CUTANEOUS MANIFESTATIONS WITH CD4 +T CELL COUNTS IN HIV SEROPOSITIVE/AIDS PATIENTS - A CROSS SECTIONAL STUDY

By

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~ Dr. Lavanya D

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

GUD – Genitoulcerative Disease

MC – Molluscum Contagiosum

NK – Natural Killer

OHL – Oral Hairy leukoplakia

OI – Opportunistic Infections

P – Ptyriasis

PPE – Pruritic Papular eruptions

PCP – Pneumocystis carinii pneumonia

RBS – Random blood sugar

RT – Reverse Transcriptase

STD – Sexually transmitted disease

STI – Sexually transmitted infections

T - Tinea

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.

ABSTRACT

Background:AIDS is currently a burning problem in India and Worldwide. Cutaneous manifestations are seen frequently in HIV infected individuals causing significant morbidity. They are valuable clinical indicators and association is established between skin conditions and CD4+T cell counts.

Objectives:

Primary Objective -To find out the correlation between CD4 + T cell counts and skin manifestations.

Secondary Objective – To find out the prevalence of cutaneous manifestations in HIV/AIDS patients.

Material & methods: A one year cross sectional study was conducted in 100 patients. All HIV seropositive patients with or without AIDS were included. The association between the CD4+T cell counts and skin manifestations was done using chi square test and Whitney – Mann test.

Results: Among the 100 patients studied – 79% had cutaneous manifestations.38 were in the age group of 31-40yrs and male to female ratio was 1.32:1.Most of the patients acquired the infection through sexual mode of transmission (54= heterosexual & 5=Homosexual).39 were on HAART treatment. The non-infectious cutaneous manifestations like xerosis, seborrhoeic dermatitis, pruritic papular eruptions, drugrash, hair and nail changes were reported in maximum number of patients. Genital warts, multidermatomal herpes zoster, molluscum contagiosum, extensive dermatophytosis,vulvovaginal candidiasis, Norwegian scabies were among the common infections that were reported. Most of these patients had CD4 + T cell counts below 200 cells/μL.40% of patients had systemic infections like tuberculosis, cryptococcalmeningitis, pneumocystis carinii pneumonia.

Conclusion: The cutaneous manifestations are more with advanced stage and considered as clinical marker of immune suppression. This study revealed that non-infectious skin manifestations were most commonly seen and thus emphasizes the

need for dermatological evaluation in HIV patients for early management and improved quality of life.

Key Words: HIV, Cutaneous manifestations,CD4+T cell counts.

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INTRODUCTION

AIDS is the current burning problem in India and worldwide. It is caused by the Human immuno deficiency virus.[1]

In 2009 there were an estimated 2.6million people who became newly infected with HIV. This is nearly 1/5th fewer than the 3.1million people newly infected in 1999.[2]

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.[3]

In many patients, mucocutaneous diseases are amongst one of the first recognized clinical manifestations of HIV/ AIDS. Over the past decade it has become increasingly clear that the cutaneous disorders are associated not only with terminal stages of immunodeficiency but also occur throughout the course of HIV infection and association between CD4+T cell counts and these skin manifestations was established.[4]

Most studies on the prevalence of cutaneous manifestations 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.[5]

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

OBJECTIVES

The objectives of the present study are:

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

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

REVIEW OF LITERATURE

HISTORICAL REVIEW[6, 7, 8,74]

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 time 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).Suniti Solomon and her colleagues documented the first evidence of HIV infection in India.
- 1987: Zidovudine became the first anti-retroviral drug to be approved by FDA.
- 1993: CDC revises its definition of AIDS.
- 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.
- 2002:The global fund is established to boost the response to AIDS,TB,Malaria.[74]

- 2009: 5.2 million people in developing and transitional countries are receiving treatment for HIV;9.5 million are still in immediate need of treatment.[74]

EPIDEMIC UPDATE[2]

The overall growth of the global AIDS epidemic appears to have stabilized. The annual number of new HIV infections has been steadily declining since the late 1990s and there are fewer AIDS related deaths due to significant scale up of antiretroviral drugs over the past few years.[2]

New infections are declining[2]

In 2009 there were an estimated 2.6million people who became newly infected with HIV.This is nearly $1/5^{th}$ fewer than the 3.1million people newly infected in 1999.This trend reflects a combination of factors, including the impact of HIV prevention efforts and the natural course of HIV epidemics .

AIDS related deaths are declining[2]

The number of annual AIDS related deaths worldwide is steadily decreasing from peak of 2.1million in 2004 to an estimated 1.8million in 2009.The decline reflects the increased availability of antiretroviral drugs as well as care and support to people living with HIV particularly in middle and low-income countries.

AIDS related mortality began to decline in sub-Saharan Africa and the Caribbean in 2005.In North America and Western and Central Europe,deaths due to AIDS began to decline soon after antiretroviral therapy was introduced in 1996.In Asia, Central and South America the number of deaths has stabilized, but there is no indication yet to decline.

TABLE 1

AIDS STATISTICS FOR ASIA,2001 AND 2009[2]

	People living with HIV	People newly infected with HIV	Children living with HIV	AIDS-related deaths
2009	4.9million [4.5-5.5 million]	3,60,000 [3,00,000-4,30,000]	1,60,000 [1,10,000-2,10,000]	3,00,000 [2,60,000-3,40,000]
2001	4.2million [3.8-4.6million]	4,50,000 [4,10,000-5,00,000]	1,00,000 [69,000-1,40,000]	2,50,000 [2,20,000-3,00,000]

The adult HIV prevalence in Asia was 1.3% in 2009, and the incidence slowed to 0.1%. Women account for 35% of total people infected with HIV.[2]

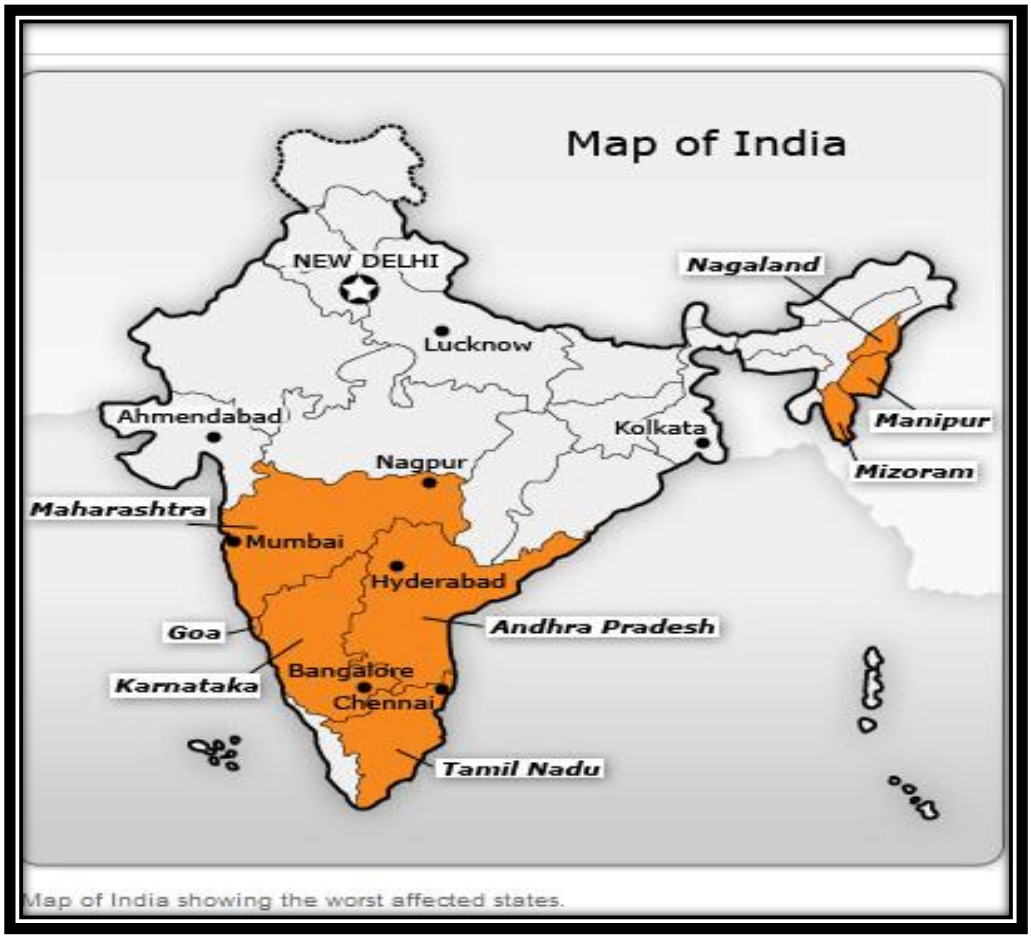
In Asia, on average, an estimated 16% of people who inject drugs are living with HIV.[2]

In 2006 UNAIDS estimated that there were 5.6 million people living with HIV in India, which indicated that there were more people with HIV in India than in any other country in the world. [2,9]

In 2007, following the first survey of HIV among the general population, UNAIDS and NACO agreed on a new estimate – between 2 million and 3.1 million people living with HIV. In 2009 it was estimated that 2.4 million people were living with HIV in India, which equates to a prevalence of 0.3%.While this may seem low,

because India's population is so large, it is third in the world in terms of greatest number of people living with HIV.[75,76]

Fig 1 – MAP OF INDIA SHOWING WORST AFFECTED AREAS



Karnataka, a diverse state in the southwest of India, has a population of around 53 million. Districts with the highest prevalence tend to be located in and around Bangalore in the southern part of the state, or in northern Karnataka's "devadasi belt". The average HIV prevalence among female sex workers in Karnataka was just over 5% in 2007, and 17.6% of men who have sex with men were found to be infected.[9]

In 2007, 1.43 percent of the adult population aged (15-49) surveyed in Belgaum was infected with HIV. HIV prevalence in rural areas was nearly 3 times

higher than that in the urban areas (1.69% compared with 0.63%: p=0.00). Similarly, the HIV prevalence was slightly higher among females (1.58%) than males (1.28%)[77.]

ETIOLOGY[10]

The retroviruses, which make up a large family (Retroviridae), mainly infect vertebrates. These viruses have a unique replication cycle whereby their genetic information 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 *Pan troglodytestroglodytes* species of chimpanzees has been established as the natural reservoir of HIV-1 and the most likely source of original human infection.

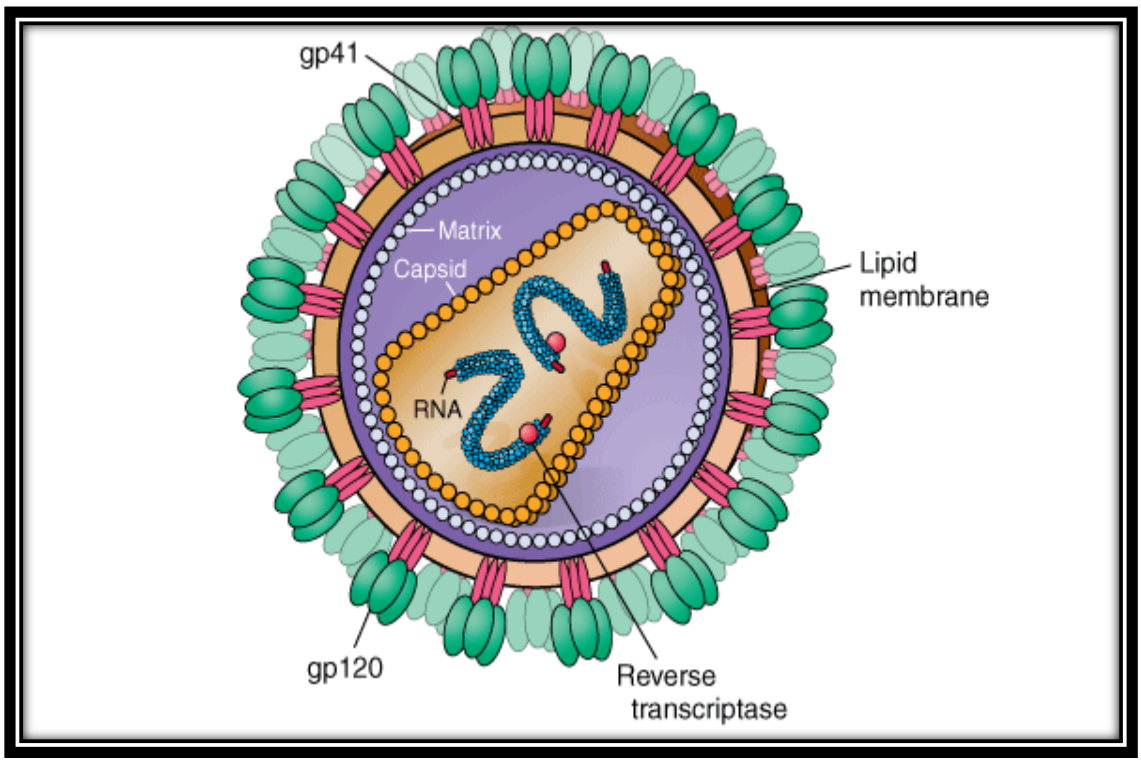
STRUCTURE AND LIFE CYCLE[10]

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*.

Fig 2 – **STRUCTURE OF HIV**



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.

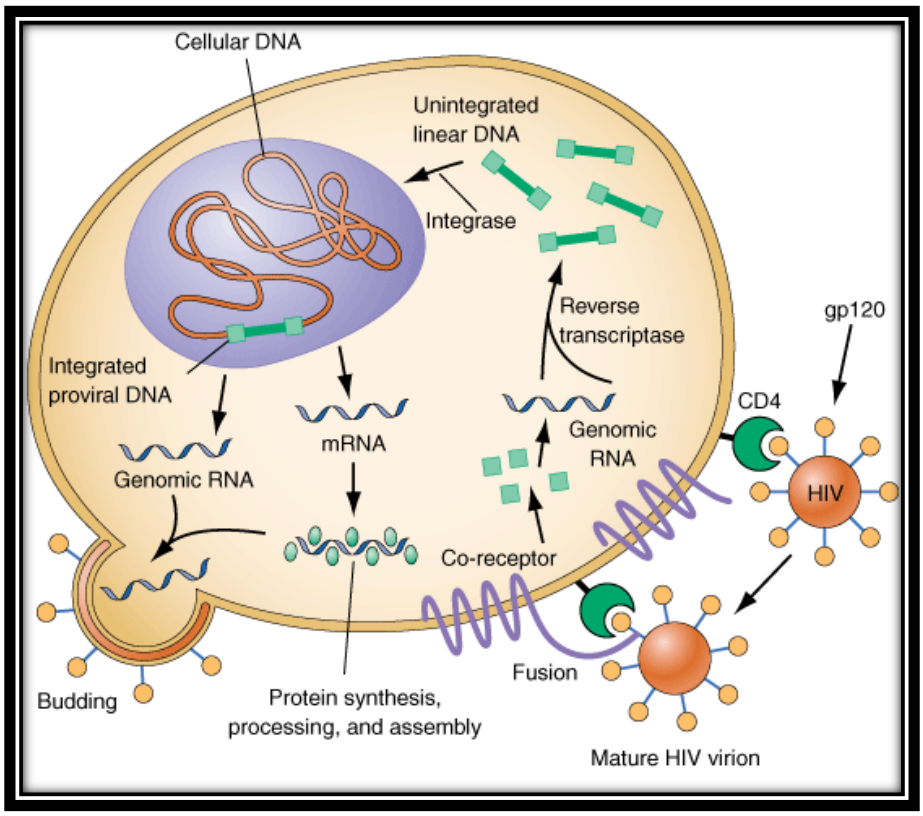
However, HIV-1 is more complex than other retroviruses, particularly those of the nonprimate group, in that it also contains at least six other genes (*tat, rev, nef, vif, vpr,* and *vpu*), which code for proteins involved in the modification of the host cell to enhance virus growth and the regulation 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.

The replication cycle proceeds in two phases:

In the first phase, the virus enters the cytoplasm after binding to a specific cell-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 viral gene 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.

Fig 3 – REPLICATION CYCLE OF HIV



TRANSMISSION[11]

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[12]

TABLE 2 - MODES OF TRANSMISSION[12]

EXPOSURE ROUTE	PERCENTAGE EFFICIENCY (WORLD OVER)	PERCENTAGE OF TOTAL (WORLD OVER)	PERCENTAGE OF TOTAL (INDIA)
Blood transfusion	90-95	5	7.05
Perinatal	20-40	10	
Sexual intercourse	0.1-1	75	74.15(Heterosexual) 0.58 (Homosexual)
Injecting drug abuse	0.5-1.0	10	7.3
Needle stick injury	<0.5	0.1	0
Others			10.92

SEXUAL TRANSMISSION[13]

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%

b)c)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:[10]

- 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[10]

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 immunegamma globulin,Hepatitis B immunoglobulin,plasma derived hepatitis B vaccine.

OCCUPATIONAL TRANSMISSION OF HIV[10]

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

MATERNAL – FETAL/INFANT TRANSMISSION[10]

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 during labour 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),premature delivery 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 INFECTION [14, 15]

Human immunodeficiency virus, the etiologic agent of AIDS, typically elicits progressive and ultimately profound immunosuppression in untreated persons. Once HIV infection is established, the clinical progression is generally steady and associated 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 the result 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 cytolytic Thl-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-infected patients.

B CELL ALTERATIONS:

Although B cells are not directly infected by HIV, functional abnormalities of B cells, as well as of humoral immune responses, are common in HIV infected patients. They include hypergammaglobulinemia, enhanced serum levels of IgG, IgA, and IgE (and also of IgM in children).

Mechanisms causing hyperactivation of the B-cell compartment in HIV-infected patients have not yet been clarified. Initially, B-cell hyperactivation was attributed to frequent association with infections by Epstein-Barr virus (EBV) and cytomegalovirus, which are well known B-cell activators.

CD4+T cells infected *in vitro* with HIV acquire the ability to induce polyclonal B-cell proliferation and immunoglobulin production. Such a property was, at least in part, mediated by the constitutive expression of membrane tumor necrosis factor (TNF)-α.

ALTERATION OF ANTIGEN PRESENTING CELLS(APC):

Infected macrophages are important reservoirs outside the blood and act as carriers of HIV to different organs.

These non-proliferating, mature cells can sustain HIV production *in vitro* for a long time without being killed by the virus. Cytokine secretion by

infectedmacrophages is also aberrant which can lead to a cascade of secondary effects.

Macrophages act as APC particularly to memory T cells in the periphery. This interaction does not appear to be significantly impaired during the asymptomatic phase of HIV infection.

However, the function of both macrophages and dendritic cells in bringing and presenting antigen to naive T cells in the lymph nodes is affected early in the course of HIV infection.

Thus, patients may survive by their memory T-cell responses, but when these cells eventually become depleted, the lack of recruitment of new memory cells, which should have occurred through the interaction of APC with naive T cells, could contribute to immune deficiency.

NATURAL KILLERCELL (NK CELLS) ALTERATIONS:

Even NK cells, which have protective activity against viral and tumor cells are affected.

A reduction in both cytolytic activity and ability to produce interferons (IFN) by NK cells from HIV-infected patients have been reported.

Of note is the recent observation that, at least *in vitro,* this defect can be reversed by IL-12, the production of which by HIV-infected macrophages appears to be defective.

Fig 4 -GENERATION OF LATENTLY INFECTED, RESTING CD4+ T CELLS IN HIV-INFECTED INDIVIDUALS

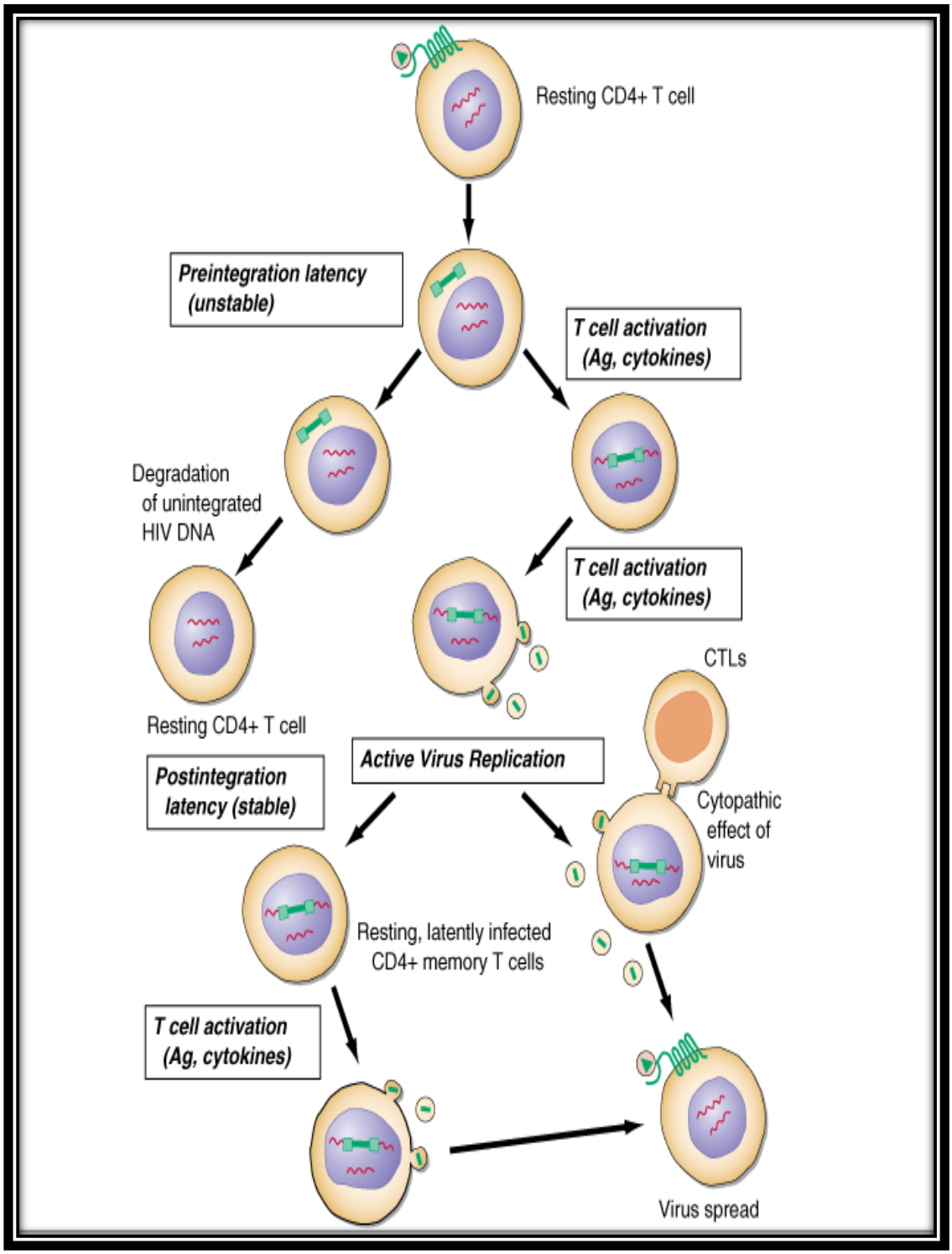
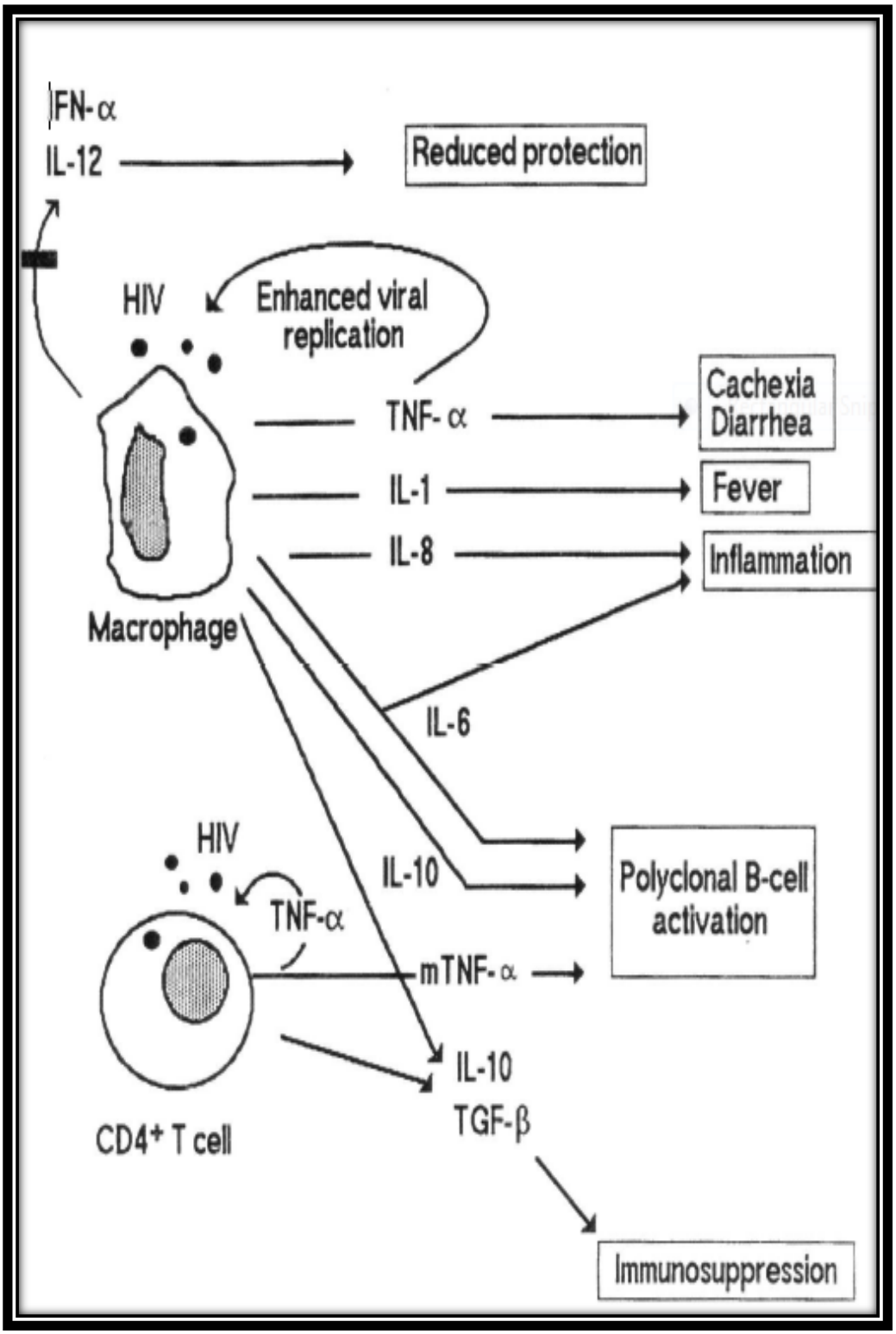


Fig 5 HIV INDUCED DYSREGULATION OF THE CYTOKINE SYSTEM



IMMUNOLOGICAL ABNORMALITIES IN CLINICAL LATENCY STAGE

Immunologic lymphocytopenia.

