapy
HIV	–	Human Immunodeficiency Virus
HLA	–	Human Leukocyte Antigen
HPV	–	Human Papilloma Virus
HSV	–	Herpes Simplex Virus
KS	–	Kaposi sarcoma
MC	–	MolluscumContagiosum
NK	–	Natural Killer
OHL	–	Oral Hairy leukoplakia
OI	–	Opportunistic Infections
PCP	–	Pneumocystis carinii pneumonia

RBS	–	Random blood sugar
RT	–	Reverse Transcriptase
STD	–	Sexually transmitted disease
STI	–	Sexually transmitted infections
TB	–	Tuberculosis
TLC	–	Total leucocyte count
TPHA	–	TreponemapallidumHaemoagglutination Assay
TPPA	–	Treponemapallidum particle Assay
VDRL	–	Venereal Disease Research Laboratory
UNAIDS	–	United Nations Programme on AIDS
WHO	–	World Health Organisation.
PR	–	Per Rectum

ABSTRACT

Background:

The HIV/AIDS epidemic remains a global health challenge. Human immunodeficiency virus causes decreased immunity & predisposition to various disease, including some rare ones in all body segments. Anorectal pathology is common in patients who are HIV positive, affecting about one third of patients at some point in their life time.

Objective:

To study the clinical profile of anorectal diseases in HIV seropositive patients and to correlate with CD4+ T cell count.

Material and Methods:

A cross sectional study was conducted from 1st September 2012 to 31st July 2014, in BLDEU's Shri B. M. Patil Medical College Hospital and Research Centre, Bijapur. Data was analyzed using SPSS software. The association between the CD4+ T cell count was done using Spearman's formula.

Result

Over a period of 1st September 2012 to 31st July 2014, 89 patients were identified with anorectal diseases who were HIV seropositive. Male: Female ratio was 3:1. The most common symptom was anorectal pain followed by mass per rectum and bleeding Per Rectum. Mean age was 37.20 years and most common anorectal pathology was fissure in ano followed by haemorrhoids. Negative correlation was established between anorectal pathology and CD4+ t cell count with P value significant at 0.024.

Conclusion

Patients with HIV infections suffered from fissure followed by haemorrhoids. Fistula was the third most common anorectal pathology identified. Other anorectal pathology identified were perianal abscess, condyloma, perianal herpes, and post traumatic perianal wound. Statistical analysis showed negative correlation between anorectal pathologies and CD4+ T cell count.

Key Words: HIV, Anorectal Diseases, CD4+ T cell count.

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INTRODUCTION

The HIV/AIDS has posed many unprecedented challenges. We are confrontedwith the problem which has no curative or palliative treatment or a preventive ortherapeutic vaccine, at least for now. Further, owing to the insidious and covert nature of the disease, the problem is compounded by a prevailing attitude of denial or resistance of complacency at all levels. Unlike epidemic of disease such as cholera, plague and polio, which manifest overtly and acutely and elicitconcrete response, the visible manifestations of HIV occur only at the last stage[1].

As a result, there is a visible lack of realization of the problem in the society. The reactive response, therefore, does not match the real magnitude and gravityof the problem. Another major challenge in the context of HIV/AIDS and sexuallytransmitted diseases is their intimate association with the issue of sexuality whichcontinues to be a taboo in our society and not discussed openly[1].

With new HIV infections occurring worldwide and better availability of lowcost anti-retroviral drugs, the number of HIV positive people in the population issteadily increasing. Surgeons will be increasingly called upon for consultation andsurgical interventions for either routine surgical conditions or for AIDS-relatedcomplications[2].

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NEED FOR STUDY

The HIV/AIDS epidemic remains a global health challenge. Human immunodeficiency virus causes decreased immunity & predisposition, including some rare ones in all body segments[3].

The wider access to ART has resulted in a decline of the number of people dying due to AIDS related causes. The trend of annual AIDS deaths is showing a steady decline since the roll out of the free ART programme in India in 2004and has led to increased number of people living with HIV infection[4].

The 2006 estimates suggest national adult HIV prevalence in India is approximately 0.36 percent, amounting to between 2 and 3.1 million people. If an average figure is taken, this comes to 2.5 million people living with HIV and AIDS. Nationally, the prevalence rate for adult females is 0.29 percent, while for males it is 0.43 percent[5].

Based on Surveillance, NACO further came up with an estimation that the adult HIV prevalence in the state was 0.63% in 2009 leading to an estimated 2.45 lakhs PLHIV in the state (KSAPS annual plan 2011-12). The only district in the state that has an HIV positivity of greater than 1% among the ANC attendees tested in PPTCT centers in 2009 is Bagalkot (1.35%). In 22 of the 29 districts, the HIV positivity among ANC attendees is low at less than 0.5%. In the remaining 6 districts (Belgaum, Bellary, Bijapur, Dharwad, Koppal, and Raichur), HIV positivity is moderate, ranging from 0.5% to 0.9%[6].

Anorectal pathology is common in patients who are HIV positive, affecting about one third of patients at some point in their life time. Anorectal pain, the presence of a mass, and bleeding per rectum are the most frequent presenting complaints [7].There are some specific conditions associated with HIV disease

syndrome which requires surgical intervention. These includes: - Perianal abscess, haemorrhoids, fistula, etc[8].

Anorectal diseases are more common in men who have sex with men (MSM) and are less frequent in those who do not engage in receptive anal sex. However, the evolution is similar in both groups. The patients may present with benign diseases, such as hemorrhoids, fistulas, fissures, and sexually transmitted infections (STIs). The STIs include gonorrhea, syphilis, condyloma, and chlamydia. There also may be ulcers caused by cytomegalovirus (CMV), herpes simplex (HSV), or Candida albicans, and idiopathic anal ulcers, which are more specific to HIV-infected individuals. Perianal tumors are more frequent in the seropositive population, particularly Kaposi's sarcoma (KS), non-Hodgkin lymphomas (NHL), and squamous-cell carcinoma (SCC); the latter is associated with human papillomavirus (HPV)[8].

Anorectal disease incidences have changed in the highly active anti-retroviral therapy. The incidences of condyloma and fissure have increased and rates of fistula, ulcers and haemorrhoids have decreased since the time of HAART. Moreover, although tumors occurred at a similar rate, SCC has become the most frequent condition since 1996 when HAART became available for AIDS treatment[9].

Much less is known about the correlation between the CD4+ count and anorectal diseases. Kaposi's sarcoma is usually associated wirh the CD4+ count of <200cells/cumm^3 , anal squamous cell carcinoma <200cells/cumm^3, anal warts 500-200cells/cumm^3, anal ulcers secondary to herpes simplex, scabies mucocutaneouscandiasis are associated with CD4+ count of <200cells/cumm3[10]. There are no studies or literature correlating between CD4+ count and Fissure, Fistula, Perianal abscess and Haemorrhoids.

Incidence of these anorectal diseases in HIV positive patients are not known in Bijapur district and as per our information, no study has been conducted in India to know the clinical profile of anorectal diseases among HIV positive patients and their correlation with CD4 counts. Hence we decided to take up this study.

AIM AND OBJECTIVE

To study the clinical profile of anorectal diseases in HIV seropositive patients and to correlate with cd4+ count.

ANORECTAL DISEASES IN HIV

Anorectal diseases are common in human immunodeficiency virus-infected individuals. As the number of individuals with HIV disease continues to increase rapidly and with improved health and survival of seropositive patients from more effective prophylaxis and treatment options, HIV-related anorectal disorders are being encountered more frequently. It is important to recognize and to understand clearly the clinical presentation and spectrum of HIV-associated anorectal disease so that these conditions can be managed appropriately and treated effectively.

Perianal diseases seem to occur mainly in male homosexuals and less frequently in those who do not practice receptive anal intercourse, although disease evolution is the same in both groups HIV-positive patients have as many as anal diseases (hemorrhoids, fistulas, and fissures) and venereal diseases (condylomas, gonorrhea, syphilis, and chlamydia) as they do typical HIV-positive diagnoses (cymmegalovirus (CMV), herpes simplex, candida, and idiopathic ulcers). Neoplasms are also referred to as being more prevalent in HIV seropositive patients than in the HIVseronegative and epidermoid anal cancer, which is associated with human papillomavirus (HPV) infection[8].

Knowledge of diagnosis and treatment for these anal diseases has importance because of the increasing number of cases around the world.

Anal Condyloma:

Condylomataacuminata is sexually transmitted and although perianal warts may be seen in heterosexual men and women, it is common among promiscuous homosexual men (Marino, 1964; Waugh, 1972; Sohn and Robilotti, 1977). Of the 80 patients with perianal warts reported by Oriel (1971), 72 were men and 95% admitted to homosexual practices. Similarly, a high proportion of women with the disease admit to having had anal intercourse (Abcarian and Sharon, 1982). Condylomata acuminate are a frequent feature among HIV-positive and AIDS patients, being found in 54% of men with AIDS (Palefsky et al, 1990). There is evidence in these patients of malignant transformation through AIN (intra-epithelial neoplasia) in 15%, which may progress to carcinoma-in-situ and invasive anogenital squamous cell carcinoma, often at an early age (Burns and van Goidsenhoven, 1970; Daling et al, 1982; Croxson et al, 1984; Longo et al, 1986; Bradshaw et al, 1992)

Anal Ulcer[9]:

These patients are in advanced stages of acquired immunodeficiency syndrome (AIDS) and have a painful anal ulceration associated with purulent anal secretion. The cause is unknown, and there is no universally accepted treatment. Medical treatment is used by some authors, intralesional steroid therapy is adopted by others, and surgery is performed when medical therapy fails to relieve symptoms.

Anal Fistula[10]:

Anal fistulas in HIV-positive patients arise from the dentate line in similar locations to human immunodeficiency virus negative patients. However, human immunodeficiency virus-positive patients were more likely to have incomplete anal fistulas than human immunodeficiency virus-negative patients. Furthermore, human

immunodeficiency virus-positive patients are predisposed to incomplete fistulas leading into a blind sinus.

Lymphoma[11]:

Colorectal lymphomas represent 6% to 12% of all gastrointestinal lymphomas. Usually, they are secondary B-cell non-Hodgkin lymphoma. Primary colorectal lymphomas account for only 0.2% of allmalignant tumors in this site. In the gastrointestinaltract, primary Hodgkin lymphoma (HL) has been reported only in 1% to 3% of all cases, and the stomach and small intestine are the sites most commonly involved. Primary HL of the rectum is rare, mainly described in HIV-infected patients or associated with inflammatory bowel disease (IBD). Epstein-Barr virus (EBV) is present in a significant proportion of cases of HL. Only 2 cases of anorectal HL have been described so far, both affecting HIV- and EBV-infected males and presenting with a concomitant lymphadenopathy[32].

Perianal Herpes[12]:

HPV infection frequently manifests as verrucous lesions (warts) that cause pruritus, discomfort, and, more rarely, pain or bleeding. However, some other infectious agents such as varicella-zoster virus (VZV), cytomegalovirus (CMV), molluscumcontagiosum (MC), and particularly herpes simplex virus (HSV), can also cause verrucous skin lesions in HIV-positive patients.

Herpes simplex virus is found in 29% of MSM with symptomatic anorectaldisease, although the majority of confirmed herpes simplex cases are reported in asymptomatic individuals. The most frequently encountered findings are ulcerated aphthous lesions, vesicles and inguinal lymphadenopathy.Additional signs

and symptoms include pain, pruritus, lymphadenopathy, superficial ulcers, vesicular erosion,urinaryretentionand constipation.

