"STUDY OF HEMATOLOGICAL AND BIOCHEMICAL MANIFESTATIONS IN HIV/AIDS AND TO ASSESS THEIR CORRELATION TO SEVERITY OF DISEASE"

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In partial fulfilment of the requirements for the degree of

MD

in

General Medicine

Under the guidance of

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2014

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Dr. SALMAN PATEL

LIST OF ABBREVIATIONS USED

HIV	–	Human immunodeficiency virus
HTLV-III	–	Human-T-lymphotrophic virus type III
ARV	–	Acquired immunodeficiency syndrome
ANC	–	Antenatal clinic
NACO	–	National AIDS control organization
SIV	–	Simian immunodeficiency virus
MHC	–	Major histocompatibility complex
CCRS	–	Chemokine receptor 5
CTLS	–	Cytotoxic T lymphocytes
LCMV	–	Lymphocytic choriomeningitis
ADCC	–	Antibody dependent cellular cytotoxicity
PCR	–	Polymerase chain reaction
ELISA	–	Enzyme linked immunosorbent asay
ART	–	Anti retroviral therapy
WHO	–	World health organization
CI	–	Confidence interval
HAART	–	Highly active antiretroviral therapy
PEP	–	Post-exposure prophylaxis
WIHS	–	Women's interagency HIV study
RR	–	Relative risk
QOL	–	Quality of life
ANC	–	Absolute neutrophil count
MAC	–	Mycobacterium avium complex
HIVAN	–	HIV-associated nephropathy
SIADH	–	Syndrome of inappropriate secretion of antidiuretic Hormone
FSGS	–	Focal segmental glomerulo sclerosis
MPGN	–	Membrano-proliferative glomerulonephritis
DPGN	–	Diffuse proliferative glomerulonephritis
MCD	–	Minimal change disease
ESRD	–	End stage renal disease

ABSTRACT

Background :

HIV/AIDS is recognized emerging disease and rapidly established itself throughout the world. Hematological and bio-chemical abnormalities are common findings in patients with HIV infection. These includes Anemia, thrombocytopenia, leucopenia, pancytopenia, altered liver function tests (LFTs) and renal function tests (RFTs).

Objectives :

To study hematological and bio-chemical manifestations in HIV/AIDS and to asses their correlation to severity of disease.

Methodology :

The peripheral blood samples of 120 patients who were confirmed by ELISA method admitted to BLDEU's Shri B M Patil's medical college hospital and research centre, Bijapur. Age of patient is more than 18 years.

Results :

120 patients are studied for period of 18 months. 77% of patients are between age group of 26-45 year. Males (67.5%) are more commonly affected than females (32.5%). Fever is predominant symptom seen in 60% of cases, weight loss was another commonly associated symptom (53%). Physical findings included Anemia 54%, oral candidiasis 30%, generalized lymphadenopathy 25%, skin lesions 15%. Respiratory system is most commonly involved. Normocytic normochromic blood picture is seen in 49% of cases. Leucopenia seen in 30% cases, Thrombocytopenia in 21% of cases. Hemoglobin, neutrophils, lymphocytes are significantly reduced according to severity criteria ($p < 0.05$). Altered liver function tests are seen in 28% of cases. Altered renal

function tests are seen 15% of cases. Bio-chemical parameters are poorly correlate with severity of the disease ($p > 0.05$).

Conclusion :

Hematological and bio-chemical abnormalities are common in HIV patients. Hemoglobin, neutrophils, lymphocytes are significantly reduced according to severity criteria.

Keywords : *HIV infection, Anemia, CD4 severity criteria.*

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Introduction

INTRODUCTION

Haemotological abnormalities are a common findings in patients with HIV infection. The common peripheral blood findings includes Anemia, thrombocytopenia, leucopenia or pancytopenia. These abnormalities may be attributable to the direct toxic effect of the virus on progenitor cells, ineffective hematopoiesis, opportunistic infections, immune mechanisms and drug reactions.[1]

Anemia is a very common finding in patients with HIV infection, particularly in individuals with more advanced HIV disease. HIV infection alone without other complicating illness may produce anemia in some patients. HIV not only causes low CD4 counts but it also associates with granulocytopenia, thrombocytopenia, loss of specific cytotoxic lymphocytes and antibody specific response.[2]

Most patients will experience hepatobiliary manifestations at some point during the course of their HIV disease, with hepatomegaly and jaundice in 50% and abnormal liver functions in over 80%. HIV can involve the liver directly, as demonstrated by presence of HIV P24 within Kuffer cells and hepatic endothelial cells and HIV messenger RNA within hepatocytes. The degree of intensity of disease can be indicated by measuring the levels of enzymes such as alkaline phosphatase, alanine amino transferase and asparatate amino trasferase, lactate dehydrogenase and creatinine phosphokinase.[3]

Renal disorders are encounted at all stages of HIV infection, and range from fluid and electrolyte imbalances commonly seen in hospitalized HIV- infected patients to HIV associated nephropathy which can progresses rapidly to end-stage renal disease (ESRD).

Hence the "STUDY OF HEMATOLOGICAL AND BIOCHEMICAL MANIFESTATIONS IN HIV/AIDS AND TO ASSESS THEIR CORRELATION TO SEVERITY OF DISEASE" is undertaken to know the magnitude of the problem, of progression and severity of disease, and guide to therapy particularly in resource limited settings.

Objectives

OBJECTIVES

1. To study the Hematological parameters in HIV affected individuals and to asses their correlation with the severity of disease.
2. To study the Biochemical parameters in HIV affected individuals and to asses their correlation with the severity of disease. (Liver function tests and renal function tests).

Review of Literature

REVIEW OF LITERATURE

A. HISTORICAL REVIEW:

At the beginning of the eighties an innocuous seeming report appeared in the New England Journal of Medicine, Homosexuals in New York and San Fransisco were succumbing to a rare form of cancer called kaposi sarcoma, and what normally was an easily curable pneumonia caused by a germ called pneumocystitis carinii. All the fight had gone out of the victims bodies as they succumbed to diseases which are minor hassles in normal times. The disease was given the name AIDS.[5]

Only 2 years after AIDS was first described in USA, scientiests in France isolated the causative agent, which they called lymphadenopathy - associated virus (LAV). The virus was independently isolated by two groups of research workers in USA who called it human - T - lymphotrophic virus type III (HTLV-III) and AIDS related virus (ARV). The virus is now generally known as HIV.[6]

At the time the disease was restricted to male homosexuals, moralists got their chance to crow about sexual "deviation" that drew the wrath of the heavens, but to medical men this was a mere curiosity. It didn't take a long time for curiosity to become a night mare. Thousands started succumbing to the disease. The disease cropped up in Intra venous drug abusers. Another punishment for sinful living, one could say, but it soon struck hemophiliacs, who had to have regular blood transfusions. Newborn babies and female prostitutes were found to have AIDS. The virus was found in several body fluids, tears, saliva, breast milk etc.

While back tracking the route of the disease, it became evident that it was pigs in Haiti, had passed it on to humans (men) who had passed it on to foreign visitors. Then focus was shifted on to green monkey in Africa. A leading French researcher LUC MONTAGNIER of pasteur research institute. PARIS, the only animal model for AIDS is

the chimpanzee. So it is likely that AIDS existed in some African monkey species which is now extinct. According to another report AIDS was born when the virus which was ostensibly being designed for biological warfare escaped from a research lab in USA.

No one is sure about the history of AIDS, we can at best only guess where and when it came into existence. An intelligent estimates suggests that the disease appeared in Africa around the same time that it came to be recognized in America - the late 1970''s and early 1980's in African countries.

LATEST THEORY, however, is that AIDS virus, primarily an animal virus, was somehow transmitted to men in Africa and from then on, the disease spread across the region through inadequately sterilized needles. John scale and ZA Medvede explain in Journal of Royal Society of Medicine that this route of spread seems highly likely in Africa considering the fact that among the infected children, only half had infected mother. The child victims of AIDS, it was found, had twice as many infection as the non infected.

From historical perspective, the infection theory seems quite plausible. Three other viral diseases spread in Africa, borne by injection needles and created epidemics. These were lassa fever, marburg viruses and Ebola virus. Fortunately not being very infective the disease died off, Not AIDS. Injections are quite popular in Africa as probably in many third world countries and bulk of these injections are mainly vitamin injections.

As the researchers plunged into the medical problem, it became evident that the killer was a virus, that was transmitted through blood and blood products. On entering the body the virus attacked a particular type of white blood cell (CD4 (helper) lymphocytes). Gary Nabel and David Baltimore of the white Head Institute for Biomedical Research in Cambridge, Massachusettes explained why AIDS viruses preferentially kill CD4 lymphocytes as they have identified a protein produced only by

activated (stimulated) T lymphocytes that turn on the AIDS virus genome thereby enabling the virus to reproduce in and kill infected CD4 cells.

It has been shown for some time that AIDS virus can persist in latent form in CD4 cells for many years and work of these scientists now provides evidence that the normal immune stimulation of CD4 cells, as may be caused by trivial day to day viral or bacterial infection, may provide the trigger that releases the virus from latency in CD4 cells and leave the body defenseless with all its resistance gone, and succumbed to opportunistic infections.[5]

After reported the first case of AIDS from India, ten more cases surfaced within a year. The scenario is changing very fast HIV epidemic in India has evolved from pattern III (Introduction or extensive spread of HIV did not begin until the mid to late 1980s or the present, overall HIV prevalence continues to remain relatively low in most populations) to pattern II (Extensive spread of HIV began in the late 1970s or early 1980s. HIV transmission has been and continues to be predominantly sexual between men and women) as found in sub saharan Africa and latin America. to be more extensively disseminated than the benign endemic form reported in some parts of Africa. However 15 of the 16 cases of kaposi sarcoma reported in India so far were homosexuals while one was heterosexual. This shows that HIV infected hetero sexual population is not immune to kaposi sarcoma.[7]

EPIDEMIOLOGY

WORLD SCENARIO

According to WHO estimates there are 35.3 million people living with HIV at the end of 2012.The highest density being in the sub-Saharan African countries which constitutes around 70%.Since the start of this epidemic around 75 million have become affected with nearly 25 million deaths. New HIV infections have fallen by 33% since 2001.AIDS related deaths have fallen by 30% since its peak in 2005.The UNAIDS in its Global Report 2013 publication on AIDS epidemic has noted a historic decline in AIDS-related deaths and new HIV infections [8].

INDIAN SCENARIO

According to the data released by NACO Annual Report 2012-2013, the revised estimate of people with HIV as of 2011 is 2.089 million (equivalent to 0.27 percent of the adult population) which is a steady decline from 0.41% in 2001 .The estimates highlight an overall reduction in adult HIV incidence (new infections) as well as AIDS related mortality in India which is similar to the global trend [9].

REGIONAL SCENARIO

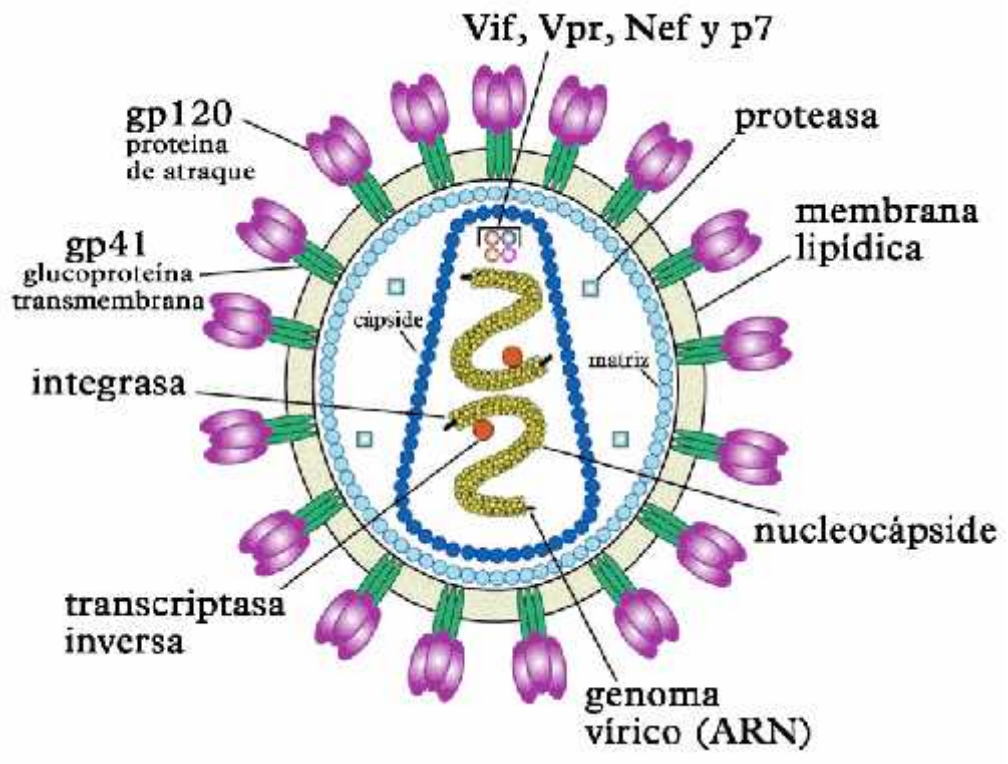
The four high prevalence States of South India (Andhra Pradesh, Karnataka, Maharashtra and Tamil Nadu) account for 53% of all HIV infected population in the country. Nonetheless they have been showing declining trend of HIV prevalence.

ICTC data shows a declining trend in the adult HIV prevalence rate in Karnataka. According to sentinel surveillance in ANC population the prevalence has dropped from 0.84 in 2007 to 0.22 in 2012 [10].

ETIOLOGIC AGENT:

The aetiologic agent of AIDS is HIV, which belongs to the family of human retro viruses and the subfamily of lenti viruses. Non oncogenic lente viruses cause diseases in other animal species, including sheep, horses, goats, cattle, cats and monkeys. The four recognized human retro viruses belong to two distinct group; The HTLV-I and HTLV-II, which are transforming viruses; and the HIV-1 and HIV-2 which are cytopathic viruses. The most common cause of HIV disease throughout the world, and certainly in the USA is HIV-1. HIV-2 was first identified in 1986 west African patients and was originally confined to West Africa. However, a number of cases have been identified in Europe, South America, Canada and USA. HIV-2 is more closely related phylogenetically to the simian immunodeficiency virus (SIV) found in Sooty Mangabeys than it is to HIV-1. HIV-1 is more closely related to an SIV isolated from chimpanzees in 1990.[11]

Electron microscopy shows that the HIV virion is an icosa hedral structure containing numerous external spikes formed by the two major envelope proteins, the external group 120 and the transmembrane group 41. The virion buds from the surface of the infected cell and incorporates a variety of host protein including major histocompatibility complex (MHC) class I and II antigens into its lipid bilayer.



[Fig 1: HIV virus structure]

LIFE CYCLE OF HIV:

HIV is an RNA virus whose hallmark is the reverse transcription of its genomic RNA to DNA by the enzyme reverse transcriptase. The life cycle of HIV begins with the high affinity binding of the group 120 protein via a portion of its VI region near the N-terminus to its receptor on the host cell surface, the CD4 molecule. The CD4 molecule is a 55-KD protein found predominantly on a subset of T lymphocytes that are responsible for helper or inducer function in the immune system. It is also expressed on the surface of monocytes or macrophages and dendritic or langerhans cells. It has recently been demonstrated that the core receptor that must be present together with the CD4 molecule for fusion and entry of T cell-tropic strains of HIV-1 is a molecule termed CXCR4, while the co-receptor for macrophage - tropic strains of HIV-1 is the-chemokine receptor CCR5. Both receptor belong to the family of seven transmembrane domain G protein coupled cellular receptors. Following binding, fusion with the host cell membrane occurs via the group 41 molecule, and the HIV genomic RNA is uncoated and internalized into the target cell. The reverse transcriptase enzyme which is contained in the infecting virion, then catalyzes the reverse transcription of the genomic RNA into double stranded DNA. The DNA translocates to the nucleus, where it is integrated randomly into the host cell chromosomes through the action of another virally encoded enzyme, integrase. This provirus may remain transcriptionally inactive (latent), or it may manifest various levels of gene expression upto active production of virus.

Cellular activation plays an important role in the life cycle of HIV and is critical to the pathogenesis of HIV disease, Following initial binding and internalization of virion into the target cell, incompletely reverse transcribed DNA intermediates are labile in quiescent cells and will not integrate efficiently into the host cell genome unless cellular activation occurs shortly after infection. Further more activation

of the host cell is required for the initiation of transcription of the integrated proviral DNA into either genomic RNA or mRNA. In this regard, activation of HIV expression from the latent state depends on the interaction of a number of cellular and viral factors. Following transcription, HIV mRNA is translated into protein that undergo modification through glycosylation myristylation, phosphorylation and cleavage. The viral core is formed by the assembly of HIV proteins, enzymes, and genomic RNA at the plasma membrane of the cells. Budding of the progeny virion occurs through the host cell membrane where the core acquires its external envelope. Each point in the life cycle of HIV is a real or potential target for therapeutic intervention. Thus far, the reverse transcriptase and protease enzymes have proven to be susceptible to pharmacologic disruption.[11]

1 Binding and Fusion: HIV begins its life cycle when it binds to a **CD4 receptor** and one of two **co-receptors** on the surface of a CD4+ **T-lymphocyte**. The virus then fuses with the host cell. After fusion, the virus releases RNA, its genetic material, into the host cell.