Reduction of relative and absolute numbers of circulating CD4+ T cells.

Increase of relative and absolute numbers of circulating CD8+ T cells.

Reduction or inversion of CD4/CD8 ratio.

Reduction or absence of delayed-type cutaneous reactivity to recall antigens.

Hypergammaglobulinemia.

Increased serum levels of IgG and IgA (also IgM in children).

Increased serum levels of neopterin,P2-microglobulin.

Increased serum levels of soluble IL-2 receptors.

NATURAL HISTORY OF HIV INFECTION[16]

The clinical spectrum of HIV infection ranges from a totally asymptomatic state to severe illness due to a multitude of oppurtunistic infections.

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

PRIMARY INFECTION/ACUTE HIV SYNDROME:

Approximately 3-6weeks after acquiring infection around 50-70% of people suffer 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 the patient is usually asymptomatic.

Viral replication is highly dynamic and continuous.

Any infection can tilt the balance between the regenerative capacity of the immune 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 also rapid.

Infected individuals may show subtle signs and symptoms indicating a compromised 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 the individual becomes highly immunocompromised.

Major opportunistic infections and malignancies start developing.

The pattern of opportunistic infections varies according to the geographical locale, the common ones being pneumocystitis jerovecii pneumonia, generalized

candidiasis, 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.

Table 3 – CLINICAL COURSE OF HIV INFECTION

Exposure to HIV infection	**Seroconversion illness**	**Asymptomatic period**	**Subtle symptoms and signs of immunodeficiency**	**Full blown AIDS. Symptoms and signs of opportunistic infections and malignancy**
Antibody titre and infectivity	Not detectable (window period) Highly infectious	Detectable antibodies Infectious	Detectable antibodies Infectious	Antibodies may or may not be detectable Highly infectious
Time period	12 weeks	3-5 years	2-3 years	1-2 years
Stage of HIV disease	Primary infection(CD4+ Tcell count near normal)	Early immunodeficiency(CD4+Tcell count > 500 cells/micro L)	Intermediate immunodeficiency(CD4+Tcell count < 500,>200 cells/ micro L)	Terminal illness(CD4 cell count<200cells/micro l)

CDC CLASSIFICATION

The current CDC classification system for HIV-infected adolescents and adults categorizes persons on the basis of clinical conditions associated with HIV infection and CD4+ T lymphocyte counts.

The system is based on three ranges of CD4+ T lymphocyte counts and three clinical categories and is represented by a matrix of nine mutually exclusive categories.

Using this system, any HIV-infected individual with a CD4+ T cell count of <200 cells/microL has AIDS by definition, regardless of the presence of symptoms or opportunistic diseases.

Table 4 -1993 REVISED CLASSIFICATION SYSTEM FOR HIV INFECTION AND EXPANDED AIDS SURVEILLANCE CASE DEFINITION FOR ADOLESCENTS AND ADULTS[17]

CD4 +T CELL (Cells/Micro L)	A	B	C
500	A1	B1	C1
200-499	A2	B2	C2
< 200	A3	B3	C3

A-Asymptomatic infection includes acute primary infection and persistent generalized lymphadenopathy.

B- Symptomatic but not AIDS indicator conditions of group C.

C- AIDS indicator.

Category A: Consists of one or more of the conditions listed below in an adolescent or adult (>13 years) with documented HIV infection. Conditions listed in categories B and C must not have occurred.

Asymptomatic HIV infection.

Persistent generalized lymphadenopathy .

Acute (primary) HIV infection with accompanying illness or history of acute HIV infection.

Category B*:* Consists of symptomatic conditions in an HIV-infected adolescent or adult that are not included among conditions listed in clinical category C and that meet at least one of the following criteria: (1) The conditions are attributed to HIV infection or are indicative of a defect in cell-mediated immunity; or (2) the conditions are considered by physicians to have a clinical course or to require management that is complicated by HIV infection. Examples include, but are not limited to, the following:

Bacillary angiomatosis.

Candidiasis, oropharyngeal (thrush).

Candidiasis, vulvovaginal; persistent, frequent, or poorly responsive to therapy.

Cervical dysplasia (moderate or severe)/cervical carcinoma in situ.

Constitutional symptoms, such as fever (38.5°C) or diarrhea lasting >1 month.

Oral Hairy leukoplakia.

Herpes zoster (shingles), involving at least two distinct episodes or more than one dermatome.

Idiopathic thrombocytopenic purpura.

Listeriosis.

Pelvic inflammatory disease, particularly if complicated by tubovarian abscess.

Peripheral neuropathy.

Category C*:* Conditions listed in the AIDS surveillance case definition.

Candidiasis of bronchi, trachea, or lungs.

Candidiasis, esophageal.

Cervical cancer, invasive.

Coccidioidomycosis, disseminated or extra pulmonary.

Cryptococcosis, extra pulmonary.

Cryptosporidiosis, chronic intestinal (>1 month's duration)

Cytomegalovirus disease (other than liver, spleen, or nodes)

Cytomegalovirus retinitis (with loss of vision)

Encephalopathy, HIV-related.

Herpes simplex: chronic ulcer(s) (>1 month's duration); or bronchitis, pneumonia, or esophagitis.

Histoplasmosis, disseminated or extra pulmonary.

Isosporiasis, chronic intestinal (>1 month's duration)

Kaposi's sarcoma

Lymphoma, Burkitt's (or equivalent term)

Lymphoma, primary of brain.

Mycobacterium avium complex or *M. kansasii*, disseminated or extrapulmonary.

Mycobacterium tuberculosis, any site (pulmonary or extrapulmonary).

Mycobacterium, other species or unidentified species, disseminated or extrapulmonary.

Pneumocystis jiroveci pneumonia.

Pneumonia, recurrent.

Progressive multifocal leukoencephalopathy.

Salmonella septicemia, recurrent.

Toxoplasmosis of brain.

Wasting syndrome due to HIV.

The symptoms which characterize the constitutional disease are as follows:

1. Fever lasting for atleast 1 month
2. Diarrhea, lasting for atleast 1 month
3. Unexplained weight loss of at least 10% in the last 6 months

Obviously, these manifestations have to be present in the absence of other disorders that may account for their development

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

CUTANEOUS MANIFESTATIONS IN HIV[19,20,21]

A large range of skin and mucosal diseases have been reported in relation to HIV infection. Infections due to a variety of pathogens (folliculitis, erysipelas, fungal infections, and HPV infections), diseases characterized by increased keratinocyte proliferation, autoimmune diseases (Grover's disease, Sjogren syndrome, and bullous diseases), neoplasms (squamous cell cancer of the anus), and other miscellaneous skin

diseases (xeroderma, atopic dermatitis) are influencing clinical course and frequency of HIV infection.[20]

In the background of the modified immune response, skin manifestations can alter:[19]

- The degree of intensity of the symptoms
- The extent of the rashes
- The sites at which they appear
- The duration of the symptoms
- The frequency of the relapses
- The response to treatment modalities.

Any modification of these characteristics is considered to be a main factor, which can lead to diagnostic approach of the immune disturbance and the diagnosis of HIV infection.

Since its emergence in the early 1980s, human immunodeficiency virus (HIV) infection has had a major impact on the field of dermatology. Cutaneous lesions may be the first sign of HIV infection or acquired immunodeficiency syndrome (AIDS).

HIV IS ASSOCIATED WITH A VARIETY OF INFECTIOUS AND NONINFECTIOUS DISEASES AS FOLLOWS: [20]

INFECTIONS AND INFESTATIONS

Viral

Herpes simplex infection

Varicella-zoster virus infection

Cytomegalovirus infection

Epstein Barr virus infection

Molluscum contagiosum virus infection

Human papilloma virus infection

Bacterial

Staphylococcus aureus infection

Bacillary angiomatosis

Mycobacterial diseases

Syphilis

Chancroid

Granuloma inguinale

Lymphogranuloma venereum

Fungal

Candidiasis

Dermatophytosis

Pityrosporum folliculitis

Cryptococcosis

Pencillinosis

Histoplasmosis

Aspergillosis

Parasitic infestations

Scabies

Demodicidosis

INFLAMMATORY DISORDERS

Seborrheic dermatitis

Psoriasis

Reiter's syndrome

Icthyosiform dermatoses

Pruritus associated with HIV

Adverse cutaneous drug reactions

NEOPLASMS

Kaposi's sarcoma

Lymphoma

Squamous cell carcinoma

HAIR & NAIL CHANGES

MISCELLANEOUS CUTANEOUS DISORDERS

Generalized hyperpigmentation

Hidradenitis suppurativa

INFECTIONS

VIRAL INFECTIONS

HUMAN HERPESVIRUS 1 AND 2[19,20,21,22]

Classic human herpes virus (HHV) 1 and 2, known as herpes simplex virus (HSV) types 1 and 2 (HSV-1, HSV-2), lead to orolabial and genital herpes, respectively.

Clinically, HSV presents as grouped vesicles on a red base that may progress to deep ulcerations and necrosis. In HIV individual lesions commonly appear in the mouth and esophagus and on genitalia, perianal areas, and distal fingers.They increase

in number, size and become more painful. Atypical morphological appearances include hyperkeratotic lesions, large ulcers, hemorrhagic and ecthymatous lesions. Increased severity, recurent outbreaks and slow healing may be seen.

Patients with HIV and orolabial herpes can be treated with acyclovir, 400 mg orally 5 times a day or 5 mg/kg intravenously (IV) every 8 hours for 7 days. Patients who need suppressive therapy can take 400 mg of oral acyclovir twice a day.

VARICELLA- ZOSTER VIRUS[19,20,21]

Varicella-zoster virus (HHV-3) affects about 25% of patients with HIV. Transmission can occur via respiratory droplets and direct contact.Serum antibodies to Varicella-Zoster virus donot appear to prevent reccurance of the infection.

Herpes zoster is a clinical indicator of faltering immunity and its occurrence should always raise the issue of HIV sero testing.It usually occurs with CD4+T cel counts< 200 cells/microL

In patients with HIV, the herpes zoster lesions may be more painful, severe, and prolonged. The vesicles often become bullous, hemorrhagic, ulcerative, necrotic, or verrucous. It is most often unidermatomal, but it may be multidermatomal, reccurent, within the same dermatome, or disseminated.

The treatment of VZV infection in HIV is not clearly defined. The treatment of choice for herpes zoster is acyclovir 800mg five times a day for ten days or more. Systemic corticosteroids, usually given to diminish post-herpetic neuralgia are contraindicated. In disseminated, visceral or ophthalmic herpes zoster, acyclovir 10mg/kg/bw intravenously every eight hours is given for seven days. Acyclovir resistant cases require foscarnet intravenously.

***EBSTEIN BARR VIRUS*[19,20,21]**

Most adults have been infected with Epstein-Barr virus (EBV),which lays dormant within B cells. Once HIV causes immunosuppression, EBV most frequently manifests as oral hairy leukoplakia (OHL), and less commonly as Burkitt's lymphoma and/or large-cell lymphoma. Up to 25% of patients with HIV can develop Oral Hairy Leukoplakia.

Lesions of Oral Hairy Leukoplakia are characterized by white corrugated plaques on the lateral aspects of the tongue, dorsal and ventral surfaces of the tongue, buccal mucosa, and soft palate. Generally, Oral Hairy Leukoplakia is asymptomatic; however, some patients may complain of dysphagia. The distribution of the lesions is related to the presence of the EBV receptors in that distribution.

Oral Hairy Leukoplakia can be differentiated from thrush by the fact that OHL cannot be easily scraped off with a tongue blade.

Because they are asymptomatic, most lesions do not need to be treated. Lesions that cause dysphagia or are cosmetically displeasing to the patient can be treated topically with retinoic acid,podophyllin or vitamin A or with surgical excision.Oral Hairy Leukoplakiahas been treated successfully with a variety of drugs: oral zidovudine, 300 mg 3 times a day; oral acyclovir, 200 to 400 mg 5 times a day; oral ganciclovir, 1 gram 3 times a day; and IV foscarnet, 40 mg/kg every 8 to 12 hours.

***CYTOMEGALOVIRUS*[19,20,21]**

Cytomegalovirus (CMV) infection is the most common viral infection in patients with HIV whose CD4+T cell counts are below 100/mm^3.

However, CMV does not commonly manifest in the skin; only a few reports in the literature discuss CMV-induced skin lesions, such as perianal and oral ulcerations that may occur as an extension of preexisting CMVinduced gastrointestinal disease. In addition, macular purpura and leukocytoclastic vasculitis on the lower extremities and small keratotic verrucous lesions on the trunk, face, and extremities can be present.

Foscarnet, 40 mg/kg IV every 8 to 12 hours; oral ganciclovir,1 gram 3 times a day; and topical anesthetics for pain are the main treatment options.

***MOLLUSCUM CONTAGIOSUM*[19,20,21]**

As CD4 + T cell counts drop below 100/mm^3, 10% to 20% of patients with HIV will develop molluscum contagiosum (MC) lesions.

These spread through direct and sexual contact. They predominate on the face and genital areas as firm, pearly pink papules with central umbilication. In patients with HIV, however, they may be more numerous, more verrucous, and larger. With progression, they become quite disfiguring.

Because the differential diagnosis for MC lesions includes histoplasmosis, cryptococcosis, and penicilliosis an accurate diagnosis is critical. Distinguishing MC from these conditions may have important considerations regarding diagnostic workup and therapy.

Treatments for MC include cryotherapy, carbondioxide laser electrodesiccation,curettage, topicals like tretinoin, imiquimod, podophyllin, intralesional interferon (1 million units once a week for 4 weeks), and zidovudine (300 mg orally 3 times a day).

BACTERIAL INFECTIONS[19, 20,21]

***STAPHYLOCOCCUS AUREUS*[19,20,21]**

Staphylococcus aureusis the most common bacterial pathogen, affecting about 85% of patients with HIV. Approximately 50% of patients with HIV harbor *S aureus* within their nares.*Saureus* may manifest in a variety of ways, including folliculitis, impetigo, cellulitis, furuncles/carbuncles, and necrotizing fasciitis (NF).

Treatment with dicloxacillin or cephalexin is usually sufficient, except in cases of NF, where the combination of penicillin, third-generation cephalosporin, and clindamycin are necessary. In patients with NF, adjuvant care with prompt extensive surgical debridement is critical to survival.

Furuncles and carbuncles also benefit from incision and drainage on a smaller scale. Topical mupirocin can be applied to nares once a day the first week of every month to decrease nasal carriage.

***BACILLARY ANGIOMATOSIS*[20,21,19]**

Bacillary angiomatosis (BA) is caused by infection with Gram negative *Bacillus Bartonella henselae*, or *B quintana*, which usually manifests in HIV-infected patients whose CD4 + T cell count is below 100/mm^3.Although skin is the most commonly involved organ, BA may occur in any organ system.

Cutaneous lesions present as firm, red-violaceous papules or nodules that may ulcerate and form a hyperkeratotic crust. Individual lesions may appear clinically similar to a pyogenic granuloma, but the generalized nature,fever, night sweats,chills, and malaise distinguish BA.

Treatment with erythromycin or doxycycline is effective. Relapses may require prophylaxis with either of these agents. Other drugs used to treat BA include

cotrimoxazole (trimethoprim and sulfamethoxazole), ciprofloxacin, rifampin, isoniazid, tetracycline, and azithromycin.

***MYCOBACTERIAL INFECTIONS*[19,20,21]**

Tuberculosis is the commonest opportunistic infection in HIV positive patients in India.

HIV related TB shows a higher prevalence of extra pulmonary and disseminated TB and adverse events because of anti tuberculosis treatment.

The rate of progression of TB infection to active disease following initial exposure is greater than 40% in people infected with HIV,compared to approximately 5% in HIV-negative individuals.

The clinical presentation is diverse, including scrofuloderma, acute military tuberculosis of skin, tuberculides, palmoplantar keratoderma.

The diagnosis of mycobacterial infection may be difficult because characteristic histopathological features such as caseating granulomas may be absent because of diminished cell mediated immunity but acid fast bacilli may be numerous for the same reason.

Treatment guidelines are same for HIV infected patients as those of non infected individuals. If DOTS is not possible, self- administered treatment with fixed dose drug combination is preffered to improve the compliance.

FUNGAL INFECTIONS [19,20,21]

***CANDIDIASIS*[19,20,21]**

Candida is the most common fungal infection in patients with HIV, developing in 30% to 50% of patients. It is an ubiquitous organism that is part of the

normal flora of the oropharynx and gastrointestinal tract. Candida may affect the mucosa, nails, and skin.

Oral candidiasis (thrush) may present in several forms, such as pseudomembranous, erythematous, hyperplastic, or angular cheilitis. It is characterized by white plaques on the tongue or buccal mucosa that can be easily scraped off with a tongue blade, producing bleeding or red macular atrophic patches on the buccal mucosa. The presence of thrush in a patient without known risk factors should raise the suspicion for HIV infection.

It may coexist with esophageal candidiasis, leading to odynophagia and dysphagia. Esophageal candidiasis is an AIDS-defining illness, occurring when CD4 + T cell counts fall below $100/mm^{3.}$

Cutaneous candidiasis appears in intertriginous areas as erythematous patches with satellite pustules. Occasionally, Candida may invade the bloodstream, leading to life-threatening fungemia.Candida onychomycosis typically affects the proximal nail, turning it white.

Effective treatment of oropharyngeal candidiasis is accomplished with topical nystatin or clotrimazole, however, patients with AIDS may need fluconazole, 100 mg orally or IV daily for 2 weeks, or 10 ml of oral itraconazole daily for 1 to 2 weeks. Vulvovaginal candidiasis can be treated with topical azoles or polyenes. Fungemia must be treated with IV fluconazole, 400 mg daily, or amphotericin B, 0.5 to 1mg/kg IV daily. The addition of oral flucytosine may be considered for HIV-infected patients with invasive candidiasis. Onychomycosis should be treated with 200 mg of oral itraconazole daily for 12 weeks.

***HISTOPLASMOSIS*[19,20,21]**

Infection with *Histoplasma capsulatum* rarely causes disease in immunocompetent patients. Inhalation of spores within the soil may lead to disseminated infection, ultimately affecting the skin in 10% to 20% of patients with HIV.

Mucocutaneous ulcerations, erythematous macules and papules, pustules,umblicated papules and psoriasiform lesions appear diffusely on the face, trunk, and extremities. Primary cutaneous histoplasmosis is extremely rare.

Treatment consists of amphotericin B, itraconazole, or fluconazole. Itraconazole is the drug of choice. Supressive therapy may be given to prevent relapse.

***CRYPTOCOCCCOSIS*[19,20,21]**

Much like histoplasmosis, cryptococcosis is caused by inhalation of contaminated soil or bird droppings, which subsequently disseminates to other organ systems in patients with HIV.

Disseminated cutaneous involvement occurs in 10% to 20% of patients. Primary cutaneous disease is also very rare. Lesions consist of erythematous papules, nodules, pustules, umblicated, verrucousor granulomatous lesions. Ulcerations appear predominantly on the head, neck, trunk and extremities.

Treatment includes fluconazole, flucytosine, or amphotericin B, with lifelong maintenance with fluconazole.

***COCCIDIOIDOMYCOSIS*[19,20,21]**

Reactivation of pulmonary coccidioidomycosis occurs in patients with HIV, leading to disseminated cutaneous involvement. Normally these papules, pustules, and

plaques are initially asymptomatic, but later coalesce into large verrucous plaques with ulcerations and draining sinuses. Mucosal ulcerations are not present. Erythema nodosum and erythema multiforme may occur as well.

Treatment with oral azoles or amphotericin B, followed by lifelong maintenance with oral azoles, is necessary.

PARASITIC INFESTATIONS[20,21,19]

SCABIES

Scabies infection with Sarcoptes scabieiis the most common parasiticinfection in patients with HIV, affecting 20% of patients. It is extremely contagious in patients with HIV and has resulted in several institutional epidemics.

Patients with HIV are more likely to be infected with crusted (Norwegian) scabies, characterized by hyperkeratotic, diffusely distributed plaques and hyperkeratotic palms and soles. This form is also seen in patients with neurologic disease. Typical burrows are often difficult to visualize in this form. Secondary bacterial infection with resultant fatal septicemia can occur.

Topical treatment with 5% permethrin, 1 week apart, or a single dose of ivermectin, 200 mcg/kg orally, are both effective. Lindane should be used cautiously because it may cause neurotoxicity. Keratolytic agents may increase the efficacy of treatment by removing some of the thick scales, allowing improved penetration.

NEOPLASMS[19,20,21]

KAPOSI SARCOMA

Kaposi sarcoma (KS) is a vascular neoplastic condition linked to infection with human herpesvirus 8 (HHV-8).