Anal Cancer[13]:

The prevalence and incidence of anogenital human papillomavirus (HPV) infection and HPV-related anal intraepithelial neoplasia (AIN), the precursors of anal cancer, were found to be higher in HIV-seropositive individuals than in HIV seronegative ones before the advent of combination antiretroviral therapy (cART) [1]. In addition, several studies showed an increased risk of anal cancer in HIV-infected patients in the precARTera. The incidence of anal cancer was reported to be two-fold higher in HIV-infected men who have sex with men (MSM) than in HIV-seronegativeMSM, whereas the relative risk of anal cancer among HIVseropositivemen and HIV-seropositive MSM was 37-fold and 59-fold higher, respectively, than in the general population [4]. Anal cancer is 14 to 175 times more frequent in HIV-infected patients than in the general population [5–9], and the prevalence of HPV infection is also higher in the former. In a recent study, Chiao et al.[10] found that anal cancer tended to be diagnosed at a younger age in HIV-infected patients and particularly in men, whereas in the general population, anal cancer is more frequent in women and usually occurs during the sixth decade of life.

Fissue and Haemorrhoids :

Incidence of fissure and haemorrhoids are low in HIV seropositive patients who are homosexual. Carr et al, found no difference in incidence of fissure and haemorrhoids in HIV seropositive patients and HIV seronegative patients who are not homosexual.

REVIEW OF LITERATURE

W L Barrett, T D Callahan, B AOrkin, Department of Surgery, The George Washington University, Washington, DC, USA, conducted a study HIV seropositive patients. Median CD4 count was 175 (range, 2-1,100) cells/mm3. The most frequent major presenting symptoms were anorectal pain (55 percent), a mass (19 percent), and blood in the stool (16 percent). Forty different perianal disorders were identified, which were categorized as benign noninfectious (18), infectious (14), neoplastic (6), and septic (2). The most common disorders were condyloma (42 percent), fistula (34 percent), fissure (32 percent), and abscess (25 percent). They concluded that perianal manifestations of human immunodeficiency virus infection are common, often multiple, and varied[7].

Nadal SR, Carmen RM, Vivianne MG, Salim BM and Manlio BS, conducted a study at Infectious Diseases Institute, Sao Paulo, Brazil, to know the prevalence and cause of anorectal disease in HIV seropositive patients and concluded that the most common anorectal lesions were condylomas (75.6 percent), ulcers (17 percent), and fistulas (12.1 percent). They Compared 1,860 human immunodeficiency virus-positive patients to 1,350 human immunodeficiency virus-negative outpatients with perianal diseases, examined from January 1989 to December 1996. They conclude that human immunodeficiency virus-positive patients have more condylomas, ulcers, tumors, fistulas, and abscesses than human immunodeficiency virus-negative patients, who have more hemorrhoids. Incidence of fissures was similar in the two groups[8].

Yuhan R, Orsay C, DelPino A, Pearl R, Pulvirenti J, Kay S, Abcarian H. Conducted a study in Nov 1998 at Source Division of Colon and Rectal Surgery, Cook County Hospital and University of Illinois, Chicago 60612, USA to assess the cause and clinical presentation of anorectal disease in this human immunodeficiency

virus-infected population & concluded that human immunodeficiency virus infection is associated with a wide spectrum of anorectal disease, of which the most common lesions are anal condylomata and painful ulcers. The majority of these anal ulcers gave negative culture and biopsy results. In addition, there seems to be a high incidence of anorectalneoplasia in this patient population. The average CD4 lymphocyte count was 160 cells/mm[16].

Retamozo P M, de Sousa JB, Santos JB. University Hospital of Brasília, Brasília, DF, Brazil. They Conducted study to know the clinical profile of Anorectal lesions in HIV-positive patients using highly active antiretroviral therapy. The study concluded with prevalence of anorectal lesions was 36.4%, and condylomaacuminata and anal fissure were the most frequent of these. Condylomaacuminata was the most prevalent anorectal lesion and was strongly associated with the use of lopinavir/ritonavir[17].

Gonzalez-R C, Heartfield W, Briggs B, Vukasin P, Beart RW, conducted study at Source Department of Colon and Rectal Surgery, Keck School of Medicine at the University of Southern California, Los Angeles, California, USA, to determine whether the prevalence and distribution of anorectal pathology in HIV-infected patients have changed after the introduction of highly active antiretroviral therapy. The pathology was distributed as follows for the early vs. late periods: 33 vs. 33 percent for ulcer, 30 vs. 34 percent for condyloma, 9 vs. 4 percent for fissure, 6 vs. 6 percent for fistula, 4 vs. 5 percent for hemorrhoids, 3 vs. 3 percent for abscess, and 15 vs. 16 percent for all other anorectal pathology. There was no statistically significant difference in any of these groups[18].

A study was conducted in BLDEU's Shri B M Patil Medical College and Research Centre, Bijapur, by DrMandar, DrTejaswini U, DrRamakanth B, DrVikram S, to know the clinical profile of surgical diseases in HIV positive patients. The study concluded that the prevalence of anorectal pathology in HIV seropositive patientswas 30%. Out of 186 patients, 41 patients were suffering from anorectal pathology (30%). Among them, 16 patients had perianal abscess, 14 patients had fissure in ano(10.3%), 8 patients had fistula in ano(5.8%), 2 patients had hemorrhoids and 1 patient was suffering from carcinoma rectum[19].

EPIDEMIOLOGY OF HIV/AIDS

Historical Milestones:

AIDS was first recognized in the United States when the US centers for diseasecontrol and prevention reported the unexplained occurrence of Pneumocysticcarinii pneumonia in 5 previously healthy homosexual men in New York and Los Angeles[20].

The first indication that the disease is caused by a retrovirus came in 1983 from French scientist, when professor Montagnierand his co-workers isolated the viral agent, which was later named as Human immunodeficiency virus. ELISA technique to detect the presence of antibodies in blood against HIV was developed in 1984. In 1986, the Montagnier's group discovered a new type of HIV in West Africa and labeled as HIV-2. In 1987, Zidovudine was reported to be useful in managing the patients with HIV infection for the first time. Later, combination therapy came in vogue which became more popular after discovery of protease inhibitors[21].

The Global Scenario:

The HIV/AIDS global epidemic has greatly exceeded all earlier predictions and although with various available preventive and therapeutic strategies, it has started stabilizing in developed countries, but it is still continuing unabated in all the developing countries[22].

Globally, an estimated 35.3 (32.2–38.8) million people were living with HIV in 2012. An increase from previous years as more people are receiving the life-saving antiretroviral therapy. There were 2.3 (1.9–2.7) million new HIV infections globally, showing a 33% decline in the number of new infections from 3.4 (3.1–3.7) million in 2001. At the same time the number of AIDS deaths is also declining with 1.6 (1.4–1.9) million AIDS deaths in 2012, down from 2.3 (2.1–2.6) million in 2005[22].

Indian Scenario:

HIV/AIDS in India came into public view in 1986 with detection of first few cases of HIV in Chennai and first AIDS case in Mumbai in 1987. The currentscenario in our country is alarming and the situation is grim. The overall prevalence is still low as compared to many other countries in South Eastern Asia,but because of our large population, even a small prevalence translates into a large number of infections[23].

Though India is a country with low HIV prevalence, it has the third largest number of people living with HIV/AIDS. As per HIV estimates 2008-09, there are an estimated 23.9 lakh people living with HIV/AIDS in India with an adult prevalence of 0.31 percent in 2009. Most infections occur through heterosexual transmission[24].

The HIV prevalence among the High Risk Groups, i.e., Female Sex Workers, Injecting Drug Users, Men who have Sex with Men and Transgender is about 20 times higher than the general population. Based on HIV Sentinel, 39 percent are female and 3.5 percent are children[24].

Of the 1.2 lakh estimated new infections in 2009, the six high prevalence states account for 39 percent of the cases, while the states of Odisha, Bihar, West Bengal, Uttar Pradesh, Rajasthan, Madhya Pradesh and Gujarat account for 41 percent of new infections[24].

Table no 1:- HIV infection in India – State wise prevalence-2011-12[24]

GROUP	STATES
Group I – High prevalence States (more than 1% of natal mothers and over 5% of STD patients positive for HIV)	Maharashtra, Tamil Nadu, Karnataka, Andra Pradesh, Manipur and Nagaland.
Group II – Low prevalence States	All other States.

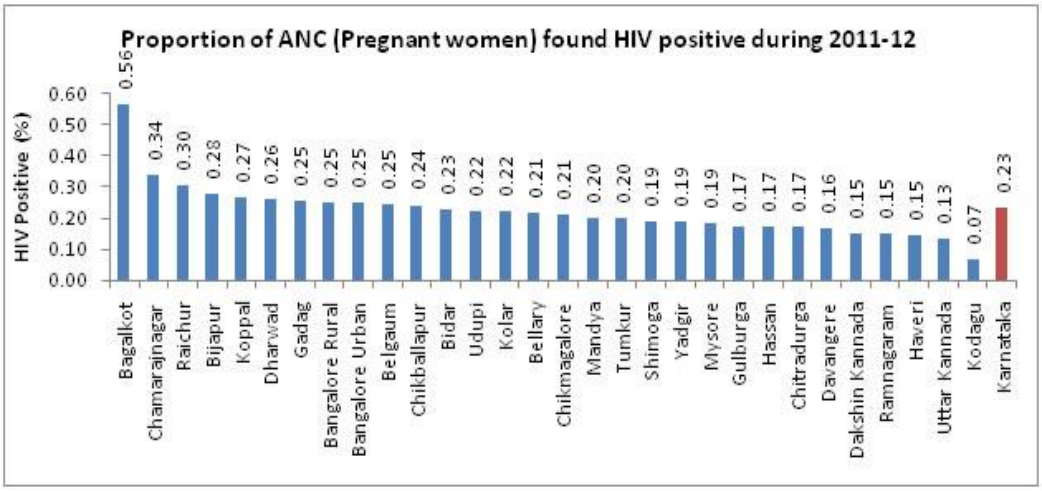
All the six high prevalence states show declining trend. However, the low prevalence states of Assam, Chandigarh, Orissa, Kerala, Jharkhand, Uttarakhand, Jammu & Kashmir, Arunachal Pradesh and Meghalaya show rising trends in the last four years[24].

Karnataka State Scenario:

HIV prevalence among the Ante Natal Clinic (ANC) attendees indicates a significant decline in adult HIV prevalence in the state, from 1.5% in 2003 and 2004 to less than 1% (0.70%) in 2010[25].

10 districts (Bagalkot, Raichur, Koppal, Chikballapur, Dharwa, Bijapur, Belgaum, Bangalore Urban, Bangalore Rural and chamrajnagar) have HIV positivity more than state average of 0.25%[25].

Figure no 1:- District wise distrubition of HIV patients



HUMAN IMMUNODEFICIENCY VIRUS

Etiologic Agent[26]:

The retroviruses, which make up a large family (Retroviridae), mainly infectvertebrates. These viruses have a unique replication cycle whereby their geneticinformation is encoded by RNA rather than DNA.

Retroviruses contain an RNA-dependent DNA polymerase (a reverse transcriptase) that directs the synthesis of a DNA form of the viral genome after infection of a host cell. The designation retrovirus denotes that information in the form of RNA is transcribed into DNA in the host cell—a sequence that overturned a central dogma of molecular biology: that information passes unidirectionally from DNA to RNA to protein.

The family Retroviridae includes three subfamilies: Oncovirinae, of which human T cell lymphotropic virus (HTLV) type I is the most important in humans; Lentivirinae, of which HIV is the most important in humans; and Spumavirinae, the "foamy" viruses, named for the pathologic appearance of infected cells.

The etiologic agent of AIDS is HIV, which belongs to the family of human retroviruses (Retroviridae) and the subfamily of lentiviruses.

The most common cause of HIV disease throughout the world is HIV-1, which comprises several subtypes with different geographic distributions.HIV-2 was first identified in 1986 in West African patients and was originally confined to West Africa.

Both HIV-1 and HIV-2 are zoonotic infections. The Pantroglodytestroglodytes species of chimpanzees has been established as the natural reservoir of HIV-1 and the most likely source of original human infection.