2 Reverse Transcription: An HIV enzyme called reverse transcriptase converts the single-stranded HIV RNA to double-stranded HIV DNA.

3 Integration: The newly formed HIV DNA enters the host cell's nucleus, where an HIV enzyme called integrase "hides" the HIV DNA within the host cell's own DNA. The integrated HIV DNA is called provirus. The provirus may remain inactive for several years, producing few or no new copies of HIV.

4 Transcription: When the host cell receives a signal to become active, the provirus uses a host enzyme called RNA polymerase to create copies of the HIV genomic material, as well as shorter strands of RNA called messenger RNA (mRNA). The mRNA is used as a blueprint to make long chains of HIV proteins.

5 Assembly: An HIV enzyme called protease cuts the long chains of HIV proteins into smaller individual proteins. As the smaller HIV proteins come together with copies of HIV's RNA genetic material, a new virus particle is assembled.

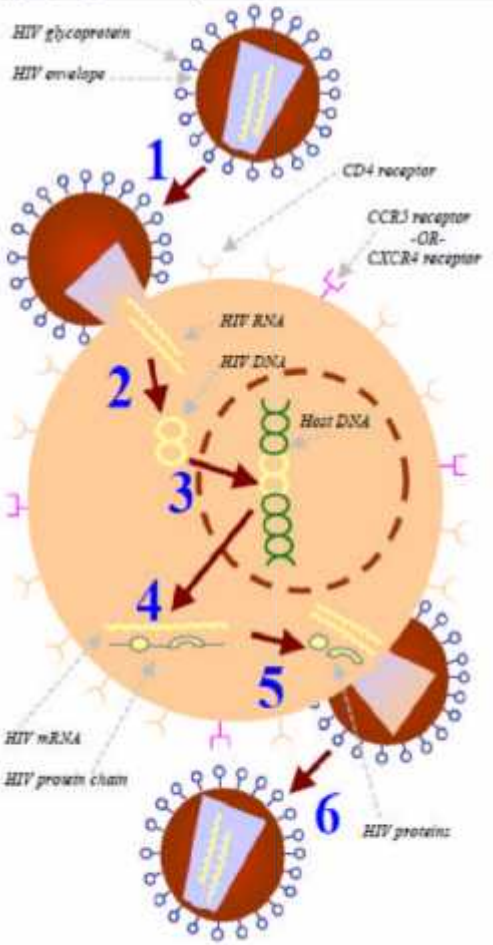
6 Budding: The newly assembled virus pushes out ("buds") from the host cell. During budding, the new virus steals part of the cell's outer envelope. This envelope, which acts as a covering, is studded with protein/sugar combinations called HIV glycoproteins. These HIV glycoproteins are necessary for the virus to bind CD4 and co-receptors. The new copies of HIV can now move on to infect other cells.

Terms Used in This Fact Sheet:

CD4 receptor: A protein present on the outside of infection-fighting white blood cells. CD4 receptors allow HIV to bind to and enter cells.

Co-receptor: In addition to binding a CD4 receptor, HIV must also bind either a CCR5 or CXCR4 co-receptor protein to get into a cell.

T-lymphocyte: A type of white blood cell that detects and fights foreign invaders of the body.



For more information:

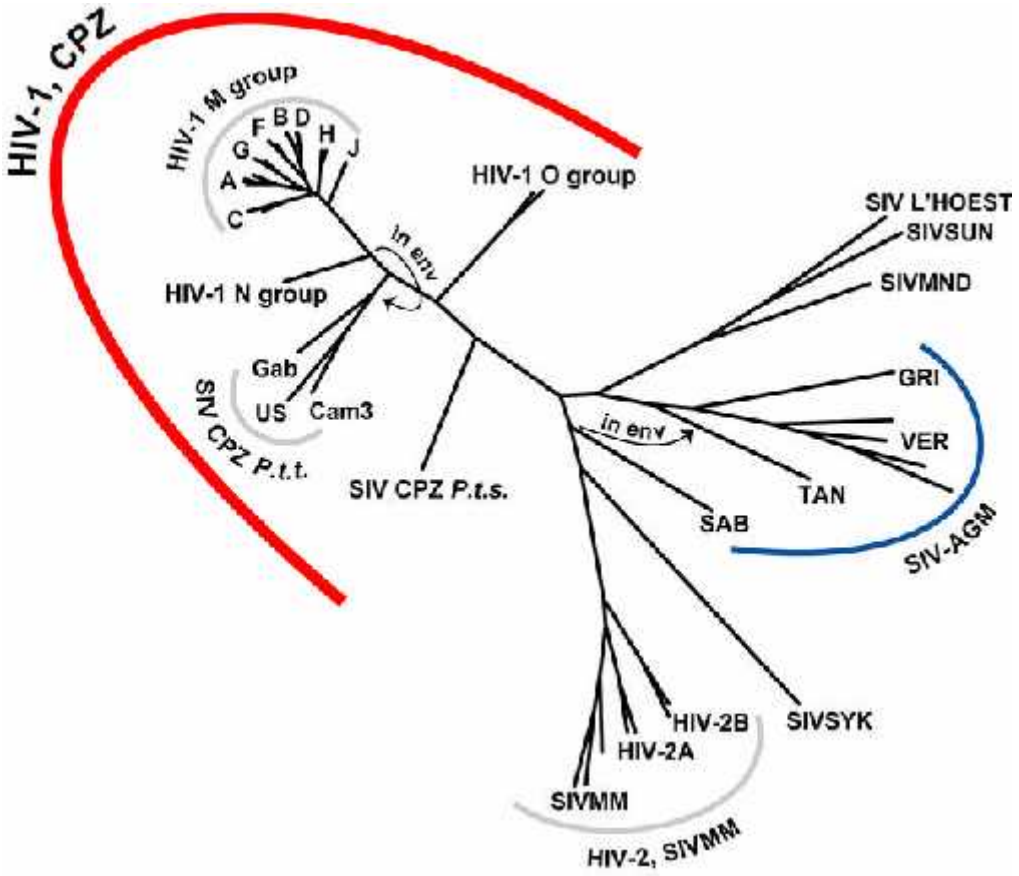
Contact your doctor or an *AIDSinfo* Health Information Specialist at 1-800-448-0440 or http://aidsinfo.nih.gov.

[Fig. 2 : The HIV life cycle]

MOLECULAR HETEROGENEITY OF HIV-1

Molecular analysis of various HIV isolates reveals sequence variation over many parts of the viral genome for eg. in different isolates, the degree of difference in the coding sequences of the viral envelope protein ranges from a few percent (very close) to 50%. These changes tend to cluster in hypervariable regions. One such regions, called V3 is a target for neutrailizing antibodies and contains recognition sites for 7' cell responses variability in this region is likely due to selective pressure from the host immune system. The extra ordinary variability of HIV-1 is in marked contrast to the relative genetic stability of HTLV-I and II.

There are two groups of HIV-1: group M (Major), which is responsible for most of the infections in the world, and group-0 (outlier), a relatively rare viral form found at this time is Cameroon, Gabon, and France. The M group comprise at least eight sequence subtypes, or clades, designated. A through H, which are distinguished by the fact that, at this time they differ from each other by 30% in their ENV coding sequences and by 14 percent in their gag coding sequences. Curiously the O-group viral sequences display subtype distances among each other of the same magnitude. As a result of the evolutionaiy process underlying these sequences differences, phylogenetic tree analyses produce star like configurations suggestive of radiation from single ancestral viruses, one for the M group and one for the O group.

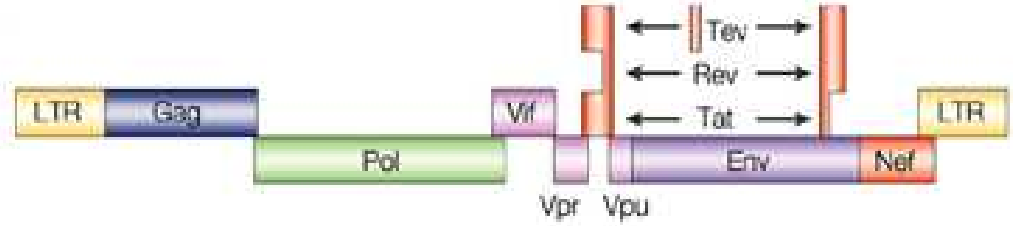


[Fig. 3 : Phylogenetic tree of HIV virus]

The global patterns of HIV-1 variation likely result from accidents of viral trafficking - subtype B viruses, which now differ by up to 17% in their ENV coding sequences, are uniformly seen in the united states it is thought that, purely by chance, this viral subtypes was seeded into the united states in the late 1970's. there by establishing an overwhelming founder effect. Subtypes A viruses (of the M group} appear to be the most common form worldwide; many countries have circulating viral subtypes that are giving mix to recombinant forms. The predominant subtypes in Europe and the Americans to subtype B. In Africa more than 75% of strains recovered to date have been of subtypes A, C, and D in Asia, HIV-1 isolates of subtypes E, C and B are found. Subtype E accounts for most infections in south East Asia, while subtypes C is prevalent in India. Sequence analysis of HIV-1 isolates from infected individuals indicate that recombination among viruses of different clades likely occurs as a result of infection of an individual with viruses of more than one clade particularly in geographic areas where clades over lap.

GENETIC DIVERSITY OF HIV & ITS IMPLICATIONS FOR INDIA:

As mentioned earlier HIV-1 can be classified into eight subtypes and HIV-2 has also been phylogenetically classified into subtypes though the number of sequenced isolate are limited, there have been very few investigation of HIV-1 strain in India available data indicates that subtype C is greater predominant in India. Subtypes A,B and E also co-exist. Genetic subtyping studies have revealed that majority of the C subtype were homologus to C3 genotype while remaining (34%) were closest to C2 genotype. Greater degree of divergence observed with in C2 genotpype as compared to C3 indicates earlier introduction of C2 in India. The C3 genotype may be a recent mutational variant of subtype C unique to India.



[Fig. 4 : HIV Genome]

As with diagnostic tests for HIV-1 most vaccine candidates are based on subtype B. It is known that vaccine efficacy is subtype specific. Hence evaluation of these candidate vaccine in areas where other subtypes predominate or where multiple subtypes are circulating like in India will pose considerable challenges.

TRANSMISSION:

Risk factors for HIV infection in Africa include multiple heterosexual sex partners, blood transmission; injections or treatment with unsterile needles, syringes or other skin piercing instruments; and mother to fetus or infant transmission before, during, or shortly after birth. Sexually transmitted diseases, in particular genital ulceration due to chancroid or herpes virus enhance the risk of sexual transmission of HIV. As noted previously, male homosexuality, intravenous drug use, and haemophilia appear to be much less important factors in HIV transmission in India and Africa than in the United States, Europe and Australia.

For adults, sexual contact appears to be by far the dominant mode of HIV transmission, followed by blood transfusion and exposure to needles, syringes, and skin piercing instruments, for children, the dominant mode of transmission is perinatal, with a secondary yet important role for blood transmission.

Sexual transmission appears to be bidirectional, from infected women to their male partners and from infected men to their partners. As with other STD's prostitute are at great risk of HIV exposure. Sexual contact with prostitutes has been documented as an

important risk factors for men in some areas genital ulcers appears to increase both the susceptibility to and the infectivity of HIV. A systemic factor that may influence infectivity during sexual contact is the clinical stage of HIV infection. Since the transmission rate to uninfected partners seems to be highest for patients with more advanced clinical disease and or lower levels of CD4 + cells.

HIV DOES NOT SPREAD BY:

- Drinking water from the same glass as an infected person.
- Swimming in pools used by people with HIV or AIDS.
- Bitten by a mosquito that has already bitten an infected person.
- Socializing or casually living with people with HIV/AIDS.
- Caring and looking after people with HIV/AIDS.
- Use of same toilets as AIDS patients or people infected with HIV.
- Shaking hands with people with AIDS/HIV.
- Hugging a person with HIV/AIDS.
- Bedbugs, flies, lice, fleas and other insects and pests DO NOT spread HIV as known till today.

PATHOGENESIS

A. Overview of course of HIV Infection

The course of untreated HIV infection spans a decade. Stages include the primary infection, dissemination of virus to lymphoid organs, clinical latency, elevated HIV expression, clinical disease, and death.

Following primary infection, there is a 4 to 11 days period between mucosal infection and initial viremia. Virus is widely disseminated throughout the body during this time, and the lymphoid organs become seeded. An acute mononucleosis like syndrome develops in many patients, 3-6 weeks after primary infection. There is a significant drop in numbers of circulating CD4T cells at this early time. An immune response to HIV occurs 1 week to 3 months after infection, plasma viremia drops, and levels of CD 4T cells rebound. However, the immune response is unable to clear the infection completely, and HIV infected cells persist in the lymph nodes.

This period of clinical latency may last for as long as 10 years, during this time, there is a high level of ongoing viral replication. It is estimated that 10 billion HIV particles are produced and destroyed each day. The half-life of the virus in plasma is about 30 to 60 minutes, and the virus life cycle averages 2 days.

Eventually, the patient will develop constitutional symptoms and clinically apparent disease, such as opportunistic infections or neoplasms. Higher levels of virus are readily detectable in the plasma during the advanced stages of infection. HIV found in patients with late-stage disease is usually much more virulent and cytopathic than the strains of virus found early in infection.

B. Lymphoid Organs

Lymphoid organs play a central role in HIV infection. It is in the lymphoid organs that specific immune responses are generated. The network of follicular dendritic cells in the germinal centers of lymph nodes traps antigens and stimulates an immune response. Throughout the course of untreated infection-even during the stage of clinical latency HIV is actively replicating in lymphoid tissues. The microenvironment of the lymph node is ideal for the establishment and spread of HIV infection.The trapped virions serve as source of immune activation causing cytokine release, and activating a large pool of CD4 T cells that are highly susceptible to HIV infection.

C. Neural Cells

Neurologic abnormalities are common in late stages of infection and are an AIDS defining condition. Central nervous system disease occurs in 40-90% of patients. These include HIV encephalopathy and peripheral neuropathies, both direct and indirect pathogenic mechanisms explain the neuropsychiatric manifestations.

The predominant cell types that are infected are monocytes and macrophages. Virus may enter the brain through infected monocytes and release cytokines that are toxic to neurons as well as chemotactic factors that lead to infiltration of the brain with inflammatory cells.

CLINICAL MANIFESTATIONS

The clinical features of HIV infection have been classified into the following categories:

1. Acute HIV Syndrome
2. Asymptomatic stage- Clinical Latency
3. Symptomatic Disease
4. AIDS

1. Acute HIV Syndrome

Around 50–70% of individuals with HIV infection experience an acute clinical syndrome 3–6 weeks after primary infection. The typical clinical findings in the acute HIV syndrome include fever, pharyngitis, lymphadenopathy, headache, arthralgia, anorexia, nausea, vomiting, and diarrhea. It has been reported that these symptoms occur less frequently in those infected by injection drug use compared with those infected by sexual contact. The syndrome is typical of an acute viral syndrome and has been likened to acute infectious mononucleosis. Symptoms usually persist for one to several weeks and gradually subside as an immune response to HIV develops and the levels of plasma viremia decrease. In most patients, primary infection with or without the acute syndrome is followed by a prolonged period of clinical latency or smoldering low disease activity. A small percentage of HIV-infected individuals treated with antiretroviral drugs during acute infection may revert to a negative EIA test during the time they remain on therapy. They rapidly re-seroconvert with the discontinuation of treatment.

2. Asymptomatic stage- Clinical Latency

There is a lot of variation between the initial infection and onset of clinical disease, the median time is considered to be around 10 years. HIV disease with active virus replication is ongoing and progressive during this asymptomatic period. The rate of disease progression is directly correlated with HIV RNA levels. Some patients referred to as long-term nonprogressors show little if any decline in CD4+ T cell counts over extended periods of time. These patients generally have extremely low levels of HIV RNA; a subset, referred to as elite nonprogressors, exhibits HIV RNA levels <50 copies per milliliter. Certain other patients remain entirely asymptomatic despite the fact that their CD4+ T cell counts show a steady progressive decline to extremely low levels. In these patients, the appearance of an opportunistic disease may be the first manifestation of HIV infection.

3. Symptomatic Disease

As mentioned above HIV is asymptomatic in its initial stages and symptoms start appearing with the decline in CD4+ count. The more severe and life-threatening complications of HIV infection occur in patients with CD4+ T cell counts <200/ L.

The virus affects the immune system of the body rendering it susceptible to opportunistic infections. While the causative agents of the secondary infections are characteristically opportunistic organisms such as P. jiroveci, atypical mycobacteria, CMV, and other organisms that do not ordinarily cause disease in the absence of a compromised immune system, they also include common bacterial and mycobacterial pathogens. Following the widespread use of cART and implementation of guidelines for the prevention of opportunistic infections, the incidence of these secondary infections has decreased dramatically.

Overall, the clinical spectrum of HIV disease is constantly changing as patients live longer and new and better approaches to treatment and prophylaxis are developed. In addition to the classic AIDS-defining illnesses, patients with HIV infection also have an increase in serious non-AIDS illnesses, including non-AIDS related cancers and, cardiovascular, renal and hepatic disease.

Non-AIDS events dominate the disease burden for patients with HIV infection receiving cART. Fewer than 50% of deaths among AIDS patients are as a direct result of an AIDS-defining illness. The physician providing care to a patient with HIV infection must be well versed in general internal medicine as well as HIV-related opportunistic diseases.