The 4 different types of KS include classic, endemic, epidemic, and idiopathic. The epidemic, or AIDS-associated type, is characterized by more aggressive and widespread mucocutaneous lesions. Several contributing factors have been associated with the development of KS, such as immune factors, coexisting viral infections, and genetics.

KS may present as red or brown-violaceous macules, patches, plaques, or nodules in areas of trauma. One third of the lesions appear on the extremities. Lesions may be distributed singly or in groups, the grouped lesions may coalesce into large areas of involvement. These lesions often ulcerate and become secondarily infected.

Treatment includes topical alitretinoin, cryotherapy, radiation, intralesional vinblastine or interferon alpha, or IV doxorubicin or daunorubicin. Improvement in CD4 +T cell counts with HAART also leads to resolution of lesions.

LYMPHOMA

The development of lymphoma is associated with immunosuppression. Partly through this mechanism, patients with HIV develop lymphoma at a greater rate than the general population.

The most commonly associated lymphomas are Hodgkin, Non-Hodgkin (NHL), cutaneous T cell (CTCL), and human Tlymphotropic virus type I (HTLV-1).

Hodgkin lymphoma and NHL lesions usually present as red-violaceous nodules on the head and neck that may ulcerate. CTCL may present as large diffuse erythematous patches or plaques, which can progress to erythroderma or tumor

formation. HTLV-1 may mimic a viral exanthem with morbilliform papules and fine vesicles.

Diagnosis can be made on histopathology, gene rearrangement, flow cytometry, and immunophenotyping.

Hodgkin lymphoma is characterized by the presence of Reed-Sternberg cells, which are large binucleated cells with irregular cell membranes.

Treatment for these lymphomas in patients with HIV does not differ from the treatment for uninfected patients.

Regimens consisting of combinations of chemotherapy, such as methotrexate, prednisone, bleomycin, doxorubicin, cyclophosphamide, and vincristine, can be given to patients with Hodgkin lymphoma, NHL, and HTVL-1. CTCL responds to standard treatments, including psoralen and ultraviolet A (PUVA) light therapy, total body electron beam, topical nitrogen mustard, and retinoids. However, some of these options are immunosuppressive, which may lead to rapid death.

NON-INFECTIOUS CUTANEOUS MANIFESTATIONS[19,20,21]

DRUG INTERACTIONS

Drug eruptions occur more frequently in patients with HIV. This observation has been attributed to several factors.

First, patients with HIV take more medications than the general population, exposing them to greater risk.

Second, medications prescribed for these patients carry a greater relative risk of causing drug reactions, such as cotrimoxazole and other sulfa medications.

Third, patients with HIV have been found to have glutathione deficiency, with subsequently reduced ability to detoxify active drug metabolites.

The most common drug eruption in patients with HIV is the generalized morbilliform exanthem, which develops 7 to 10 days after the patient has taken the culprit medication and resolves after the medication is discontinued.

Vasculitis, urticaria, anaphylaxis, erythema multiforme, more severe drug reactions which include Stevens-Johnson syndrome and toxic epidermal necrolysis (TEN) may also occur.

Drug reactions can be treated with IV antihistamines and IV or topical steroids, as well as immediate withdrawal of the medication causing the reaction. One exception is TEN, which should be treated with IV immunoglobulin, supportive care in the intensive care unit, and aggressive wound care.

SEBORRHEIC DERMATITIS

The occurrence of seborrheic dermatitis (SD) in the general population varies between 2–4%, however, its incidence in patients with HIV is significantly higher.

Seborrheic dermatitis is the most common skin manifestation of HIV disease, occurring most frequently on the scalp, face, and chest. As the disease progresses, the clinical findings worsen and subside after highly-active antiretroviral treatment (HAART).

Although the frequency, duration and severity of the rash are common findings at the first stages of the disease, they are basically related to later stages and decreased numbers of CD4 +T lymphocytes.

Some believe that infection with pityrosporum may be associated with seborrheic dermatitis.

Seborrheic dermatitis usually affects sebaceous areas on the face, scalp, chest, back, and intertriginous areas as yellowwhite greasy scales on erythematous patches. It may even progress to erythroderma.

The exacerbation of SD, or its presentation in atypical and severe forms, are related to impending progression of HIV infection, and constitute a clinical index of deterioration of the underlying immunological disorder.

Treatment options include UVB light therapy, ketoconazole shampoo or cream, topical steroids, sulfur, coal tar, and salicylic acid.

PSORIASIS

The frequency of common psoriasis in HIV patients is slightly higher than that in general population. Nevertheless, psoriatic arthritis has a higher frequency that is related to the presence of HLA-27.

De novo appearance of psoriasis or sudden worsening of pre-existing lesions in a person with a high-risk sexual behavior is an indication for undertaking a HIV test.

Psoriatic lesions in the context of a modified immune response are commonly atypical. The frequent appearance of guttate form is reported, which normally is a post-streptococcal infection, or located in the genitourinary or auxiliary folds (inverse type), as well as in the palmar and plantar surfaces. Severe onychodystrophy, as well as generalized erythrodermic type have been reported.

Psoriasis is usually refractory to treatment. Avoidance of immunosuppressive treatment options, such as cyclosporin and methotrexate, in patients with HIV is recommended. Although potentially immunosuppressive, phototherapy has been used uneventfully in patients with HIV.Other treatment options include topical steroids or retinoids.

PRURITIC PAPULAR ERUPTION

Pruritus is one of the most prominent symptoms reported during HIV infection and is commonly an indicator of thesubjacent HIV immunodeficiency.

Furthermore, prurituscan be the first clinical symptom of HIV infection.

Pruritus can be related with atopy as a result of the immune disorder with changes of the cytokine levels and with the inversion of the type of the immune response with domination of Th-2 and with eosinophilia.

Pruritic papular eruption (PPE), is a common atypical papular pruritic eruption appearing in HIV patients. Etiology and the exact pathogenesis of eruptions of the type of PPE remain unclear and controversial.

The most constant finding in HIV patients with PPE is hypereosinophilia in the lesions or/and in peripheral blood, although eosinophilia is a usual finding in advanced HIV infection.

PPE is correlated to latent HIV infection, decreased CD4+Tlymphocytes (100cells/MicroL), and high HIV viral load, and constitutes a marker of underlying immune disorder.

Idiopathic pruritus, PPE, and EF are correlated with advanced HIV immunodeficiency and can coexist with other symptoms or indicators of HIV

infection. However, their appearance is not related with prognosis aggravation and faster progress of the disease to AIDS.

Although their diagnostic significance is important as indicative of the underlying immunodeficiency, their prognostic value as skin markers remains obscure.

PPE is normally recalcitrant to most conventional antipruritic therapies. Success has been reported with UVB with or without oral sedating antipruritics, as well as pentoxifylline.

XEROSIS/ACQUIRED ICHTHYOSIS

Xerosis/acquired ichthyosis may be present in 30% of patients with HIV. The exact pathogenesis of xerosis is unknown, but poor nutrition, immunosuppression, and chronic illness play a role.

Disease severity does not correlate with the level of immunosuppression. However, the lower the CD4 +Tcell counts, the more severe and unremitting the disease is in these cases.

Emollients, topical steroids, and oral antihistamines may be of some benefit.Acquired ichthyosis usually requires the use of keratolytics or low-dose acitretin.

ATOPIC DERMATITIS

Patients with atopic dermatitis (AD) may present with the triad of allergic rhinitis, asthma, and AD.

Patients with AD have a Th1 cytokine profile, which is similar to the cytokine profile seen in HIV disease. The Th1 cytokine profile is characterized by elevated IgE

levels, increased eosinophils, and increased interleukin 4 and 5. Therefore, patients who are HIV-positive commonly manifest AD and often have severe disease that is recalcitrant to therapy.

Treatment options include emollients, oralantihistamines, topical steroids, and avoidance of irritants. Immunosuppressant medications should be avoided, but phototherapy has been used with success.

HIV AND SEXUALLY TRANSMITTED INFECTIONS[20,22,23]

SYPHILIS

Syphilis is caused by Treponema pallidum. The risk of transmission is greatest in the early stages of the disease, especially if skin or mucosal ulcers are present.

For a single unprotected sexual contact, the risk of transmission is about 30 to 60 %. Like other STDs, syphilis favors the transmission of HIV due to lesions in the genital mucosa.

Symptoms

Patients may have multiple primary chancres, giant chancres which may become painful owing to superinfection.

Secondary syphilis may present as leus maligna.

There is more rapid progression to tertiary manifestations.

Patients have high RPR titre and a limited or absent antibody response to syphilis and treponemal antibody testing in the serum or CSF.

Increased predilection for the development of the Jarisch-Herxheimer reaction.

Likelihood of treatment failure and relapses.

More likelihood of progression to neurosyphilis in the first two years after diagnosis often despite appropriate therapy.

Diagnosis

Routine screening for syphilis with TPHA, TPPA or VDRL may not be reliable in HIV-infected patients. False-negative results can be explained by inadequate production of antibodies or by suppression of IgM production due to exorbitant IgG levels. In case of doubt, specific tests such as FTA-ABS (IgG and IgM) or cardiolipin tests should be carried out.

In erosive skin or mucosal lesions, dark field microscopy should be performed to demonstrate Treponema pallidum directly.

In cases where infection has been proven serologically, a neurological examination should be performed, especially on HIV-infected patients because of the merging of clinical stages.

Therapy

Primary and Secondary Syphilis Among HIV-Infected Persons

Treatment

Treatment of primary and secondary syphilis among HIV-infected persons is benzathine penicillin G, 2.4 million units IM in a single dose.

Available data demonstrate that additional doses of benzathine penicillin G, amoxicillin, or other antibiotics in early syphilis do not result in enhanced efficacy, regardless of HIV status.

In cases of penicillin intolerance, doxycycline 100 mg two times daily, tetracycline or erythromycinfour times dailycan be administered orally for 4 weeks, but these drugs are considered to be less effective than penicillin.

Neurosyphilis is usually treated with 5 MU benzyl penicillin given intravenously every 4 hours for 21 days. Other recommendations prefer administration of benzyl penicillin for 14 days, followed by three intramuscular doses of 2.4 MU benzathine penicillin given at weekly intervals.

In cases of penicillin intolerance, neurosyphilis can also be treated with 2 g intravenous ceftriaxone once daily for 14 days. Observational studies in small groups suggest ceftriaxone to be as effective as penicillin in the treatment of syphilis. However, cross-sensitivity may occur.

Follow-Up

HIV-infected persons should be evaluated clinically and serologically for treatment failure at 3, 6, 9, 12, and 24 months after therapy.

LYMPHOGRANULOMA VENEREUM

Infections with Chlamydia trachomatis are nearly twice as prevalent as gonococcal infections.

The serovars L1-3 cause Lymphogranuloma venereum. This disease is usually considered to be a tropical disease, rarely occurring in industrialized countries.

It may present clinically as primary (transient genial sore),secondary(inguinal) and tertiary(rectal) lesions.

In both HIV positive and HIV negative patients diagnosis is made by a combination of clinical presentation and high chlamydial complement fixation

antibody titres(>1:64).Co-infection with HIV has no effect on the clinical presentation.

Therapy

The therapy of choice is doxycycline 100 mg two times daily for 7 days. International guidelines also recommend 1 gm azithromycin, given as a single dose, as an equally potent therapy.

Lymphogranuloma venereum requires a longer treatment, with doxycycline being administered for minimum of 3 weeks.

Persons with both LGV and HIV infection should receive the same regimens as those who are HIV negative. Prolonged therapy might be required, and delay in resolution of symptoms might occur.

CHANCROID

Chancroid, also called *Ulcus molle*, is caused by Haemophilus ducreyi, a gram negative bacterium. It is an endemic infection found primarily in tropical or subtropical regions of the world.

Symptoms

Usually, the incubation period is about 2-7 days. The incubation may be increased in HIV patients. The ulcer may have a longer duration, greater numbers, necrotizing form and multilocular buboes. It may affect atypical sites such as the legs and digits. It may lead to increased severity, slow healing and treatment failure.

Therapy

The current CDC recommendations for the treatment of chancroid in immunocompetent and HIV infected patients are the same. Therapy should be

conducted using a single dose of 1 gm oral azithromycin. Ceftriaxone 250 mg intramuscularly, as a single dose, is equally potent. Alternative therapies are ciprofloxacin 500 mg two times daily for three days or erythromycin four times daily for 7 days. In fluctuant buboes, needle aspiration of pus may be indicated.

HIV-infected patients who have chancroid should be monitored closely because, as a group, they are more likely to experience treatment failure and to have ulcers that heal more slowly. HIV-infected patients might require repeated or longer courses of therapy than those recommended for HIV-negative patients.

GONORRHOEA

Gonorrhoea is caused by Neisseria gonorrhea.It primarily affects the urethra in both sexes but it may spread to paraurethral glands,cervix,endometrium,peritoneum.

The symptoms start with mild irritation,scanty mucopurulent discharge or mucoid discharge.As it progresses,the discharge becomes thick,purulent and profuse with intense burning and pain during micturition.

Therapy: Patients who have gonococcal infection with HIV should receive the same treatment regimen as those who are HIV negative.

Uncomplicated Gonococcal Infections of the Cervix, Urethra, and Rectum

Recommended Regimens

Ceftriaxone 250 mg IM in a single dose
OR
Cefixime 400 mg orally in a single dose
OR
Single-dose injectable **cephalosporin** regimens
PLUS
Azithromycin 1g orally in a single dose

OR

Doxycycline 100 mg twice a day for 7 days

Disseminated Gonococcal infection

Recommended Regimen

Ceftriaxone 1 g IM or IV every 24 hours

Alternative Regimens

Cefotaxime 1 g IV every 8 hours

OR

Ceftizoxime 1 g IV every 8 hours

All of the preceding regimens should be continued for 24--48 hours after improvement begins, at which time therapy can be switched to cefixime 400 mg orally twice daily to complete at least 1 week of antimicrobial therapy.

DONOVANOSIS

Granuloma inguinale caused by Klebsiella(calymmatobacterium) granulomatis is endemic in South India.

It typically presents with a chronic,destructive,beefy red,non-tender granulomatous ulcer.In HIV positive patients the mean duration to complete ulcer healing is prolonged and they are associated with greater tissue damage and extracellular dissemination.

Currently the CDC recommends the same treatment for both HIV positive and HIV negative patients with the note that gentamicin(1mg/kg administered intravenously every 8 hours) should be strongly considered for the HIV patients.

HERPES GENITALIS

Genital herpes as well as other genitoulcerative diseases are risk factors for acquisition of HIV infection during sexual intercourse.

Symptoms

In HIV individuals:

Herpes lesions increase in number and size,and become painful.

Atypical morphological appearances like hyperkeratotic lesions,hemorrhagic and ecthymatous.

Atypical sites like buttocks and lower back may be involved.

Increased severity,reccurent outbreaks and slow healing may be seen.

Necrotizing lymphadenitis, urinary retention, intestinal obstruction,pneumonitis, transverse myelitis may be seen.

Therapy

First Clinical Episode of Genital Herpes

Recommended Regimens*

Acyclovir 400 mg orally three times a day for 7--10 days
OR
Acyclovir 200 mg orally five times a day for 7--10 days
OR
Famciclovir 250 mg orally three times a day for 7--10 days
OR
Valacyclovir 1 g orally twice a day for 7--10 days

*Treatment can be extended if healing is incomplete after 10 days of therapy.

Established HSV-2 Infection

Almost all persons with symptomatic first-episode genital HSV-2 infection subsequently experience recurrent episodes of genital lesions; recurrences are less frequent after initial genital HSV-1 infection. Antiviral therapy for recurrent genital herpes can be administered either as suppressive therapy to reduce the frequency of recurrences or episodically to ameliorate or shorten the duration of lesions.

***Recommended Regimens for Daily Suppressive Therapy in Persons with HIV And Genital Herpes*[22]**

Safety and efficacy have been documented among patients receiving daily therapy with acyclovir for as long as 6 years and with valacyclovir or famciclovir for 1 year

Acyclovir 400--800 mg orally twice to three times a day
OR
Famciclovir 500 mg orally twice a day
OR
Valacyclovir 500 mg orally twice a day

Recommended Regimens for Episodic Infection in Persons with HIV And Genital Herpes

Effective episodic treatment of recurrent herpes requires initiation of therapy within 1 day of lesion onset or during the prodrome that precedes some outbreaks. The patient should be provided with a supply of drug or a prescription for the medication with instructions to initiate treatment immediately when symptoms begin.

Acyclovir 400 mg orally three times a day for 5--10 days

OR

Famciclovir 500 mg orally twice a day for 5--10 days

OR

Valacyclovir 1 g orally twice a day for 5--10 day

CONDYLOMATA ACUMINATA

Condylomata acuminata are caused by human papillomaviruses (HPV). They are usually present as genital warts, but other locations (oral) are known to be involved.

HIV-infected patients have a higher risk of acquiring genital warts. The incidence of warts is reported to be between 5% and 27%.

The typical pathogens, human papillomavirus type 6 or type 11, are not normally considered to be cancerogenic. Of genital warts, 90% are caused by HPV 6 or 11. HPV types 16, 18, 31, 33, and 35 can be associated with foci of high-grade intraepithelial neoplasia.

In HIV patients the lesions are extensive, dysplastic and may be subclinical. They tend to be infected with more HPV serotypes than control populations. These patients are at more risk of cervical, anal and other genital cancers.

Therapy

Treatment of genital warts is performed surgically by electrosurgery, cryotherapy, curettage, or laser. Chemical cautery with podophyllin, trichloroaceticacid is also helpful. In daily clinical practice, a surgical intervention followed by adjuvant immunotherapy with interferon beta or with imiquamod reduces the rate of relapse and seems to be the best choice for patients.

GENITAL MOLLUSCUM CONTAGIOSUM

In HIV infected patients, molluscum contagiosum manifests itself most commonly when the immune function has been dramatically reduced.

Giant lesions of molluscum contagiosum are seen in those cases who have progressed to AIDS. It is a clinical sign of marked HIV progression and very low CD4+T cell count,usually less than 200cells/microL

Molluscum contagiosum in HIV-positive patients is difficult to treat and spontaneous resolution does not occur. Most widely used methods are curettage and cryosurgery. Topical application of cidofovir and imiquamod 5% are helpful in refractory cases.

LABORATORY DIAGNOSIS[24,25,22]

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 commercially available tests with “Rapid protocols” and also by “Elaborate Test protocols”.

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

Laboratory Tests For The Diagnosis Of HIV Infecion-[24,25]

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 of Ministry 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 2

antibodies 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 solid surface bound HIV antigen and circulating antibody. These tests are highly sensitive and 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 co-cultivating 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 a

template to perform PCR. Nested PCR is a modified PCR for greater specificity and sensitivity.

ORASURE – (SALIAVA) HIV TESTS:

Non-invasively collected specimens of oral fluids are used, although generally referred to as saliava. This test uses antibodies that are comparable to or exceed those from serum samples. The first test employed is ELISA and then Western blot.

ORAQUICK ADVANCE RAPID HIV TESTS:

This test was approved in 2004.It gives results in 20mins.The blood, plasma, oralfluid 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 virologic 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.[22]

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. [22]

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.[22]

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.[22]

THERAPY OF HIV INFECTION [26,27,28]

HIV is a devastating disease caused by the human immunodeficiency virus. Symptoms of illness can manifest in every organ system, including the skin. Although there is no definitive cure, the creation of antiretroviral drugs and aggressive treatment regimens have dramatically altered disease morbidity and mortality.

In 2009, the total number of people who received anti-retroviral therapy was about 5.2 million, a 30% increase over 2008.

Currently, there are five broad categories of antiretroviral therapies:

- Nucleoside reverse transcriptase inhibitors (NsRTIs)
- Nucleotide reverse transcriptase inhibitor (NtRTI)
- Protease inhibitors (PIs)
- Nonnucleoside reverse transcriptase inhibitors (NNRTIs)
- Fusion inhibitors (FIs)

Zidovudine, an NsRTI, was the first drug on the market in 1987. Because of the virus's extraordinary ability to mutate, monotherapy was found to be largely ineffective. Studies showed that suppression of plasma HIV RNA was better sustainedwith three drugs, rather then one or even two drugs alone . HAART, typically a cocktail of two nucleoside analogs and a PI (protease inhibitor) or an NNRTI, became the cornerstone of HIV management in 1996 in the United States. Efavirenz, lamivudine, and zidovudine are often drugs of choice for initiating a patient on HAART.

Although HAART can reduce plasma HIV viral titers to undetectable levels in as little as eight weeks, the term "undetectable" is simply a reflection of the inadequate sensitivity of the test.

A realistic goal of treatment is one log reduction of viral load with eight weeks of therapy. Plasma HIV RNA levels and CD4 + T cell counts should be monitored throughout treatment . A viral load rebound may signify drug resistance and a need for therapy change.

Table 5 – CURRENT FDA APPOVED ANTIRETOVIRAL DRUGS

CURRENT FDA-APPROVED ANTIRETROVIRAL DRUGS				
Nucleoside reverse transcriptase inhibitors	**Nucleotide reverse transcriptase inhibitors**	**Non-nucleoside reverse transcriptase inhibitors**	**Protease Inhibitors**	**Fusion inhibitors**
zidovudine Didanosine zalcitabine Stavudine Lamivudine Abacavir Emtricitabine Lamivudine + zidovudine Lamivucine + zidovudine + abacavir	Tenofovir	Nevirapine Efavirenz Delaviridine	Saquinavir: hard gel Saquinavir: soft gel Ritonavir Indinavir Nelfinavir Amprenavir Fosamprenavir Atazanavir Lopinavir + ritonavir	Enfuvirtide

GENERAL GUIDELINES FOR INITIATION OF ANTIRETROVIRAL THERAPY

Start antiretroviral therapy earlier :Begin antiretroviral therapy when the CD4 cell count is less than 350cells/$mm^{3.}$

Use less toxic and more patient friendly options: Reduce the risk of adverse events and improve adherence by using less toxic drugs and fixed- dose antiretroviral therapy combinations.

Improve management of co-infections between HIV and TB or hepatitis B: Start anti retroviral therapy in all people living with HIV who have active TB and chronic active hepatitis B disease irrespective of CD4 + T cell counts.

Promote strategic use of laboratory monitoring: Use laboratory monitoring such as CD4 + T cell counts and viral load counts to improve the efficiency and quality of HIV treatment and care.

NsRTIs were the first family of antiretrovirals to be created in the battle against AIDS.

Although zidovudine was initially used as monotherapy, viral resistance quickly arose. Subsequently, substantial evidence supported the use of combination therapies. Treatment with indinavir, zidovudine, and lamivudine resulted in superior efficacy against rising viral titers and maintenance of CD4 + T cell counts. This led to the development of potent, aggressive multidrug regimens, or HAART, as the current standard treatment for HIV infection.

REVISED GUIDELINES ON INITIATION OF ART IN ADULTS AND ADOLESCENTS[79]

WHO CLINICAL STAGE	RECOMMENDATIONS
HIV INFECTED ADULTS & ADOLESCENTS(INCLUDING PREGNANT WOMEN)	
Clinical Stage I and II	Start ART if CD4 count< 350/mm^3
Clinical Stage III and IV	Start ART irrespective of CD4 counts
HIV AND TB CO-INFECTED PATIENTS	
Patients with HIV and TB co-infections(Pulmonary and Extra-pulmonary	Start ART irrespective of CD4 counts and type of TB(Start ATT first,initiate ART as early as possible between 2weeks to 2months,when TB treatment is tolerated
HIV AND HEPATITIS B/C CO-INFECTED PATIENTS	
HIV and HBV/HCV co-infection – without any evidence of chronic active hepatitis	Start ART if CD4 count< 350/mm^3
HIV and HBV/HCV co-infection –with documented evidence of chronic active hepatitis	Start ART irrespective of CD4 counts

Examples of preferred initiating drug regimens for treatment naive HIV patients include the following:[28]

- Non-nucleoside reverse transcriptase basedregimens efavirenz + lamivudine + zidovudine(or tenofovir or stavudine).
- Protease inhibitor based regimens lopinavir/ritonavir + lamivudine + zidovudine (or stavudine).
- Triple nucleoside reverse transcriptase basedregimens (used only when all other NNRTI or PI based regimens cannot be used).
- Abacavir + lamivudine + zidovudine (or stavudine).

NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NSRTIS)[28]

Mechanism of action : NsRTIs are dideoxynucleoside analogs that lack the 3' hydroxy group. Once phosphorylated intracellularly into active triphosphate metabolites,they bind avidly to the viral reverse transcriptase and become incorporated into the growing DNA strand, leading to DNA strand chain termination. These compounds, in essence, block RNAdependent DNA synthesis.

All the drugs in the class act in a similar manner, but differ in their side effects and toxicity profiles, although mitochondrial cytotoxicity is often associated with all NsRTIs.

Resistance to one NsRTI typically leads to resistance across the entire line.

NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITOR[28]

Tenofovir is an FDA-approved nucleotide analog reverse transcriptase inhibitor licensed for use in HIV combination therapies. Its mechanism of action is the

same as nucleoside analogs. Tenofovir causes DNA chain termination by competing against the natural substrate for the HIV reverse transcriptase active binding site. Clinical studies demonstrate that long-term use of HAART with tenofovir to be effective at suppressing resistant HIV-1 RNA titers.

Tenofovir shows activity against HBV and may be advantageous for patients with HIV/HBV coinfection.

NON-NUCLEOSIDE REVERSE TRANSCRIPTASEINHIBITORS (NNRTIS)[28]

NNRTIs are another family of antiretroviral medications approved by the FDA for treatment of HIV-1 infection. NNRTI binds non-competitively to the viral RNA dependent DNA polymerase outside of the active site and induces a conformational change that renders the enzyme inactive without affecting human DNA polymerases.

NNRTIs are active in their native state, do not require phosphorylation, and are not incorporated into the viral DNA chain. They are licensed for use in combination therapies selectively against HIV-1 infections only.They have no effect on HIV-2 infections.

PROTEASE INHIBITORS (PIS)[28]

In 1995, a new family of antiretroviral was added to the therapeutic arsenal for use in combination therapy against HIV infection. Protease inhibitors function at a point downstream of reverse transcriptase inhibitors in the viral replication cycle by inhibiting the cleavage of viral polyproteins, resulting in the formation of immature, nonfunctional viruses.

The new family of antiretroviral ismore potent than their nucleoside analog counterparts and improved the quality of life of patients on treatment.

FUSION INHIBITORS[28]

In order to enter a human cell, HIV must first attach itself to proteins on the cell's surface. The virus always begins by latching on to a protein called CD4. The next stage involves proteins called co-receptors, of which there are two main types: CCR5 and CXCR4. Some strains of HIV use CCR5, others use CXCR4, and some can use either.

CCR5 antagonists are a type of entry inhibitor that bind to the CCR5 co-receptor so that HIV cannot exploit it to gain entry to a cell. The main drawback of these drugs is that they don't work against all strains of HIV.

MATURATION INHIBITORS[28]

Maturation inhibitors are a potential new drug class which seeks to halt the development of immature HIV particles after they have emerged from human cells.

Table 6: SIDEEFFECTS OF DRUGS:[78]

ADVERSE EVENTS	OFFENDING AGENTS
Anemia Leukopenia	Zidovudine
Peripheral Neuropathy	Stavudine Didanosine
Lactic Acidosis	Stavudine Didanosine
Pancreatitis	Stavudine Didanosine
Lipoatrophy Lipohypertrophy	Protease inhibitors Stavudine
Dyslipidaemia	Stavudine Efavirenz All boosted Protease inhibitors except Atazanavir
Hyperglycemia	Protease inhibitors Stavudine

Table 7: NEWER ANTI-RETROVIRAL DRUGS[28]

DRUG	RECENTLY APPROVED	DISCONTINUED TRIALS	PHASE II TRIALS	PHASE III TRIALS
ENTRY INHIBITORS	Maraviroc	Vicriviroc	BMS-663068 TNX-355 – also known as ibalizumab PRO 140 Cenicriviroc is a CCR5 anatagonist	
INTEGRASE INHIBITORS	Raltegravir		Dolutegravir	Elvitegravir
MATURATION INHIBITORS		Bevirimat		Vivecon (MP-9055)
NNRTI	Etravirine Rilpivirine		Lersivirine	
NRTIs			KP-1461 Apricitabine, Elvucitabine Racivir Festinavir (previously OBP-601)	
Fixed Dose Combination (FDC)				**Quad pill**
Fixed Dose Combination (FDC)	**Rilpivirine + FTC + TDF (Complera) - Aug. 2011**			

Because rilpivirine is a low dose, once daily medication, it is easier to use it in the development of new fixed dose combinations (FDCs), which combine several different drugs into one pill. A new FDC comprising tenofovir, emtricitabine and rilpivirine (marketed as Complera) was approved by the FDA in 2011[28].

POST EXPOSURE PROPHYLAXIS [80]

Transmission

The risk of HIV transmission is present if an HIV-negative person comes into contact with the blood, semen or vaginal fluids of an HIV-positive source person. But exposure of intact skin to HIV-contaminated body fluids (e.g. blood) is not sufficient to transfer the virus.

Transmission is possible if HIV-containing material enters the body by:

. Accidental needlestick injury or incision by surgical instruments

. Exposure of damaged skin or mucosal membranes

. Unprotected sexual intercourse with an infected person

. IDU sharing needle or equipment

. Transfusion of HIV-contaminated blood or blood products

Type of Exposure	**Relative Risk**
Deep needlestick injury or cut	16 : 1
Fresh blood on the penetrating instrument	5 : 1

Penetrating needle previously placed in blood vessel	5 : 1
Source person with high viral load	6 : 1
Exposition of mucosal membrane	1 : 10
Exposition of inflammatory damaged skin	1 : 10

Initiation of PEP

Time is the most important factor for initiation of PEP. The best chance to prevent transmission is within the first 24 hours of exposure. After that time period, the risk of systemic spread of the virus increases. Initiating PEP after more than 72 hours following exposure does not seem reasonable.

PEP should be initiated as soon as possible, preferably within 2 hours of exposure.

Actual recommendations prefer a regimen with a combination of antiretroviral substances given over 4 weeks, preferably consisting of two NRTIs and one PI . NNRTIs, especially nevirapine, should not be used for PEP because of the risk of severe adverse effects (hepatotoxicity) (CDC 2001). For efavirenz such severe in the first weeks of intake, limits its use for PEP.

Recommended antiretroviral combinations for HIV Post-exposure Prophylaxis *

NNRTI	**PI**
Zidovudine + Lamivudine	Lopinavir
Tenofovir + Emtricitabine	PLUS Saquinavir

Tenofovir + Lamivudine	Fosamprenavir
Stavudine+ Lamivudine	Nefinavir

HIV VACCINES[29]

Vaccines against HIV are being developed, and they are in various stages of clinical trial but at present none have proven effective.

Since 1987, more than 30 HIV candidate vaccines have been tested in approximately 60 Phase I/II trails, involving more than 10,000 healthy volunteers. Most of these trials have been conducted in the United States and Europe, but several have also been conducted in developing countries (Brazil, China, Cuba, Haiti, Kenya, Peru, Thailand, Trinidad, and Uganda). The results have confirmed the safety of the vaccines, and have provided important scientific information to develop newer generations of candidate vaccines with better ability to induce anti-HIV specific immune responses.

At the present time, there are only two related candidate vaccines being evaluated in Phase III efficacy trials.

Strategies must be put in place to ensure that once an HIV vaccine is discovered, delivery systems are in place so that it can be made available without unnecessary delay to all people in need.

Subunit vaccines: Also known as "component" or "protein" vaccines, contain only individual parts of HIV, rather than the whole virus. They Can prompt the body to produce an anti-HIV immune response, although that response may be too weak to actually protect against future HIV infection.

Recombinant vector vaccines: Take advantage of non-HIV viruses that either don't cause disease in humans or have been deliberately weakened so that they can't cause disease. These weakened (attenuated) viruses are used as **vectors**, or carriers, to deliver copies of HIV **genes** into the cells of the body. As with subunit vaccines, these HIV proteins can stimulate an anti-HIV immune response.

DNA vaccines also introduce HIV genes into the body. Unlike recombinant vector vaccines, DNA vaccines do not rely on a virus vector. Instead, "naked" DNA containing HIV genes is injected directly into the body. The HIV proteins trigger the body to produce an immune response against HIV.

METHODOLOGY

The present study titled CUTANEOUS MANIFESTATIONS WITH CD4 +T CELL COUNTS IN HIV SEROPOSITIVE/AIDS PATIENTS - A CROSS SECTIONAL STUDY was conducted in Department of Dermatology, Venereology & Leprosy, KLE'S Dr Prabhakar Kore Hospital and Medical Research Centre, Belgaum.

Study period

The present study was conducted during January 2010 to December 2010.

Study design: Cross sectional study

Sample selection criteria: All HIV seropositive/AIDS patients attending KLE's Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum, were recruited as per the Inclusion and Exclusion criteria.

Inclusion Criteria:

- All confirmed HIV seropositive cases.
- All HIV positive patients with or without AIDS.

Exclusion Criteria:

- Pediatric age group.
- All pregnant mothers.
- Cases who do not provide informed consent.

Main parameters Studied

- Association between CD4+T lymphocyte cell count and cutaneous manifestations of HIV/AIDS**.**

- Prevalence rate of cutaneous manifestations in HIV/AIDS patients.

Sample size: Considering the formula $4pq/d^2$

Where p=prevalence=50%

q = 100-p=100-50 = 50

d=absolute error=10%

n=4x50x50/10X10

=100

Therefore the sample size = 100

The association between CD4+Tcell counts and different skin manifestations was done by Chi Square test and Mann - Whitney U test. Statistical significance was assumed if $p<0.05$.

Ethical clearance has been obtained from the Institution.

After obtaining the informed consent, patients were enrolled in the study. A detailed history of all patients was recorded as per the proforma. Chief complaints were recorded in the form of duration and evolution of the lesions on the skin, mucous membrane, hair and nails and other associations with them. History regarding nature of work, occupation and type of work, income and marital status was also taken. Past history of similar complaints and family history regarding spouse or partner being sero reactive was also elicited. Personal history regarding the sexual behaviour, use of condoms and presence of any risk factors or practices were also taken.

General physical examination and systemic examination 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 Organization (WHO) clinical staging criteria. The HIV status of all the patients verified and the CD4+ T cell count was obtained.

The patients were clinically examined in good light, for various cutaneous manifestations of HIV such as skin lesions, nail changes, mucous membrane involvement etc.

Following investigations were done in all the patients:

1) Routine haematological and urine investigations such as Hb%, TLC, DLC, ESR, RBS, Urine routine and microscopy were done in all patients.

2) CD4+ T lymphocyte count estimation by flow cytometry.

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 count. 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.

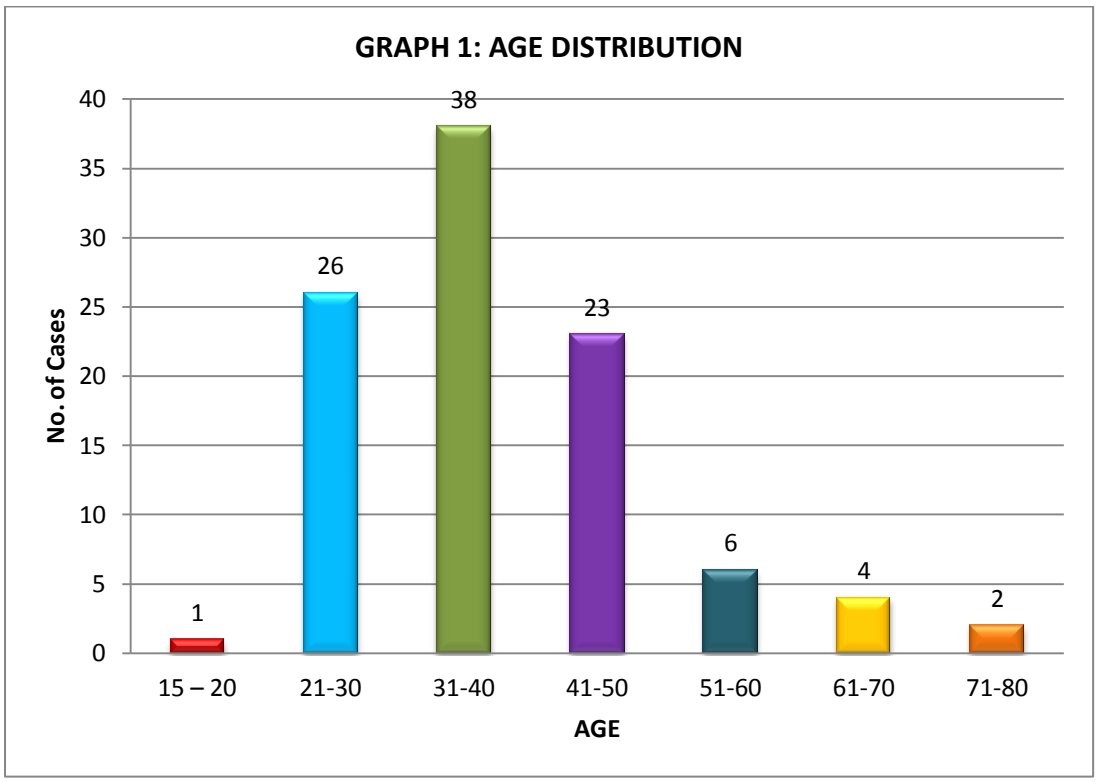
RESULTS

The present study titled CUTANEOUS MANIFESTATIONS WITH CD4+T CELL COUNTS IN HIV SEROPOSITIVE/AIDS PATIENTS - A CROSS SECTIONAL STUDY was conducted in Department of Dermatology, Venereology & Leprosy, KLE'S Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum.

AGE DISTRIBUTION

Table 8

Sr.No	AGE	NO OF PATIENTS
1	15 – 20	1
2	21-30	26
3	31-40	38
4	41-50	23
5	51-60	6
6	61-70	4
7	71-80	2
	TOTAL	**100**

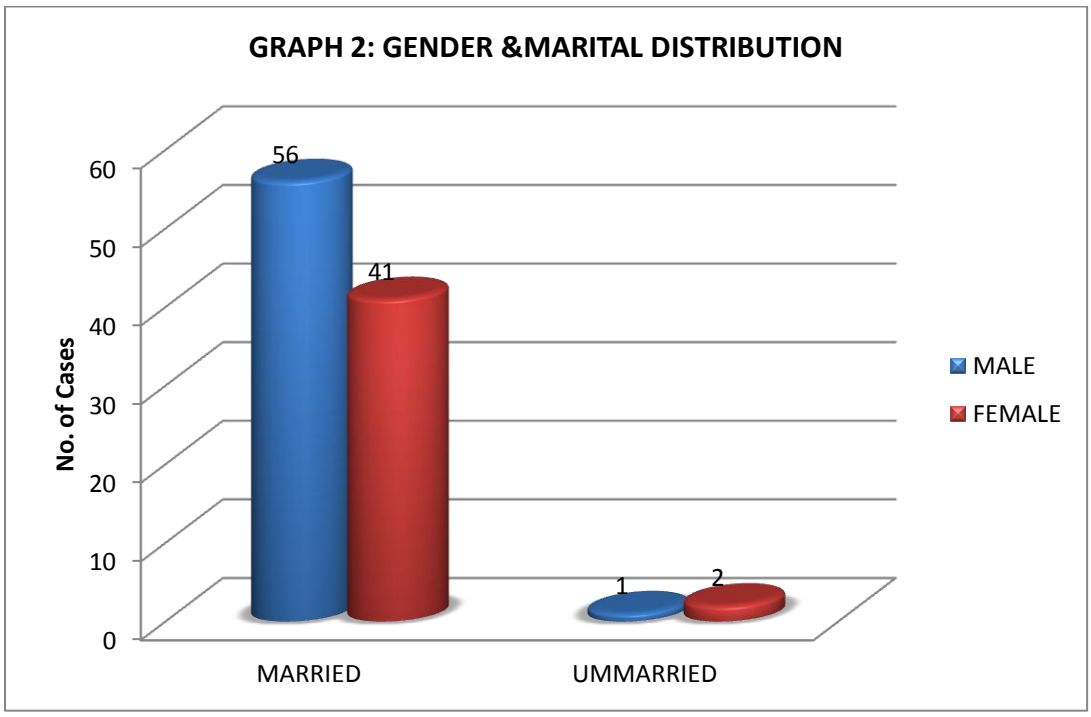


In the present study, the age of the patients ranged between 15 years to 80 years. Among the 100 patients studied, most of them were in the range of 31-40 years (38%) followed by 41-50years(23%).Youngest patient in the study was of 17years and highest age noted was 76years.The mean age in females was 31.93years and in males is 42.31years.

GENDER &MARITAL DISTRIBUTION

Table 9

Sr.No	GENDER	PERCENTAGE	MARRIED	UMMARRIED
1	MALE	57	56	1
2	FEMALE	43	41	2
	TOTAL	**100**	**97**	**3**

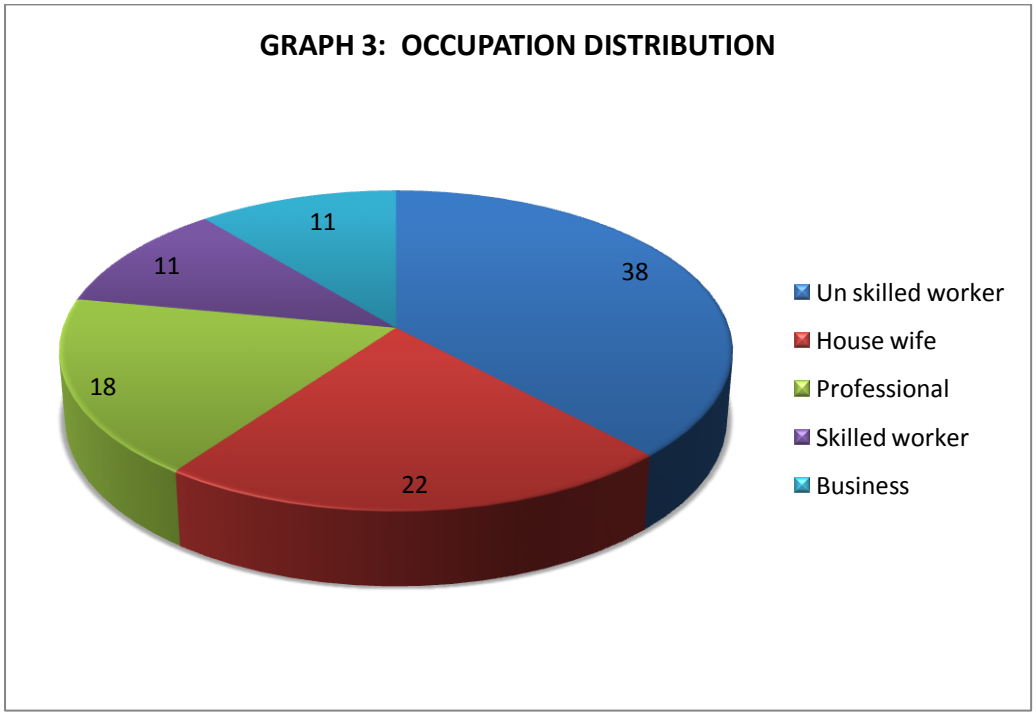


In the present study the total number of married patients were 97(M=56,F=41). Among 57 male patients,56 were married and 1 was unmarried(17 years).Of the total 43 female patients,41 were married and 2 unmarried with mean age of 22 years. Male to female ratio for the HIV reactive patients in the study was 1.32:1.

OCCUPATION DISTRIBUTION

Table 10

OCCUPATION	NO.OF CASES PATIENTS CASES
Un skilled worker	38
House wife	22
Professional	18
Skilled worker	11
Business	11
TOTAL	**100**



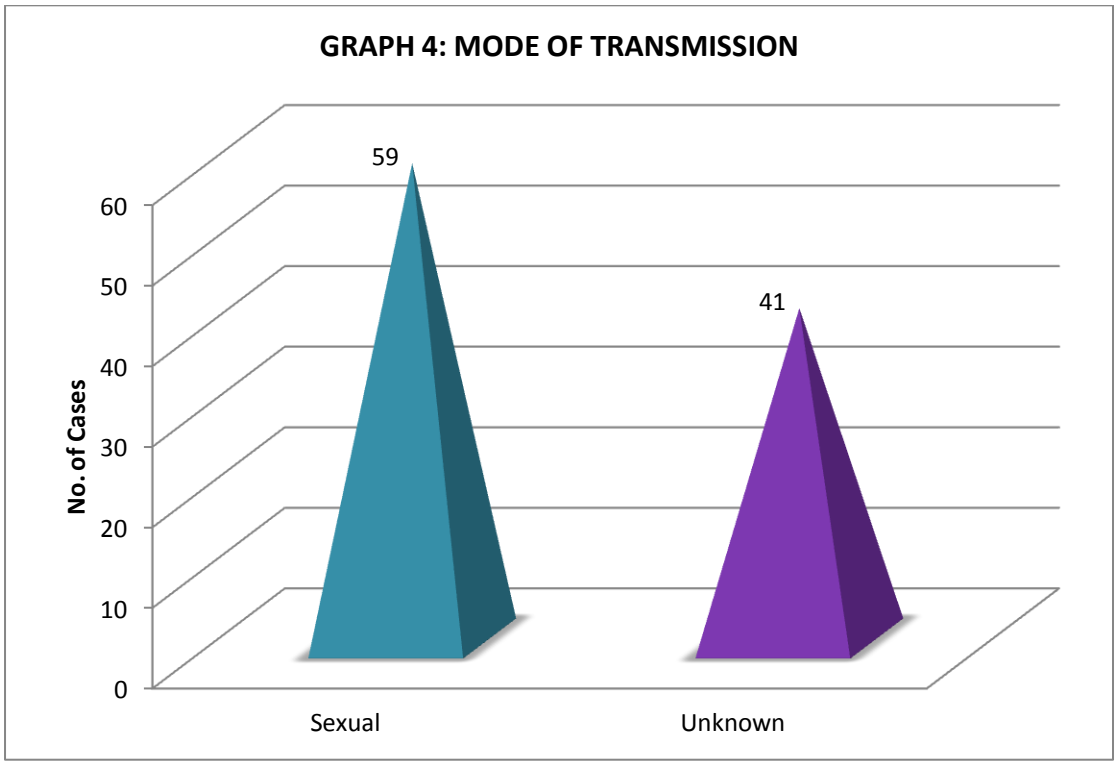
In this study majority of the patients that is 38 (38%) were unskilled workers.

Most of the males were farmers (28 patients, 28%), followed by drivers & cooliesi.e. 9 (9%) patients each. Among females most of them were house wives (22 patients, 22%). 11 (11%) patients were into business.