The virion[26]:

Despite the wide range of biologic consequences of retroviral infection, all retroviruses are similar in structure, genome organization, and mode of replication.

Retroviruses are 70–130 nm in diameter and have a lipid-containing envelope surrounding an icosahedral capsid with a dense inner core. The core contains two identical copies of the single-strand RNA genome.

The RNA molecules are 8–10 kb long and are combined with reverse transcriptase and tRNA. Other viral proteins, such as integrase, are also components of the virion particle .However, the retroviral RNA is not translated; instead it is transcribed into DNA. The DNA form of the retroviral genome is called a provirus.

Retroviral genomes include both coding and noncoding sequences:

The coding regions include the gag (group-specific antigen, core protein), pol (RNA-dependent DNA polymerase), and env (envelope) genes.

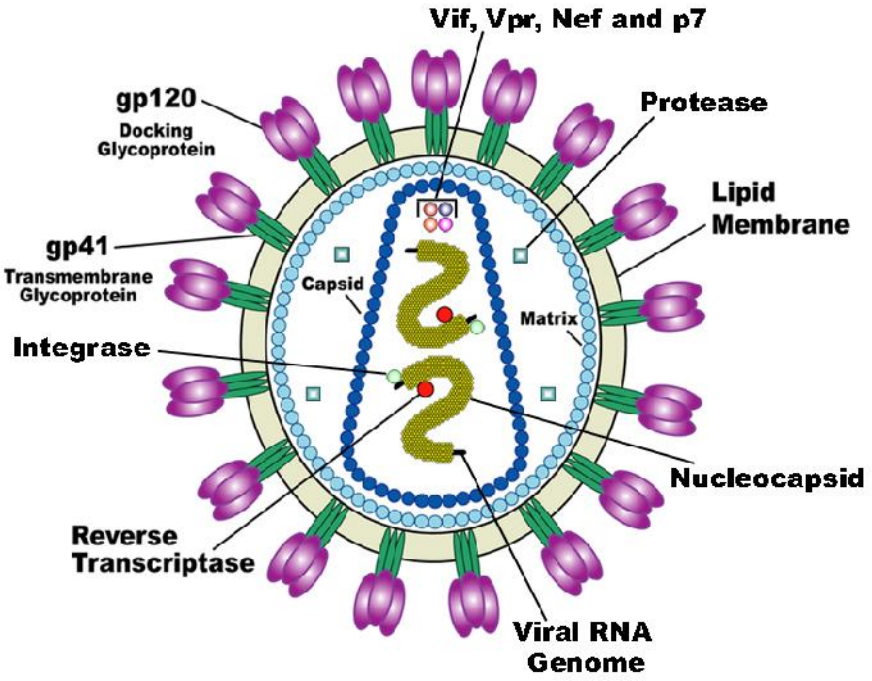
The gag gene encodes a precursor polyprotein(including P 24 antigens) that is cleaved to form three to five capsid proteins. A fraction of the Gag precursor proteins also contain a protease responsible for cleaving the Gag and Pol polyproteins.

The pol gene encodes three proteins: the reverse transcriptase, the integrase, and the protease. The reverse transcriptase functions to copy the viral RNA into the double-strand DNA provirus, which inserts itself into the host cell DNA via the action of integrase. The protease functions to cleave the Gag-Pol polyprotein into smaller protein products.

The env gene encodes the envelope glycoproteins: one protein that binds to specific surface receptors and determines what cell types can be infected and a smaller transmembrane protein that anchors the complex to the envelope.

However, HIV-1 is more complex than other retroviruses, particularly those of the nonprimate group, in that it also contains at least six other genes (tat, rev, nef, vif, vpr, and vpu), which code for proteins involved in the modification of the host cell to enhance virus growth and the regulation of viral gene expression. Several of these proteins are thought to play a role in the pathogenesis of HIV disease. The major difference between the genomes of HIV-1 and HIV-2 is the fact that HIV-2 lacks the vpu gene and has a vpx gene not contained in HIV-1.

Figure no 2:- STRUCTURE OF HIV

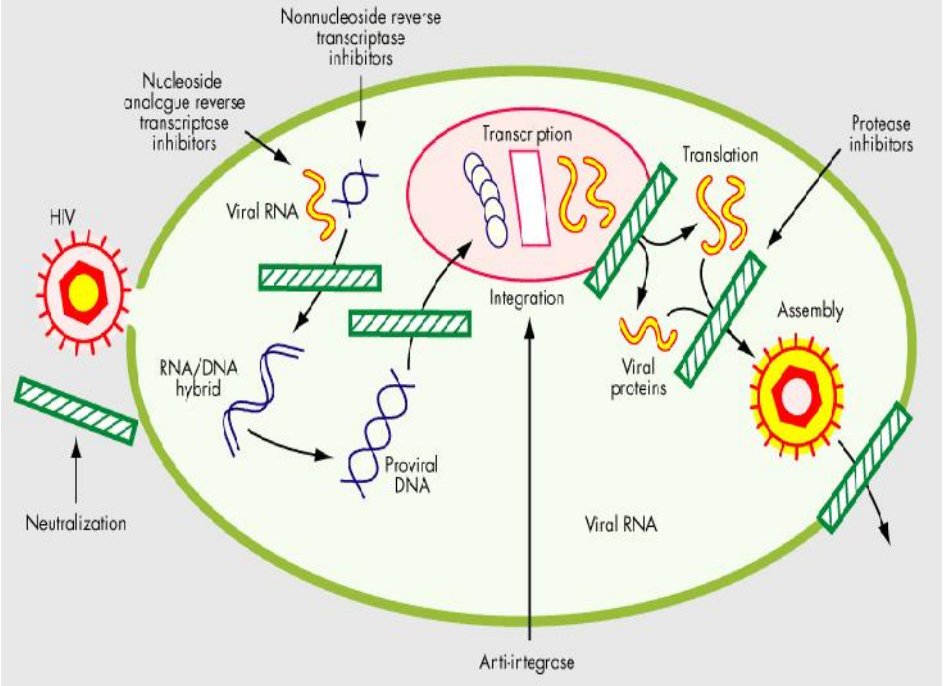


Replication cycle of HIV[26]:

In the first phase, the virus enters the cytoplasm after binding to a specificcell-surface receptor; the viral RNA and reverse transcriptase synthesize a double strand DNA version of the RNA template; and the provirus moves into the nucleus and integrates into the host cell genome. This proviral integration is permanent.

The second phase includes the synthesis and processing of viral genomes,mRNAs, and proteins using host cell machinery, often under the influence of viralgene products. Virions are assembled and released from the cell by budding from the membrane; host cell membrane proteins are frequently incorporated into the envelope of the virus. Proviral integration occurs during the S-phase of the cell cycle; thus, in general, nondividing cells are resistant to retroviral infection. Only the lentiviruses are able to infect nondividing cells. Once a host cell is infected, it is infected for the life of the cell.

Figure no 3:- REPLICATION OF HIV



TRANSMISSION OF HIV[27]:

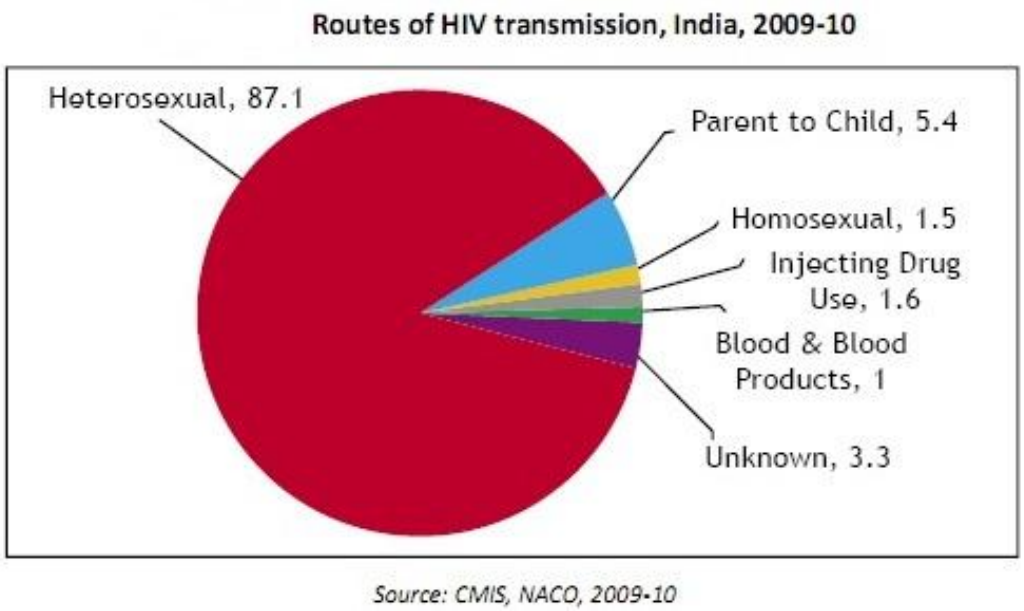
HIV is a sexually transmitted disease, but there are other ways to contract the virus. There is lack of awareness related to the other ways of transmission. Therefore, HIV positive people are shunned by the society, where sexual relations other than legal partner are a taboo.

This lack of awareness, empathy as well as humanity makes the lives of those affected a living hell. It important to know how is HIV transmitted to be able to help those affected.

MODES OF TRANSMISSION

Efficiency of different routes of HIV transmission and their contribution to total number of cases

Figure no 4:-



SEXUAL TRANSMISSION[28]

Most common route of spreading of HIV in India.

- Male to male, unprotected, anal sex - 0.5 to 3%
- Male to female, unprotected, vaginal sex - 0.1 to 0.2%
- Female to male, unprotected, vaginal sex - 0.03 to 0.1%

Risk factors for sexual transmission:

- Male to female transmission is 2-4 times more efficient than female to male transmission.

Factors associated with increased risk of HIV transmission[26]:

Ulcerative and non-ulcerative sexually transmitted disease, lack of circumcision, oral contraceptivepills, alcohol consumption, illicit drug use are associated with unsafe sexual behavior leading to an increased risk of HIV infection. Anal intercourse because the mucosa is thin, unlike vaginal mucosa is more prone for injuries.

Oral sex is a much less efficient mode of transmission of HIV than is receptive anal intercourse.

TRANSMISSION BY BLOOD AND BLOOD PRODUCTS[26]

The most efficient (90-95%) vehicle of HIV transmission is blood.

Blood and blood products which can transmit HIV virus are:

- Transfusion of whole blood, packed red blood cells,leukocytes,platelets, fresh frozen plasma, concentrates of clotting factors, transplanted tissues.
- The products which have not been associated with HIV transmission are:hyper immunegammaglobulin,Hepatitis B immunoglobulin,plasma derived hepatitis Bvaccine.

Occupational Transmission Of Hiv[26]

There is a small but definite occupational risk of HIV transmission in healthcare workers. The risk of transmission following a skin puncture from a needle orsharp object is 0.3% and for mucous membrane it is 0.11%.

Maternal – Fetal/Infant Transmission[26]

The HIV can be transmitted to the fetus as early as the first and second trimester of pregnancy. But 50-70% of transmission occurs late in the gestation or duringlabour or after delivery.

The probability of transmission ranges from 15-25% in the industrialized countries, 25-35% in the developing countries.

Factors which increase the risk of transmission:

Maternal factors:

Advanced maternal HIV disease,P24 antigenemia,CD4+ T cell counts, high plasma HIV-1 RNA levels, acute HIV -1 infection during pregnancy, genital STDs and inflammation at the time of delivery,Vitamin A deficiency, smoking and drug abuse during pregnancy.

Labour and delivery factors:

Chorioamnoitis, prolonged rupture of membranes(>4hours),prematuredelivery before 34weeks gestation, obstetric procedures – amniocentesis, amnioscopy, episiotomy with severe lacerations, first born twin is more commonly infected. Caesarean section results in decreased transmission to the infant.