In general, it should be stressed that a key element of treatment of symptomatic complications of HIV disease, whether they are primary or secondary, is achieving good

control of HIV replication through the use of cART and instituting primary and secondary prophylaxis for opportunistic infections as indicated.

4. AIDS

AIDS is the end-stage of HIV infection. Acquired Immune Deficiency Syndrome(AIDS) diagnosis is made in anyone with HIV infection with a CD4+ T cell count <200/ L and in anyone with HIV infection who develops one of the HIV-associated diseases considered to be indicative of a severe defect in cell-mediated immunity. A number of opportunistic infections commonly occur at this stage and or cancers that occur in people with otherwise unexplained defects in immunity. Death is due to uncontrolled or untreatable infection. Tuberculosis and Kaposi sarcoma are usually seen relatively early. Serious fungal infections such as Candida oesophagitis, Cryptococcus meningitis and Penicillosis, and parasitic infections such as Pneumocystis carinii pneumonia or Toxoplasma gondii encephalitis tend to occur, when T-helper cell count has dropped to around 100. People whose counts are below 50 have the late opportunistic infections such as cytomegalovirus retinitis.

WHO CASE DEFINITION FOR HIV INFECTION [12]

Adults and children 18 months or older

HIV infection is diagnosed based on: positive HIV antibody testing (rapid or laboratory-based enzyme immunoassay). This is confirmed by a second HIV antibody test (rapid or laboratory-based enzyme immunoassay) relying on different antigens or of different operating characteristics; and/or; positive virological test for HIV or its components (HIV-RNA or HIV-DNA or ultrasensitive HIV p24 antigen) confirmed by a second virological test obtained from a separate determination.

Children younger than 18 months:

HIV infection is diagnosed based on: positive virological test for HIV or its components (HIV-RNA or HIV-DNA or ultrasensitive HIV p24 antigen) confirmed by a second virological test obtained from a separate determination taken more than four weeks after birth1. Positive HIV antibody testing is not recommended for definitive or confirmatory diagnosis of HIV infection in children until 18 months of age.

Table 1: WHO immunological classification for established HIV infection

HIV-associated immunodeficiency	**Age-related CD4 values**			
	<11 months (%CD4+)	12–35 months (%CD4+)	36 –59 months (%CD4+)	>5 years (absolute Number per mm3 or %CD4+)
None or not significant	>35	>30	>25	> 500
Mild	30–35	25–30	20–25	350−499
Advanced	25–29	20–24	15−19	200−349
Severe	<25	<20	<15	<200 or <15%

Table 2 : WHO clinical staging of HIV/AIDS for adults and adolescents with confirmed HIV infection

Clinical stage 1	Asymptomatic Persistent generalized lymphadenopathy
Clinical stage 2	Moderate unexplained weight loss (<10% of presumed or measured body weight)I Recurrent respiratory tract infections sinusitis, tonsillitis, otitis media and pharyngitis) Herpes zoster Angular cheilitis Recurrent oral ulceration Papular pruritic eruptions Seborrhoeic dermatitis Fungal nail infections

Clinical stage 3	Unexplained severe weight loss (>10% of presumed or measured body weight) Unexplained chronic diarrhoea for longer than one month Unexplained persistent fever (above 37.6°C intermittent or constant, for longer than one month) Persistent oral candidiasis Oral hairy leukoplakia Pulmonary tuberculosis (current) Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis or bacteraemia) Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis Unexplained anaemia (<8 g/dl), neutropaenia (<0.5 × 109 per litre) or chronic thrombocytopaenia (<50 × 109 per litre)
Clinical stage 4	HIV wasting syndrome Pneumocystis pneumonia Recurrent severe bacterial pneumonia Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration or visceral at any site) Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs) Extra-pulmonary tuberculosis Kaposi's sarcoma Cytomegalovirus infection (retinitis or infection of other organs)

	Central nervous system toxoplasmosis HIV encephalopathy Extra-pulmonary cryptococcosis including meningitis Disseminated non-tuberculous mycobacterial infection Progressive multifocal leukoencephalopathy Chronic cryptosporidiosis (with diarrhoea) Chronic isosporiasis Disseminated mycosis (coccidiomycosis or histoplasmosis) Recurrent non-typhoidal Salmonella bacteraemia Lymphoma (cerebral or B-cell non-Hodgkin) or other solid HIV-associated tumours Invasive cervical carcinoma Atypical disseminated leishmaniasis Symptomatic HIV-associated nephropathy or symptomatic HIV-associated cardiomyopathy

WHO case definition for AIDS surveillance [13]

For the purposes of AIDS surveillance an adult or adolescent (> 12 years of age) is considered to have AIDS if at least 2 of the following major signs are present in combination with at least I of the minor signs listed below, and if these signs are not known to be due to a condition unrelated to HIV infection.

Table 3 : Major and Minor signs of AIDS

Major signs • Weight loss ≥ 10% of body weight • Chronic diarrhea for-more than 1 month • Prolonged fever for more than I month (intermittent or constant) Minor signs • Persistent cough for more than 1 month. • Generalized pruritic dermatitis • History of herpes zoster. • Oropharyngeal candidiasis • Chronic progressive or disseminated herpes simplex infection. • Generalized lymphadenopathy.
The presence of either generalized Kaposi Sarcoma or cryptococcal meningitis is sufficient for the diagnosis of AIDS for surveillance purposes.

LABORATORY INVESTIGATIONS

Screening tests: As antibodies to HIV are far easier to detect than the virus itself, their presence or absence in blood stream is the basis for the most widely used test of HIV infection. A person whose blood contains HIV antibodies is said to be HIV positive, or seropositive. There is now a wide range of screening tests based on detection of HIV antibodies. [14]

Table 4 : Laboratory findings with HIV infection

Test	Significance
HIV enzyme linked immunosorbent assay (ELISA)	Screening test for HIV infection. Sensitivity> 99.9%; to avoid false positive results, repeatedly reactive results must be confirmed with Western Blot.
Western Blot	Confirmatory test for HIV. Specificity when combined with ELISA >99.99%. Indeterminate results with early HIV infection, HIV-2 infection, autoimmune disease, pregnancy and recent tetanus toxoid administration.
Complete Blood Count	Anemia, neutropenia, and thrombocytopenia common with advanced HIV infection
Absolute CD4 lymphocyte count	Most widely used predictor of HIV progression. Risk of progression to an AIDS opportunistic infection or malignancy is high with CD4 <200 cel1s/µL.
CD4 lymphocyte percentage	Percentage may be more reliable than the CD4 count. Risk of progression to an AIDS, opportunistic infection or malignancy is high with percentage < 20%.
HIV viral load tests	These tests measure the amount of actively replicating HIV virus. Correlates with disease progression and response to antiretroviral drugs.
B-Microglobulin	Cell surface protein indicative of macrophage. Monocyte stimulation levels>*3.5* mg/dl associated with rapid progression of disease.
p24 antigen	Indicates active HIV replication. Tends to be positive prior to seroconversion and with advanced disease.

Table 5: TREATMENT :[10]

Antiretroviral drugs :

Drug	**Dose**	**Common side effects**	**Special monitoring**
Nucleoside reverse transcriptase inhibitors			
Zidovudine (AZT)	600 mg orally daily in two divided doses	Anemia, neutropenia, nausea, malaise, headache, insomnia, myopathy	No special monitoring
Didanosine (ddl)	400 mg orally daily (enteric-coated capsule) for persons 60 kg	Peripheral neuropathy, pancreatitis, dry months, hepatitis	Bimontly neurologic questionnaire for neuropathy, K^+, amylase, bilirubin, triglycerides
Zalcitabine (ddC)	0.375-0.75 mg orally three times daily	Peripheral neuropathy, aphthous ulcers, hepatitis	Monthly neurologic questionnaire for neuropathy
Stavudine (D4T)	40 mg orally twice daily for persons 60 kg	Peripheral neuropathy, hepatitis, pancreatitis	Monthly neurologic questionnaire for neuropathy, amylase
Lamivudine (3TC)	150 mg orally twice daily	Rash, peripheral neuropathy	No special Monitoring
Emtricitabine	200 mg orally once Daily	Skin discoloration palms/soles (mild)	No special Monitoring
Abacavir	300 mg orally twice daily	Rash, fever-if occur, rechallenge may be fatal	No special Monitoring

Nucleotide reverse transcriptase inhibitors			
Tenofovir Protease inhibitors	300 mg orally once daily	Gastrointestinal distress	Renal function
Saquinavir hard gel	1000 mg orally twice daily with 100 mg ritonavir orally twice daily	Gastrointestinal distress	Cholesterol, Triglycerides
Ritonavir	600 mg orally twice daily or in lower doses (eg, 100 mg orally once or twice daily) for boosting other PIs	Gastrointestinal distress, peripheral paresthesias	Cholesterol, Triglycerides
Indinavir	800 mg orally three times daily	Kidney stones	Cholesterol, triglycerides, billirubin level
Nelfinavir	750 mg orally there times daily or 1250 mg twice daily	Kidney stones	Cholesterol, triglycerides
Amprenavir	1200 mg orally twice daily	Gastrointestinal, Rash	Cholesterol, triglycerides
Fosamprenavir	1400 mg orally twice daily or 1400 mg orally once daily with ritonavir 200 mg orally once dialy	Same as amprenavir	Same as amprenavir
Lopinavir/ritonavir	400 mg/100 mg orally twice daily	Diarrhea	Cholesterol, triglycerides

Atazanavir	400 mg orally once daily	Hyperbillirubinemia	Billirubin level; when used with ritonavir: cholesterol and triglycerides
Tipranavir/ritonavir	500 mg of tipranavir and 200 mg of ritonavir orally twice daily	Gastrointestinal, Rash	Cholesterol, Triglycerides
Darunavir/ritonavir	600 mg of darunavir and 100 mg of ritonavir orally twice daily	Rash	Cholesterol, Triglycerides
Nonnucleoside reverse transcriptase inhibitors (NNRTIs)			
Nevirapine	200 mg orally daily For 2 weeks, then 300 mg orally twice daily	Rash	No special Monitoring
Delavirdine	400 mg orally three times daily	Rash	No special Monitoring
Efavirenz	600 mg orally daily	Neurologic disturbances	No special Monitoring

Table 6: WHO recommendations for initiating antiretroviral therapy in adults and adolescents (2006) [15]:

WHO clinical stage	**CD_4 testing not Available**	**CD4 testing available**
1	Do not start ART	Start ART if CD4 is < 200/mm3
2	Do not start ART	
3	Start ART	Consider starting ART if CD4 < 350/mm^3, starting before it drops to < 200/mm^3 Recommended for all HIV + pregnant women if CD4 < 350/mm^3
4	Start ART	Start all irrespective if CD4

Table 7: WHO recommendations for initiating antiretroviral treatment in infants and children :

Age	Criteria to start ART in infants and children			
	Infants < 12 months	**12 months through 35**	**36 months through 59**	**5 years or over**
% CD4	All	< 20	< 20	< 15
Absolute CD4*		< 750 mm^3	< 350 mm^3	As in adults (<

*Absolute CD4 count is naturally less constant and more age-dependent than % CD4; it is not therefore appropriate to define a single threshold.

Table 8: Summary of WHO preferred antiretroviral treatment recommendation for infants, children and adults[15] :

Patient group	Preferred first line regimen	Preferred second line regimen
INFANTS		
Infant not exposed to ARY	NVP + 2 NRTI	LPV/r + 2 NRTI
Infant exposed to NVP	Boosted PI + 2NRTI	NNRTI + 2 NRTI
Infant with unknown ARV exposure	NVP + 2 NRTI	LPV/r + 2 NRTI
CHILDREN		
Children e years or over	NNRTI + 2NRTI	Boosted PI + 2 NRTI
ADULT OR ADOLESCENTS		
Adult or adolescent	NVP + 2NRTI	Boosted PI + 2 NRTI
Woman starting ART in Pregnancy	NVP + 2 NRTI	Doesn't apply
6women starting ART within 6 months of single dose NVP	NVP + 2 NRTI or 3 NRTI	Doesn't apply

Concomitant conditions		
Child, adolescent or adult with severe anaemia	NVP + 2 NRTI (avoid	Boosted PI + 2 NRTI
Child, adolescent or adult with TB	EFV + 2 NRTI or 3 NRTI	Boosted PI* + 2 NRTI
Adult or adolescent with hepatitis B Adult or adolescent with Hepatitis C	TDF + 3TC + NNRTI ETV + 2 NRTI	Boosted PI + 2 NRTI** Boosted PI + 2 NRTI
IDU	NNRTI + 2 NRTI	Boosted PI + 2 NRTI
HIV-2 or dual infection	3 NRTI	Boosted PI + 2 NRTI

*If using RMP in the TB regimen, LPV/r + extra dose of RTV is the recommended PI option, based on pK interactions. If RFB or an alternative TB regimen without RMP is used, any bPI at its conventional dosage can be used.

**If long term anti-HBV therapy is still needed consider maintaining 3TC and/or TDF, in addition to the new 2 NRTI backbone.

NNRTI = Non nucleoside reverse transcriptase inhibitor, NRTI = nucleoside / nucleotide reverse transcriptase inhibitor, PI = Protease inhibitor, IDU = Injecting drug user, AZT = Zidovudine, EFV = Elavirenz, NVP = Nevirapine, LPV = Lopinavir/r = booster dose ritonavir, RTV = Ritonavir, TDF = Tenofovir, 3TC = Lamivudine, RMP = Rifampicin, RFB = Rifabutin, HBV = Hepatitis B virus.

Table9: Recommended first line combination antiretroviral treatment regimens for pregnant women[15] :

Mother	
Ante-partum	AZT + 3TC + NVP twice daily
Intra-partum	AZT + 3TC + NVP twice daily
Post-partum	AZT + 3TC + NVP twice daily

Table 10: Recommended antiretroviral regimens for prophylaxis in pregnant women not yet eligible for ART.

Mother	
Ante-partum	AZT starting at 28 weeks of pregnancy or as soon as feasible thereafter
Intra-partum	Sd-NVP + AZT/3TC
Postpartum	AZT/3TC x 7 days

Table 11: Recommended antiretroviral regimens for prophylaxis in infants

> 4 weeks maternal ART or ARV	Sd-NVP + AZT x 7 days
< 4 weeks maternal ART or ARV	Sd-NVP + AZT x 4 weeks

Occupational post-exposure prophylaxis (PEP) :[16]

Post-exposure prophylaxis (PEP) is a necessary secondary prevention measure in health care settings, since there will always be rare instances in which primary prevention fail and healthcare workers or patients may be accidentally or through unsafe procedures be exposed to the risk of HIV transmission.

PEP for HIV consists of a comprehensive set of services to prevent infection developing in an exposed person, including : first aid care; counseling and risk assessment; HIV testing and counseling; and depending on the risk assessment, the short term (28-day) provision of antiretroviral drugs, with support and follow up.

Occupational PEP should also be available to all other workers who could be exposed while performing their duties (e.g., social workers, police or military personnel, rescue workers, and refuse collectors). There should be appropriate training for service providers to ensure the effective management and follow up of PEP. ARVs for PEP should be initiated as soon as possible after exposure within the first few hours and no later than 72 hours. ARV drugs for PEP should not be prescribed to people already known to have been injected with HIV prior to the exposure incident. HIV testing is recommended. The administration of ARV drugs for PEP should never be delayed because of testing procedures. If the first test is negative it should be repeated after three and six months. Who recommends that the PEP ARV regimen contain two NRTI drugs. If drug resistance is suspected the addition of a protease inhibitor (PI) may be considered. ARVs for PEP should be administered for a duration of 28 days.

Any occupational exposure to HIV should lead to an evaluation of the working environment and procedures and, when appropriate, improvement of working condition and safety precautions.

IMMUNOLOGICAL TESTS :

The hallmark of immunodeficiency in AIDS patients is a qualitative and quantitative defect of CD4 + cells. Nearly all AIDS patients have cutaneous anergy, a decreased number (<500 for mm3) of T-helper cells (CD4 +), a decreased T-helper to T-suppressor cell ratio (CD4 + : CD8 + < 0.9), and evidence of polyclonal B-cell activation with mainly IgA and IgG, besides immunological abnormalities. The technique for determining lymphocytic sub populations is difficult and expensive. However, when available, the total number of T- helper cells and the percentage of T.

helper cells are very useful prognostic markers. Patients are at risk of developing opportunistic infections if their T-helper cells is below 20%. T-helper cell levels are also increasingly used to decide, whether antiretroviral therapy should he initiated in asymptomatic patients with HIV injection or whether prophylactic treatment (Eg. against pneumocytitis carinii pneumonia) should be started.