MODE OF TRANSMISSION

Table 11

Mode of transmission	NO.OF CASES
Sexual	59
Unknown	41
Total	**100**

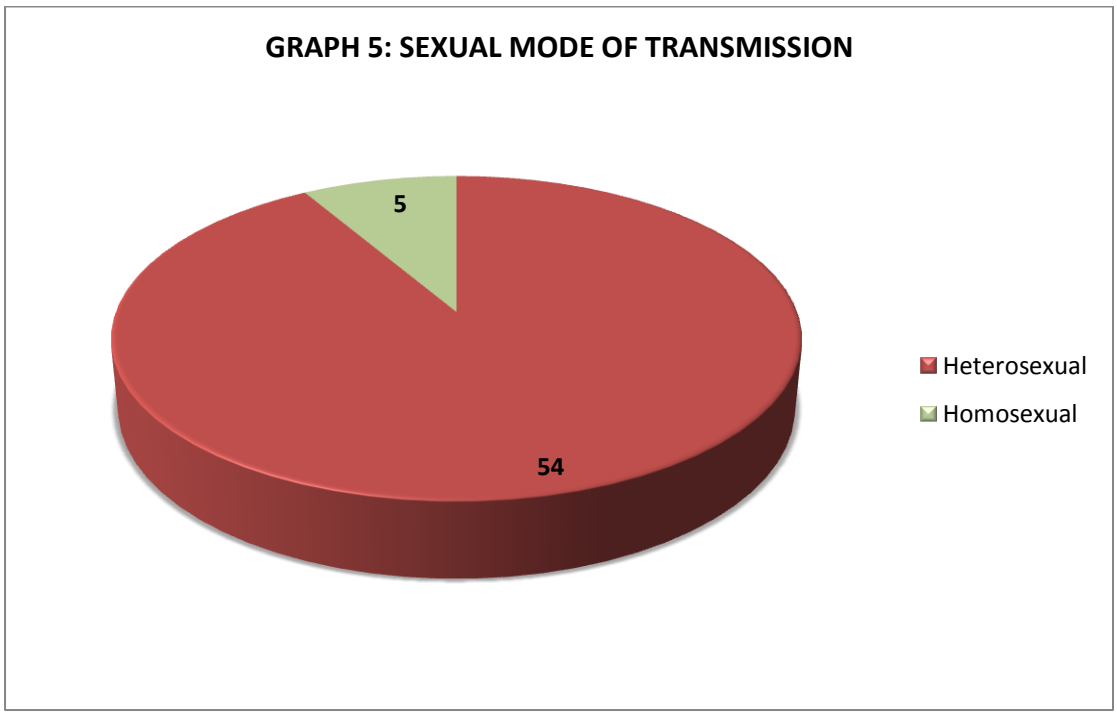


Of the total 100 patients majority i.e.59 (59 %) patients had acquired HIV infection by sexual transmission.41(41%) patients denied any of the other modes of transmission like blood transfusion, needle stickinjury, injecting drug abuse.

SEXUAL MODE OF TRANSMISSION

Table 12

SEXUAL	NO.OF CASES	PERCENTAGE
Heterosexual	54	91.52%
Homosexual	5	8.47%
TOTAL	**59**	**100**



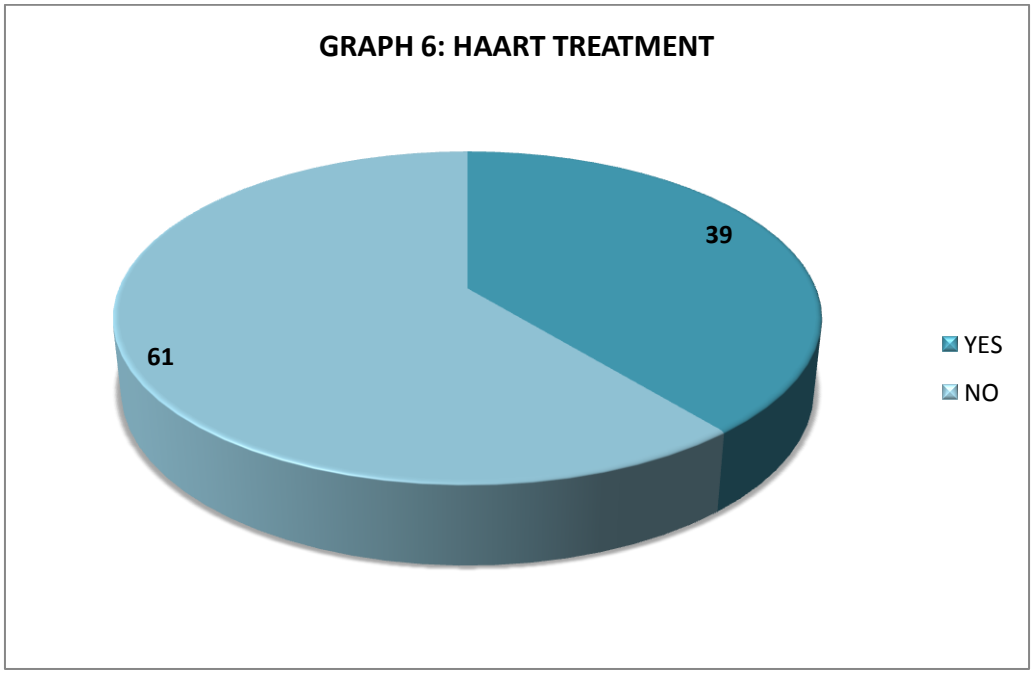
Of the 59 total cases of sexual mode of transmission, majority showed heterosexual mode (91%).

8.47% of patients were noted to have acquired infection through homosexual route.

HAART TREATMENT

Table 13

TREATMENT	NO.OF CASES
YES	39
NO	61
TOTAL	**100**

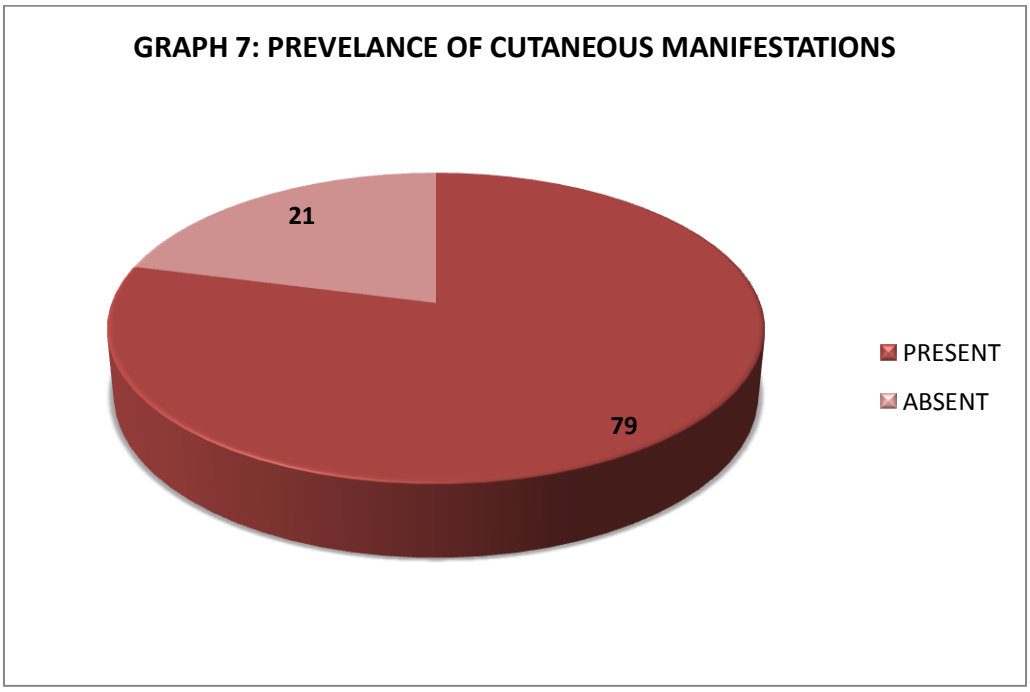


In the present study, 61 patients(61%) did not receive HAART treatment while 39 patients were on treatment.

PREVELANCE OF CUTANEOUS MANIFESTATIONS

Table 14

CUTANEOUS MANIFESTATIONS	NO OF CASES
PRESENT	79
ABSENT	21
TOTAL	**100**

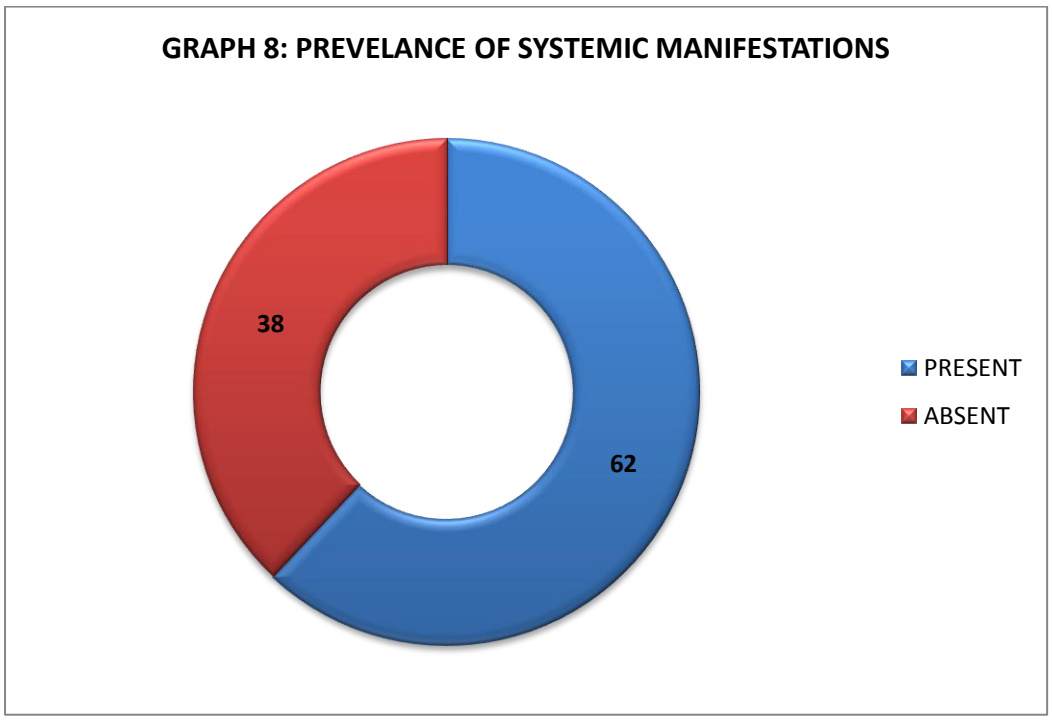


In the present study, among the 100 patients the cutaneous manifestations of HIV infection/AIDS were found in 79% of the patients. 21% patients with HIV infection/AIDS had no cutaneous manifestations.

PREVELANCE OF SYSTEMIC MANIFESTATIONS

Table 15

SYSTEMIC MANIFESTATIONS	NO OF CASES
PRESENT	62
ABSENT	38
TOTAL	**100**

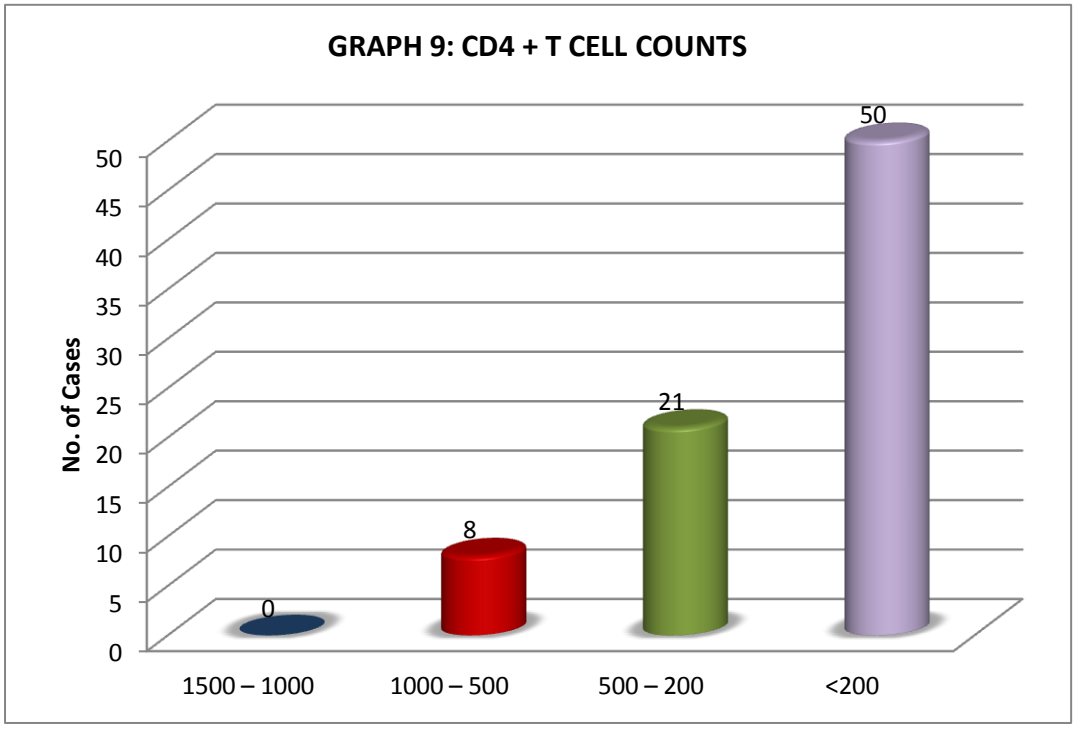


In the present study, the systemic manifestations of HIV were found in 62 (62%) of the patients. 38 (38%) patients with HIV infection/AIDS had no systemic involvement.

CD4 + T CELL COUNTS

Table 16

CD 4+ T cell counts	No of Patients	Percentage
1500 – 1000	-	-
1000 – 500	8	10.12
500 – 200	21	26.58
<200	50	63.29
TOTAL	**79**	**100**



In the study out of the total number of 79 patients with skin manifestations, majority had CD4+T cell counts falling below 200 cells/microL i.e,50(63%).Only 10% of patients showed CD4+T cell counts levels between 500 – 1000cells/microL.

DISTRIBUTION OF CASES ACCORDING TO WHO CLINICAL STAGE

Table 17

WHO clinical stage	No. of Cases
I	9
II	3
III	65
IV	23
TOTAL	**100**

In the present study 9 patients belonged to clinical stage I, 3 patients to stage II,65 patients to clinical stage III and 23 were in stage IV.

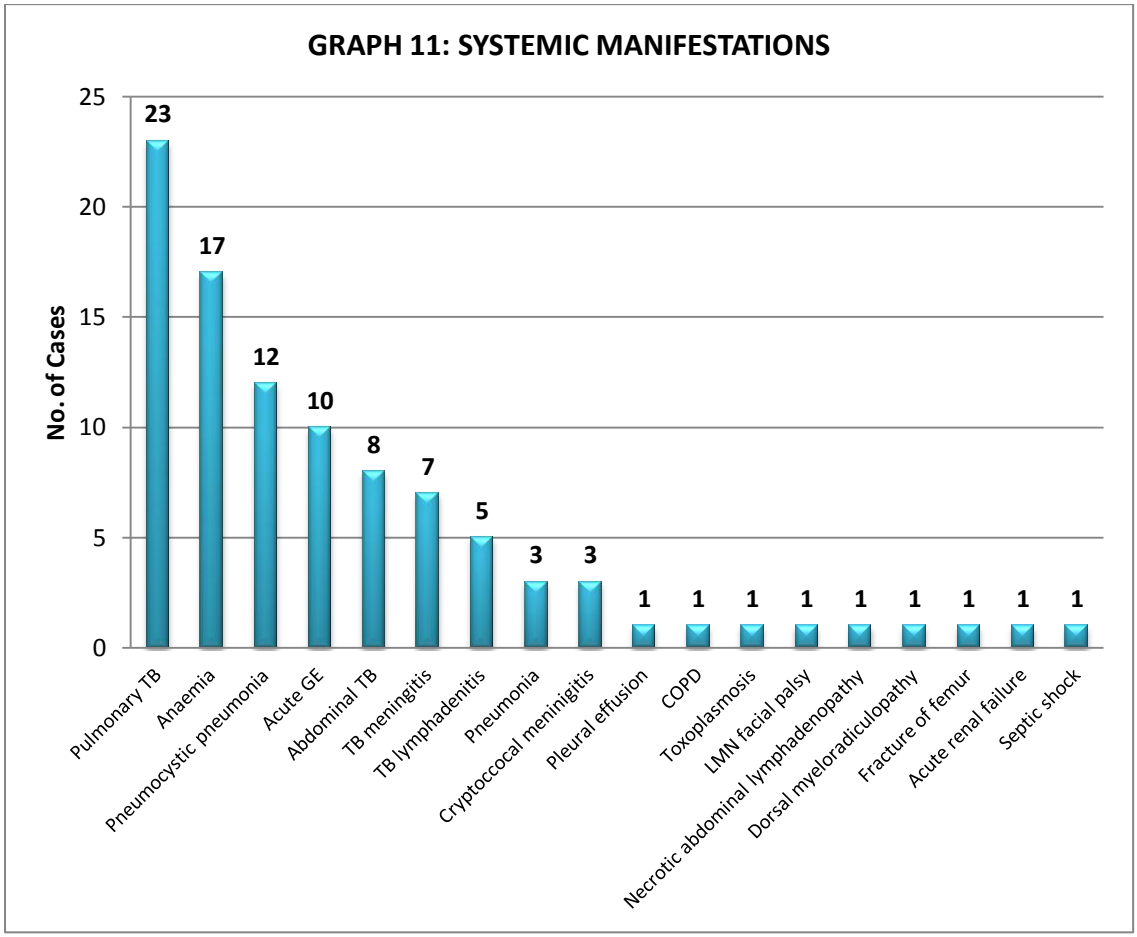
SYSTEMIC MANIFESTATIONS

Table 18

Pulmonary TB	23
Anaemia	17
Pneumocystic pneumonia	12
Acute GE	10
Abdominal TB	8
TB meningitis	7
TB lymphadenitis	5
Pneumonia	3
Cryptoccocal meninigitis	3
Pleural effusion	1
COPD	1
Toxoplasmosis	1
LMN facial palsy	1
Necrotic abdominal lymphadenopathy	1
Dorsal myeloradiculopathy	1
Fracture of femur	1
Acute renal failure	1
Septic shock	1

In the present study majority of them i.e. 40 patients had respiratory system involvement mainly in the form of pulmonary tuberculosis (23 patients),Pneumocystitis carinii pneumonia (12 patients),Pneumonia (3 patients),Pleural effusion(1 patient),COPD(1 patient).

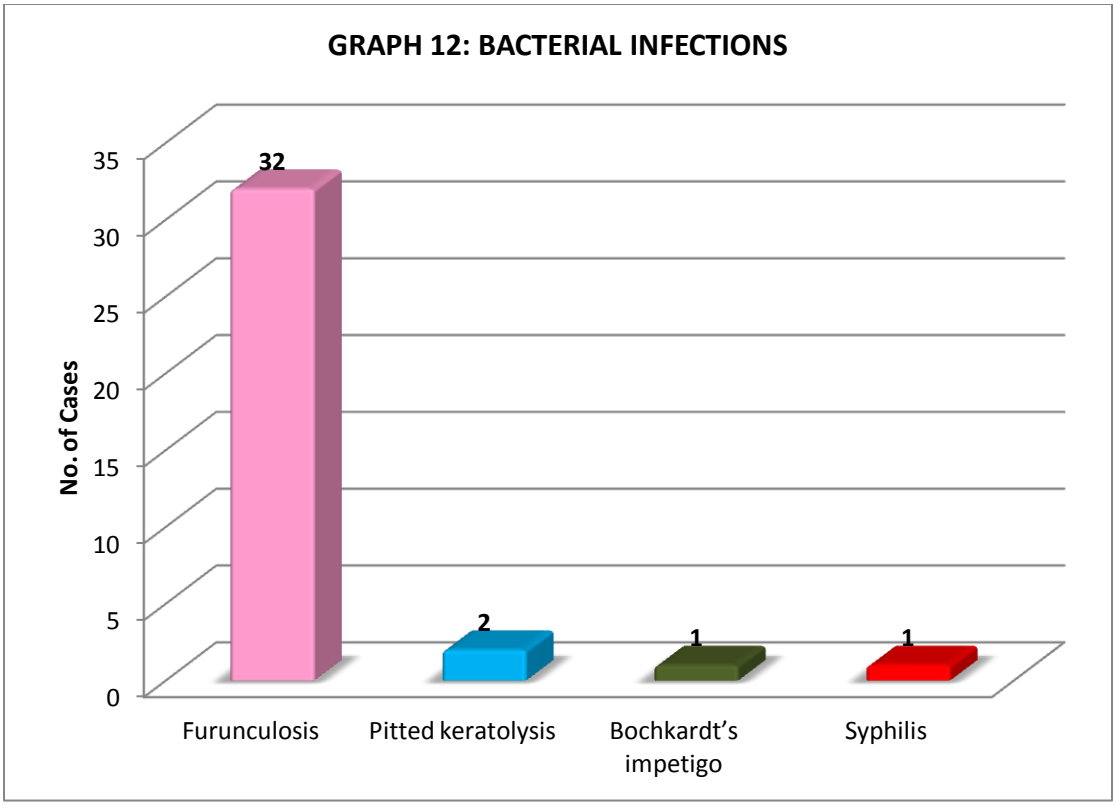
Other forms of TB like abdominal TB(8 patients),TB meningitis(7 patients),TB lymphadenitis(5 patients). CNS involvement in the form of Cryptococcal meningitis, Toxoplasmosis were seen in 3 and 1 patient respectively .17 patients were diagnosed to be having Anaemia of chronic disease and 10 patients suffered from Acute gastro enteritis.



BACTERIAL INFECTIONS

Table 19

Furunculosis	32
Pitted keratolysis	2
Bockhart's impetigo	1



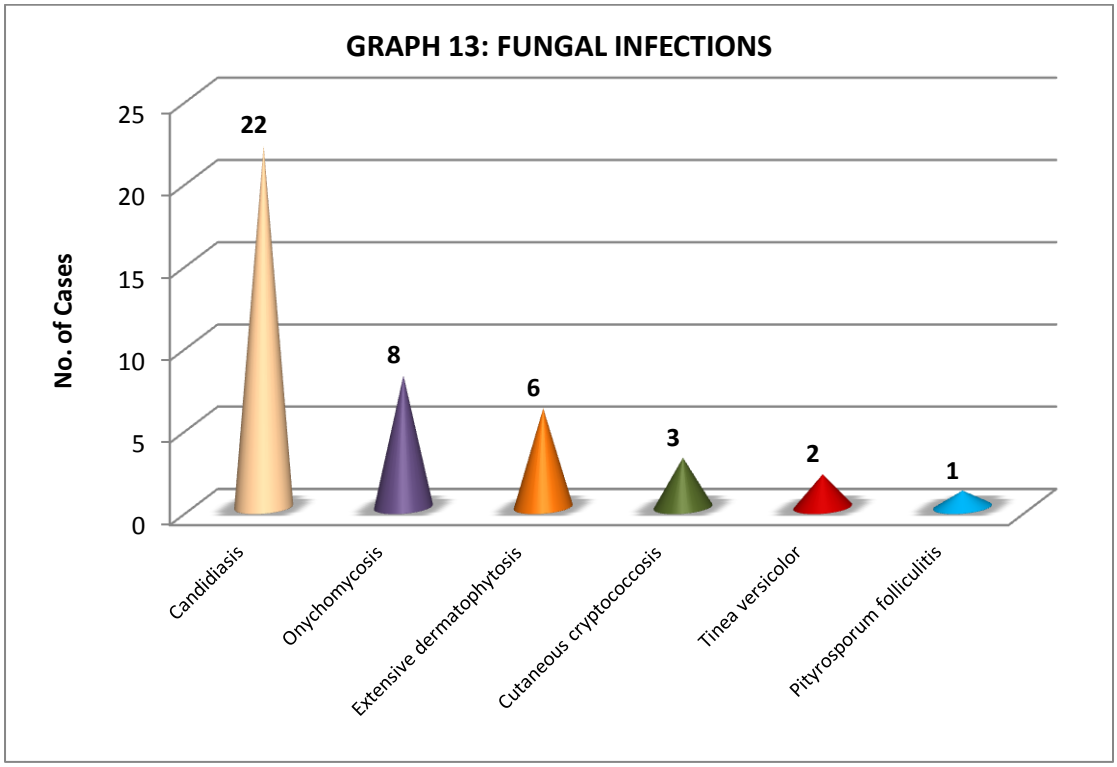
In the present study of the total 79 patients with cutaneous manifestations bacterial infections like furunculosis was the most common one reported in about 32 patients. Pitted keratolysis was seen in 2 patients,Bockhart's impetigo in 1 patient.