Breast feeding:

Account for 5-15% of infants becoming infected after delivery.

Risk factors are: detectable levels of HIV in breast, presence of mastitis, low CD4 T cell counts in the mother, maternal vitamin A deficiency.

IMMUNOPATHOGENESIS OF HIV/AIDS[29,30]:

Human immunodeficiency virus, the etiologic agent of AIDS, typically elicitsprogressive and ultimately profound immunosuppression in untreated persons. Once HIV infection is established, the clinical progression is generally steady andassociated with progressive destruction of the immune system.

Without treatment, HIV disease progresses to AIDS over a median interval of about 10 years, eventually causing death in most cases. The course of HIV disease is determined by the interaction between the virus and its host, by the rapidity of viral replication, and the magnitude of the immune response that is generated.

HOST IMMUNE RESPONSES

The natural history of HIV infection is variable among individuals and is theresult of the complex interaction between the virus and the host immune response. High levels of HIV replication are associated with more rapid clinical progression.

The ability of the host to mount a vigorous virus-specific immune response and the capacity of the virus to persist determine the course of HIV disease.

A small percentage of HIV infected individuals have demonstrated lack of disease progression for periods of up to 20 years. Such individuals maintain normal.

CD4 + T-cell counts and some demonstrate low to undetectable plasma viral loads in the absence of antiviral therapy.

ROLE OF CD4+ T HELPER CELLS:

The CD4+T helper cells play a critical role in regulating production of antibodies, induction and maintenance of cutaneous T lymphocyte (CTL) responses, and activation of macrophages and natural killer cells.

During acute infection, T helper (Th) cells are activated and help in orchestrating an effective antiviral response, as one would expect in any viral infection.

However, because HIV is able to selectively infect activated CD4 + T cells, these cells could preferentially become infected and deleted. Alternatively, these cells may undergo activation-induced cell death at the time of high viral load. This in turn would lead to insufficient HIV-specific Th cells to maintain antiviral Cutaneous TLymphocyte responses, and thus the Cutaneous TLymphocyte responses induced during acute infection would progressively diminish. This gradual loss of Cutaneous TLymphocyte has been observed in the majority of infected persons.

Mechanisms thought to cause functional abnormalities and quantitative depletion of CD4+ T cells

Caused by HIV, its components, or both:

- Directly HIV-mediated cytopathic effects (single-cell killing).
- HIV-mediated formation of syncytia.
- Apoptosis induced by gp120 or gp120-anti-gp120 immune complexes.
- Super antigen-mediated perturbation of T-cell subsets.
- Infection of bone marrow or thymic precursors.

Caused by immune response against HIV

- HIV-specific cytolytic T cells.
- Antibody-dependent cellular cytotoxicity (ADCC).
- Th1/Th2 switch.
- Autoimmune mechanisms.

ROLE OF CD8 + T CYTOTOXIC CELLS:

CD8+ T cells play a dual protective and detrimental role in HIV infection. In regard to the former, antigen-specific, cytotoxic T lymphocytes (CTL), normally important in combating viral infections, are readily detectable in HIV infection.

They have been detected in various tissues and can lyse target cells expressing HIV proteins, including env, gag, pol, nef and vif.

Closer examination of the CD8 + T cell population in HIV-infected patients has revealed alterations in several subsets of CD8 +T cells. In particular,percentages of CD8 + T cells that express CD38, CD57, or HLA-DR increase early after HIV infection and usually continue to increase over time.

This oligoclonal CD8+ Tcell expansion appears to be strongly associated with rapid progression towards the full-blown disease, suggesting a critical role for the CD8+T cell mediated response in the development of the disease.

Last, but not least, a switch of CD8+T cells from the cytolyticThl-like functional profile to Th2-like cells showing B-cell helper function and reduced cytolytic activity.

This switch may explain, at least in part, the reduced defense against viral infections and intracellular parasites, and account for the elevated IgE serum levels,eosinophilia, and the allergic-like clinical manifestations seen in some HIV-infectedpatients.

Three dominant patterns of evolution of HIV infection:

Typical progressors: 80%-90% of HIV infected persons are typical progressors and experience a course of HIV disease with a median survival time of approximately 10yrs.

Rapid progressors: 5%-10% of HIV infected persons are rapid progressors and experience an unusually rapid (3-4yrs) course of HIV disease.

Long-term nonprogressors: About 5% of HIV infected persons do not experience disease progression for an extended period of time and are termed long-term nonprogressors.

Natural history of HIV Infection[26]:

The clinical spectrum of HIV infection ranges from a totally asymptomaticstate to severe illness due to a multitude of opportunistic infections.

The signs and symptoms of infection with HIV are varied and complex. Fourstages of HIV infection can be described:

PRIMARY INFECTION/ACUTE HIV SYNDROME:

Approximately 3-6weeks after acquiring infection around 50-70% of peoplesuffer from seroconversion illness in the form of fever, skin rashes, pharyngitis and myalgia similar to the mononucleosis syndrome.

The CD4 +T cell count falls rapidly during this phase and the viremia is high.

Most patients recover spontaneously and majority develop a prolonged phase of clinical latency.

The duration of asymptomatic phase varies from 5-15years.

EARLY IMMUNE DEFICIENCY(CD4+ T CELL COUNT>500 cells/ Micro L):

During this phase the immune system efficiently controls the virus,and thepatient is usually asymptomatic.

Viral replication is highly dynamic and continuous.

Any infection can tilt the balance between the regenerative capacity of theimmune system and the decline of CD4+ T cell counts.

INTERMEDIATE IMMUNE DEFICIENCY(CD4 + T CELLCOUNT 200-500 cells/MicroL):

In this stage viral replication is very high and the CD4+T cell turnover is alsorapid.

Infected individuals may show subtle signs and symptoms indicating acompromised immune system.This is termed AIDS – related complex.

ADVANCED IMMUNE DEFICIENCY (CD4+T CELL COUNT<200 cells/ Micro L):

With continuous viral replication, the CD4 +T cell count falls further and theindividual becomes highly immunocompromised.

Major opportunistic infections and malignancies start developing.

The pattern of opportunistic infections varies according to the geographicallocale, the common ones being pneumocystitisjerovecii pneumonia, generalizedcandidiasis, tuberculosis, CMV retinitis, toxoplasmosis and generalized herpes virus infections.

A CD4+T cell count < 200 cells/microL in a HIV-infected individual is defined as AIDS.

LABORATORY DIAGNOSIS[32, 33,34]:

Various HIV specific antibodies are produced in the early part of infection. They are directed against the major gene products gp 160, gp120, gp41 (env), p66 p51, p33, (pol), p55, p24 and p70 (gag) and can be detected with commerciallyavailable tests with “Rapid protocols” and also by “Elaborate Test protocols”.

Tests commonly employed for the diagnosis of HIV infection may be classified intofollowing groups.

Laboratory Tests For The Diagnosis Of HIV Infecion-

I. Tests for HIV -specific antibodies in serum /plasma

a. Screening test –

i. ELISA

ii. Rapid Tests

b. Supplementary test -

i. Western blot

ii. Immunofluoresecence Test

II. Test for HIV specific antibody in saliva

III. Confirmatory Tests

a. Virus isolation

b. Detection of HIV – specific core antigen (p24)

c. Polymerase chain reaction (RT –PCR/b DNA)

National AIDS Control Programme Technical Advisory Committee ofMinistry of Health & Family Welfare, Government of India recommended the implementation of following HIV antibody testing policy.

NACO Guidelines For HIV Antibody Testing Strategies

Testing Algorithm I

For transfusion purpose: Only one highly sensitive, reliable and economically feasible and technically easy EIA (enzyme immune assay) for both HIV 1 and HIV 2antibodies must be carried out, if reactive, blood is discarded and no further testing is required.

Testing Algorithm II

For surveillance purpose: HIV 1 and HIV 2 testing kits are used. All sera are tested with one EIA, if found reactive is retested with second EIA based on different antigen preparation or principle. Any serum which is reactive on first test but non-reactive on second test is considered antibody negative.

Testing Algorithm III

For identification of asymptomatic individuals: First test with one EIA, if reactive, samples are tested with another EIA based on different antigen preparation or principle. Sample found reactive to second test are subjected to third EIA based on different antigen preparation or principle. Serum reactive on all three tests is considered HIV antibody positive. Serum which is non-reactive in either first test or in second test is considered non-reactive. Samples reactive in first two tests and negative in third test is considered equivocal/borderline positive.

Screening Test-

Enzyme Linked Immuno Sorbent Assays (ELISA)-

These assays use enzymes as indicator system for the detection and quantitation of analyte present in the immune complexes formed as a result of reaction between solidsurface bound HIV antigen and circulating antibody. These tests are highly sensitiveand specific and take 90 minutes for completion.

ELISA Generations:

First generation – Whole viral lysate

Second generation – Recombinant antigen

Third generation – Synthetic peptide

Fourth generation – Antigen+Antibody (simultaneous detection of HIV antigen and antibody-HIV Duo)

Rapid Test-

Most popular ones are dot blot assays. In them microscopic particles are coated with a synthetic peptide and then immobilized on a nitrocellulose membrane. Patient's serum containing antibodies, conjugate, developer and stop solutions are then added in sequence with usual incubation and washing steps. These tests have a total reaction time of less than 30 minutes.

Supplement Tests-

Western Blot-

Specific viral proteins from whole virus lysate are separated by polyacrylamide gel electrophoresis according to their molecular weight and then transferred onto a nitrocellulose membrane by a process called electro blotting. A serum sample is reacted with HIV protein immobilized on the strip. If sample has antibodies, coloured bands will appear where ever human IgG binds to viral proteins on the strip.

Immuno fluorescence Test-

In this test HIV infected cells are acetone fixed onto glass slides and then reacted with serum followed by fluorescein conjugated anti-human antibody. An apple green fluorescence of the membrane is considered positive.

Confirmatory Tests-

Virus Isolation-

Virus can be isolated from the blood of the infected individual by cocultivating peripheral blood mononuclear cells (PBMC) with those from uninfected donors. It generally takes 4-8 weeks for isolation and identification of the virus. This assay is 100% specific but its sensitivity ranges with stage of HIV infection.

Detection of HIV specific core antigen-

The antigen test detects HIV free antigen (p 24) in the serum. This test is useful in window period, during late disease when patient is symptomatic, to detect HIV infection in a newborn because diagnosis is difficult due to presence of maternal antibodies, etc. The test employs indirect ELISA technology in which a specific antibody is bound to a solid phase and the serum containing free HIV antigen is made to react with this antibody.

Polymerase Chain Reaction (PCR)-

This technique allows detection of HIV infection prior to the detection by antibody assays. A single copy of proviral DNA can be amplified and then be detected by the probe. The PCR can be used to detect HIV RNA in the blood by an additional step of converting RNA from plasma to a complementary DNA (cDNA) strand using enzyme reverse transcriptase. The cDNA obtained can be used as atemplate to perform PCR. Nested PCR is a modified PCR for greater specificity and sensitivity.

ORAQUICK ADVANCE RAPID HIV TESTS:

This test was approved in 2004.It gives results in 20mins.The blood, plasma, oral fluid is mixed in a vial with the developing solution and the results are read from stick like testing device.

URINE TESTS

Intact IgG antibodies are found in urine whose origin is not known. It is simple, inexpensive and non-invasive and widely used by physicians, medical officers etc.

HIV infection can be diagnosed by serologic tests that detect antibodies against HIV-1 and HIV-2 and by virological tests that can detect HIV antigens or ribonucleic acid (RNA). Antibody testing begins with a sensitive screening test (e.g., the conventional or rapid enzyme immunoassay [EIA]). Currently available serologic tests are both highly sensitive and specific and can detect all known subtypes of HIV-1. Most can also detect HIV-2 and uncommon variants of HIV-1 (e.g., Group O and Group N).