HEMATOLOGIC ABNORMALITIES :

ANEMIA IN HUMAN IMMUNODEFICIENCY VIRUS INFECTION INCIDENCE OF ANEMIA

Anemia is common in HIV-infected individuals, occurring in approximately 10 to 20 percent at initial presentation and diagnosed in approximately 70 to 80 percent of patients over the course of disease.[17] In an attempt to ascertain the precise incidence of anemia in the setting of HIV infection, data derived from the case records of 32,867 HIV-infected persons followed from 1990 through 1996 were evaluated.[18] This cohort, termed the Multistate Adult and Adolescent Spectrum of HIV Disease Surveillance Project, consists of individuals who receive HIV care in hospitals and HIV clinics in nine US cities. Using a hemoglobin level of less than 10 g/dl to define anemia, the

1-year incidence of anemia was 37 percent among patients with clinical AIDS; 12 percent among patients with immunologic AIDS, as defined by a CD4 cell count of less than 200 cells/ l and 3 percent among HIV- infected individuals with neither clinical nor immunologic AIDS. Using a hemoglobin cutoff value of 12 g/dl as the criterion for anemia in a large group of participants from the Women's Interagency HIV Study (WIHS), a higher prevalence of anemia was found in HIV- infected women compared to HIV-uninfected controls.[17] Thus, 37 percent of the 2056 HIV infected women were anemic at baseline, compared to 1 7 percent of the 569 HIV negative controls ($p < 0.001$). In the HAART era, an observational. cohort study of 6725 HIV- infected patients from across Europe also documented a high prevalence of anemia.[19] Thus, 58.2 percent had mild anemia, defined as hemoglobin level of 8 to 14 g/dl in males or 8 to 12 g/dl in females; whereas 1.4 percent had severe anemia, defined as a hemoglobin level of less than 8 g/dl. These data thus confirm the high incidence of anemia among HIV infected patient s m both the pre-HAART and HAART eras. Fur ther, the frequency and severity of anemia in HIV- infected patients appear to correlate with HIV-related factors, such as CD4 cell count less than 200 cells/ l (0.2×10^9/liter), higher plasma HIV-1 RNA levels, and a history of clinical AIDS-defining condition[20].

Table 12: Mechanisms and causes of anemia in human immunodeficiency virus infection

Mechanism of anemia	Cause of anemia
Decreased red cell production	Neoplasm infiltrating the marrow Lymphoma Kaposi sarcoma Other Infection Atypical tuberculosis (Mycobacterium avium intracellular or Mycobacterium avium complex) Mycobacterium tuberculosis Cytomegalovirus B19 parvovirus Fungal infection Medications HIV infection Abnormal growth of burst forming unit- erythroid
Ineffective production	Folic acid deficiency Vitamin B_{12} deficiency
Increased red cell destruction	Coombs-positive hemolytic anemia Hemophagocytic syndrome Thrombotic thrombocytopenic purpura Disseminated intravascular coagulation Medications Sulfonamides, dapsone Oxidant drugs in glucose-6-phosphate dehydrogenase deficiency

CONSEQUENCES OF ANEMIA IN HUMAN IMMUNODEFICIENCY VIRUS INFECTION :

Decreased Survival Several large cohort studies have shown that anemia is an independent risk factor for shorter survival in HIV-infected patients.[21] In the Multistate Adult and Adolescent Spectrum HIV Disease Surveillance Project, anemia, defined as a hemoglobin level less than 10 g/dl or a physician's diagnosis of anemia, was found to be associated with an increased risk of death for all CD4 ranges in this cohort. However, the greatest risk of death was noted in patients with baseline CD4 cell counts greater than 200 cells/µl, with a relative risk of death 150 percent higher than for individuals in the same CD4 cell count strata without anemia (relative risk, RR, 2.3, $p < 0.001$). In comparison, the risk of death was increased y approximately 60 percent for anemic patients with baseline CD4 cell counts less than 200 cells/µl (0.2×10^9 liter). Recovery from anemia was shown to be independently associated with improved survival. Thus, among anemic patients with baseline CD4 counts less than 50 cells/µl. Those who remained anemic (hemoglobin level < 10 g/dl) had a 160 percent higher risk of death than patients who recovered from anemia following treatment. In another series of 2348 HIV-infected patients from Baltimore, Maryland development of any grade of anemia was found to be independently associated with decreased survival, with the risk of death approximately threefold increased in those with a hemoglobin level of 7 to 8 g/dl and fourfold increased in those with a hemoglobin level less than 6.5 g/dl. Use of erythropoietin was associated with a decreased risk of death, as was use of antiretroviral therapy. Similarly, an additional study of 6725 European HIV- infected patients demonstrated that hemoglobin level at baseline. CD4 count, and viral load were independent prognostic factors for survival.[22] For each 1 g/dl decrease in hemoglobin level, the relative hazard of death was 1.39 (95% confidence interval [CI] 1.34-1.43; < 0.0001). A large

multicenter prospective study of 2056 HIV- infected women confirmed the independent association between anemia and decreased survival.[23.] Further work is required to elucidate the precise mechanisms underlying this strong prognostic association. It is conceivable that anemia may simply serve as a surrogate marker for more advanced systemic illness.

DISEASE PROGRESSION :

Anemia has been shown to be independently associated with more rapid clinical progression of HIV infection. In one large European study aimed at identifying predictive factors for disease progression among HIV- infected patients receiving HAART, the most recent measured hemoglobin level, CD4 cell count, and HIV-1 viral load, and a history of clinical AIDS before initiation of HAART all were independently related to the risk of disease progression.[24] Thus, with mild anemia (hemoglobin 8 - 14 g/dl for men and 8 - 12 g/dl for women) the relative hazard of disease progression or death was 2.2 (95% CI 1.6-2.9. $p < 0.0001$), whereas for severe anemia (hemoglobin <8 g/dl) the relative hazard was 7.1 (95% CI 2.5-20.1, $p = 0.0002$).

QUALITY-OF-LIFE PARAMETERS :

Anemia has been associated with decreases in quality of life (QOL), as measured by the linear analogue self assessment (LASA) scale and other such instruments.[25.26]

PREVENTION OR CORRECTION OF ANEMIA WI TH HIGHLY ACTIVE ANTIRETROVIRAL THERAPY :

HAART can correct or improve the anemia of HIV infection. In a study of6725 HIV-infected patients from across Europe,[27] use of HAART was statistically associated with improvement in hemoglobin levels. In addition, prolonged HAART use was associated with a greater likelihood of correcting anemia. Thus, 65.5 percent of the cohort were anemic before the use of HAART, 53 percent were anemic after 6 months HAART, and 46 percent were anemic after 12 months of HAART. In a study of 905 HIV-infected patients from Baltimore, use of HAART was associated with an increase in hemoglobin levels after 1-year follow up.[28] Among the patients with a baseline hemoglobin level less than 14 g/dl, 21 percent of patients receiving HAART recovered from anemia (hemoglobin >14 g/dl) compared to only 8 percent of patents not receiving HAART ($p = 0.0006$).[29] In multivariate analysis, use of HAART was strongly associated with freedom from anemia, after adjusting for CD4 cell count, HIV-1 RNA level, sex, race, history of injection drug use, and use of various therapies for anemia. Data from the WIHS demonstrated that use of HAART for as few as 6 months was independently associated with a higher likely hood of resolution of anemia, and longer use was associated with more profound improvements.[30]

Additionally, use of HAART for at least 12 months was significantly associated with a reduced risk of developing anemia.

The mechanisms whereby HAART may protect against development of anemia or correct preexisting anemia are not yet fully understood. Nonetheless, because HIV infection directly contributes to the development of anemia, it is conceivable that HAART may protect against or correct anemia simply by decreasing the level of HIV-1 viral burden and/or by overcoming the factors responsible for the anemia of chronic disease. Additionally, use of HAART has been associated with an increase in hematopoietic progenitor cell growth, while ritonavir, a protease inhibitor, has been shown to directly stimulate progenitor cell growth and to inhibit apoptosis of hematopoietic progenitors in vitro.[30]

NEUTROPENIA :

Etiology Of Neutropenia And Decreased Granulocyte Function In Human Immunodeficiency Virus :

Neutropenia is reported in approximately 10 percent of patients with early, asymptomatic HIV infection and in more than 50 percent of individuals with more advanced HIV-related immunodeficiency.[31] As with other blood cytopenias in the setting of HIV infection, multiple etiologies may be present, either singly or in combination. Thus, decreased colony growth of the progenitor cell colony forming unit- granulocyte-macrophage may lead to decreased production of both granulocytes and monocytes. Soluble inhibitory substances produced by HIV-infected cells have been noted to suppress neutrophil production in vitro, suggesting that autoimmunity plays a part in the development of neutropenia in HIV infection.[33] However, other studies have shown that the presence of neutrophil bound Ig correlates best with stage of disease rather than with neutropenia per se. Decreased serum levels of granulocyte colony stimulating factor (G-CSF) have been described in HIV-seropositive subjects with afebrile neutropenia (<1000 neutrophils/µl), indicating that a relative deficiency

of this specific hematopoietic growth factor also may contribute to persistent neutropenia. [34] The other causes of neutropenia in HIV infection include the presence of opportunistic infections, malignancies, and HIV-related myelodysplasia affecting marrow function.[35] Myelosuppression and neutropenia may result from any one of several medications that arc commonly prescribed for HIV-infected patients.

Beside from absolute neutropenia, patients with HIV infection also may experience decreased function of granulocytes and monocytes. Thus, abnormal Fc processing by macrophages has been described. Decreased opsonization and intracellular killing of bacterial or fungal organisms by granulocytes also have been noted.[36]

Risk factors for infection in neutrpenic patients with human immunodeficiency virus :

In patient s with cancer who receive chemotherapy, multiple studies have shown that the risk of bacterial infection rises when the absolute neutrophil count (ANC) falls below 1000cells/ l and increases further when the ANC falls below 500 cells/µl.[37] Several studies have confirmed the same relationship in patients with HIV infection. Thus Moore and colleagues[38] found that the risk of bacterial infection increased 2.3-fold for HIV-infected individuals with ANC less than 1000 cells/ l and rose by 7.9-fold in those with ANC levels less than 500 cells/ l. Lower ANCs have been associated with increased risk of hospitalization for serious infection[39], as shown in a review of 2047 HIV-positive patients. On multivariate analysis, the severity and duration of neutropenia[40] were found to be significant predictors of the incidence of hospitalization for serious bacterial infections.

In a study of 62 HIV-infected patients with ANCs of 1000 cells/ l or less, 24 percent developed infectious complications, most commonly within 24 hours after onset of neutropenia. On multivariate analysis, the three factors independently associated with infectious complications were presence of a central venous catheter, neutropenia in the previous 3 months, and a lower nadir of granulocyte count (250 cells/µl in those with infections vs. 622 cells/ µ1 in those without infections). Among patients with medication associated neutropenia, the most common cause was zidovudine, followed by trimethoprim-sulfamethoxazole and ganciclovir. Neutropenia was less likely to be associated with infection in these patients than in individuals who were neutropenic because of cancer chemotherapy.

Another study, however, has suggested that the risk of serious infectious complications in neutropenic HIV-infected patients is low.[41] In this prospective study of neutropenia (defined as ANC < 1000 cells/µl) in 87 consecutive HIV-infected patients, ail except three episodes of neutropenia were associated with known myelosuppressive medications. The majority of patients had received co-trimoxazole (62%), lamivudine (56%), and/or zidovudine (40%). The mean ANC of these individuals was 660 cells/µl (range 100-900 cells/µl), and the median duration of neutropenia was 13 days. However, severe neutropenia was uncommon; only three patients had ANC nadirs less than 200 cells/ µl, Serious neutropenia related sepsis in this setting was uncommon, with culture-proven infection occurring in only 8 percent of patients and presumed infection in another 8 percent. No patient died of infection. As expected, patients with infections had significantly lower ANC nadirs (mean 460 vs. 710 cells/µl) and significantly lower CD4 cell counts (mean 64 vs. 126/µl) but did not have a longer duration of neutropenia than patients who did not develop infection.

IMPACT OF EFFECTIVE ANTIRETROVIRAL. THERAPY ON NEUTROPENIA :

Evidence indicates that use of HAART may be associated with improvement of leukopenia and neutropenia in treated patients. Thus, in a group of 66 HIV- infected patients treated with HAART, significant increases in total leukocyte counts and absolute granulocyte counts were seen after 6 months of treatment. A stimulatory effect of protease inhibitors by human hematopoiesis has been demonstrated. These data indicate that mild to moderate levels of neutropenia can be managed by use of HAART alone, although several months of therapy are required to achieve the desired effect.

THROMBOCYTOPENIA :

Thrombocytopenia is relatively common during the course of HIV infection, occurring in approximately 40 percent of patients and serving as the first symptom or sign of infection in approximately 10 percent.[42] Evaluation of the 1- year incidence of thrombocytopenia (<50,000/µl) in a group of 30,214 HIV-infected patients as part of the retrospective Adult and Adolescent Spectrum of Disease Project found the incidence of thrombocytopenia over 1 year was 8.7 percent in patients with clinical AIDS, 3.1 percent in patients with immunologic AIDS (CD4 <200 cells/ µl), and 1.7 percent in patients with neither clinical nor immunologic AIDS. Development of thrombocytopenia was associated with (1) history of clinical or immunologic AIDS, (2) injection drug use, (3) history of anemia or lymphoma, and (4) being an American of African descent. After controlling for multiple factors (AIDS, CD4 count, anemia, neutropenia, antiviral therapy, receipt of prophylaxis against P. carinii), thrombocytopenia was significantly associated with shorter survival (risk ratio 1.7,95% CI 1.6-1.8).[43]

The incidence of thrombocytopenia, defined as a platelet count less than 150,000/ l, was evaluated among 1990 HIV-infected and 553 HIV-negative women who were part of the WIHS. At baseline, 15 percent of HIV-positive women were thrombocytopenic compared to 1.6 percent of HIV-negative women ($p < 0.001$).[44] Factors associated with increased risk of thrombocytopenia included (1) HIV infection, (2) low CD4 levels, (3) increasing viral load, (4) smoking, and (5) being an American of European descent. The study also found thrombocytopenia was a significant predictor of both all-cause and AIDS-related mortality among women infected with HIV. Thus, HIV-infected women with a platelet count less than 50,000/µl had a fivefold increased risk of death from any cause compared to women with normal platelet counts (hazard ratio [HR] 5.10, 95% CI 2.71-9.58) and an approximate threefold increased risk of death from AIDS (HR 3.36, 95% CI 1.44-7.83).

Highly Active Antiretroviral Therapy in Immune Thrombocytopenic Purpura :

HAART has been shown to be effective for treatment of HIV-related ITP. In a report of 37 such patients, effective use of HAART was associated with a significantly increased platelet count after 3 months, independent of baseline platelet count or concomitant use of zidovudine.[45] Similarly, in a retrospective study involving 15 patients with HIV-related ITP treated with HAART, 11 (73%) had an increase in platelet count to values of 50,000/µl or greater, and 8 (53%) had an increase in platelet count to values of 100,000/µl or greater after 6 months of HAART therapy.[46] Consistent with these findings, data from the WIHS demonstrated a strong association between use of HAART and resolution of thrombocytopenia (defined as a platelet count > 150,000/µl). Thus, compared to thrombocytopenic women not receiving antiretroviral therapy, women taking a non-AZT-containing HAART

regimen were nearly two times more likely to improve their thrombocytopenia (odds ratio [OR], 1.84, 95% CI 1.31-2.59, $p < 0.001$), whereas women taking an AZT- containing HAART regimen were even more likely to resolve their thrombocytopenia (OR 2.85, 95% CI 1.96-4.15, $p < 0.0001$). Thus, HAART is an important treatment modality in patients with HIV-related ITP and should be the initial treatment of choice in these patients. Effective use of HAART probably significantly decreases HIV viral load and, in so doing, ameliorates many of the effects of HIV on megakaryocytes, platelet production, and destruction.

Hepatobiliary abnormalities :

Most patients will experience hepatobiliary manifestations at some point during the course of their HIV disease, with hepatomegaly and or Jaundice in 50% and abnormal liver function tests in over 80%. Most liver disorders that are diagnosed in patients with AIDS reflect advanced immunosuppression and occur late in natural history of AIDS, when little can be done to improve overall outcome. HIV can involve the liver directly, as demonstrated by presence of HIV P24 with in Kupffer cells and hepatic endothelial cells[47] and HIV messenger RNA within hepatocytes. Hepatic macrophages and endothelial cells express CD4 surface molecule and have been shown to support viral replication invitro.[48] It remain unclear, however, whether HIV itself directly damages the liver. The quantity of HIV antigens in immunohistochemical studies does not correlate with the degree of histologic abnormalities and histology can be seen.

Mycobacterium avium complex (MAC) is the most common opportunistic pathogen found when liver biopsy of performed in patients with HIV disease, accounting for 38% of diagnoses in one series.[49] Because hepatic involvement occur

in the setting of disseminated disease, systemic symptoms dominate the clinical picture, although a prominent elevation of serum alkaline phosphatase is common.

Hepatic involvement with MAC must be distinguished from infection with mycobacterium tuberculosis. Extra pulmonary tuberculosis occurs in 50% of infected patients with AIDS.[50]

Peliosis hepatic has been recognized as a bacterial syndrome in patients with AIDS, following the discovery of its causative agent, Bartonella hensalae. Early in the AIDS epidemic, a syndrome consisting of dilated, blood- filled hepatic sinusoids and elevated liver functions tests. Fungi usually involve the liver only with disseminated disease. These infections share a nonspecific clinical presentation, including unexplained fever, hepatomegaly and elevated alkaline phosphatase levels. Pneumocystis carinii is the most common pathogen among patients with AIDS, and liver involvement occurs in 38% of patients.[51] Kaposi's sarcoma is seen almost exclusively in homosexual men with AIDS, as opposed to other risk groups. Although serum alkaline phosphatase may be elevated, visceral disease is often a symptomatic, even with extensive involvement. Extranodal presentation of non-hodgkins lymphoma is common in patients with advanced AIDS, with liver disease typically in the setting of multi-organ involvement. Serum alkaline phosphatase elevations are most sensitive for hepatic involvement, with elevated transaminases and bilirubin in advanced disease.