FUNGAL INFECTIONS

Table 20

Candidiasis	22

Onychomycosis	15
Extensive dermatophytosis	6
Cutaneous cryptococcosis	3
Tinea versicolor	2
Pityrosporum folliculitis	1



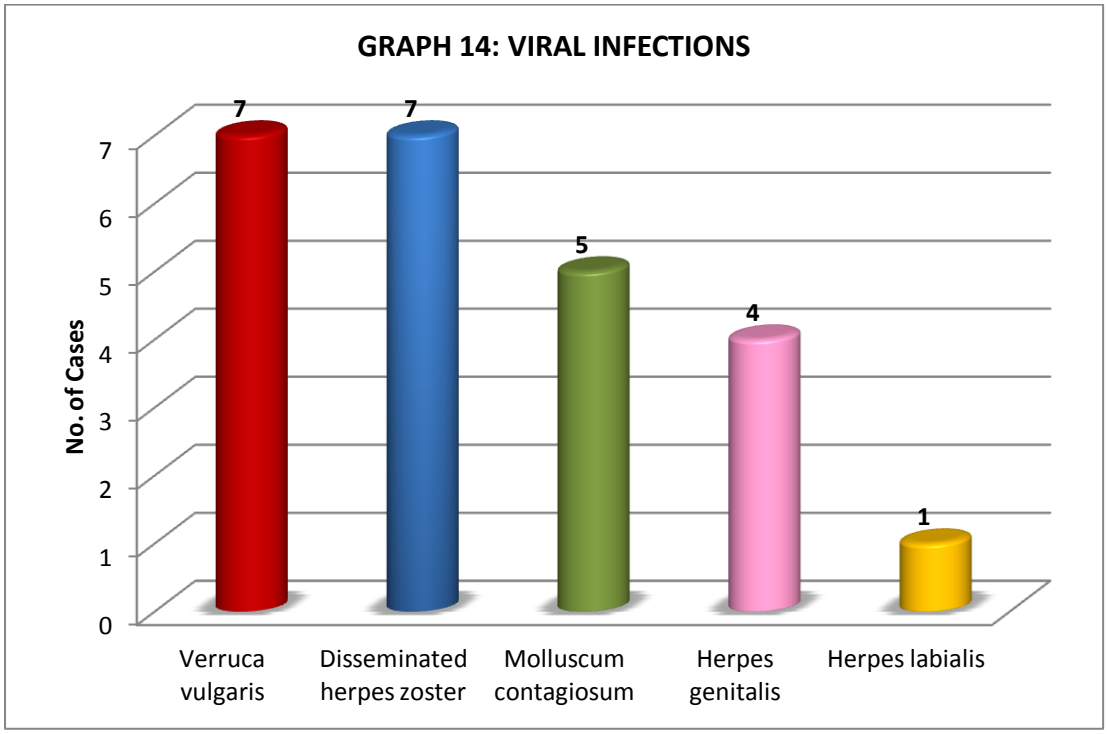
Among the fungal infections candidiasis was the most common one reported in 22 patients followed by onychomycosis and extensive dermatophyosis in 15 and 6 patients respectively.

VIRAL INFECTIONS

Table 21

Verruca vulgaris	7

Disseminated herpes zoster	7
Molluscum contagiosum	5
Herpes labialis	1



Among the viral infections, verruca vulgaris, herpes zoster were the commonest ones seen in 7 patients each. Next in frequency is molluscum contagiosum in 5 patients and herpes labialis in 1 patient.

PARASITIC INFESTATIONS

Table 22

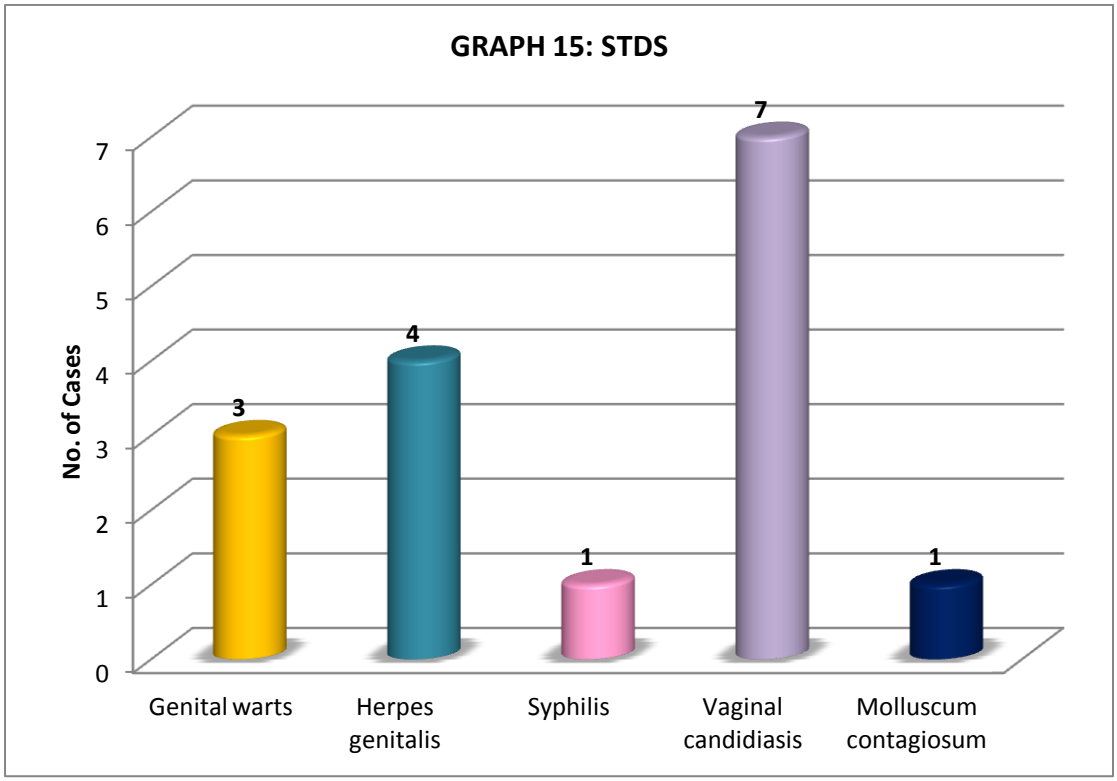
Scabies	12

The only parasitic infestation noted in this study was scabies(12 patients) and 2 among them were of Norwegian variety.

SEXUALLY TRANSMITED INFECTIONS

Table 23

Vulvovaginal candidiasis	7
Herpes genitalis	4
Genital warts	3
Genital molluscum contagiosum	1
Syhilis	1

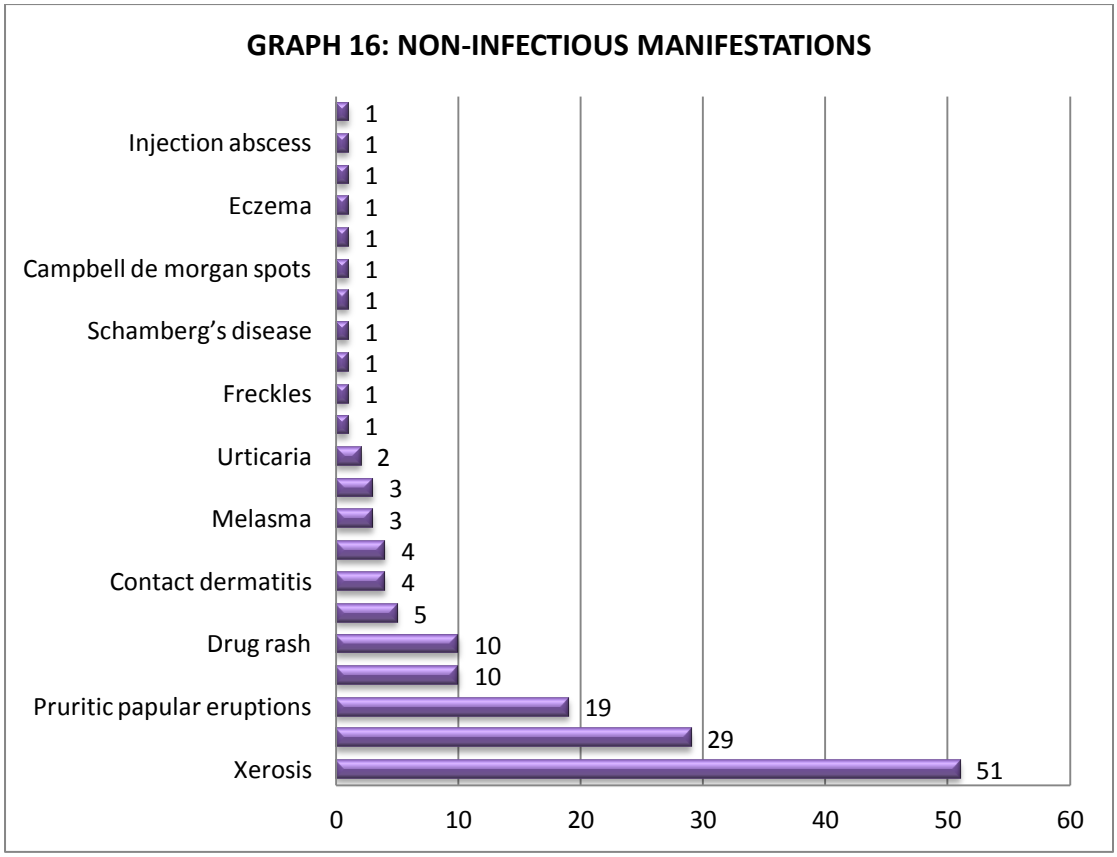


In the present study,patients presented with genital complaints,of which majority had vulvovaginal candidiasis 7 patients.Herpes genitalis was noted in 4 followed by genital warts in 3 patients. One patient each of syphilis and genital molluscum contagiosum.

NON-INFECTIOUS MANIFESTATIONS

Table 24

Xerosis	51
Seborrheic dermatitis	29
Pruritic papular eruptions	19
Lipodystrophy	10
Drug rash	10
Apthous ulcers	5
Contact dermatitis	4
Generalized hyperpigmentation	4
Melasma	3
Acne vulgaris	3
Urticaria	2
Plantar keratoderma	1
Freckles	1
Photodermatitis	1
Schamberg's disease	1
Portwine stain	1
Campbell de morgan spots	1
Acanthosis nigricans	1
Eczema	1
Keratolysis exfoliativa	1
Injection abscess	1
Idiopathic guttate hypomelanosis	1

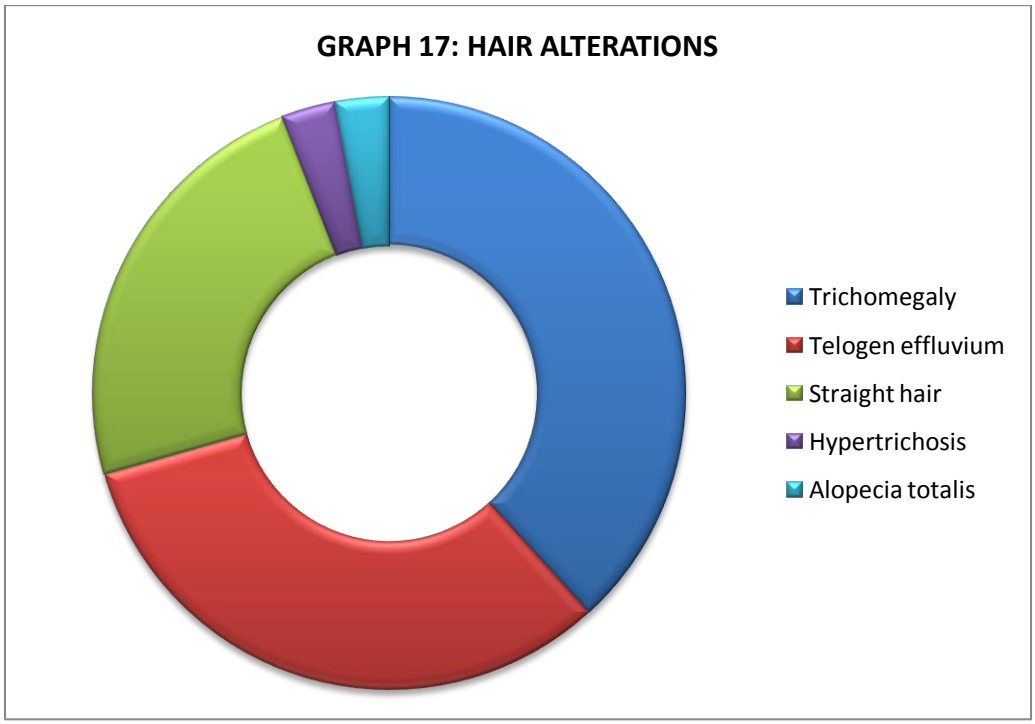


In the present study, among the non-infectious manifestations, xerosis was observed in 51 patients (51%), seborrheic dermatitis in 29 patients (29%), pruritic papular eruptions in 19 patients (19%).Drug rash,lipodystrophy were observed in 10 patients each.

HAIR ALTERATIONS

Table 25

Trichomegaly	13
Telogen effluvium	11
Straight hair	8
Hypertrichosis	1
Alopecia totalis	1

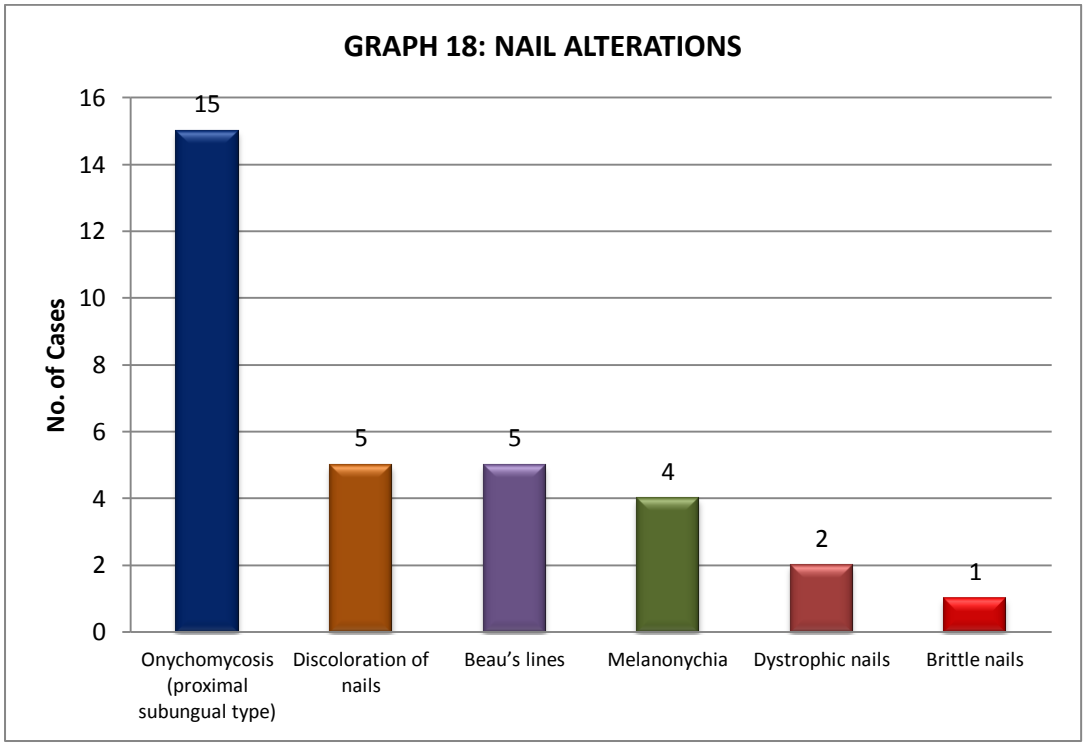


Hair changes noted were trichomegaly in 13 patients followed by telogen effluvium in 11.Alopecia totalis was seen in one patient.

NAIL ALTERATIONS

Table 26

Onychomycosis (proximal subungual type)	15
Discoloration of nails	5
Beau's lines	5
Melanonychia	4
Dystrophic nails	2
Brittle nails	1



Nailchanges noted were in onychomycosis in 15 patients,followed by beau's lines in 5,longitudinal melanonychia in 4 patients.

COMPARSION OF CUTANEOUS MANIFESTATIONS WITH CD4 + T CELL COUNTS

In the present study,most patients were having more than one cutaneous manifestations which are tabulated as follows:

Table 27

CD4 COUNTS	INFECTIOUS	NON - INFECTIOUS	TOTAL
<200 cells/ MicroL	Furunculosis(17) Candidiasis(11) Herpetic infections(8) Verruca vulgaris(7) Scabies(7) Molluscum contagiosum(5) Extensive dermatophytosis(4) Cutaneous cryptococcosis(3) Pityrosporum infections(2) Syphilis(1)	Xerosis(31) Hair changes(24) Nail changes(22) Seborrheic dermatitis(18) Pruritic papular eruptions(11) Drugrash(7) Apthous ulcers(5) Lipodystrophy(5) Generalized hyperpigmentation(3) Melasma(3) Urticaria(2) Contact dermatitis(2)Plantar keratoderma(1) Acne(1) Eczema(1) Keratolysis exfoliativa(1) Injection abscess(1) Schamberg's disease(1) Port wine stain(1) Campbell de morgan spots(1)	50
500 – 200	Bacterial folliculitis(11)	Xerosis(16)	21

Cells/MicroL	Herpetic infections(5) Candidiasis(5) Scabies(5) Pityrosporum infections(1)	Seborrheic dermatitis(9) Hair changes(7) Nail changes(6) Pruritic Papular Eruptions(6) Lipodystrophy(4) Drug rash(3) Contact dermatitis(2) Photodermatitis(1) Generalized hyperpigmentation(1) Freckles(1) Acne(1) Acanthosis nigricans(1)	
1000 – 500 Cells/MicroL	Furunculosis(4) Herpetic infection(3) Extensive dermatophytosis(2) Intertrigo(1)	Xerosis(4) Nail changes(4) Hair changes(3) Pruritic papular eruptions(2) Seborrheic dermatitis(2) Idiopathic guttate hypomelanosis(1) Acne(1) Lipodystrophy(1)	8
1500 – 1000 Cells/MicroL	NIL	NIL	0
Total			**79**

In the present study, the cutaneous manifestations in HIV seropositive patients were observed with all ranges of CD4+Tcell counts but it was found that patients with lowered CD4+ T cell counts were associated with increased incidence of xerosis, seborrheicdermatitis, pruritic papular eruption, adverse drug eruptions when compared with those patients of high CD4+T lymphocyte counts. Patients with

CD4+T cell counts less than 200cells/microliter were found to have more incidence of infectious conditions like genital herpes, viral warts, candidiasis,furunculosis, and Norwegian scabies.

FREQUENCY OF SKIN DISORDERS AS A FUNCTION OF CD4 + T CELL COUNTS

Table 21

SKIN MANIFESTATION	TOTAL	<200 Cell count	>200 Cell count	*P* value
Xerosis	51	31	20	0.533
Hair alterations	34	24	10	0.242
Nail alterations	32	22	10	0.406
Seborrheic dermatitis	29	18	11	0.864
Pruritic papular eruption	19	11	8	0.576
Lipodystrophy	10	5	5	0.351
Drug rash	10	7	3	0.638
Apthous ulcers	5	5	0	0.094
Furunculosis	32	17	15	0.122
Candidiasis	16	11	5	0.612
Scabies	12	7	5	0.699
Verruca vulgaris	7	7	0	**0.034**
Herpetic infections	16	8	8	0.217
Extensive dermatophytosis	6	4	2	0.858
Molluscum contagiosum	5	5	0	0.094

Generalized hyperpigmentation	4	3	1	0.378
Cutaneous cryptococcosis	3	3	0	0.248
Pitysporum infections	3	2	1	0.449
Melasma	3	3	0	0.248
Urticaria	2	2	0	0.397
Acne vulgaris	3	1	2	0.256
Contact dermatitis	2	2	0	**0.055**
Pitted keratolysis	2	2	0	0.397
Plantar keratoderma	1	1	0	0.632
Freckles	1	0	1	0.632
Photodermatitis	1	0	1	0.632
Schamberg's disease	1	1	0	0.632
Port wine stain	1	1	0	0.632
Campbell de morgan spots	1	1	0	0.632
Acanthosis nigricans	1	0	1	0.632
Eczema	1	1	0	0.632
Keratolysis exfoliativa	1	1	0	0.632
Injection abscess	1	1	0	0.632
IGH	1	0	1	0.632
Syphilis	1	1	0	0.632

In the present study it was observed that patients with CD4+Tcell counts < 200 cells/mm^3 had more infectious conditions like genital warts, furunculosis and

non-infectious conditions like xerosis than those with CD4+Tcell counts >200 cells/mm^3 which is statistically significant.

DISCUSSION

HIV infection/AIDS results in various mucocutaneous manifestations which may be due to HIV infection itself, due to decreasing immunity or due to various opportunistic infections. Mucocutaneous disorders are not only associated with the terminal stages of immunodeficiency but occur throughout the course of HIV infection. [20]

The present cross sectional study was conducted on 100 patients who were known to be positive for HIV infection with or without AIDS, and have determined their CD4+T lymphocyte cell count, at Department of Dermatology, Venereology& Leprosy, KLES Dr. PrabhakarKore Hospital and Medical Research Centre, Belgaum during the study period of January 2010- December 2010.

AGE& SEX DISTRIBUTION

In the present study the age of the patients ranged between 15 years to 80 years. In both males and females most of the patients were in the range of 31-40 years (38 patients) followed by 21-30 years(26 patients),41-50years(23 patients).The youngest patient in the study was of 17years old and the highest age noted was 76years.The mean age in females was 31.93years and in males is 42.31year.Male to female ratio was 1.36:1.

In a study conducted by Boon-Kee Gog et al,the mean age of the patients was 40.2years.89.6% were male and 10.4% were female thus with male to female ratio of 8.6:1.[30]

Similar findings in age distribution were also found by Harish MR et al[31], CritonS et al[32], Ganesh Pai et[33] al where maximum numbers of patients were between

the age group of 25-35years. This age group is most susceptible may be because of it being sexually most active age group.

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.[34]

The present study in accordance with the previous studies has a similar pattern of age and sex distribution. The probable male to female ratio could be that most female patients belong to the low socio-economic strata, have low literacy levels and may not seek medical attention as early as males.

MARITAL DISTRIBUTION

In the present study the total number of married patients were 97(M=56,F=41).Among 57 male patients,56 were married and 1 was unmarried(17 years).Of the total 43 female patients,41 were married and 2 unmarried with mean age of 22 years.

OCCUPATION

In the present 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 & coolies i.e 9 (9%) each. Among females most of them were house wives (22 patients, 22%). 11 (11%) patients were into various types of business.

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 [35]. A study by Sharma SK et al reported similar results in which majority of the participants were unskilled laborers (29%) followed by businessmen (17.9%), drivers (10.4%), and others 18%.[36]

This is because the hospital renders free service and hence is attributed more by people belonging to middle and low income group. The higher prevalence among unskilled workers is due to the lack of education and awareness regarding the modes of transmission.

Among women, majority(22%) were housewives. This again emphasizes the main route and source of infection in females i,e through heterosexual contact with their spouse.

ROUTE OF TRANSMISSION

Of the total 100 patients majority i.e.59 % patients had acquired HIV infection by sexual transmission.41% of patients denied any of the other modes of transmission like blood transfusion, needle stick injury, injecting drug abuse.