The advent of HIV rapid serologic testing has enabled clinicians to make an accurate presumptive diagnosis of HIV infection within half an hour.

Reactive screening tests must be confirmed by a supplemental antibody test (i.e., Western blot [WB] and indirect immunofluorescence assay [IFA]) or virologic test (i.e., the HIV-1 RNA assay). A confirmed positive antibody test result indicates that a person is infected with HIV and capable of transmitting the virus to others. HIV antibody is detectable in at least 95% of patients within 3 months after infection. Although a negative antibody test result usually indicates that a person is not infected, antibody tests cannot exclude recent infection.

Virologic tests for HIV-1 RNA can also be used to identify acute infection in persons who are negative for HIV antibodies. However, HIV-2 infection should be suspected in persons who have epidemiologic risk factors or an unusual clinical presentation.

Epidemiologic factors associated with HIV-2 infection include having lived in or having a sex partner from an HIV-2 endemic area (e.g., West Africa and some European countries such as Portugal)where HIV-2 prevalence is increasing. Specific testing for HIV-2 is also indicated when clinical evidence of HIV infection exists but tests for HIV-1 antibodies or HIV-1 viral load are negative, or when HIV-1 WB results exhibit the unusual indeterminate pattern of gag (p55, p24, p17) plus pol (p66, p51, p31) bands in the absence of env (gp160, gp120, gp41) bands.

Suspicion of acute retroviral syndrome should result in prompt nucleic acid testing (HIV plasma RNA) in addition to an HIV antibody test to detect the presence of HIV.

A positive HIV nucleic acid test should be confirmed by subsequent antibody testing to document seroconversion.

ANTI RETROVIRAL THERAPY[35]

Antiretroviral agents are drugs which act at various stages of the life cycle of HIV in the body and work by interrupting the process of viral replication. Theoretically, ARV drugs can act in any of the following ways during different stages of viral replication:

(i) Block binding of HIV to target cell (fusion inhibitors)

(ii)Block viral RNA cleavage and one that inhibits reverse transcriptase (reverse transcriptase inhibitors)

(iii) Block the enzyme, integrase, which helps in the incorporation of the proviral DNA into the host cell chromosome (integrase inhibitors)

(iv)Block the RNA to prevent viral protein production

(v) Block the enzyme protease (protease inhibitors)

(vi) Inhibit the budding of virus from host cells

The currently available agents target the virus mainly by inhibiting the enzymes reverse transcriptase (RT inhibitors) and protease (protease inhibitors), and preventing fusion of the virus with CD4 cells (fusion inhibitors). New classes of drugs are emerging.

GOALS OF ART (ACCORDING TO NACO GIUDELINES)

The currently available ARV drugs cannot eradicate the HIV infection from the human body. This is because a pool of latently infected CD4 cells is established during the earliest stages of acute HIV infection and persists within the organs/cells and fluids (e.g., liver and lymphoid tissue) even with prolonged suppression of plasma viraemia to <50 copies/ml by antiretroviral therapy. The goals of therapy are as follows.

- **Clinical goals:** Prolongation of life and improvement in quality of life
- **Virological goals:** Greatest possible reduction in viral load for as long as possible
- **Immunological goals:** Immune reconstitution that is both quantitative and qualitative
- **Therapeutic goals:** Rational sequencing of drugs in a fashion that achieves clinical, virological andimmunological goals while maintaining treatment options, limiting drug toxicity and facilitating adherence
- **Reduction of HIV transmission in individiuals:** Reduction of HIV transmission by suppression of viral load

INITIATION OF ART(ACCORDING TO NACO GIUDELINES)

All persons registered for care and treatment at ART centre's should have their full history taken and undergo clinical examination, including determining the clinical stage of HIV. The initiation of ART is based on the clinical stage and the CD4 count is used to guide treatment and follow-up. **The lack of a CD4 result should not delay the initiation of ART if the patient is clinically eligible according to the WHO clinical staging, but a CD4 test should be done as soon as possible.**

Table No. 2 Initiation of ART based on CD4 count and WHO clinical staging

Classification of HIV-associated clinical disease	**WHO clinical stage**	**CD4 test not available (or result pending)**	**CD4 test available**
Asymptomatic	**1**	**Do not treat**	**Treat if CD4 <200**
Mild symptoms	**2**	**Do not treat**	**Treat if CD4 <200**
Advanced symptoms	**3**	**Treat**	**Consider treatment if CD4 <350and initiate ART before CD4drops below 200**
Severe/advanced symptoms	**4**	**Treat**	**Treat irrespective of CD4 count**

ANTIRETROVIRAL THERAPY REGIMENS(ACCORDING TO NACO GIUDELINES)

Principles for selecting the first-line regimen

1. Choose 3TC (lamivudine) in all regimens

2. Choose one NRTI to combine with 3TC (AZT or d4T)

3. Choose one NNRTI (NVP or EFV)

Table No. 3 Recommended first-line antiretroviral regimens

Recommendation	Regimen	Comments
Preferred firstline regimen	AZT + 3TC + NVP	AZT may cause anaemia, which requires Hb monitoring, but is preferred over d4T because of d4T toxicity (lipoatrophy, lactic acidosis, peripheral neuropathy) Patients who develop severe anaemia while on an AZTbased regimen should not be re-challenged with AZT. In such cases, the patient should receive either d4T or TDF in place of AZTFor women with CD4 > 250 cells/mm3, monitor for hepatotoxicity closely if started on the NVP-based regimen
Alternative first -line regimens	AZT + 3TC + EFV D4T + 3TC + (NVP or EFV)	EFV is substituted for NVP in cases of intolerance to thelatter or if patients are receiving rifampicin-containing anti-TB treatment.EFV should not be used in patients with grade 4 or higherelevations of ALT If the patients have anaemia, a d4T-based regimen should be prescribed
Other options	TDF + 3TC + (NVP or EFV) or AZT + 3TC + TDF	TDF is supplied on a case-to-case basis by SACS after evaluation by the SACS clinical expert panel

METHODOLOGY

SOURCE OF DATA:

The HIVseropositive patients admitted in or attending surgical OPD or diagnosed at B.L.D.E.U.'s Shri. B. M. Patil Medical College Hospital & Research Centre Bijapur, with history suggestive of anorectal disease were included in the study.

METHOD OF COLLECTION OF DATA:

The HIV seropositive patients admitted or diagnosed in B.L.D.E.U.'s Shri. B.M.Patil Medical College Hospital Bijapur/ attending surgical OPD during period of Oct 2012 to July 2014.

Details of patients were recorded including history, clinical examination, and investigations done.

Detailed information regarding anorectal disease was entered in the proforma. These patients underwent appropriate treatment as necessary.

INCLUSION CRITERIA

The HIVseropositive patients admitted or diagnosed in B.L.D.E.U.'s Shri. B. M. Patil Medical College Hospital Bijapur/ attending surgical OPD. All HIV seropositive patients with anorectal disease were included in the study.

EXCLUSION CRITERIA

Patients with anorectal disease who were seronegative for HIV were.

STATISTICAL ANALYSIS

1. Correlation was established between anorectal pathology and CD4+ T cell count using Spearman's method by SPSS software.
2. Mean± 2SD

RESULT

During a period of 1st September 2012 to 31st July 2014, 89 patients were identified in BLDEU's ShriB.M.Patil Medical College Hospital and Research Centre, Bijapur.

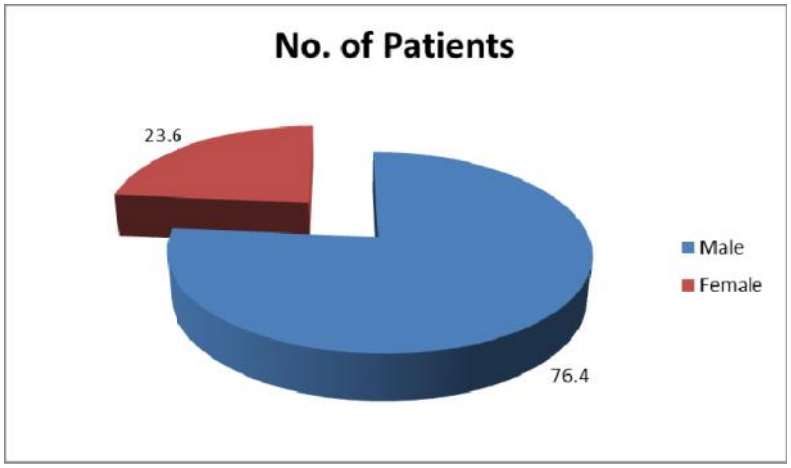
During study period 59,744 patients were admitted and 430 were HIV seropositive patients. Of, those eighty nine had anorectal symptoms. Incidence of anorectal diseases in HIV seropositive patients was 20.7%.

Table no. 4- Sex distribution

Sex	No. of Patients
Male	68
Female	21

In the present study the total number are 89. Among these 68 patients are male and 21 are female. Male to female ratio for the HIV reactive patients in the study was 3:1.

Graph no. 1- Sex Distribution (%).



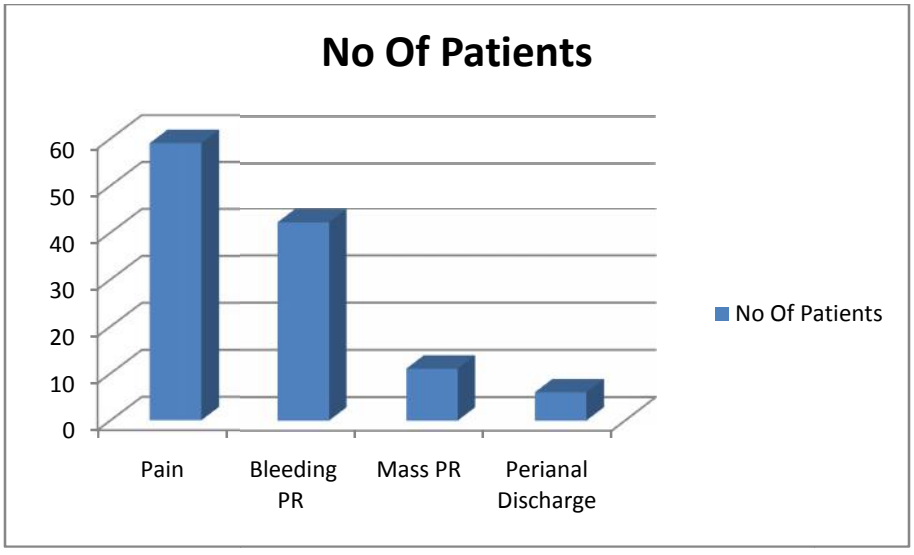
Symptomatology

Table No 5:- Symptom Distribution

Symptoms	No Of Patients
Pain	59
Bleeding PR	42
Mass PR	11
Perianal Discharge	6

Among the study group most common symptom was pain while defecation (59 patients), followed by bleeding per rectum (42 patients). Other symptoms were mass per rectum and perianal discharge.