Co-infection with HBV and HIV is common is not surprising given their similar modes of acquisition. The prevalence of seropostivity for past for present infection with HBV approaches 90% in HIV infected homosexuals.[52] Several studies have described reappearance of HBsAg in HIV- infected patients previously thought to be immune to HBV, as indicated by presence of anti- Hbs. Vaccination against HBV has been

recommended for all patients infected with HIV.

Hepatitis C (HCV) shares a parenteral mode of transmission with HIV and is seen more commonly among intravenous drug users than in other risk groups. Biliary abnormalities in patients with AIDS falls into three general categories. Non-HIV associated conditions of the bile duct, acalculous cholecystitis, and AIDS cholangiopathy.

The role of liver biopsy in patients with AIDS has been especially controversial. Several reported series have shown that histologic abnormalities are seen on almost all biopsy specimens, the majority of which are non specific.[53]

Renal manifestations of HIV :

Renal disorders are encounted at all stages of HIV infection, and range from fluid and electrolyte imbalances commonly seen in hospitalized HIV-infected patients, to HIV-associated nephropathy (HIVAN) which can progress rapidly to end- stage renal disease (ESRD).

Mild ARF, defined as a peak serum creatinine > = 2.0 mg/dL has been reported to occur in up to 20% of hospitalized HIV-infected patients.[54] This percentage campares to an incidence rate of 4-5% hospitalized non-HIV patients.[55]The two most common causes of ARF in this population are dehydration and acute tubular necrosis (ATN). A study of kidney biopsy specimens in HIV-infected patients with severe ARF not thought to be due to pre-renal causes or ATN reported the following distribution of renal lesions : 53% Hemolytic Uremic Syndrome; 40% ATN either of ischemic toxic origin or due to rhabomyolysis, 26% obstructive renal failure that was either Entnnsic, drug induced or secondary to

paraprotein precipitation; 23% HIV associated nephropathy; 3% acute interstitial nephritis and 6% various glomerulonephritides.[56]

Common causes of ATN include sepsis, hypotension, and medications commonly used in the treatment of HIV-related infections such as aminoglycosides, pentamidine, acyclovir, foscarnet, amphotericin, tenofovir, adefovir, and cidofovir.[57]

In addition to ATN, foscarnet may produce a dose related ionized hypocalcemia, with normal total serum calcium. Foscarnet also is frequently associated with a transient hyperphosphatemia during the second week of induction therapy. In HIV-infected patients, sepsis contributes to the development of severe renal failure, defined as a peak creatinine > = 6mg/dL, in upto 75% of cases.[58] The probability for survival and recovery from ARF is dictated by the nature and severity of underlying illness. Severe renal failure in HIV-infected patients may be associated with terminal conditions in which acute dialysis would be inappropriate. When the acute underlying illness is reversible, however ARF will usually reverse with dialysis and conventional supportive care.

Acute interstitial nephritis has been found in 13% of autopsies done in patients with renal dysfunction, and an inciting agent is usually not identified. Roughly 4% of patients receiving the protease inhibitor indinavir may develop nephrolithiasis. Symptomatic urinary tract disease, including nephrolithiasis, with renal colic, pain without evidence of stones, dysuria or urgency, has occurred in 8% of patients taking the drug.

Hyponatremia has been reported in 30-60% of patients hospitalized with HIV infection.[59] Hyponatremia is associated with increased morbidity and mortality,

in HIV- infected patients. Volume depletion due to diarrhea or vomiting is the usual cause of hyponatremia present at the time of hospital admission. The syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is the likely culprit in those who develop hyponatremia during hospitalization. Both hypokalemia and hyperkalemia are common in HIV-infected patients. Hypokalemia is predictably seen secondary to gastro intestinal losses of potassium in HIV- infected patients with gastrointestinal infections.[60]

Drug induced hyperkalemia is common in patients receiving either high-dose trimethorpim-sulfamethoxozole or intravenous pentamidine. The mechanism underlying hyperkalemia with both during consists of inhibition of distal nephron sodium transport, leading to a decrease in distal potassium secretion.

A systemic abnormality in potassium equilibrium, which favours the development of hyperkalemia by a mechanisms unrelated to renal potassium excretion, has also been identified in HIV- infected individuals.[61]

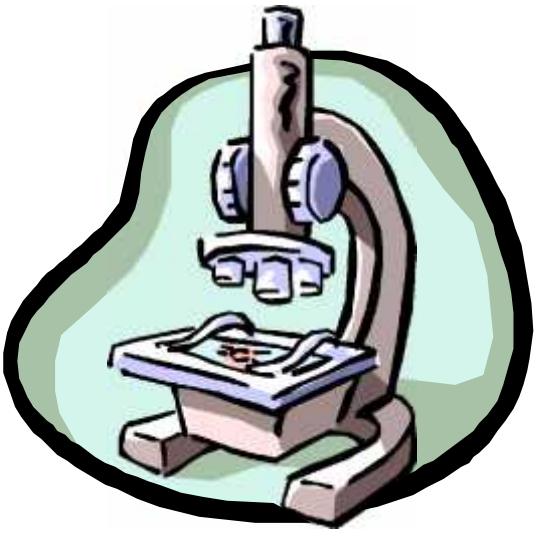
Acid-base disturbances in HIV-infected patients are commonly due to infections or drugs. Respiratory alkalosis and respiratory acidosis may occur in opportunistic infections of the lungs or central nervous system. Nonunion gap metabolic acidosis may occur as a result of several different processes, including intestinal base losses from diarrhoea or renal acidosis due to adrenal insufficiency, the syndrome of hyporeninemic hypoaldosteronism or drug toxicity. High anion gap metabolic acidosis in this population results from chronic kidney disease, type a lactic acidosis due to tissue hypoxia (sepsis) and type B lactic acidosis.

HIV-Associated Nephropathy (HIVAN) is a unique clinical and histopathologic entry and it is thought to develop as result of HIV gene expression in

renal tissue. Proteinuria occurs in upto 30% of HIV-infected patients, but not all of these patients have HIVAN.[62] The pathogenesis of HIVAN has been studied intensely over the past 15 years, and the accumulated data in humans and animal moderate provides substantial evidence that HIVAN is caused by HIV gene expression in renal tissue, resulting in injury of glomerular and tubular epithelial cells. Although the mechanism for HIV entry into renal cells remain unknown, recent studies in humans indicate that HIV gains entry into the epithelium and that full-length mRNA is generated.

Despite the wide spread use of effective an ART over the last 6 years, limited evidence exists that ART can reverse or improve the progression of HIVAN. The rationale for treating HIVAN with corticosteroids is that steroids are the mainstay of treatment for idiopathic FSGS. The ACE-1s captopril and fosinopril have also been studied on renal biopsy, show FSGS followed by MPGN. Other less common renal lesions include DPGN, IgA nephropathy, MCD, and membranous or mesangio proliferative glomerulonephritis. The FSGS characteristically reveals collapse of the glomerular capillary tuft called collapsing glomerulopathy, visceral epithelial cell swelling, microcytic dilatation of renal tubules and tubuloreticular inclusions.

Although evidence from large well-designed clinical trails lacking, many feel that effective anti retroviral therapy benefits both the patient and the kidney.



Methodology

METHODOLOGY

Source of data:

Patients admitted in medical college hospital and research centre, , India during a period of 18 months.

Method of collection of data :

Patients admitted medical college during 18 months duration (2013 and 2014) was included in the study after fulfilling inclusion and exclusion criteria. A predetermined pretested performa is used to record the details of history, physical examination and investigations.

Inclusion criteria :

1. The patients diagnosed HIV I and II reactive by ELISA method (Both symptomatic and asymptomatic).
2. Age > 18 years.

Exclusion criteria:

1. Patients with previously known hematological disorder prior to HIV infection.
2. Patients with hepatic disorders and renal disorders due to other causes are excluded.

Severity criteria : According to 1993 revised classification system for HIV infection.

CD4 count		**Severity**
> 500/ L	→	Mild
200-499/ L	→	Moderate
< 200/ L	→	Severe

After a detailed history and thorough clinical examinatio n patients will be subjected to routine investigations including complete hemogram, CD4 count, liver function tests, renal function tests.

Investigations :

1) Complete hemogram.

2) CD4 count.

3) Liver function tests (LFT)

Serum bilirubin

SGOT

SGPT

Alk. Phosphatase

Sr. proteins

4) Renal function tests (RFT) Blood urea

Sr. creatinine

STATISTICAL ANALYSIS :

1) Cross sectional study design

2) Mean = $\frac{\text{sum of value}}{\text{number of value}} = \frac{\Sigma X}{n}$

3) Standard deviation = $\frac{\Sigma (X - x)^2}{(n - 1}$

4) Anova study(Analysis of variance)

5) F - value (Anova test value)

6) p-value (probability)

Results

RESULTS

TABLE 13 : AGE WISE DISTRIBUTION

Age group	Number of cases (Per 120)
16-25	8
26-35	41
36-45	52
46-55	13
56-65	4
66-75	2

Most of the patients are belonged to age group between 26-45.
No patients above 75 years.

GRAPH 1 : AGE WISE DISTRIBUTION

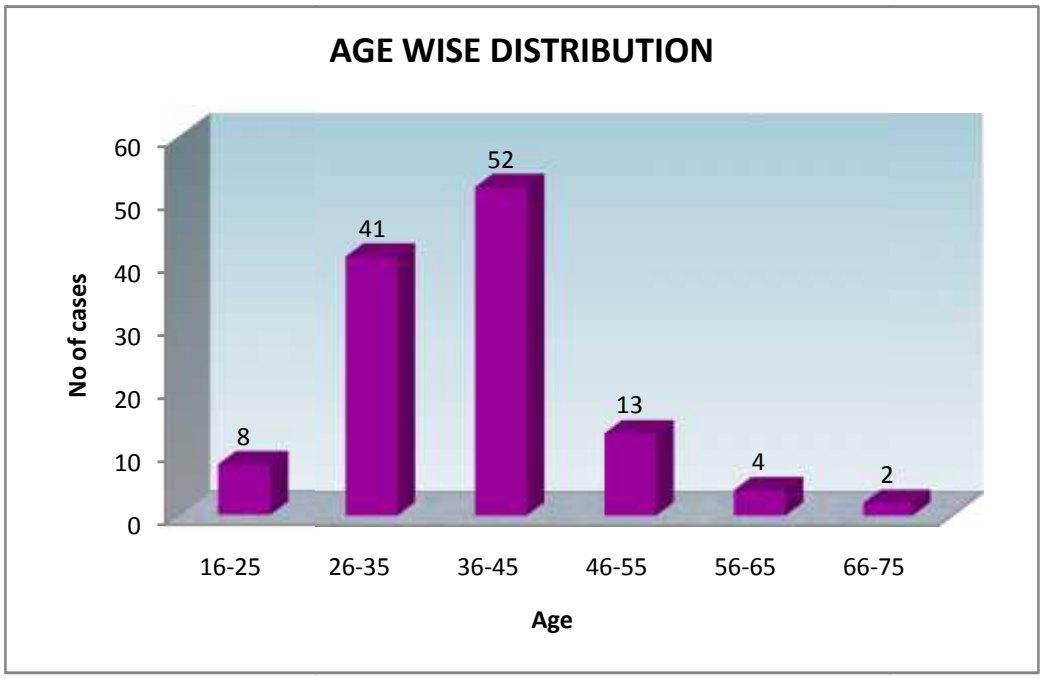


TABLE 14 : SEX WISE DISTRIBUTION

Gender	Number of cases (Per 120)
Male	81
Female	39
Total	120

Males are commonly affected than females. (Males 81% & females 39%)

GRAPH 2 : SEX WISE DISTRIBUTION

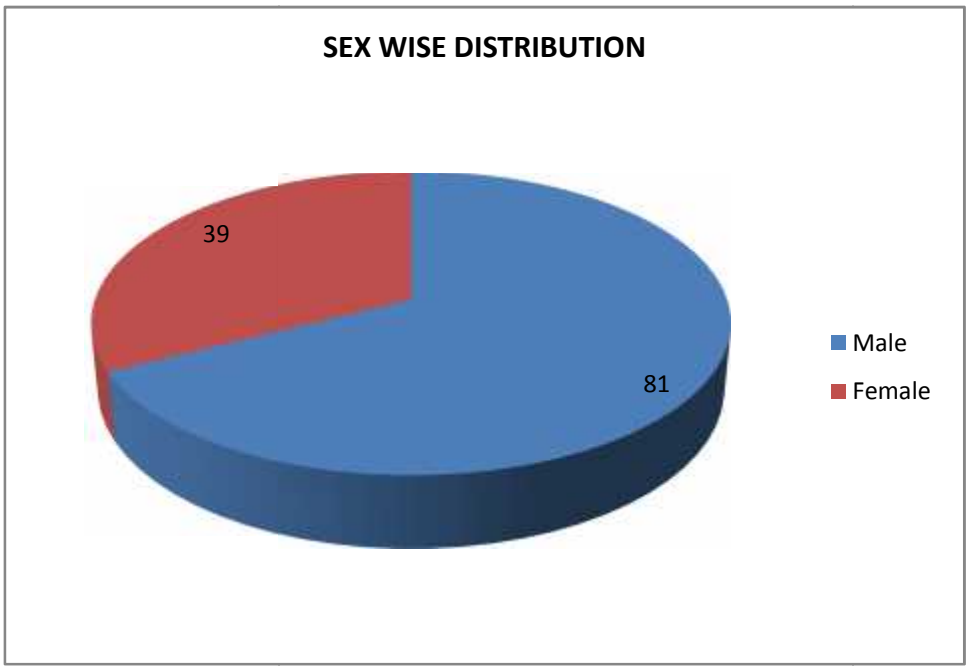


TABLE 15: CLINICAL SYMPTOMS

Symptoms	Number of cases (Per 120)
Fever	73
Vomiting	34
Diarrhea	35
Headache	33
Cough	46
Weight loss	62

In my study fever is the most common symptom followed by weight loss, cough, diarrhoea, vomiting, headache.

GRAPH 3 :CLINICAL SYMPTOMS

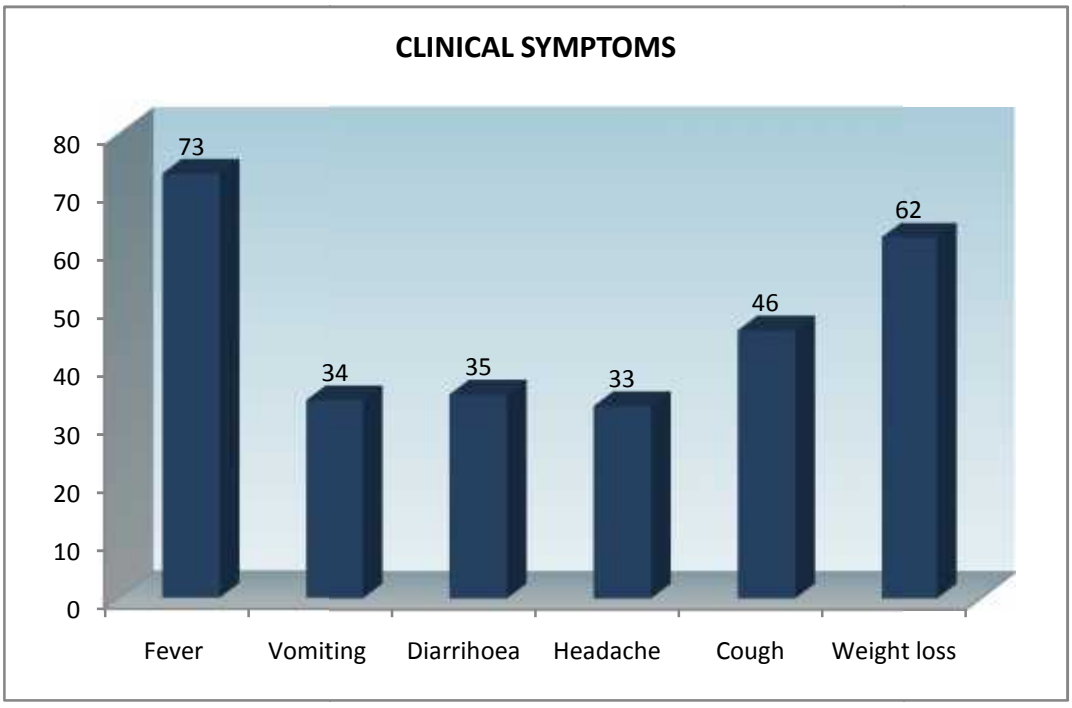


TABLE 16 : CLINICAL SIGNS

Signs	Number of cases (Per 120)
Pallor	75
Oral candidiasis	36
Jaundice	36
Clubbing	18
Cyanosis	1
Generalized lymhadenopathy	34
Pedal edema	19
Skin lesions	17

Most common sign is pallor followed by oral candidiasis, jaundice, clubbing, Generalized lymphadenopathy, Pedal edema,Cyanosis.