Of the 59 total cases of sexual mode of transmission,majority showed heterosexual mode (91%).

8.47% of patients were noted to have acquired infection through homosexual route.

Findings according to NACO shows an average of 85.34% of sexual transmission[37] and in study conducted by Nair et al shows 78.50%[38].According to Boon-Kee et al the most common mode of HIV transmission was heterosexual(75%) followed by homosexual/bisexual contacts(22%).[30]

Still there exists a stigma about HIV infection especially in low socio-economic strata and thus most patients do not reveal the mode of acquiring the infection. The government is taking every possible effort regarding the safety of blood transfusion thus reducing the chances of acquiring infections like HIV, Hepatitis B and other blood-borne infections.

PREVALENCE OF CUTANEOUS MANIFESTIONS

In the present study, the cutaneous manifestations of HIV infection/AIDS were found in 79% of the patients. 21% patients with HIV infection/AIDS had no cutaneous manifestations.

Dermatological diseases are among the first recognized clinical manifestations of AIDS[39,40].They are seen at every stage of HIV infection and are often its presenting features[41].Approximately 90% of HIV infected patients develop cutaneous disease. These skin manifestations not only act as markers but also reflect the underlying immune status.[42]

In study conducted by Shobana et al [43] and kumaraswamy et al [44] the incidence of skin manifestations ranged between 40-50%.Thus the present study data is in accordance with the above studies.

PREVALANCE OF SYSTEMIC MANIFESTATIONS

In the present study, the systemic manifestations of HIV were found in 62% of the patients. 38% patients with HIV infection/AIDS had no systemic involvement.

In the present study majority of them i.e. 40 patients had respiratory system involvement mainly in the form of pulmonary tuberculosis (23 patients),Pneumocystitis carinii pneumonia (12 patients),Pneumonia (3 patients),Pleural effusion(1 patient),COPD(1 patient).

Other forms of TB like abdominal TB(8 patients),TB meningitis(7 patients),TB lymphadenitis(5 patients).

A study conducted in Chennai in 1999 reported tuberculosis as the most frequently associated systemic illness in 50% of the patients and oral candidiasis was observed in 29% of the patients.[45] Pathai S et al in a study have reported similar findings in which 53% of the patients had either current or a previous history of tuberculosis .[46]

The present study 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.

CD4+T CELL COUNTS AND AIDS STAGING

In the study out of the total number of 79 patients with skin manifestations, majority had CD4 +T cell counts falling below 200 cells/microL i.e,50(63%).These patients had maximum number of cutaneous manifestations. Only 10% of patients show CD4 +T cell count levels between 500 – 1000cells/microL.

In the present study 9 patients belonged to clinical stage I, 3 patients to stage II,65 patients to clinical stage III and 23 were in stage IV

MUCOCUTANEOUS MANIFESTATIONS IN PATIENTS OF HIV/AIDS

It is well known that more than 80% [42] of HIV-infected patients will develop at least one or other type of dermatologic disorder during the course of their HIV infection, with an increased risk for both rare and common infectious and inflammatory skin conditions.

In the present study the mucocutaneous manifestations were classified into infectious and non-infectious manifestations. Among the infections bacterial, viral, fungal, parasitic and various STDs were reported while in non-infectious xerosis, pruritic papular eruptions, seborrheic dermatitis, hair and nail changes etc were observed.

Correlation between the Cutaneous manifestations and CD4 +T cell counts was established using Chi-square test and Whitney-Mann test.

In the present study of the total 79 patients with cutaneous manifestations, 35patients (44.30%) had bacterial infections. Among the 35 bacterial infections,furunculosis was the most common one reported in about 32 patients. Pitted keratolysis was reported in 2 patients. These are comparable with the incidence in various studies which varied from 1% [54] to 25%[33]

The present scenario may be due to various factors like personal hygiene, environmental conditions, economic status, nutritional status, sanitation etc. playing an important role in its occurrence.

Of the total 79 patients with cutaneous manifestations fungal infection were seen in 42 patients(53.16%).Among the fungal infections candidiasis was the most common one reported in 22 patients followed by onychomycosis(proximal subungual type) and extensive dermatophytosis in 15 and 6 patients respectively. Cutaneous cryptococcosis in 3 patients and Tineaversicolor was observed in 2 patients.

Among various types of candidiasis recorded the most common type was oral thrush(pseudomembranous type).

Oral candidiasis precedes most other opportunistic infections[55.] The most common pattern of oral thrush in HIV/AIDS patients is the pseudo membranous type.[55]

The incidence of oral candidiasis in the present study was 27.84% which is in correlation with the incidences reported in various studies from 9%, 12% respectively in studies by Rajagopalan G et al[54] and Pradeep N[56.] While 40.6% and 45% cases respectively have been reported in studies by Ganesh pai[33] and Kumarasamy et al[44]. The large variation in the incidence may be due to various factors like malnutrition, poverty, oral hygiene, trauma due to sharp tooth, tobacco chewing which vary in different groups included in various studies.

Dermatophyte infections in various studies ranges from 5.2%[51] to 37.5%[57] which is in agreement with present study(7.59%).

In the present study, among the 20 viral infections, verruca vulgaris,herpes zoster were the commonest ones seen in 7 patients each.

Next in frequency is molluscum contagiosum,herpes labialis infections in 5 patients and one patient respectively.

Herpes zoster is a clinical indicator of faltering immunity and its atypical occurrence should always raise the issue of HIV serotesting. In present study Herpes zoster was seen in 7 patients (8.86%). Incidence of Herpes zoster varied from 3% and 4% patients respectively in studies of Muhlemann et al[58] and Khopkar et al[50] to 9.8% and 13.1% respectively in studies of Chacko S[59] et al and Ghate et al[60].

Molluscum contagiosum was seen in 5 patients(6.32%) which is similar to the study conducted by Goodman et al in which a prevalence of 9% was noted[61]

Verruca vulgaris were seen in 8.86% patients. Reports of verruca in various studies ranged from 7% to 40%[61,62]

In the present study 15.18% of patients had scabies infection. Two patient had subungual hyperkeratosis secondary to scabies. This percentage is slightly more compared to that observed in a study conducted by Shobana A et al which revealed 5%.[43]

STI in Patients of HIV/AIDS

STI is a cofactor for HIV infection. There is increased risk of HIV infection associated with ulcerative STIs (like genital herpes, Syphilis, Chlamydia, etc).[47]

The exigencies of containment of HIV infection have focused considerable attention on the control of genital ulcer disease (GUD),following an insight that sexually transmitted diseases (STDs), apart from being a marker of sexual activity, may enhance HIV transmission[63]

If STI causes ulceration in the genital or perineal region of the uninfected, partner, it becomes far easier for HIV to pass in his or her tissues. STI also causes inflammation. T cells monocytes / macrophages get concentrated in the genital area.

In person already infected with HIV, some of these key cells of the immune system will be carrying the virus, which magnifies the risk of transmission to uninfected partner.[47]

In present study patients presented with various genital complaints (20.25%),majority of them had vulvo-vaginal candidiasis followed by herpes genitalis and genital warts. One patient was diagnosed of syphilis. The prevalence in HIV/AIDS patients in different studies from India varied from 1% [64] to 47.5% [65]

In advanced HIV disease, the lesions of herpes genitalis are atypical, large, painful and deep with raised margin which was seen in two patients in present study.

Syphilis in present study was seen in 1 patient.Its prevalence varied from 3% [64] to 44% [65] in different studies from India.

Prevalence Of STI In Various Studies

Diagnosis / Study	N	HG %	GW %	NGU %	VC %	Ch %	Sy %	GU %	MC %	Tr %	CBP %	LGV %	GI %
Gupta S et al.[65]	40	47.5	32.5	-	-	2.5	15	2.5	7.5	-	5	-	-
Kar PK et al.[66]	11	-	-	9.1	-	63.3	9.1	-	-	-	-	18.2	-
Khopkar U et al.[50]	86	10.5	7.5	-	-	34.5	07	8.5	3	-	3	-	2
Nair S. P. et al.[38]	37	07.4	6.6	0.83	-	-	40.5	2.5	-	.83	-	-	-
Seema G. et al.[67]	09	-	11.1	-	11.1	-	44.4	11.1	11.1	-	-	-	-
Vibhu M. et al.[68]	09	11.1	22.2	-	-	-	-	-	-	-	-	22.2	-
Present Study	10	5.06	3.79	-	8.86	-	1.26	-	1.26	-	-	-	-

The decreased prevalence of STDs in HIV could be because of growing awareness of HIV prevention steps like increased practice of condom usage, and attending high-quality STI clinics.

NON-INFECTIOUS CUTANEOUS MANIFESTATIONS

Among the non-infectious manifestations, xerosis was observed in 51 patients(64.5%),seborrheic dermatitis in 29 patients(36.7%),pruritic papular eruptions in 19 patients(24.05%).Cutaneous manifestations secondary to ART were observed in 20 patients,10 patients each of adverse drug rash and lipodystrophy.

NAIL CHANGES

Among 100 patients studied, nail changes were noted in 32 patients of which onychomycosis was seen in 15 patients followed by beau's lines in 5,longitudinal melanonychia in 4 patients. Nail involvement in crusted scabies was seen in one patient. Brittle nails, discoloration of nails were the other changes noted.

Chronic, severe hypocalcaemia as seen in severe malnutrition probably can contribute to abnormal nails.[48]

In HIV disease, an immune dysregulated state occurs which is supported by elevation of cytokines such as IL-1,IL-6 and TNF –α,increased levels of which induce a febrile response acting through the hypothalamus, and also increase the neuropeptide α-MSH.IL-1 also upregulates α-MSH receptor expression by melanocytes as well as melanin production in the presence of MSH. α-MSH is a potent stimulant for melanocytic activation and pigmentation.[49]

Pigmentation, half and half nail, clubbing, onychomycosis, paronychia, yellow nail syndrome are seen in patients of HIV/AIDS. [47]

Thus the nail changes noted here are in accordance with various studies.[30,41]

HAIR ALTERATIONS

Lusterless hair, thin hair, various types of alopecia, discoloration of hair, graying of hair, long eye lashes are found in HIV/AIDS patients.[47]

Among 100 patients studied, hair changes were noted in 34 patients of which trichomegaly was maximum(13),followed by telogen effluvium which constituted 11.

Trichomegaly was seen in many patients. Though previous reports have suggested longer eyelashes to be a marker for late-stage HIV disease[52]. The present study did not show any such correlation with the disease stage.

Straightening of hair occurs in upto 36% of patients.[43] Alopecia totalis was seen in one patient. Diffuse alopecia in various studies ranges from 3.9% to 10%[43,50,51]

The increased prevalence of hair alterations in the present study can be attributed to more number of patients in progressed stage of the HIV infection.

PAPULO SQUAMOUS:

In an established HIV infection pruritus, xerosis and ichthyosis are common and can be variably symptomatic.[53]. Xerosis could be a secondary change attributable to the nutritional status of the patients. [32] Itching is an important symptom of AIDS, which may be associated with numerous causes including xerosis, scabies, staphylococcal folliculitis, drug reactions etc. Mechanism is uncertain but cutaneous peptidergic neuronal loss and histological follicular damage with associated eosinophilic infiltrate could be responsible.[53]

In present study generalized xerosis was seen in 64.5%, seborrheic dermatitis in 36.7%.

Various studies showed xerosis ranging from 0.2 to 50%[43,57,69]

Diffuse xeroderma or acquired icthyosis are known to be closely correlated with more advanced phases of AIDS.[70]

In the present study it has also been observed that xerosis, seborrheic dermatitis, etc did not show any direct and specific relationship with CD4+ T cell

counts. Various studies also reported wide variations of CD4+ T cell counts that is 44[71]/179[72] in xerosis, 204[56]/189[72] in seborrheic dermatitis.

May be it is more of subjective symptoms and related with nutritional status and personal hygiene, medications etc.

PRURITIC PAPULAR ERUPTIONS

In the present study pruritic papular eruptions were found in 19 patients(24.05%) of which 11 patients had CD4+Tcell counts<200 cells/mm^3 which is comparable to the study conducted by Boon-KeeGoh where 32.29% of patients showed pruritic papular eruptions, of which 24 patients had CD4 counts < 200 cells/mm^3,while 7 patients had CD4 counts >200 cells/mm[30]

DRUG RASH

In our study of the 79 patients with cutaneous manifestations,10 patients(12.6%) showed various kinds of drug reactions like maculopapularexanthem, steven-johnson syndrome. Of the 10 patients 5 were on ART while 4 patients were on ATT and 1 patient gave history of taking trimethoprim and sulfamethaxazole (TMX-SMX) tablets.

Among ART maculopapular eruption is commonly associated with NNRTIs and efavirenz, amprenavir. Mostpatients in present study developed rashes secondary to nevirapine. Drug rash has direct relation with CD4+Tcell counts,ie patients were lowered CD4 +T Cell counts(<200 cells/mm^3) developed more drug rashes(7 patients) compared to those with CD4 +T Cell counts> 200 cells/mm.[3]

Similar observation was made in a study conducted byBoon-Kee Goh where out of the 17 patients who showed drug rash majority(15 patients) had CD4+T cell counts < 200 cells /mm^3.[30]

In study conducted by Nair et al drug rash was observed in 15% of patients which is in accordance with the present study.[38]

In present study apthous ulcers were seen in 6.32% of patients. One patient had major apthae involing lips, tongue mucosae while 5 patients had minor apthae.

Pigmentary disorders were noted in 13 patients(16.45%), like generalized hyperpigmentation(4 patients),longitudinal melanonychia(4 patients),melasma(3 patients),freckles(1 patient),idiopathic guttate hypomelanosis(1 patient)were reported.

Diffuse hyperpigmentation reported in various studies ranges from 3.6% to 35.9%.[30,43]

The importance of hyperpigmentation other than being one of the cutaneous markers of HIV and cosmetic significance is that it may be an indication to investigate for other opportunistic infections and endocrine causes.

Other cutaneous manifestations observed in the study are contact dermatitis secondary to nickel, parthenium, potassium-dichromate etc.in 4 patients(5.06%) of which 3 patients had CD4 +T cell counts<200 cells/$mm^{3.}$

Other manifestations noted were acne vulgaris in 3.79%,urticaria in 2.53%.One case each of plantar keratoderma,photodermatitis, schamberg's disease, port wine stain,campell de Morgan spots, acanthosis nigricans, eczema, keratolysis exfoliativa were reported.

Correlations of Cutaneous Manifestations

With CD4+ T Cell Count in Patients Of HIV/AIDS

In this study, we surveyed the spectrum of skin disorders at different stages of HIV disease according to CD4+T cellcounts. The CD4+T cell count categories used in the analysis were based on the categories defined by AIDS Surveillance Case Definition for Adolescents and Adults, 1993.

Of the 100 patients studied,79 had cutaneous manifestations(79%).The correlation between the various CD4+T cell counts and the cutaneous manifestations was established by Chi-Square test.50 patients had CD4+T cell counts below 200 cells/mm^3 while 29 patients had values above 200 cells/mm^3.Statistical analysis between these two variables were analyzed using Whitney-Mann test.It was also difficult to analyze our data on the basis of antiretroviral therapy, as many of our patients who were initially on treatment had stopped their therapy because of financial difficulties, on-compliance or adverse reactions.

The spectrum of skin disorders in present study showed preponderance of inflammatory dermatoses like xerosis, seborrheic dermatitis, pruritic papular eruption and certain infections like pyodermas, dermatophytosis, verruca vulgaris.

The relation between the CD4+T cell counts and skin disorders is tabulated as follows:

<200 cells/microL	Furunculosis, candidiasis, herpes genitalis, infections, verruca vulgaris, genital warts, syphilis, molluscum contagiosum, scabies, xerosis, hair and nail changes, seborrheic dermatitis, pruritic papular eruptions, drugrash, opportunistic infections
500 – 200 cells/microL	Herpes labialis,bacterialfolliculitis, scabies Pityrosporum infections, xerosis seborrheic dermatitis, photodermatitis generalized hyperpigmentation, contact dermatitis, acne, acanthosis nigricans
>500 cells/microL	Intertrigo, folliculitis, pigmentary disorders, nail and hair changes
1000 – 500 cells/microL	NIL

The above findings are comparable to the study conducted by Waugh M where the following findings are noted[73]

<200 cells/microL	Herpes simplex, acquired icthyosis,papular eruptions,oral candidiasis, oral hairy leukoplakia, Norwegianscabies, opportunistic infections
500 – 200 cells/microL	Bacterial folliculitis,pityriasis versicolor, warts, molluscum contagiosum, herpes zoster
>500 cells/microL	Tineacorporis,seborrheicdermatitis,bullousimpetigo
1000 – 500 cells/microL	Seroconversion and HIV exanthema

Thus comparing the two tables the above study is in accordance with that conducted by Waugh M.[73]

Cutaneous infections are less frequently seen compared to the non-infectious manifestations and skin tumors (such as Kaposi sarcoma) are absent.

It is well recognized that Kaposi sarcoma develops almost exclusively in HIV-positive homosexual men, and that homosexual contact is a risk factor for HHV-8 .Relative to Western studies, the proportion of homosexual individuals in our study is significantly lower. This difference together with the low prevalence of HHV-8 in Asians, may explain the apparent absence of Kaposi sarcoma in the present study.

Of the 100 patients studied 79 had cutaneous manifestations at the time of examination and nearly 62 patients (78.48%) had two or more skin diseases. Furthermore the number of skin disorders increased with the degree of immune suppression.

In the present study comparisons of the skin disorders with CD4+T cell counts less than 200 cells/microL with that of those above 200 cells/microL was done.Statistically significant values were obtained for infections like verruca vulgaris, genital warts and non-infectious conditions like contact dermatitis. Similar findings were observed in a study conducted by Boon-KeeGoh were statistically significant values were obtained for few manifestations like pruritic papular eruptions, psoriasis, adverse drug reactions.[30]

CONCLUSION

Mucocutaneous manifestations are one of the most important clinical markers and may be the first clue to HIV infection.

Of the 100 patients studied,79 had cutaneous manifestations. The correlation between the various CD4+T cell counts and the cutaneous manifestations was established by Chi-Square test and Whitney Mann test.50 patients had CD4+T cell counts below 200 cells/mm^3 while 29 patients had values above 200 cells/mm^3.

Majority of the patients in the present study showed more of non-infectious conditions like xerosis, seborrheic dermatitis, pruritic papular eruptions, adverse drug reaction. Infections conditions like furunculosis, candidiasis, viral warts were also observed.

These manifestations were compared in two groups with CD4 + T cell counts less than 200cells/microL and those with counts above 200 cells/MicroL using Whitney-Mann Test. Although both groups exhibited almost same cutaneous manifestations, statistically significant values were obtained for genital warts, and contact dermatitis.

Thus all dermatologists should have adequate and updated knowledge of the various mucocutaneous manifestations. This would help not only in diagnosis of HIV/AIDS but also in further management of the patients.

SUMMARY

The present study was undertaken to know the spectrum of cutaneous manifestations in HIV/AIDS. A total of 100 HIV/AIDS patients with cutaneous manifestations were studied.

The observations and results were tabulated and graphically represented; their significance was discussed after reviewing the available literature.

- In the present study the age of the patients ranged between 15 years to 80 years. Among males and females most of the patients were in the range of 31-40 years (38 patients,38%) followed by 41-50years(23 patients,23%).Youngest patient in the study was of 17years and highest age noted was 76years.
- Male to female ratio for the HIV reactive patients in the study was 1.32:1
- In the present study the total number of married patients were 97(M=56,F=41).Among 57 male patients,56 were married and 1 was unmarried(17 years).Of the total 43 female patients,41 were married and 2 unmarried with mean age of 22 years.
- 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 (22 patients, 22%). 11 (11%) patients were into business.
- Of the total 100 patients majority i.e.59 (59 %) patients had acquired HIV infection by sexual transmission.41(41%) of patients denied any of the other modes of transmission like blood transfusion, needle stick injury, injecting drug abuse.

- Of the 59 total cases of sexual mode of transmission, majority showed heterosexual mode (91%).8.47% of patients were noted to have acquired infection through homosexual route.
- In the present study,61 patients(61%) did not receive HAART treatment while 39 patients are on treatment.
- In the present study, the cutaneous manifestations of HIV infection/AIDS were found in 79 (79%) of the patients. 21 (21%) patients with HIV infection/AIDS had no cutaneous manifestations.
- In the present study, the systemic manifestations of HIV were found in 62 (62%) of the patients. 38 (38%) patients with HIV infection/AIDS had no systemic involvement.
- In the study out of the total number of 79 patients with skin manifestations, majority had CD4 counts falling below 200 cells/microL i.e,50(63.29%).These patients had maximum number of cutaneous manifestaions. Only 10% of patients show CD4 count levels between 500 – 1000cells/microL.
- In the present study majority of the patients had pulmonary tuberculosis (23 patients) and its related complications like abdominal TB(8 patients),TB meningitis(7 patients),TB lymphadenitis(5 patients). CNS involvement in the form of Cryptococcalmeningitis, Toxoplasmosis were seen in 3 and 1 patient respectively .
- Out of 79 patients with cutaneous manifestations,bacterial infections commonly seen was furunculosis reported in about 32 patients. Pitted keratolysis was reported in 2 patients.

- Total number of patients with fungal infection were 35.Among the fungal infections candidiasis was the most common one reported in 22 patients followed by onychomycosis and extensive dermatophyosis in 15 and 6 patients respectively
- Among the viral infections, verrucavulgaris, herpes zoster were the commonest ones seen in 7 patients each. Next in frequency is molluscumcontagiosum in 5 patients and herpes labialis in one.
- The only parasitic infection noted in this study is scabies (12 patients) and two patients of Norwegian variety
- Among the various genital complaints, majority of them had vulvo-vaginal candidiasis,herpes genitalis followed by genital warts. One patient was diagnosed of syphilis
- In the present study, among the non-infectious manifestations, xerosis was observed in 51 patients(51%), seborrheic dermatitis in 29 patients(29%),pruritic papular eruptions in 19 patients(19%). Cutaneous manifestations secondary to ART were observed in 20 patients,10 patients each of adverse drug rash and lipodystrophy.
- Among 79 patients studied,nail changes were noted in 32 patients of which onychomycosis was seen in 15 followed by beau's lines in 5,longitudinal melanonychia in 4 patients,discoloration of nails in 5 patients,dystrophic nails in 2 and brittle nails in 1.
- Hair changes were noted in 34 patients of which trichomegaly was seen in maximum number of patients 13,followed by telogen effluvium which constituted 11.Diffuse alopecia was seen in one patient.

- In the present study, the cutaneous manifestations in HIV seropositive patients in relation to CD4 counts proved that a low CD4 count was associated with increased incidence of xerosis, seborrheicdermatitis, pruriticpapular eruption, adverse drug eruptions when compared with high CD4 lymphocyte counts. Patients with CD4 counts less than 200cells/microlitre were found to have more incidence of infectious conditions like genital herpes, viralwarts, furunculosis, Norwegian scabies.
- In the present study it was observed that patients with CD4 counts < 200 cells/mm3 had more infectious conditions than those patients with CD4 counts >200 cells/mm3 which is statistically significant.

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ANNEXURE – I: SCREENING FORM

SI NO:

IP/PO NO : ☐

Date of examination **:** ☐☐ ☐☐ ☐☐☐☐

Name: ☐ ☐ ☐

(First name) (Middle name) (Last name)

Age: ☐ Years

Sex: ☐ 1-Male; 2-Female

Address with phone no:_____

_____

Occupation: ☐

Income: _____

Religion: ☐ 1.Hindu 2.Muslim 3.christian 4.sikh 5.others

HIV status: 1.Positive 2.Negative

AIDS: Clinical stage: 1.stage 1 ☐

2.stage 2

3.stage 3

4.stage 4

Is the patient eligible for the study? 1.Yes 2.No ☐

Has informed consent been taken? 1.Yes 2.No ☐

Final Result Information ☐

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

Investigator's Name: _____

Investigators's signature

ANNEXURE - II : INFORMED CONSENT FORM

I.DO.NO. ☐☐☐

CUTANEOUS MANIFESTATIONS WITH CD4 COUNTS IN HIV SEROPOSITIVE/AIDS PATIENTS - A CROSS SECTIONAL STUDY

The study is conducted by Dr. D.Lavanya Post graduate student in M.D Dermatology under guidance of Dr. B.S.Manjunathswamy,Professor and Head of Department of Dermatology, J N Medical College, Belgaum.