Graph No 2:- Symptom Distribution

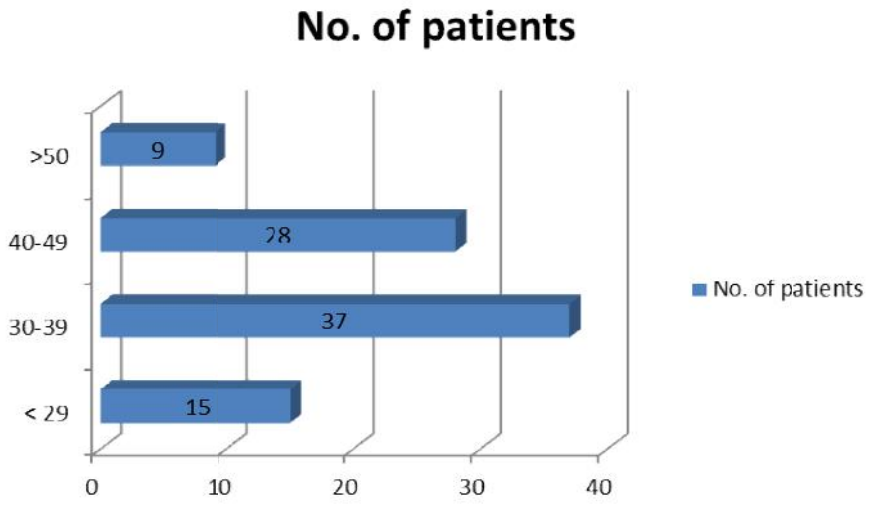


Age distribution:

Table No. 6- Age Distribution.

Age (yrs)	< 29	30-39	40-49	>50
No. of patients	15	37	28	9

Graph No. 3- Age Distribution.



In the present study, the age of the patients ranged between 16 years to 55 years.Amongthe 89 patients studied, most of them were in the range of 30 - 39 years(41%) followed by 40-49 years(31%).Youngest patient in the study was of 16years and highest age noted was 55years.The mean age in is 37.43±7.83years.

Anorectal Disease Distribution

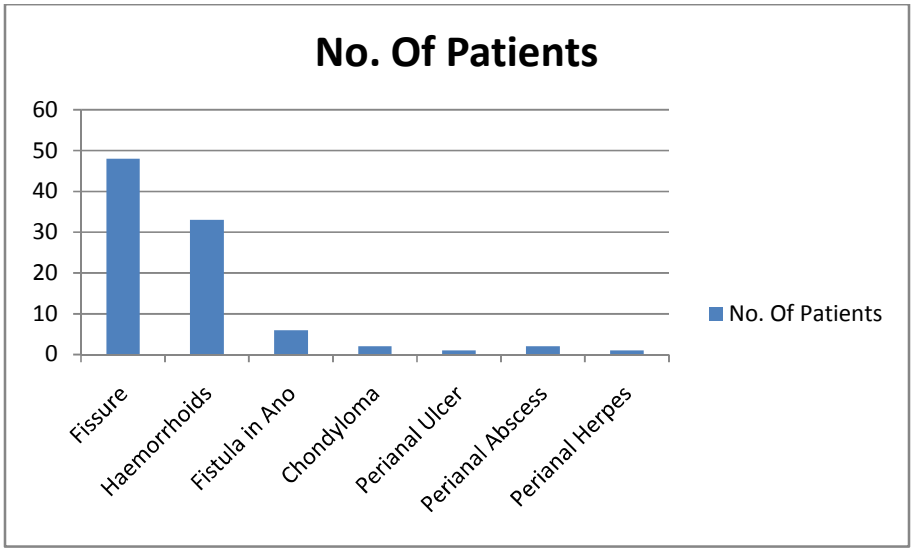
Table No. 7-Anorectal Disease Distribution

Anorectal Disease	No. Of Patients
Fissure	48
Haemorrhoids	33
Fistula in Ano	6
Chondyloma	2
Perianal Ulcer	1
Perianal Abscess	2
Perianal Herpes	1

In the present study, the most common anorectal pathology was fissure in ano (54%), hameorrhoids(37%). Other anorectal pathology were fistula in ano, perianal abscess, condyloma, perianal herpes and post traumatic perianal ulcer.

Eight patients had more than one disorder.

Graph No. 4- Anorectal Disease Distribution



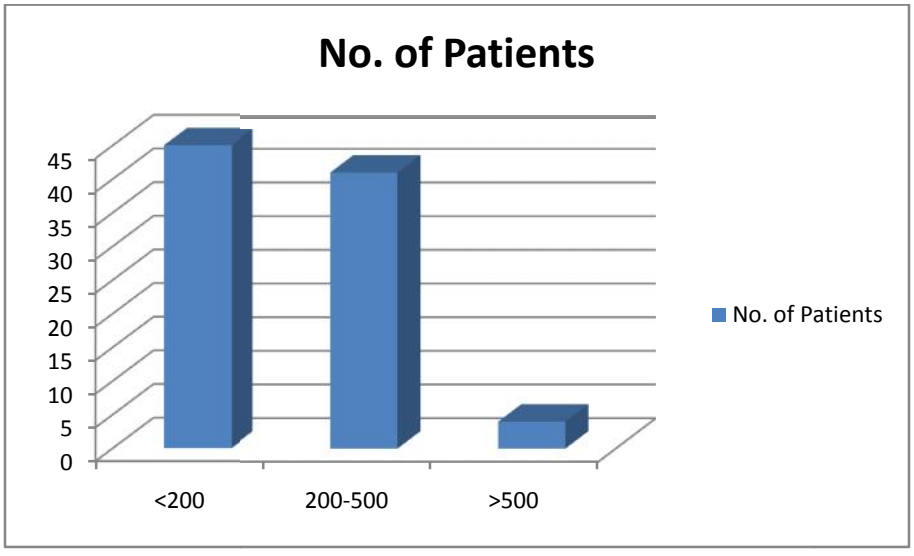
Correlation with CD4+ T Cell Count

Table No. 8- Distribution of Patients

CD 4+ T Cell Count (cells/cumm)	No. of Patients
<200	45
200-500	40
>500	4

Amongthe 89 patients studied, most of them were in the range of <200cells/mm^3, 45 patients (50.5%) followed by 200-500 cells/mm^3, 40 patients (45%). Remaining 4 patients were in the group of >500 cells/mm^3. Average CD4+ T cell count was 232.49±135.65 cells/cumm.

Graph NO. 5- Distribution Of Patients



Correlation with CD4+ T Cell Count

Table No 9- Distribution of Diseases

CD4 + T Cell Count (cells/cumm)	Anorectal Pathology
<200	Fistula, fissure, haemorrhoids, perianal abscess
200 – 500	Fissure, haemorrhoids, chondyloma, perianal ulcer, perianal herpes
>500	Fissure, haemorrhoids

In this study, with CD4+ of <200 cells/cummfistula, fissure, haemorrhoids, perianal abscess were identified. With CD4+ count of 200-500 cells/cumm Fissure, haemorrhoids, chondyloma, perianal ulcer, perianal herpes were identified and with CD4+ of >500 fissure and haemorrhoids were identified.

Spearman's correlation between anorectal pathology and CD 4+ T cell count, interpreted negative correlation between different anorectal pathology and CD 4+ T cell count.

R= -0.258

P= 0.024

Table No 10- Systemic Diseases

Disease	No. of Patients
Tuberculosis	6
Viral hepatitis	2
Alcoholic Liver Disease	5
Others	8

Of the 89 patients, 21 patients suffered from other systemic disorders. Pulmonary tuberculosis. Alcoholic liver disease and vital hepatitis were common. Other systemic disorders were meningitis, COPD, pyrexia of unknown origin and gastric outlet obstruction.

DISCUSSION

The present study titled "CLINICAL PROFILE OF ANORECTAL DISEASES IN HIV SEROPOSITIVE PATIENTS AND ITS CORRELATION WITH CD4+ COUNTS" was conducted at BLDEU's, ShriB.M.Patil Medical College, Hospital and Research Center, Bijapur.

The objective of the study was to know the clinical profile of anorectal disease among HIV positive patients.

In a study conducted by Yuhan R, et al, in 1993 at the Division of Colon and Rectal Surgery, Cook County Hospital and University of Illinois, Chicago, Illinois. The mean age of this cohort was 33 years, with a male-to-female ratio of 14:1, showing that HIV infection is most prevalent in young men. The majority of this group comprised homosexual or bisexual males (55 percent). The actual percentage of this risk group may be even higher because another 18 percent would not disclose their sexual orientation. The homosexual population seems to be particularly susceptible to anorectal lesions.

Anorectal Pathology

Pathology	Number	Percent
Condyloma	78	43
Ulcers	57	32
Fistula	26	14
Abscess	22	12
Hemorrhoid	11	6
Malignancy	4*	2

Sixteen percent of patients with HIV had multiple lesions.

The most common symptom was anorectal pain, followed by lumps or warts, with many patients complaining of more than one anorectalsymptom.The most common anorectal condition encountered was anal or perianal condylomata, noted in

43 percent of all patients with HIV. Anal ulcers were the most common noncondylomatous HIV-associated anorectal condition. Two cases of anal Kaposi's sarcoma were observed, one case of non-Hodgkin's lymphoma was seen in a patient with AIDS who had anorectal pain.

In a study conducted by Barret L W, et al, at Division of Colon and Rectal Surgery, Department of Surgery, The George Washington University, Washington, D.C. Their mean age was 34.9 (range, 19-58) years. Mean duration of known HIV positivitywas 5 years, 5 months (range, up to 11 years, 5 months). In 5 percent of our patients, a perianal complaint was the first sign of HIV infection, and tile HIV test was ordered by the colorectal surgeon. Median CD4 count was 175 (range, 2-1,100) cells per mm^3.

The three most common major presenting symptoms were anorectal pain (142 patients (55 percent)), presence of a mass (50 patients (19 percent)), and blood in the stool (41 patients (16 percent)).

Forty different disorders were identified. The three most common overall were condyloma (111 patients (42 percent)), fistula (87 patients (34 percent)), and fissure (82 patients (32 percent)). These 40 disorders were divided into four categories: benign noninfectious (18 types), infectious (14), neoplastic (6), and septic (2).

In our study over a period of two years, 89 HIV seropositive patients with anorectal pathology were referred to surgical clinic.

Most common symptom was anorectal pain, followed by bleeding per rectum and mass per rectum. Study conducted by Yuhan R had anorectal pain as most common symptom followed by lumps or warts, and rectal bleeding. Study conducted

by Barret L had anorectal pain as most common symptom, followed by mass and bleeding per retum.

Most common anorectal pathology identified in our study is anal fissure, haemorrhoids, and fistula. Study by Yuhan R, anal condyloma, anal ulcer and fistula were the most common anorectal pathology. Study by Barret*et al* (1996), anal condyloma, anal ulcer, fistula and anal fissure were the most common anorectal pathology.

In our study no neoplastic anorectal diseases were identified.

Table No 11:- Comparision with Other Studies

Pathology	Our Experience (%)	Barret et al (1989-1996) (%)	Yuhan et al (1993-1997) (%)
Condyloma	2.2	32	43
Anal ulcer	1.1	33	32
Fissure	54	6.5	N/A
Fistula	6.8	6	14
Haemorrhoids	37	4.5	6
Abscess	2.2	3	12

In a study by Claudia Gonzalez-Ruiz, et al at Department of Colon and Rectal Surgery, Keck School of Medicine at the University of Southern California,Los Angeles, California to know the impact of anitretroviral therapy (ART) on anorectal pathology.

Total of 117 patients were identified in pre ART era (early period) and 107 in ART era (late period). Ninety-five percent of the patients were male, with the vastmajority being MSM. The average age of the patients treated in the early period was 44 years, and for those of the late period it was 40.

HIV-related pathology was distributed as follows for the early vs. late periods: 33 vs. 33 percent for anal ulcer, and 30 vs. 34 percent for anogenitalcondyloma. For non-HIV-pathology the distribution was 9 vs. 4 percent for anal fissure, 6 vs. 6 percent for fistulas (all of which were cryptoglandular), 4 vs. 5 percent for hemorrhoids, and 3 vs. 3 percent for perianal abscess.

They did not see a significant difference in the prevalence of anorectal pathology for the overall clinic population between the studied time periods before and after the appearance of HAART. The percentage of HIV/AIDS patients presenting to the colorectal clinic during these 18-month periods remained approximately 4.5 percent.