GRAPH 4:CLINICAL SIGNS

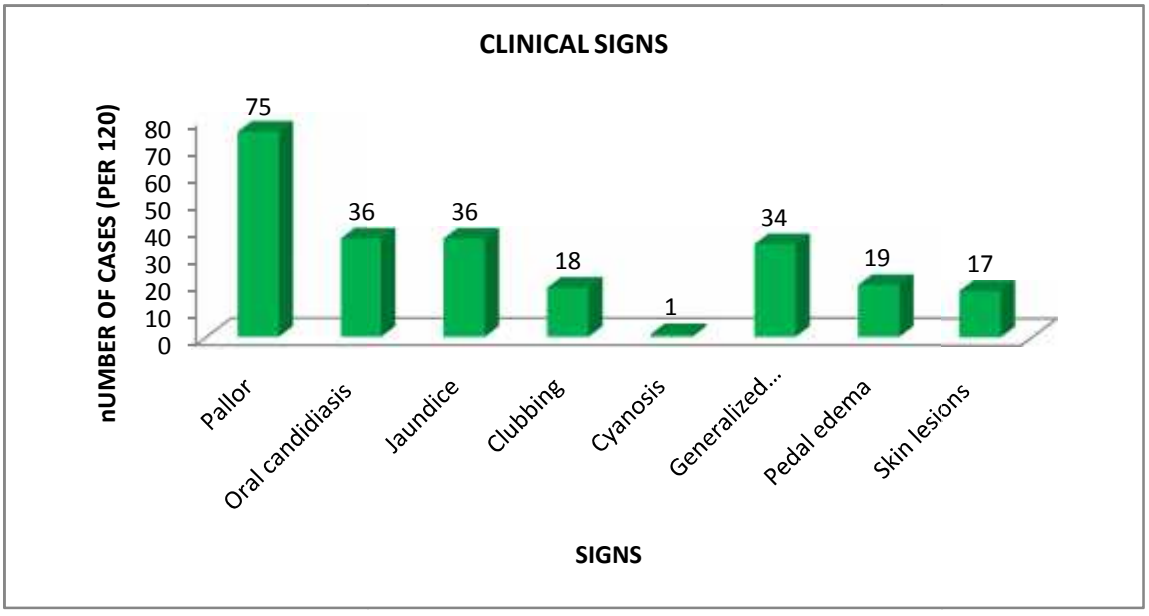


TABLE NO 17 : SYSTEMIC EXAMINATION

	Signs	**Number of cases (Per 120 cases)**
CNS	Neck rigidity	15
Res	Brochial sounds	13
	Crepitations	15
P/A	Hepatomegaly	11
	Hepato – splenomegaly	7
	Spelnomegaly	3
CVS	-	-

On systemic examination respiratory system is involved more commonly involved than other systems.

TABLE 18 : BLOOD PICTURE

Blood picture	Number of cases (Per 120)
Dimorphic	23
Macrocytic	3
Microcytic hypochromic	9
Normocytic hypochromic	26
Nomocytic Normochromic	59
Total	120

Thrombocytopenia - 25cases
Leucopenia - 37 cases

Most common type of blood picture is normocytic normochromic type seen 59% of the patients. Thrombocytopenia seen in 25% of patients. Leucopenia is seen in 37% of patients.

GRAPH 5 : BLOOD PICTURE

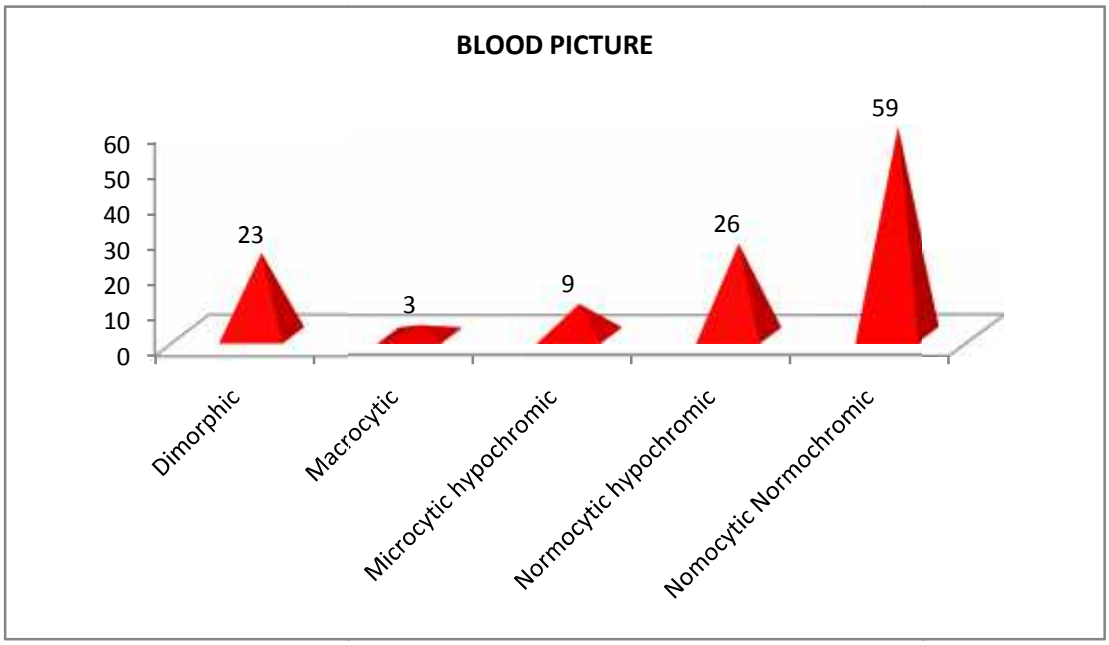
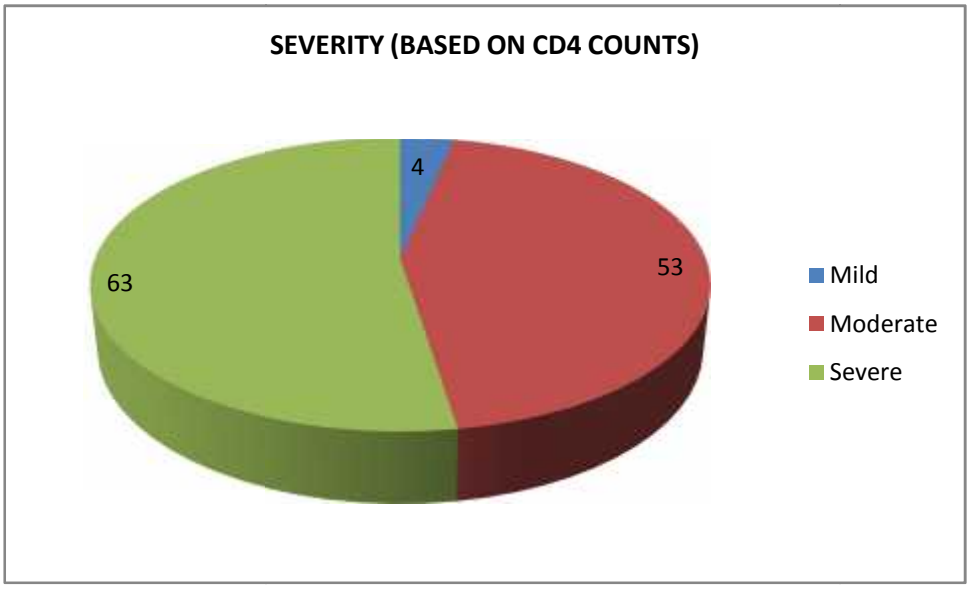


TABLE 19 : SEVERITY (BASED ON CD4 COUNTS)

Severity	CD4	Number of cases (Per 120 cases)
Mild	>500 / µl	4
Moderate	200 – 499 / µl	53
Severe	<200	63
Total		120

GRAPH 6: SEVERITY (BASED ON CD4 COUNTS)



Bio-chemical parameters :

1) Altered liver function tests (LFTs) seen in 28% of patients.

2) Altered renal function tests (RFTs) seen in 15% of patient

Table 20 : HEMATOLOGICAL PARAMETERS ACCORDING TO SEVERITY CRITERIA

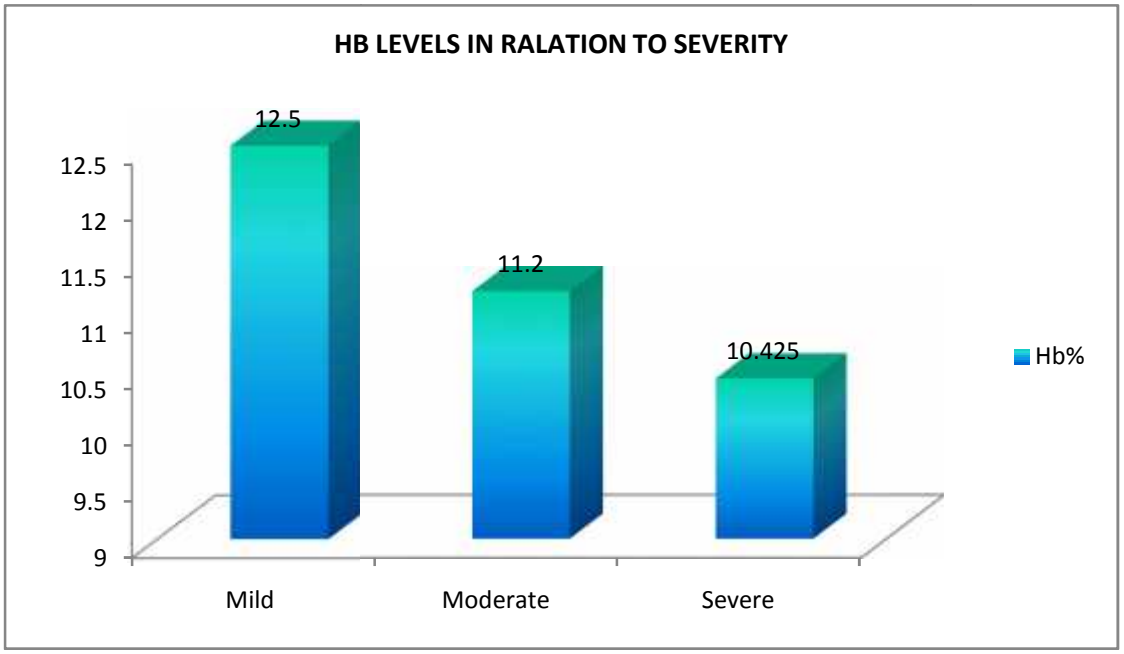
Severity	No. of cases	CD4	Hb%	TLC	Neutrophils	Lymphocytes	Eosinophils	Monocytes	Basophils	PLT (Platelets)
Mild	4	597±111.2	13.0± 1.82	5575± 492.4	56.7 ±5.3	38.5 ±3.6	4.2±1.70	0.5±0.57	0±0	2.9±0.82
Moderate	55	314.6±86.8	11.2±2.5	7126±6044	55±9.5	37.3±8.18	4.39±2.33	0.88±0.725	0.07±0.26	2.6±1.74
Severe	63	175.4±40.63	10.425±2.44	4700±4137.1	68.0±11.73	27.0±9.62	3.7±1.91	0.6±0.794	0.08±0.27	2.32±1.10
Anova	F	174.4	3.230	3.318	21.53	20.47	1.258	1.85	0.17	0.718
	P	< 0.05,S	< 0.05,S	0.04,NS	< 0.05,S	< 0.05,S	0.29,NS	0.16,NS	0.84,NS	0.49,NS

Analysis of variation (ANOVA)

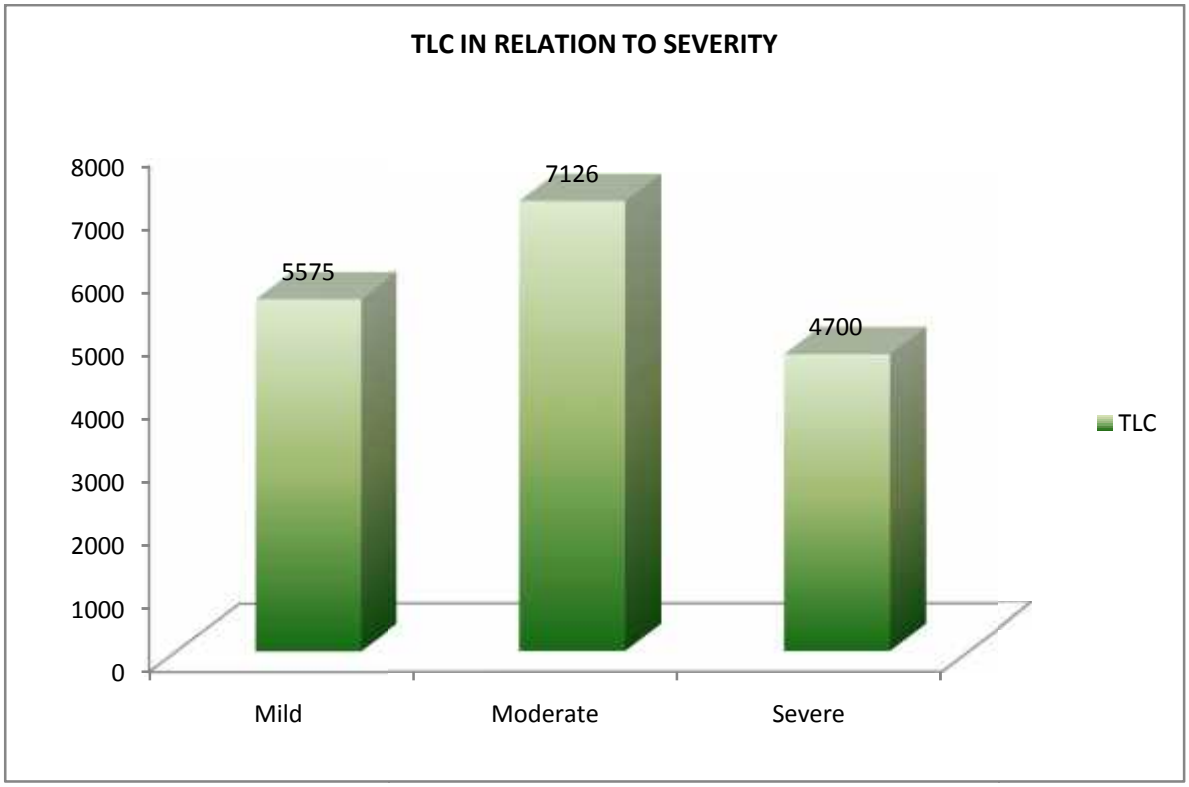
P - Probability
F - ANOVA test value
S - significant ($p < 0.05$)
NS - Not significant ($p > 0.05$)

According to severity criteria, Hemoglobin, neutrophils, lymphocytes are significantly reduced ($p < 0.05$). Total lymphocyte count shows decreasing trend, but not significantly reduced because eosinophils, monocytes, basophils are not significantly reduced.

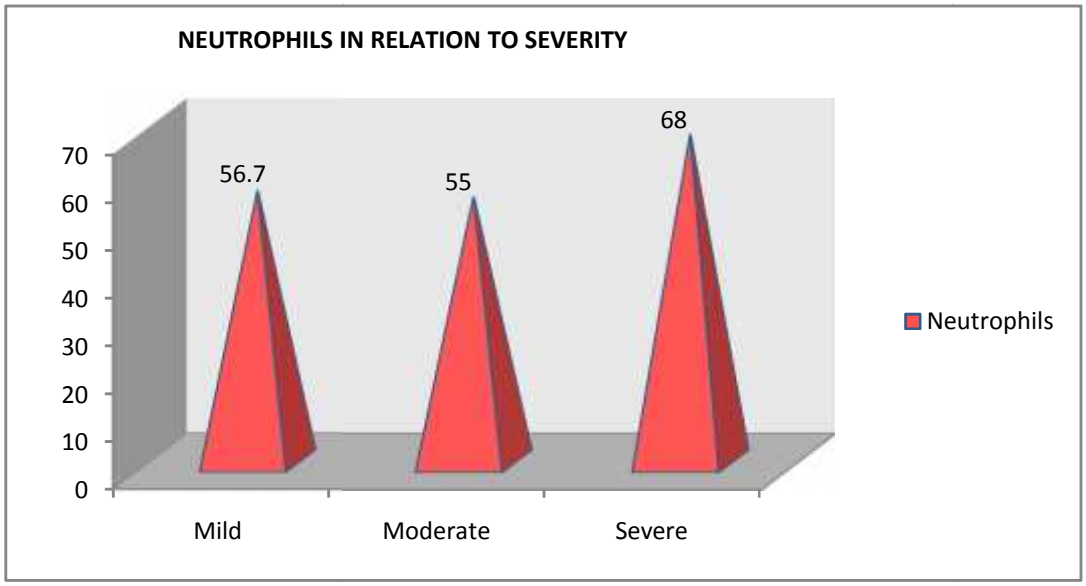
GRAPH 7 : HB LEVELS IN RELATION TO SEVERITY



GRAPH 8 : TLC IN RELATION TO SEVERITY



GRAPH 9:NEUTROPHILS IN RELATION TO SEVERITY



GRAPH 10: LYMPHOCYTES IN RELATION TO SEVERITY

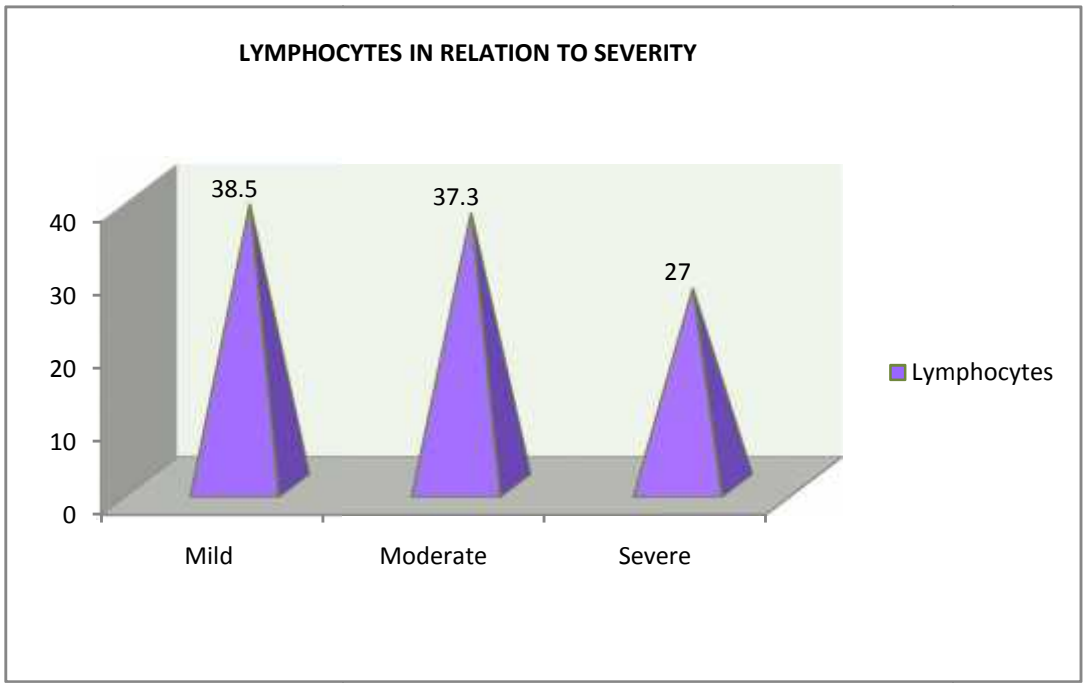


Table 21 : BIOCHEMICAL PARAMETERS ACCORDING TO SEVERITY CRITERIA

Severity	No. of cases	RBS	Bl. Urea	Sr. Creat.	Billirubin	SGOT	SGPT	Alk. Phos.	Sr. protein
Mild	4	126.5±33.7	40.0±21.3	1.67±1.04	1.37±0.66	38.2±9.6	33.7±10.96	81.0±16.69	6.37±0.48
Moderate	53	114.4±43.19	37.6±17.3	1.4±0.64	1.90±1.30	112.4±169.5	120.9±164.66	90.4±36.2	6.4±0.74
Severe	63	121.9±38.2	39.9±19.3	1.70±0.81	2.28±1.35	159.7±238.6	165.6±259.34	107.8±68.4	6.51±0.87
Anova	F	0.522	0.2262	2.735	1.79	1.192	1.104	1.628	0.1190
	P	0.59,NS	0.80,NS	0.069,NS	0.17,NS	0.31,NS	0.33,NS	0.20,NS	0.89,NS