Respected Sir/Madam, we invite you to participate in our study as, you are eligible for the same. During the study you will be asked some questions in detail regarding your present complaints.

The purpose of this study is to know the various skin manifestations of HIV in association with CD4 lymphocyte counts. You are being asked to participate in this research because you have been diagnosed to be HIV positive. All patients attending the hospital, who are diagnosed to have this disease, will be requested to participate in this study during the period of one year.

Should you choose to participate, you will be asked to give a detailed history of your disease, undergo a physical examination, and consent to a few routine blood and urine investigations. . In addition to this, you will agree to undertake CD4 Lymphocyte counts examination and if required other relevant investigations.

You may undergo some amount of discomfort during the process of investigations, which may include slight pain and bleeding. However all necessary steps and precautions will be taken to ensure your safety. The result of you taking part

in this research would help health care providers towards a better understanding of this disease, and thus we will be able to provide improved patient care

If you decide not to participate in this study, you will still be receiving the usual standard care for your disease.

Your privacy will be respected and all information collected about you during the course of this study will be kept confidential. Your identity will remain undisclosed.

The J N Medical College will provide, within the limitations of the laws of the State of Karnataka, facilities and medical attention to patients who suffer injuries as a result of participating in this project. In the event if you suffer any physical injury as the result of your participation in this study, you may contact Dr.Lavanya , Telephone No.9620845750 or Dr. B.S.Manjunathswamy, Telephone No.9449734433. In the event of an emergency, you should contact KLE'S Dr. Prabhakar Kore Hospital and MRC on Telephone No. 08312473777.

You shall not be receiving any payment or any financial incentives for participating in this study.

The results of this study may be published for scientific purpose or presented to a scientific group. Your identity, however, will be maintained confidential at all times.

Your participation in this study is voluntary. Your decision whether or not to participate will neither affect the care of your current disease, nor your future relations with the doctor or the hospital. You are free to discontinue participation in this study at any time and for any reason. In case you need further information regarding your

rights as a study participant, you may please contact Dr. V.D. Patil, principal and chairman of the ethical committee, J N Medical College, Belgaum on telephone No. 0831473777

STATEMENT OF CONSENT

I.D.NO: | | | |

I Mr/Ms/Mrs

_____

volunteer and consent to participate in this study. I have read the consent document or it has been read to me in my vernacular language. I accept to participate in this study. All the information regarding this study is provided to me and I have understood the same. I have been given the opportunity to ask questions and obtain appropriate answers.

Participants's name:

Signature or left thumb print of participant:

Witness name:

Signature of witness:

Signature of Investigator:

Date:

If the participants are Minors (under 18), the parents sign the form, rather than the participants.

ANNEXURE – III: PROFORMA

CUTANEOUS MANIFESTATIONS WITH CD4 COUNTS IN HIV SEROPOSITIVE/AIDS PATIENTS - A CROSS SECTIONAL STUDY

Case No. ☐☐ **OP/IP No.** ☐☐☐☐☐☐☐

Name: First name ☐☐☐☐☐☐ Middle name ☐☐☐☐☐☐☐

Last name ☐☐☐☐☐☐

Age: ☐☐

Sex:

1. Male ☐

2. Female

Occupation:

1. Business
2. Housewife
3. Professional
4. Driver
5. Any other ☐

Income: Monthly income (In Rs.):

a. Above poverty line b. Below poverty line**:** ☐

Address with phone number:

Presenting complaints and duration:

History of present illness:

1. a. Onset:

1. Sudden
2. Gradual ☐

b 1. Progressive 2.Stationary ☐

Site of lesion:

Face

1. Present
2. Absent

Oral cavity

1. Present
2. Absent

Neck

1. Present
2. Absent

Back

1. Present
2. Absent

Trunk

1. Present
2. Absent

Palms

1. Present
2. Absent

Soles

1.Present

2.Absent

External genetalia

1.Present

2.Absent

Initial Lesion: ☐

1. Dryness
2. Red lesion
3. Wheals
4. Fluid filled lesion
5. Pus filled lesion
6. Oozing lesion
7. Change in skin color
8. Swelling
9. Ulcer
10. Scaly lesion

Any associated factors:

1. Itching ☐
2. Pain
3. Burning
4. Discharge
5. Asymptomatic

Sexual History:

Extra marital Exposure: ☐

1. Present
2. Absent

If present.

No.of Partners ☐

H/o contact with ☐

1.sex workers

2.wife ☐

3.Unknown

No.of Times ☐

Nature of contact ☐

1.protected

2.unprotected

Type of contact:

1.Heterosexual ☐

2.Homosexual

3.Bisexual

H/O of blood Transfusion ☐

1.Present

2.Absent

H/O of IV Drug abuse ☐

1. Present

2. Absent

Systemic complaints: ☐

1.Present

2.Absent

Cough ☐

Fever. ☐

Loss of appetite ☐

Loose motions ☐

Generalised weakness ☐

Loss of weight

Past History:

History of similar illness: ☐

1. Present
2. Absent

History of Diabetes Mellitus: ☐

1. Present
2. Absent
3. If Yes,Duration _____months/years

History of Hypertension: ☐

1. Present
2. Absent
3. If yes,Duration_____months/years

History of anyother medical disorders:_____

Family History:

Marital Status**:** ☐

1. Married
2. Unmarried
3. Divorcee

☐

Married life in years:

Health status of spouse:1.Healthy 2.Diseaesd 3.Dead ☐

If dead specify the cause _____

Number of children ☐

☐

Health status of children 1.Healthy 2.Diseased 3.Dead

If dead specify the cause _____

Treatment History

HAART 1-On treatment ☐

2-Not on treatment

Personal History:

Diet ☐

1. Veg
2. Mixed

Appetite ☐

1. Normal
2. Poor

Bowel/ Bladder ☐

1. Normal
2. Altered

Sleep

1. Normal ☐
2. Altered

Alcohol

1. Present ☐
2. Absent

Smoking

1. Present ☐
2. Absent

General Physical Examination:

Built

1. Poor ☐
2. Moderate
3. Good

Vitals

Pulse / min ☐☐☐

BP(mm/hg):Systolic ☐☐☐

Diastolic ☐☐☐

Temperature ☐☐☐ ^{0}F

Weight ☐☐ Kg

Pallor

1. Present
2. Absent

Icterus

1. Present
2. Absent

Cyanosis

1. Present
2. Absent

Clubbing

1. Present
2. Absent

Lymph nodes

1. Palpable
2. Non palpable

Edema

1. Pitting
2. Non Pitting
3. Absent

Mucocutaneous Examination:

Type of lesion:

Macules

1. Present
2. Absent

Patches

1. Present
2. Absent

Papules ☐

1. Present
2. Absent

Plaque ☐

1.Present

2.Absent

Vesicles ☐

1.Present

2.Absent

Bullae ☐

1.Present

2.Absent

Pustule ☐

1.Present

2.Absent

Nodule ☐

1.Present

2.Absent

Erythema ☐

1.Present

2.Absent

Ulcer ☐

1.Present

2.Absent

Wart ☐

1.Present

2.Absent

Atrophy

1.Present

2.Absent

Swelling

1.Present

2.Absent

Distribution:

1. Symmetrical
2. Assymetrical

Colour of lesion:

1. Hyperpigmented
2. Hypopigmented
3. Erythematous
4. Mixed
5. Others

Size of lesion:

Discharge from lesion:

1.Present

2.Absent

Associated features:

Atrophy 1.Present 2.Absent

Scaling 1.Present 2.Absent

Telengectasia 1.Present 2.Absent

Mucosal Examination:

Genital lesion:

1. Present
2. Absent

Oral lesion:

1. Present
2. Absent

Hair lesion

1. Present
2. Absent

Nail lesion

1.Present

2.Absent

Systemic Examination:

Cardiovascular system: Heart sounds

1. Normal
2. Abnormal;if abnormal specify the finding_____

Respiratory system: Breath sounds

1. Normal
2. Abnormal;if abnormal specify the finding_____

Per abdomen:

1. Normal
2. Abnormal;if abnormal specify the finding_____

Central nervous system: Neurological examination

1. Normal
2. Abnormal;if abnormal specify the finding_____

Investigations

Diagnosis:-

Signature:

Guide's Signature

KEY TO MASTER CHART

ARF – Acute renal failure

AV – Acne vulgaris

Cut – cutaneous

Crypt - Cryptococcus

D – Denial

Ext - Extensive

F – Female

Fac - Factor

GE – Gastroenteritis

Gen - Generalized

HW – House wife

HSM – Hepatosplenomegaly

HK - Hyperkeratosis

LMN – Lower motor neuron

Lng - Longitudinal

M – Male

MAR - Married

NAD –No abnormality detected

NAL –Necrotic abdominal lymphadenopathy

PPE – Pruritic papular eruptions

PCP –Pneumocystiscarinii pneumonia

PK – Plantar keratoderma

OCM - Onychomycosis

S- Sexual

Seb Dermatitis – Seborrheic dermatitis

Sec – Secondary

SJS – Stevens-Johnson syndrome

T- Tinea

TCM –Trichomegaly

TB-Tuberculosis

TE- Telogen effluvium

UM - Unmarried

W - Worker

ANNEXURE – IV: MASTER CHART

S.NO	IP/OP.NO	AGE	SEX	MARITAL STATUS	OCCUP	MOT	HAART	SKIN DISORDERS	SYST ILLNESS	1500-1000	1000-500	500-200	<200
1	382738	25	F	MAR	HW	S	NO	Oral candidiasis, warts, pitted keratolysis	PulmonaryTB				67.48
2	352593	22	F	UM	HW	S	NO	Herpes genitalis, xerosis, seborrheic dermatitis	NAD				117.26
3	347678	24	F	MAR	HW	S	NO	PPE, seborrheic dermatitis, furunculosis	Anemia		720.05		
4	348544	30	F	MAR	HW	S	NO	Xerosis, furunculosis, TE	Acute GE		823.07		
5	366551	34	F	MAR	COOLI	D	NO	Freckles, acanthosis nigricans, xerosis, furunculosis	LMN Facial palsy			253.48	
6	1377049	30	F	MAR	FARMER	S	NO	Scabies with sec. bacterial infection, xerosis, discoloration of nails	NAD			315	
7	1229862	40	F	MAR	FARMER	D	YES	Herpes zoster opthalmicus, PPE, TCM	NAD			393	
8	1243853	21	F	UM	HW	S	NO	Scabies with sec. bacterial infection, xerosis	NAD			450	
9	345811	26	F	MAR	FARMER	D	NO	PPE, seborrheic dermatitis, folliculitis, TE	Pneumonia			477	
10	814795	25	F	MAR	HW	D	NO	Herpes genitalis, PPE, oral thrush, TE	NAD				152.53
11	1264981	36	F	MAR	BUSINESS	S	YES	Herpes genitalis, oral candidiasis, xerosis, OCM	NAD			303	
12	381764	55	F	MAR	HW	D	YES	Post herpetic neuralgia, IGH,	NAD		634.45		

								intertrigo, TCM					
13	391016	50	F	MAR	FARMER	D	NO	Generalized xerosis, oral thrush, generalized hyperpigmentation	NAD				63.18
14	1367114	36	F	MAR	HW	S	YES	Maculopapular rash sec AKT4,apthous ulcers	TB meningitis, Toxoplasmosis				144
15	3732905	52	F	MAR	FARMER	D	NO	Herpes zoster, xerosis, dystrophic nails	Dorsal myeloradiculopathy			253.48	
16	357864	45	F	MAR	HW	S	NO	Syphilis, oral thrush, seborrheic dermatitis, TCM, xerosis	PulmonaryTB				13.82
17	373501	34	F	MAR	FARMER	S	YES	Xerosis, PPE, Kerotolysis exfoliativa	PulmonaryTB				106.76
18	1267290	32	F	MAR	HW	D	NO	Seborhheic dermatitis, Injection abscess, brittle nails, discoloration of nails, TE	NAD				173.19
19	354114	40	F	MAR	HW	D	NO	Norwegian scabies, melasma, TE, beau's nails, folliculitis	Abdominal TB				109
20	348108	23	F	MAR	FAC WKR	S	NO	Cut. Cryptococcosis, seborrheic dermatitis	Crypt meningitis				82
21	345848	38	F	MAR	COOLI	S	NO	NAD	Fracture femur, Anaemia		NAD		
22	353400	32	F	MAR	HW	D	NO	Oral candidiasis, PPE, TE, dystrophic nails	Acute GE				170.01
23	383018	40	F	MAR	HW	S	YES	Oral candidiasis, PPE, TCM, seborrheic dermatitis, lipodystrophy	Acute GE			335	
24	383237	22	F	MAR	FARMER	S	YES	Oral candidiasis, malar melasma, TCM	PCP				30.83
25	433467	25	F	MAR	FARMER	S	YES	Ext dermatophytosis, Distal onychomycosis,	NAD		789.89		

								AV- 2,TE,xerosis					
26	377754	25	F	MAR	HW	S	NO	Chronic eczema, molluscum contagiosum, xerosis	Anaemia				196.31
27	1279604	30	F	MAR	BUSINESS	S	YES	Molluscum contagiosum, xerosis, TE, discoloration of nails	Acute GE				81.4
28	583691	40	F	MAR	FARMER	S	YES	PPE, TCM, Beau's lines, furunculosis	NAD		530.1		
29	1265901	35	F	MAR	HW	D	YES	Phototoxic drug rash sec ART, apthous ulcers, xerosis, TE	NAD				42
30	392492	38	F	MAR	BUSINESS	D	NO	Seborhheic dermatitis, common warts, PK	Anaemia				15.7
31	377219	32	F	MAR	HW	D	NO	Vaginal candidiasis, clubbing, PPE, xerosis, TE	PCP				33.1
32	1308199	30	F	MAR	HW	S	YES	Herpes zoster, TE, AV	NAD			480	
33	1113857	45	F	MAR	FARMER	S	YES	Maculopapular rash sec ART	NAD				107.98
34	377028	32	F	MAR	FARMER	D	YES	NAD	PulmonaryTB			NAD	
35	382127	22	F	MAR	COOLI	D	NO	NAD	PCP,acute GE			NAD	
36	382738	34	F	MAR	HW	S	YES	oral candidiasis, warts, pitted keratolysis, TE	PulmonaryTB				67.48
37	382820	34	F	MAR	HW	S	NO	NAD	PCP			NAD	
38	389573	30	F	MAR	BUSINESS	D	NO	NAD	TB Lymphadenitis			NAD	
39	391402	35	F	MAR	HW	S	YES	NAD	Pulmonary TB, anaemia			NAD	
40	398052	35	F	MAR	HW	D	NO	NAD	PulmonaryTB			NAD	
41	399271	24	F	MAR	BUSINESS	S	NO	NAD	Pleural effusion, abdominal TB			NAD	
42	399982	29	F	MAR	HW	S	NO	NAD	PCP,anaemia			NAD	
43	402771	48	F	MAR	HW	S	YES	NAD	PulmonaryTB			NAD	

44	1279604	36	M	MAR	BUSINESS	D	YES	Molluscum contagiosum	PulmonaryTB				20.97
45	366997	28	M	MAR	FARMER	S	YES	Ext dermatophytosis, melanonychia, TCM	PulmonaryTB				78.89
46	385540	43	M	MAR	DRIVER	S	YES	Seborrheic dermatitis, Ext. Tinea cruris, xerosis, furunculosis	NAD		593		
47	357697	40	M	MAR	BUSINESS	S	YES	Oral candidiasis, xerosis, drug rash sec nevirapine	NAD			290.16	
48	354764	42	M	MAR	BUSINESS	S	NO	Norwegian scabies, acute urticaria, subungual HK	NAD				47.35
49	386634	30	M	MAR	FARMER	S	NO	Molluscum contagiosum, dystrophic nails, xerosis, furunculosis	NAD				25.43
50	351861	45	M	MAR	FARMER	S	NO	Xerosis, PPE	TB Meningitis				112.81
51	350614	30	M	MAR	FARMER	S	NO	Gen. Hyperpigmentation, campell de morgan spots, xerosis, seb. dermatitis	PulmonaryTB				45.44
52	369722	40	M	MAR	BUSINESS	S	YES	Herpes genitalis, oral thrush, lng ridges nails (melanonychia),TCM	NAD		652		
53	3588912	32	M	MAR	FARMER	D	NO	Melasma, xerosis, PPE	NAD			279.8	
54	353525	57	M	MAR	FARMER	D	NO	Cryptococcosis, TCM, seb. dermatitis, furunculosis	Crypt meningitis				11.44
55	354701	55	M	MAR	BUSINESS	D	YES	Maculopapular rash sec. ATT, apthous ulcers, xerosis, furunculosis	Abdominal TB				34.96
56	349480	50	M	MAR	FARMER	D	NO	Scabies, hypertrichosis, beau's lines, xerosis, folliculitis	Acute GE			201.9	

57	375187	40	M	MAR	FARMER	S	YES	NAD	Pneumonia, anaemia			NAD	
58	1638050	63	M	MAR	MECHANIC	S	YES	Photodermatitis, seborrheic dermatitis, diffuse alopecia, PPE, furunculosis	NAD			310.56	
59	357538	35	M	MAR	BUSINESS	S	NO	Seborrheic dermatitis, oral thrush, xerosis, straight hair, furunculosis	PCP, ARF, septic shock			212.53	
60	3733968	65	M	MAR	FARMER	D	YES	Xerosis, TCM, furuncle	PCP, anaemia				69.12
61	358161	49	M	MAR	FARMER	S	YES	Herpes labialis, xerosis, seb. dermatitis, lipodystrophy	Acute GE				12.4
62	1024917	48	M	MAR	FARMER	S	NO	Xerosis, TCM, PPE, seb.dermatitis, folliculitis, lipodystrophy	Acute GE				105.92
63	355244	45	M	MAR	FARMER	S	NO	Pityrosporum folliculitis, Gen hyperpigmentation, xerosis, seb. dermatitis	Anaemia				36.23
64	1200831	34	M	MAR	CONDUCTOR	S	NO	Multiple genital warts, schamberg's disease, OCM, xerosis, PPE	NAD				155.04
65	357010	45	M	MAR	FARMER	S	NO	Disseminated Herpes zoster, apthous ulcers, furunculosis, xerosis	Abdominal TB				175.06
66	368697	25	M	MAR	COOLI	S	NO	NAD	PulmonaryTB, anaemia			NAD	
67	1349147	45	M	MAR	FARMER	D	NO	Genital warts, folliculitis, xerosis, seb. dermatitis	TB meningitis				26.83
68	367442	29	M	MAR	FARMER	S	YES	Common warts, melanonychia, seb.dermatitis, furunculosis	TB meningitis				132.47

69	353157	40	M	MAR	FARMER	D	NO	Recurrent furunculosis, genital warts, PPE, xerosis, straight hair	NAD				23.83
70	1226559	34	M	MAR	BUSINESS	S	YES	PPE, Gen. xerosis, seb.dermatitis, lipodystrophy, furunculosis	Pulmonary TB, anaemia			303	
71	1340082	50	M	MAR	FARMER	S	YES	Gen. Hyperpigmentation, oral thrush, seb.dermatitis, xerosis, lipodystrophy	TB meningitis			216.18	
72	1277327	35	M	MAR	FARMER	D	NO	Steven johnson's syndrome, xerosis, furunculosis, beau's lines	PulmonaryTB			477	
73	353350	35	M	MAR	BUSINESS	S	NO	Extensive dermatophytosis, OCM, Xerosis, seb. dermatitis, straight hair	Pulmonary TB				156.98
74	356005	48	M	MAR	BUSINESS	S	NO	NAD	TB Lymphadenitis			NAD	
75	374981	35	M	MAR	FARMER	S	NO	NAD	Pulmonary TB			NAD	
76	386459	27	M	MAR	FARMER	S	NO	Portwine stain, OCM, apthous ulcers, xerosis, seborrheic dermatitis	PulmonaryTB				101.7
77	1238009	28	M	MAR	FARMER	D	NO	Bockhardt's impetigo, PPE, xerosis	Anaemia				35.96
78	347161	40	M	MAR	BUSINESS	D	NO	NAD	TB Lymphadenitis, TB meningitis			NAD	

79	356831	17	M	UM	HOSTEL WORKER	D	YES	Scrotal dermatitis, recurrent folliculitis, seb.dermatitis, T.versicolor, xerosis	NAD				421	
80	1250366	46	M	MAR	MECHANIC	S	NO	Norwegian scabies, TCM, xerosis, folliculitis, straight hair	Pulmonary TB					152.53
81	347968	30	M	MAR	DRIVER	S	NO	Contact dermatitis sec nickel, OCM, xerosis, seb.dermatitis	TB Lymphadenitis, Anaemia				201.97	
82	350684	43	M	MAR	SERVICE	D	YES	SJS sec nevirapine, TCM, beau's lines, straight hair, furunculosis, lipodystrophy	Abdominal TB					32.41
83	346320	47	M	MAR	FARMER	S	YES	NAD	PCP,anaemia				NAD	
84	1220463	43	M	MAR	FARMER	S	NO	Maculopapular rash sec phenytoin, scabies, xerosis, seb.dermatitis, lipodystrophy	Abdominal TB					167
85	351861	45	M	MAR	FARMER	D	YES	Maculopapular rash sec nevirapine, PPE, furunculosis, lipodystrophy	TB meningitis					112.81
86	385855	60	M	MAR	FARMER	D	NO	Acquired icthyosis, seborrheic dermatitis, furunculosis	PCP					16.32
87	582597	44	M	MAR	FARMER	S	YES	Post herpetic neuralgia, Lipodystrophy, xerosis, straight hair	Acute GE			521		
88	388390	38	M	MAR	BUSINESS	S	YES	Seborrheic dermatitis, xerosis, cryptococcosis	Crypt meningitis, ANM					62.6
89	387797	37	M	MAR	DRIVER	S	NO	Molluscum contagiosum, chronic urticaria, xerosis, seb.dermatitis, straight hair	Pulmonary TB					29.51

90	347972	35	M	MAR	DRIVER	D	NO	Extensive dermatophytosis, OCM, xerosis, straight hair	TB Lymphadenitis					17
91	378145	54	M	MAR	BUSINESS	D	NO	Pityriasis versicolor, T.corporis, OCM, furunculosis	Pulmonary TB					44.78
92	396860	40	M	MAR	BUSINESS	D	YES	SJS sec nevirapine, melanonychia, xerosis, lipodystrophy	pulmonary TB				246.58	
93	374198	71	M	MAR	BUSINESS	D	NO	NAD	COPD, anaemia				NAD	
94	378590	42	M	MAR	DRIVER	S	YES	NAD	Pulmonary TB, anaemia				NAD	
95	387031	68	M	MAR	FARMER	D	NO	Herpes zoster, xerosis, furunculosis	Acute GE				271.84	
96	379303	33	M	MAR	BUSINESS	S	YES	Herpes zoster opthalmicus, xerosis	PCP					92.15
97	383985	68	M	MAR	FARMER	D	NO	NAD	Pneumonia, Abdominal TB				NAD	
98	R1057195	52	M	MAR	FARMER	D	NO	Herpes zoster opthalmicus, xerosis	PulmonaryTB					84.37
99	377227	76	M	MAR	FARMER	D	NO	NAD	PCP				NAD	
100	377461	55	M	MAR	FARMER	D	NO	NAD	PCP				NAD	