Study was conducted by N. D. Carr, on Non-condylomatous perianal disease in homosexual men. Of 34 homosexuals 20 presented with anorectal sepsis. Lesions included chronic intersphincteric abscess (eight patients), anal fistula (seven patients) and chronic intersphincteric abscess and fistula (five patients). Anal fissure occurred in 15 patients, anal ulcer in three, skin tags in six, haemorrhoids in two and Kaposi's sarcoma in one.

CONCLUSION

In our study majority of the patients with HIV infections suffered from fissure followed by haemorrhoids. Fistula was the third most common anorectal pathology identified.

Other anorectal pathology identified were perianal abscess, condyloma, perianal herpes, and post traumatic perianal wound.

Due lower incidence of male to male sex, HIV related anorectal pathology was low in our study.

SUMMARY

This study was conducted from September 2012 to July 2014, at BLDEU's Shri B M Patil Medical College and Research Centre.

Incidence of anorectal diseases in HIV seropositive patients was 20.7%.

Eighty Nine patients presented to surgical opd with anorectal symptoms who were HIV seropositive over this study period. Anorectal pathology were more common among middle aged male patients.

Anorectal pain was the most common symptom followed rectal bleedin and rectal mass. Anal fissure was the most common anorectal pathology followed by haemorrhoids and fistula in ano.

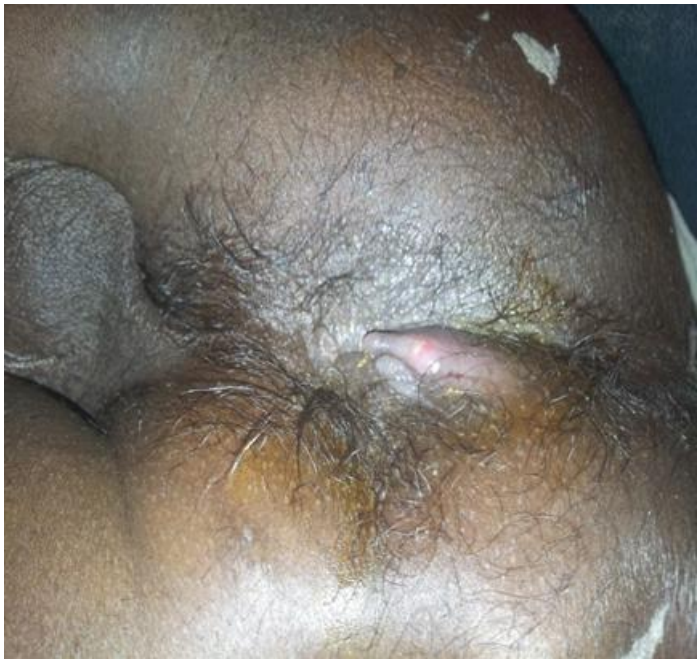
Other anorectal pathology identified were anal condyloma, perianal abscess, perianal herpes and post traumatic perianal wound.

Spearman's correlation between anorectal pathology and CD 4+ T cell count, interpreted negative correlation between different anorectal pathology and CD 4+ T cell count.

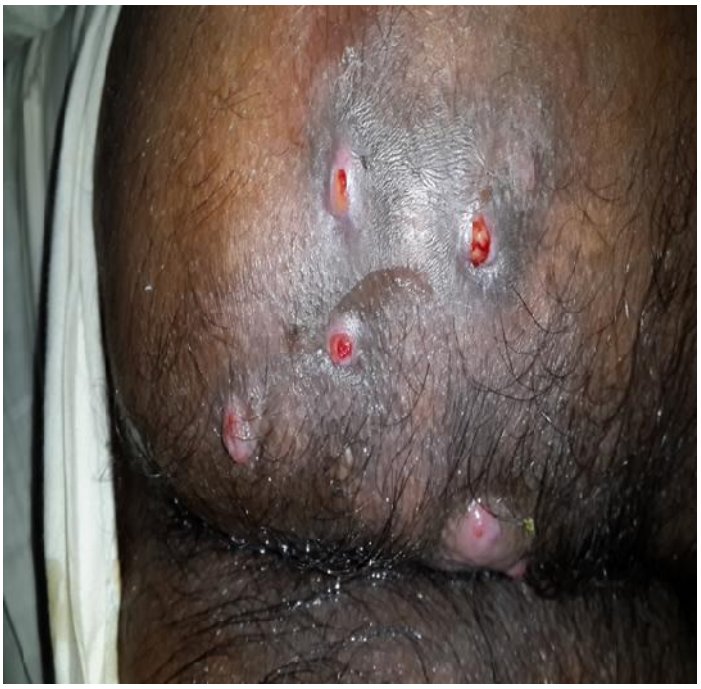
R= -0.258

P= 0.024

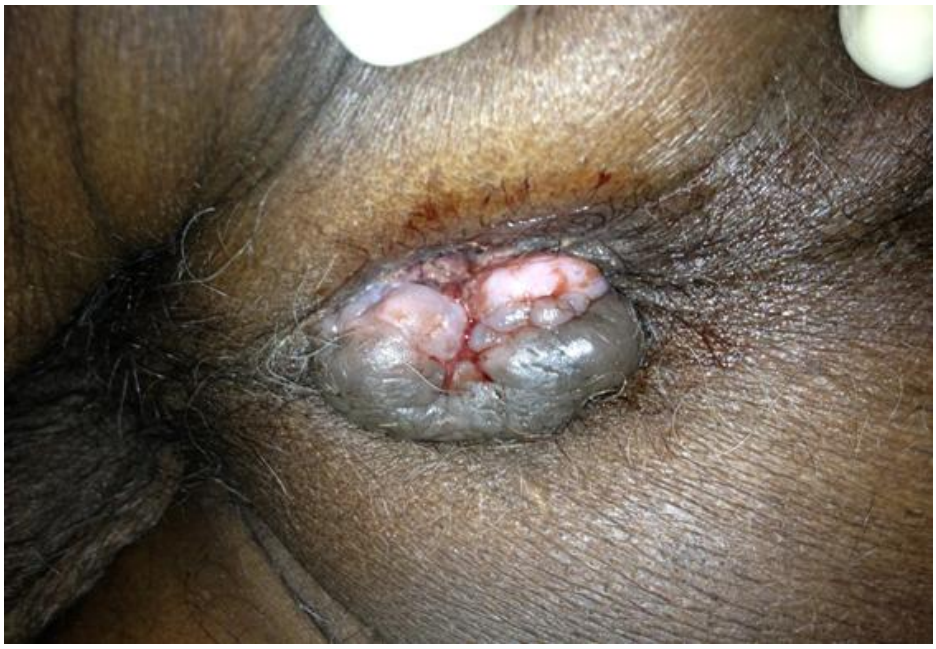
PHOTOGRAPHS



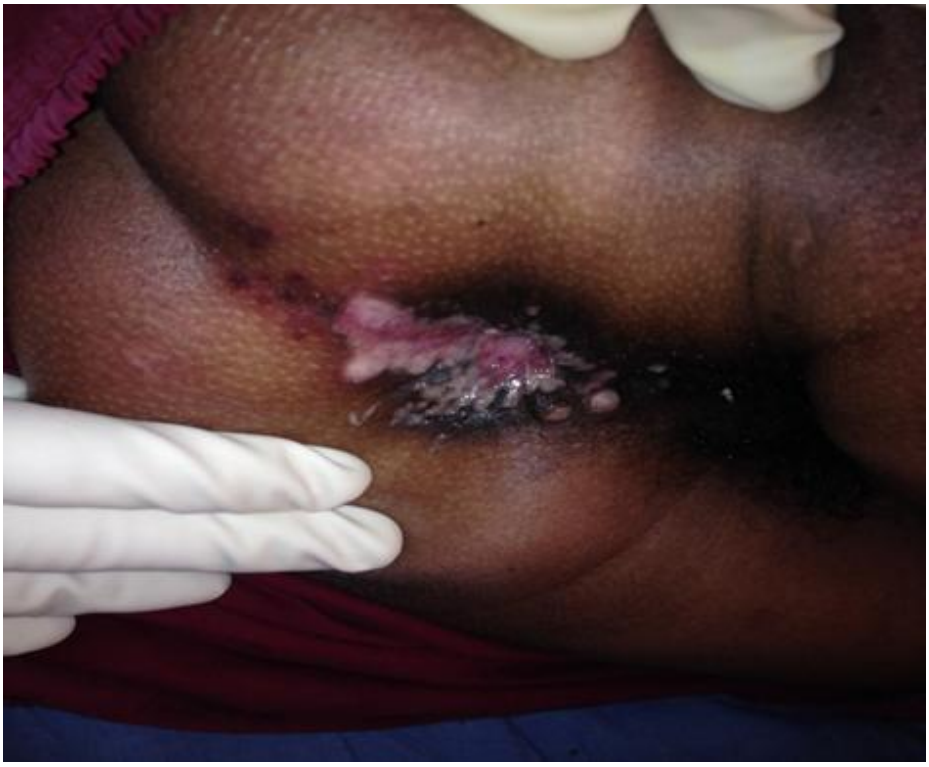
Photograph No. 1- Perianal Abscess



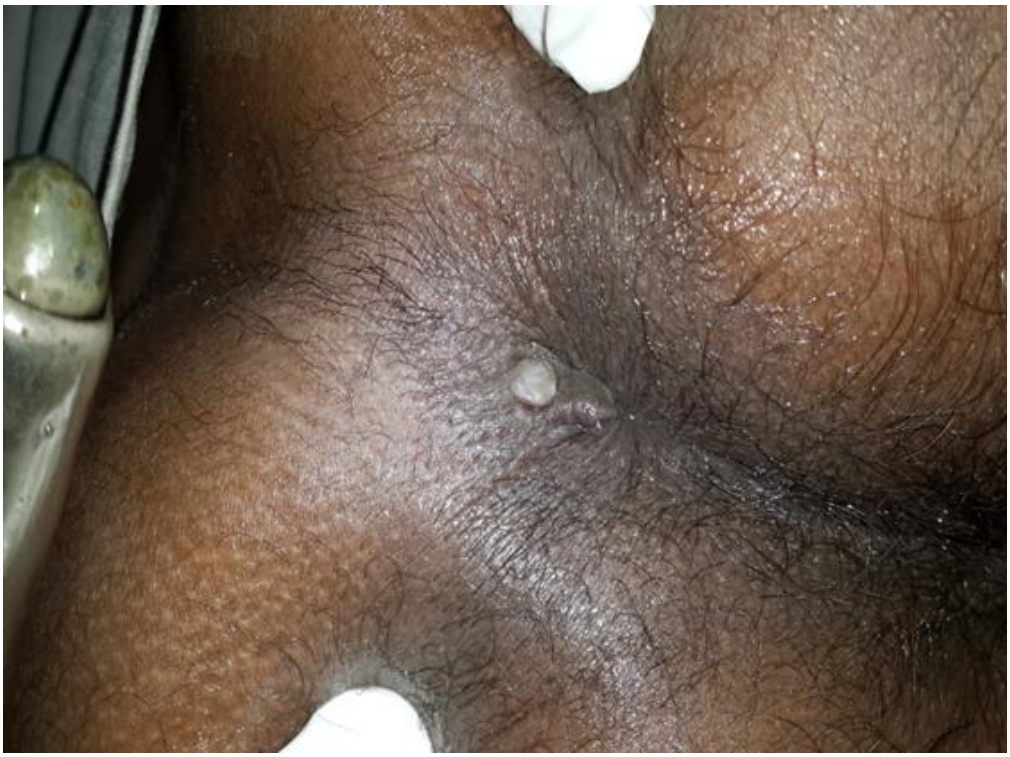
Photograph No. 2- Complex Fistula InAno



Photograph No. 3- Prolapsed Haemorrhoids



Photograph No. 4- Perianal Herpes



Photograph No. 5- Perianal Condyloma

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ANNEXURE

Institutional Ethical Committee
BIJAPUR-586 103.
OUTWARD
No. 246/12
Dt: 18/10/12

B.L.D.E. UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 18-10-2012 *at* 3-30pm *to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.*

Title "clinical profile of anorectal diseases in HIV seropositive patients and its correlation with CD4+ counts"

Name of P.G. student Dr. Harshavardhan. P. Biradar
Surgery

Name of Guide/Co-investigator Dr Tejaswini Vallabha.
Prof & HOD Surgery

DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

PROFORMA

SCHEME OF CASE TAKING:

1) Name	:			CASE NO	:
2) Age/sex	:			IP NO	:
3) Religion		DOA	:		
				DOS	:
4) Occupation	:			DOD	:
5) Residence	:				

6) Chief Complaints :

7) Past History-

8) Treatment history – Any surgery

Systemic illness.