Analysis of variation (ANOVA)

P - Probability
F - ANOVA test value
s - significant ($p < 0.05$)
NS - Not significant ($p > 0.05$)

Biochemical parameters are poorly correlated with severity of the disease. ($p>0.05$)

Discussion

DISCUSSION

These observations made in 120 patients of HIV I and II positive by ELISA method, admitted in BLDEU's Shri B M Patil's medical college hospital and research centre, Bijapur. During a period of 18 months from jan 2013 to june 2014

1) Age :

Age distribution in study was > 18 years. Maximum numbers of patients belong to 26-45, that was 77.5% of all cases.

	S. Sitalakhmi et al[1]	**Nantayachanarat et al[2]**	**Present study**
Maximum number of cases (age range)	25 – 55	24 – 52	26 – 45

2) Sex :

In my study out of 120 patients 81 cases are males and 39 cases are females. So males are more commonly affected than females.

Sex	**Nantaya Chanarat et al[2]**	**S. Sitalakshmi et al[1]**	**Present study**
Male	61%	60%	67.5%
Female	39%	40%	32.5%

3) Clinical presentation (Symptoms) : (Cases out of 120)

Cases	**S. Sitalakshmi et al[1]**	**Nantaya Chanarat et al[2]**	**Present study**
Fever	45%	40%	60%
Vomitings	46%	41%	28%
Diarrhoea	42%	39%	29%
Headache	31%	30%	27%
Cough	25%	35%	38%
Weight loss	59%	60%	51%

In my study most common symptom is fever, followed by weight loss. But in S. Sitalukshmi et al study most common symptom is weight loss and vomitings. In Nantaya Chanarat et al study most common symptom is weight loss.

4) Clinical signs : In number of cases out of 120

	S. Sitalakshmi et al[1]	**dNantayaChanarat et al[2]**	**Present study**
Pallor	60%	59%	62%
Oral candidiasis	25%	32%	30%
Jaundice	30%	19%	30%
Clubbing	10%	15%	15%
Cyanosis	2%	4%	0.8%
Generalized lymphadenopathy	30%	40%	28%
Pedal edema	12%	5%	15%
Skin lesions	20%	17%	14%

In my study most common sign is pallor followed by oral candidiasis, jaundice and generalized lymphadenopathy. In Sitalakshmi et al study, most common sign is pallor, jaundice, generalized lymphadenopathy. In Nantaya Chanarat et al study most common sign is pallor, generalized lymphadenopathy, oral candidiasis.

5) Blood picture :

Total cases out of 100	**Bodey GP et al[32]**	**Moore RD et al[33]**	**Present study**
Normocytic normochromic	50%	60%	59%
Dimorphic	20%	15%	19%
Macrocytic	5%	5%	2.5%
Normocytic hypochromic	20%	10%	19%
Microcytic hypochronic	5%	10%	7.5%

Most common type of blood picture seen in my study is normocytic normochromic blood picture. Other studies, Bodey et al, Moore RD et al shown most common type is Normocytic normochromic blood picture.

6) Leucopenia :

Zon LI et al[31]	Bagnaro et al [32]	Present study
39%	41%	30%

My study shown 30% of patients have Leucopenia, Zon LI et al study shown 39%, Bangara et al shown 41%.

7) Thrombocytopenia :

Pechere M et al[42]	Sullivan PS et al[43]	Present study
13%	15%	21%

In my study, thrombocytopenia in HIV patients is 21%, in Pechere M et al study thrombocytopenia is 13%, in Sullivan PS et al study it is 15%.

8) Liver function tests :

In my study, liver abnormalities in the form raised bilirubin and liver enzymes are noted in 28% of cases. In Housset et al study, liver abnormalities are seen in 80% of cases.

In Schmitt M et al study liver abnormalities are seen in 43% of cases.

Attered LFT	Housset C et al[47]	Schmitt M et al[48]	Present study
Altered LFT (Liver function tests)	80%	43%	28%

9) Renal function tests :

Altered renal function tests are seen in 15% of cases in the form raised blood area and serum creatinine. In Valeri A et al study, altered renal function tests are seen in 20 cases. In Shasterman N et al study altered renal functions are seen in 25% of cases.

	Valeri A et al Study[54]	**Shusterman N et al study[55]**	**Present study**
Altered RFT (Renal function tests)	20%	25%	15%

Conclusion

CONCLUSION

By this it was concluded that,

1) Peak incidence of HIV occurred in age group of 26-45 year.
2) Males are affected more than females.
3) Fever, weight loss are most common symptoms, other associated symptoms are vomiting, diarrhoea, headache, cough.
4) Pallor, oral candidiasis, generalized lymphadenopathy, jaundice, skin lesions are most common clinical signs noted in HIV patients.
5) Respiratory system was most commonly involved system, followed by gastro-intestinal system.
6) Normocytic, normochromic blood picture was most commonly seen in HIV patients.
7) Leucopenia was seen in 30% of cases.
8) Thrombocytopenia was seen in 21% of cases.
9) Altered liver function tests (LFT) was seen in 28% of cases.
10) Altered renal function tests (RFT) was seen in 15% of cases.
11) Hemoglobin, neutrophils, lymphocytes were significantly reduced according to severity criteria ($P < 0.05$).
12) Bio-chemical parameters were poorly correlated with severity of the disease ($P > 0.05$).

Summary

SUMMARY

120 cases of HIV diagnosed by ELISA method, admitted in BLDEU's Shri B M Patil's medical college hospital and research centre, Bijapur. During a period of 18 months from jan 2013 to june 2014

1) Of the 120 cases, 77% of cases were in the age group of 26 – 45.
2) 81 % of patients were males.
3) Fever and weight loss were most common symptoms, seen in almost 60% of patients.
4) Pallor (62%), oral candidiasis (30%), Generalized lymphadenopathy (28%), Jaundice (30%) were most common signs noted in HIV patients.
5) Respiratory system was most common system involved.
6) Hematological abnormalities were common in HIV patients.
7) Normocytic Normochromic blood picture was seen in 59% of cases.
8) Leucopenia was seen in 30% cases.
9) Thrombocytopenia was seen in 21% cases.
10) According severity criteria, Hemoglobin, Neutrophils, Lymphocytes were reduced significantly ($P < 0.05$).
11) Eosinophils, Basophils, Monocytes, Platelets were not shown any significant reduction according severity criteria.
12) Biochemical abnormalities were common in HIV patients.
13) Altered Liver function tests (LFT) was seen in 28% of patients.
14) Altered Renal function tests (RFT) was seen in 15% of patients.
15) Bio-chemical parameters poorly correlated with the severity of the disease ($p > 0.05$).

Finally my study proves the Hematological and Bio-chemical abnormalities were common in HIV patients, like reported in many other studies. The study further strengthened the relation between hematological and bio-chemical parameters to the severity of the disease.

"It helps in clinical practice, particularly in resource limited settings, where CD4 counts are not available and guide to therapy based on simple hematological profile".

Bibliograpy

BIBLIOGRAPHY

1. Sitalakshmi S, Srikrishna A, Damodar P. Haematological changes in HIV infection. Indian J Pathol Microbiol 2003;46(2):180-183.
2. Chanrat N, Chanarat P. Bio-chemical and hematological manifestations of HIV/AIDS in Chiang Mai, Thailand. Southeast Asian J Trop Med Public Health 2001 Sep;32(3):500-3.
3. Billah MM, Islam KMD, Ahasan MM et al. Transmission, bio-chemical manifestation and CD4 cell count HIV. Pakistan J Biological Sciences 2004;7(2):292-300.
4. Valeri A, Neusy AJ. Acute and chronic renal disease in hospitalized AIDS patients. Clin Nephrol 1991 Mar;35(3):110-8.
5. Malaviya AN. Aids we could do without. Science Age 1987;Vol33-43.
6. Piot P et al. Aids in Africa. Manual for physicians. WHO Geneva 1992;4:13.
7. Sengupta D et al. AIDS in India – An update and reappraisal. APICON-98 Medicine update 1998;8:209-214.
8. GLOBAL REPORT - UNAIDS report on the global AIDS epidemic 2013 [Internet].[place unknown]:Nov 2013.Available from http://www.unaids.org/en/resources/campaigns/globalreport2013/factsheet
9. Annual Report 2013- 2014 NACO[Internet].[place unknown]:2013.Available from :http://naco.gov.in/NACO/Quick_Links/Directory_of_HIV_Data/
10. Karnataka State AIDS Prevention Society.HIV Data Karnataka For the Year 2007-2008 and 2011-2012[Internet]:2013.Available from http://ksaps.gov.in/HIVDataKaranataka.htm

11. Anthony S, Fauci H, Chifford L. HIV disease. In : Aids and related disorders.Harrison principles of internal medicine. 17th edn., Vol. 2 1791-1854:308.
12. WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children.2007. [Internet]. [place unknown]. Available from www.who.int/hiv/pub/guidelines/hivstaging/en/
13. Park K; Park's textbook of Preventive and social medicine; 20th edition;Jabalpur:Banarsidas Bhanot;2009.
14. Low PA,Benanoch EE.CLINICAL AUTONOMIC DISORDERS. 3rd Edition. Philadelphia. Lippincott, Williams and Williams.2008.
15. Tie rncy LM et al. Current Medical Diagnosis and Treatment, 47th Ed., A Lange Medical Publ. 2008.
16. WHO. Priority interventions, HIV/AIDS Prevention treatment and care in the health sector, WHO HIV/AIDS Department. 2008 August.
17. Mitsuyasu R. AIDS Clin Review 1993/4, p. 189. Marcel Dekker, New York1993.
18. Sullivan PS, Hanson DL, Chu SY et al. Epidemiology of anemia in human immunodeficiency virus infected persons : Results from the Multistate Adult and Adolescent Specturm of HIV Disease Surveillance Project. Blood 1998;91:301.
19. Mocroft A, Kirk O, Barton SE et al. Anaemia is an independent predictive marker for clinical prognosis in HIV infected patients from across Europe. AIDS 1999;13:943.
20. Levine AM, Berhane K, Masri- Lavine L. Prevalence and correlates of anemia in a large cohort of HIV-infected women : Women's

Interagency HIV Study. J Acquir Immune Defic Syndr 2001;26:28.

21. Sullivan PS, Hanson DL, Chu SY et al. Epidemiology of anemia in human immunodeficiency virus infected persons : Results from the Multistate adult and adolescent spectrum of HIV disease surveillance Project. Blood 1998;91:301.
22. Mocroft A, Ledergerber B, Katlama C et al. Decline in the AIDS and death rates in the EuroSIDA study : An observational study. Lancet 2003;362:22.
23. Berhane K, Karim R, Cohen MH. Impact of highly active antiretroviral therpay on anemia and relationship between anemia and survival in a large cohort of HIV- infected women : Women's Interagency HIV Study. J Acquir Immune Defic Syndr 2004;37:1245.
24. Lundgren JD, Mocroft A, Gatell JM et al. A clinically prognostic scoring system for patients receiving highly active antiretroviral therapy : Results from the EuroSIDA study. J Infect Dis 2002;185:178.
25. Saag MS, Bowers P, Leitz GJ et al. Once-weekly epoetin alfa improves quality of life and increases hemoglobin in anemic HIV + patients. AIDS Res Hum Retroviruses 2004;20:1037.
26. Grossman HA, Goon B, Bowers P et al. Once-weekly epoetin alfa dosing is as effective as three times-weekly dosing in increasing hemoglobin levels and is associated with improved quality of life in anemic HIV-infected patients. J Acquir Immune Defic Syndr 2003;34:368.
27. Mocroft A, Kirk O, Barton SE et al. Anaemia is an independent predictive marker for clinical prognosis in HIV infected patients from across Europe AIDS 1999;13:943.
28. Moore RD, Forney D. Anemia in HIV- infected patients receiving highly active antiretroviral therapy. J Acquir Immune Defic Syndr 2002;29:54.

29. Isgro A, Mezzaroma I, Aiuti A et al. Recovery of hematopoietic activity in bone marrow from human immunodeficiency virus type 1 infected patients druing highly active antiretroviral therapy. AIDS Res Hum Retroviruses 2000;16:1471.
30. Huang SS, Barbour JD, Deeks SG et al. Reversal of human immunodeficiency virus type 1 associated hematosuppression by effective antiretroviral therapy. Clin Infect Dis 2000;30:504.
31. Zon LI, Arkin C, Groopman JE. Hematologic manifestations of the human immunodeficiency virus (HIV). Semin Hematol 1988;25:208.
32. Bagnara GP, Zauti G, Giovannini M et al. Early loss of circulating hemopoietic progenitors in HIV-1 infected subjects. Exp Hematol 1990;18:426.
33. Leiderman I, Greenberg M, Adelsberg B et al. Autoantibodies against peripheral blood cells appear early in HIV infection and their prevalence increases with disease progression. Clin Exp Immunol 1990;81:11.
34. Mauss S, Steinmetz HT, Willers R et al. Induction of granulocyte colony-stimulating factor by acute febrile infection but not by neutropenia in HIV seropositive individuals. J Acquir Immune Defic Syndr 1997;14:430.
35. Karcher DS, Frost AR. The bone marrow in human immunodeficiency virus (HIV)-related disease. Morphology and clinical correlation. Am J Clin Pathol 1991;95:63.
36. Elis M, Gupta S, Galant S et al. Impaired neutrophil function in patients with AIDS or AIDS-related complex : A comprehensive evaluation J Infect Dis 1988;158:1268.
37. Bodey GP, Buckley M, Sathe US et al. Qualitative relationships

between circulating leukocytes and infection in patients with acute leukemia. Ann Intern Med 1966;64:328.

38. Moore RD, Keruly J, Chaisson RE et al. Neutropenia and bacterial infection in acquired immunodeficiency syndrome. Arch Intern Med 1995;155:1965.
39. Jacobson MA, Cohen PT, Liu RC et al. Risk of hospitalization for serious bacterial infection associated with neutropenia severity in patients with HIV (abstract 231). 11th International Conference on AIDS, Vancouver, Canada, 1996.
40. Meynard J- L, Guiguet M, Arsac S et al. Frequency and risk factors of infectious complications in neutropenic patients infected with HIV AIDS 1997;11:995.
41. Moore DAJ, Benepal T, Portsmouth S et al. Etiology and natural history of neutropenia in human immunodeficiency virus disease : A prospective study. Clin Infect Dis 2001;32:469.
42. Pechere M, Sami K, Hirschel B. HIV related thrombocytopenia. N Engl J Med 1993;328:1785.
43. Sullivan PS, Hanson DL, Chu Sy et al. Surveillance for thrombocytopenia in persons infected with HIV : Results from the multistate adult and adolescent spectrum of disease project. J Acquir Immune Defic Syndr 1997;14:374.
44. Pearce CL, Wendy JM, Levine AM et al. Thrombocytopenia is a strong predictor of All-Cause and AIDS-Specific Mortality in Women with HIV : The Women's Interagency HIV Study. 46th Annual Meeting of the American Society of Haematology, San Diego California 2004.
45. Caso JAA, Mingo CS, Tena JG. Effect of highly active antiretroviral

therapy on thrombocytopenia in patients with HIV infection. N Engl J Med 1999;16:1239.