9) Personal History – Diet

Appetite

Bowel/Bladder

Sleep

Habits

10) Family History -

11) General Physical Examination -

Built	Nourishment
Pulse rate	Pallor:
Blood pressure	Respiratory rate
Temperature	Jaundice
Clubbing	Cyanosis
Edema	Lymphadenopathy

12) Per rectal examination.

Digital examination

Proctoscopy

Sigmoidoscopy

Colonoscopy

13) Other systemic examination

- Abdominal system
- Respiratory system.
- Cardiovascular system.
- Central nervous system.
- Other system

14) INVESTIGATIONS UNDERGONE BY PATIENT:

Complete blood count

Urine routine

Bleeding time and clotting time

Random blood sugar

Blood urea

Serum creatinine

HIV

CD4 Count

HBsAG

15) FINAL DIAGNOSIS

INFORMED CONSENT FORM

TITLE OF THE PROJECT	:	To study the clinical profile of anorectal diseases in human immunodeficiency virus seropositive patients.
GUIDE	:	Dr. TEJASWINI VALLABHA (PROFESOR and HOD)
P.G. STUDENT	:	Dr. HARSHAVARDHAN P BIRADAR

PURPOSE OF RESEARCH:

I have been informed that this study is conducted to know the profile of anorectal diseases human immunodeficiency virus-positive patients.I have also been given free choice of participation in this study.

PROCEDURE:

I am aware that in addition to routine care received I will be asked series of questions by the investigator. I have been asked to undergo the necessary investigations and treatment, which will help the investigator in this study.

RISK AND DISCOMFORTS:

I understand that I may experience some pain and discomforts during the examination or during my treatment. This is mainly the result of my condition and the procedures of this study are not expected to exaggerate these feelings which are associated with the usual course of treatment.

BENEFITS:

I understand that my participation in the study will help to know the clinical profile of anorectal disease in HIV seropositive patients.

CONFIDENTIALITY:

I understand that the medical information produced by this study will become a part of hospital records and will be subject to the confidentiality. Information of sensitive personal nature will not be part of the medical record, but will be stored in the investigations research file.

If the data are used for publication in the medical literature or for teaching purpose, no name will be used and other identifiers such as photographs will be used only with special written permission. I understand that I may see the photograph before giving the permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at anytime Dr. Harshavardhan P Biradar at the department of surgery who will be available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of the study, which might influence my continued participation. A copy of this consent form will be given to me to keep for careful reading.

REFUSAL FOR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice. I also understand that Dr. Harshavardhan P Biradar may terminate my participation in the study after he has explained the reasons for doing so.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me resulting directly from my participation in this study, if such injury were reported promptly, the appropriate treatment would be available to me. But, no further compensation would be provided by the hospital. I understand that by my agreements to participate in this study and not waiving any of my legal rights.

I have explained to _____the purpose of the research, the procedures required and the possible risks to the best of my ability.

_____ _____

Dr. Harshavardhan P Biradar Date

(Investigator)

STUDY SUBJECT CONSENT STATEMENT:

I confirm that Dr. Harshavardhan P Biradar has explained to me the purpose of research, the study procedure, that I will undergo and the possible discomforts as well as benefits that I may experience in my own language. I have been explained all the above in detail in my own language and I understand the same. Therefore I agree to give consent to participate as a subject in this research project.

_____ _____

(Participant) Date

_____ _____

(Witness to signature) Date

MASTER CHART

NAME	IPD/OPD NO.	SEX	AGE	DIAGNOSIS	CD4 COUNT	SYMPTOMS
Dareppa masali	23448/12	Male	40	Hemorrhoids	398	Bleeding PR
Siddu	5750/13	Male	32	Fissure with Hemorrhoids	124	Pain and Bleeding PR
Sharanappa	23967/12	Male	40	Traumatic Perineal Ulcer	214	Bleeding PR
Sandeep	5094/13	Male	28	Fissure	400	Pain and Bleeding PR
Gouramma	532/12	Female	48	Fissure with Hemorrhoids	140	Bleeding PR and Mass PR
Siddappa	108277/12	Male	28	Fissure with Molluscum Contagiosum	564	Mss PR and Pain
Bhimashi	11927/13	Male	43	Hemorrhoids with Portal hypertension	78	Bleeding PR
Hiragappa	20748/13	Male	55	Fissure	230	Pain
Renuka	3911/13	Female	30	Fissure	88	Pain
Roopa	7675/13	Female	45	Fissure with Hemorrhoids	102	Pain
Mahadevi	1654/13	Female	36	Fissure	180	Bleeding PR and Pain
Neelawwa	26472/12	Female	35	Fissure	230	Pain
Sharanappa	26342/12	Male	38	Fissure	132	Pain
Kareppa	2089/13	Male	30	Hemorrhoids	160	Bleeding PR
Bhimashankar	567/13	Male	35	Fissure	204	Pain and Bleeding PR
Siddappa	4070/13	Male	46	Fissure	640	Pain
Chandrashekar	1628/13	Male	40	Hemmorhoids	246	Bleeding PR
Sunil	5916/13	Male	30	Hemmorhoids	480	Bleeding PR
Tukaram	24221/12	Male	41	Hemmorhoids With Fissure	84	Bleeding PR
Shankramma	2923/13	Female	28	Fissure	178	Bleeding PR and Pain
Basu Pawar	3008/13	Male	43	Fissure With Haemorrhoids	200	Pain and Bleeding PR
Mallappa	2685/13	Male	38	Fissure	220	Pain
Basavaraj	25048/12	Male	50	Fissure	230	Pain
Manjunath	48642/13	Male	36	Fissure	242	Pain
Barappa	12142/13	Male	40	Fissure	124	Pain
Basappa	7574/13	Male	55	Hemmorhoids	132	Bleeding PR
Hanamantaraya	30478/13	Male	30	Hemmorhoids	272	Bleeding PR
Tippanna	2432/13	Male	38	Fissure with Hemorrhoids	370	Pain and Bleeding PR
Mahantesh	166547/13	Male	32	Fissure	188	Pain
Sujata	174312/13	Female	28	Fistula in ano	140	Pain And perianal Discharge
Hanamanth	14561/13	Male	35	Hemmorhoids	180	Mass PR and Bleeding PR
Kamala	183417/13	Female	33	Fissure	96	Pain and Bleeding PR
Siddappa	184343/13	Male	45	Complex fistula in ano	54	Perianal Disharge And Pain
Balawwa	190284/13	Female	47	Fissure	108	Pain and Mass PR
Kumar Vijay	14671/13	Male	35	Hemmorhoids	145	Bleeding PR And Pain
Suvarna	16681/13	Female	27	Hemmorhoids	283	Mass PR and Bleeding PR
Shashikanth	201469/13	Male	30	Fissure	210	Pain
Suresh	17777/13	Male	34	Fistula in ano	18	Perinal Disharge
Nagappa	231689/13	Male	52	Hemmorhoids	488	Mass And Bleeding PR
Shrinath	222704/13	Male	37	Fissure	290	Pain
Chandrashekar	18054/13	Male	40	Fissure	346	Pain and Bleeding PR
Pooja	19179/13	Female	21	Fistula in ano with Fissure	128	Perianal Discharge And Pain
Suresh	221054/13	Male	40	Fissure	600	Pain
Prabhavati	231124/13	Female	48	Fissure	180	Pain
Parvati	323106/13	Female	28	Hemmorhoids	430	Mass And Bleeding PR
Gurulingayya	304186/13	Male	30	Fissure	176	Pain
Rajendra	344124/13	Male	31	Hemmorhoids	123	Mass PR and Bleeding PR
Sumitra	326428/13	Female	25	Fissure	148	Pain and Bleeding PR
Tukaram	358140/13	Male	50	Fissure	172	Pain and Bleeding PR
Prassanna	206126/13	Male	29	Fissure	340	Pain and Mass PR
Prabhakar	214308/13	Male	40	Hemmorhoids	344	Bleeding PR
nagappa K	400328/13	Male	36	Hemmorhoids	380	Pain and Bleeding PR
Basappa	409134/13	Male	40	Fissure	288	Pain
Balawwa	948/14	Female	35	Fissure	240	Pain
Mahadev	1048/14	Male	42	Hemmorhoids	255	Bleeding PR And Pain
Tasleema	5312/14	Female	29	Fissure	100	Pain with Bleeding PR

Rajashekar	3038/14	Male	43	Fissure	128	Pain
Chandappa	6148/14	Male	34	Fissure	230	Pain
Anil	7894/14	Male	30	Hemmorhoids	368	Bleeding PR And Pain
Chandrashekar	108413/14	Male	35	Fissure	346	Pain
Gurmappa	11342/14	Male	47	Hemmorhoids	600	Bleeding PR
Bherappa	21440/14	Male	52	Hemmorhoids	320	Bleeding PR And Pain
Harishchandra	2034/14	Male	28	Fissure with Hemorrhoids	198	Pain and Bleeding PR
Mudakappa	1770/14	Male	31	Fissure	470	Pain
Suresh	2620/14	Male	33	Fistula in ano	144	Perianal Discharge
Tukaram	8785/14	Male	48	Fissure	78	Pain
Annapurna	9545/14	Female	40	Fissure	180	Pain
Shivantha	9591/14	Male	35	Perineal abscess	126	Pain
Shrishail	41368/14	Male	34	Fissure	304	Pain and Bleeding PR
Shashikala	50476/14	Female	32	Hemmorhoids	170	Bleeding PR And Pain
Gurushanth	66147/14	Male	44	Fissure	300	Pain and Bleeding PR
Nandappa	71325/14	Male	41	Hemmorhoids	234	Bleeding PR
Siddappa	100102/14	Male	39	Perineal herpes	218	Pain
Channabasappa	5812/14	Male	28	Fissure	60	Pain
Karavati T	7412/14	Female	29	Fistula in ano	190	Perianal Discharge And Pain
Hanamanth	8424/14	Male	32	Molluscum contagiosum	140	Perianal Wrats
Lingayya	189564/14	Male	43	Hemmorhoids	458	Bleeding PR
Dareppa	201258/14	Male	50	Fissure	214	Pain and Mass PR
Alajalghari	3893/14	Male	37	Fissure	108	Pain
Shrikanth	2882/14	Male	30	Hemmorhoids	172	Mass PR and Bleeding PR
Siddappa	198413/14	Male	44	Hemmorhoids	94	Bleeding PR
Meeraji	11714/14	Female	38	Hemmorhoids	114	Pain and Bleeding PR
Tukaram	8785/14	Male	41	Fissure	168	Pain
Ramlingappa	204175/14	Male	51	Fissure	102	Pain
Lalitha	224562/14	Female	28	Hemmorhoids	370	Bleeding PR
Rajendra	11233/14	Male	25	Hemmorhoids	146	Mass PR and Bleeding PR
Annapurna	9594/14	Female	40	Fissure	448	Pain
Vijay kumar	12901/14	Male	38	Fissure	278	pain and Bleeding PR
Dyamanna	16091/14	Male	54	Perineal abscess	104	Pain