46. Carbonara S, Fiorentino G, Serio G et al. Response of severe HIV associated thrombocytopenia to highly active antiretroviral therapy in cluding protease inhibitors. J Infect 2001;42:251.
47. Housset C, Boucher O, Girard P. Immunohistochemical evidence for human immunodeficiency virus-1 infection of liver Kupffer cells. Hum Pathol 1990;21:104-408.
48. Schmitt M, Lafon M, Gendrault J. Primary cultures of endothelial cells from the human liver sinusoid are permissive for human immunodeficiency virus type 1. Proc Natl Acad Sci USA 1992;89:1582-1586.
49. Schneiderman D, Arensen D, Cello J. Hepatic disease in patients with the acquired immune deficiency syndrome (AIDS). Hepathology1987;7:925-930.
50. Cappell MS. Hepatobiliary manifestations of the acquired immune deficiency syndrome. Am J Gastroenterol 1991;86(1):1-15.
51. Cohen O, Stoeckle M. Extrapulmonary pneumocystis carinii infection in the acquired immunodeficiency syndrome. Arch Intern Med 1991;151:1205-1214.
52. Dove L, Wright T. Hepatitis/HIV coinfection – infection with hepatitis viruses in patients with human immunodeficiency virus : Medical dilemma or inconsequential coincidence. Adv Gastroenterol Hepatol Clin Nutr 1997;1(5):231-239.
53. Lebovies E, Thung S, Schaffner F et al. The liver in the acquired immunodeficiency syndrome : A clinical and histologic study. Hepatology 1985;5:293.

54. Valeri A, Neusy AJ. Acute and chronic renal disease in hospitalized AIDS patients. Clin Nephrol 1991 Mar;35(3):110-8.

55. Shusterman N, Strom BL, Murray TG, Morrison G, West SL, Maislin G. Risk factors and outcome of hospital-acquired acute renal failure. Clinical epidemiologic study. Am J Med 1987 Jul;83(1):65-71.

56. Peraldi MN, Maslo C, Akposso K, Mouge not B, Rondeau E, Sraer JD. Acute renal failure in the course of HIV infection : a single-institution retrospective study of ninety-two patients and sixty renal biopsies. Nephrol Dial Transplant 1999 Jun;14(6):1578-85.

57. Berns JS, Cohen RM, Stumacher RJ, Rud nick MR. Renal aspects of therapy for human immunodeficiency virus and associated opportunistic infections. J Am Soc Nephrol 1991 Mar;1(9):1061-80.

58. Rao TK, Friedman EA.Outcome of severe renal failure in patients with acquired immunodeficiency syndrome. Am J Kidney Dis 1995 Mar;25(3):390-8.

59. Agarwal A, Soni A, Ciechanowsky M, Chander P, Treser G. Hyponatremia in patients with the acquired immunodeficiency syndrome. Nephron 1989;53(4):317-21.

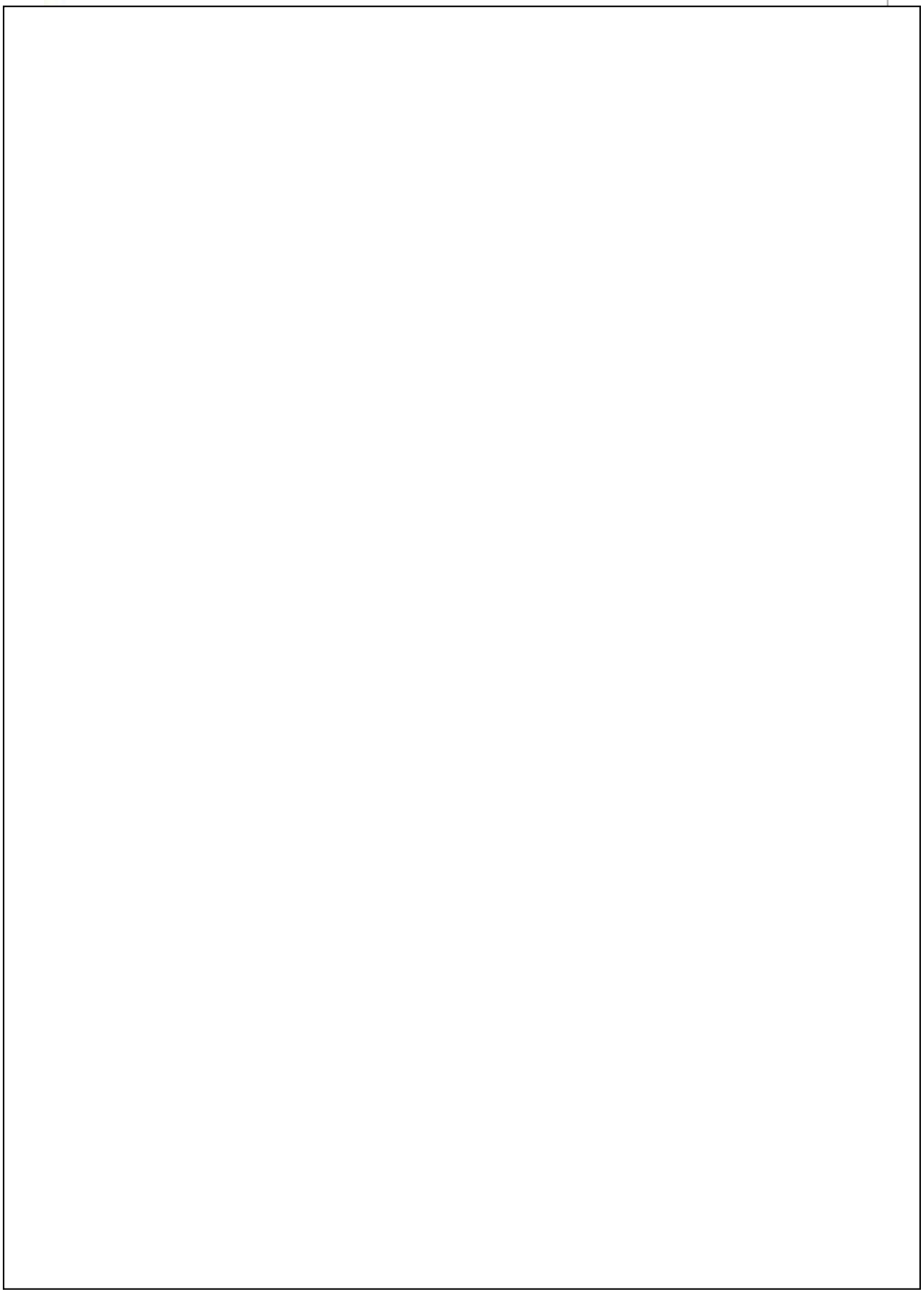
60. Tang WW, Kaptein EM, Feinstein EI, Massry SG. Hyponatremia in hospitalized patients with the acquired immunodeficiency syndrome (AIDS) and the AIDS-related complex. Am J Med 1993 Feb;94(2):169-74.

61. Caramelo C, Bello E, Ruiz E, Rovira A, Gazapo RM, Alcazar JM et al. Hyperkalemia in patients infected with the humanimmunodefic iency virus : involvement of a systemic mechanism. Kidney Int 1999 Jule;56(1):198-205.

62. Luke DR, Sarnoski TP, Dennis S. Incidence of microalbuminuria in

ambulatory patients with acquired immunodeficiency syndrome. Clin Nephrol 1992 Aug;38(2):69-74.

ANNEXURE



PROFORMA

Name :

Age :

Sex :

Occupation :

Socio-economic status :

I.P. No. : Exposure :

Presenting symptoms :

1) Fever
2) Headache
3) Vomitings
4) Diarrhea
5) Cough with expectoration
6) Loss of weight

Past history :

Long fever / Intermittent fever

Prolonged cough

Repeated diarrhea and vomitings

Hemoptysis History

of surgery History

of exposure

History of blood transfusion

Personal history :

History of alcoholic

History of smoking

History of drug abuse and needle sharing

CLINICAL EXAMINATION :

General examination :

1) Built – normal average / below average
2) Nutrition – well nourished / moderate / poor
3) Hydration status
4) Pallor
5) Jaundice
6) Clubbing
7) Cyanosis
8) Generalized lymphadenopathy
9) Pedal edema
10) Oral candidiasis
11) Skin lesions

Vital sings :

B.P. →

P.R. →

R.R. →

Temp →

Systemic examination :

1) Respiratory system :

Signs of consolidation

Collapse

Cavity

Fibro-cavitory

Effusion

Pneumothorax

2) C.V.S. :

Signs of pericardial effusion

Constrictive pericarditis

Pericardial rub

3) G.I.T. :

- Doughy abdomen
- Ascites
- Hepatomegaly
- Splenomegaly
- Lymphnode mass

C.N.S. :

- Consciousness
- Higher mental functions
- Speech
- Cr. Nr palsies and papilledema
- Neck rigidity

Investigations :

1) C.B.C :

1) Hb%

2) TLC

3) DLC

- Neutrophils

- Lymphocytes
- Eosinophils
- Monocytes
- Basophils

4) CD4 count

5) Platelet count

6) Blood picture

- Type of anemia
- Leucopenia / Leucocytosis
- Thrombocytopenia / Thrombocytosis

2) RBS :

3) RFT :

1) Bl. Urea
2) Sr. Creatinine

4) LFT :

1) Sr. Bilirubin
2) SGOT
3) SGPT
4) Alk. Phosphatase
5) Sr. proteins.

5) HIV I and II

(ELISA)

Treatment given :

Comments :

INFORMED CONSENT FORM

I ……. exercising free power of choice hereby give my written consent to be included as a subject in the study **"STUDY OF HEMATOLOGICAL AND BIOCHEMICAL MANIFESTATIONS IN HIV/AIDS AND TO ASSESS THEIR CORRELATION TO SEVERITY OF DISEASE"** conducted by and undergo the necessary investigations required for this study and I fully consent for the same.

I am over 18 yrs of age and I have been explained to my satisfaction by the attending Physician, in the language I understand, about the purpose of the study .I have also understood that the investigator will maintain confidentiality regarding my identity.

SIGNATURE OF DOCTOR **SIGNATURE OF PATIENT/RELATIVE**

NAME OF THE DOCTOR **NAME OF PATIENT/RELATIVE**

RELATIONSHIP (IF RELATIVE)

DATE:

KEY TO MASTER CHART

IPNO	–	In patient No
GL	–	Generalized lymphadenopathy
PE	–	Pedal edema
OC	–	Oral candidiasis
SL	–	Skin lesions
CNS	–	Central Nervous System
Res	–	Respiratory System
P/A	–	Per abdomen
CVS	–	Cardio Vascular System
BS	–	Bronchial breath Sounds
H	–	Hepatomegaly
HS	–	Hepatosplenomegaly
S	–	Splenomegaly
Hb	–	Hemoglobin
TLC	–	Total leucocyte count
N	–	Neutrophils
L	–	Lymphocytes
E	–	Eosinophils
M	–	Monocytes
B	–	Basophils
CD_4	–	CD4 cells (Cluster of differentiation)
PLT	–	Platelets
MH	–	Microcytic hypochromic
NH	–	Normocytic hypochromic
DM	–	Dimorphic
NN	–	Normocytic Normochromic
MA	–	Macrocytic
Bl.Pic	–	Blood Picture
RBS	–	Random blood sugar
Bl.Ur	–	Blood urea
Sr.Cr	–	Serum ceratinine
Sr.Pro	–	Serum proteins

MASTER CHART

Sl No	Name	IP No	Age	Gender	Exposure	Fever	Vomiting	Diarrhoea	Headache	Cough	Weight loss	oc	pallor	Jaundice	Clubbing	Cyanosis	SL	GL	PE	CNS	RS	PA	CVS	Hb(gr)	TLC(cumm)	N(%)	L(%)	E(%)	M(%)	B(%)	CD4(µl)	PLT(lakhs)	Bl.Plc	Thrombocyte	Leukopenia	RBS(gm)	Bl.Ur(mg)	Sr.Cr(mg)	Bilirubin(mg)	SGOT(U/L)	SGPT(U/L)	Alk.P(U/L)	Sr.Pro(gm)	HIV I & II
1	Sadashiv	30424	45	M	+	+	-	-	-	+	+	-	+	-	-	-	-	-	-	-	Crep	-	-	8.4	32000	57	38	3	1	0	462	2.82	MH	-	-	105	21	0.8	0.9	41	27	120	6	Reactive
2	Kareppa	2089	37	M	+	-	+	+	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	10.2	8200	60	31	1	1	0	404	7.91	NH	-	-	80	40	1.2	1	64	39	44	5.4	Reactive
3	Siddu	3286	40	M	+	+	-	-	+	-	+	+	+	-	-	-	-	+	-	NR	-	-	-	9.2	3500	55	37	8	0	0	382	2.1	DM	-	-	94	26	0.7	0.8	18	20	112	6	Reactive
4	Siddu k	4070	52	M	+	+	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	10.3	5100	68	30	1	1	0	386	8.5	NH	-	-	86	23	0.7	0.7	37	40	90	6.9	Reactive
5	Chandrashaker	4798	38	M	+	+	+	-	-	-	-	-	-	+	-	-	+	-	-	-	-	-	-	14.5	31000	74	19	1	1	0	322	5.4	NN	-	-	70	53	0.9	5.1	200	305	110	6.1	Reactive
6	Narsing	12224	37	M	+	-	-	+	-	-	+	+	-	-	+	-	-	+	-	-	-	-	-	13	2000	75	21	2	2	0	121	1	NN	+	-	80	40	2.2	2	25	35	80	5.8	Reactive
7	Basangouda	16041	60	M	+	+	-	-	+	-	-	-	+	+	-	-	-	-	-	-	-	H	-	8	4000	43	45	6	2	1	234	2.5	NH	-	+	90	35	1.5	3.5	230	310	150	6	Reactive
8	Shantabai	16205	40	F	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	9.9	9000	60	34	4	2	0	136	3	MH	-	-	110	27	1.8	2.1	39	40	100	6.2	Reactive
9	Sharda	16319	35	F	+	+	-	+	-	-	-	-	+	-	-	-	+	-	-	-	-	-	-	7.5	8500	82	16	2	0	0	131	2.7	NH	-	-	75	60	2.5	1.9	40	41	80	6	Reactive
10	Sangappa	16319	41	M	+	+	-	-	+	+	+	-	+	+	-	-	-	+	+	NR	Crep	-	-	10.2	3000	70	22	6	1	1	112	3.7	DM	-	+	105	37	2	4.5	300	150	100	6.5	Reactive
11	Ranjana	17138	32	F	+	-	+	+	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	11	4900	62	34	4	0	0	377	0.9	NH	+	-	99	45	2.2	0.7	25	30	105	5.9	Reactive
12	Tarubai	2467	38	F	+	+	-	-	-	-	+	+	+	-	-	-	-	+	-	-	-	-	-	9.3	5300	49	48	2	1	0	411	1.7	DM	-	-	120	40	1.7	1.2	50	45	80	6	Reactive
13	Mahesh	17147	38	M	+	+	-	-	+	+	+	-	+	-	-	-	+	-	-	NR	-	-	-	10	2500	60	35	4	1	0	149	1.5	NH	-	+	88	20	1.4	1.7	42	39	40	6.1	Reactive
14	Parasappa	17770	36	M	+	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	BS	HS	-	14.1	6000	52	40	8	0	0	432	2.1	NN	-	-	100	30	0.8	3.5	120	105	90	5	Reactive
15	Suresh	17777	34	M	+	-	+	+	-	+	+	+	-	-	-	-	-	-	-	-	-	-	-	13	6900	72	26	4	0	0	174	3	NN	-	-	92	55	2.8	1.3	25	30	80	5.9	Reactive
16	Suvarna	16681	35	F	+	+	+	-	-	-	-	-	+	+	-	-	-	-	-	-	-	H	-	7	3000	82	16	2	0	0	49	3.1	DM	-	+	110	29	1.8	4	390	275	150	6.1	Reactive
17	Sunil	18536	42	M	+	-	-	-	-	-	+	+	-	-	+	-	+	-	-	-	-	-	-	13.7	5000	49	45	6	0	0	154	2.7	NN	-	-	220	33	1.9	1.9	39	20	105	6	Reactive
18	Sangeeta	18788	41	F	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	10	4200	58	39	3	0	0	199	1.1	NH	+	-	69	60	3.1	0.7	18	20	112	6.1	Reactive
19	Bashasah	18536	45	M	+	+	-	-	-	+	+	+	+	+	-	-	+	+	-	-	BS	-	-	11	6000	78	20	2	0	0	444	3.5	NN	-	-	78	31	1.3	3.9	205	197	130	5.9	Reactive
20	Ahmed	18512	34	M	+	+	+	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	12.9	2600	69	22	7	1	0	150	0.8	NN	-	+	105	34	1	1	37	20	84	6.8	Reactive
21	Jagadish	18744	28	M	+	+	+	+	+	-	-	+	-	+	-	-	-	-	-	-	-	-	-	14.1	7000	45	49	1	3	0	197	1.9	NN	-	-	131	29	1.1	3	405	391	190	5.7	Reactive
22	Imran	18681	29	M	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	NR	-	-	-	6.2	3600	65	29	6	0	0	290	1.2	MH	+	+	150	58	2.7	1.8	42	27	74	6.4	Reactive
23	Balappa	17928	55	M	+	+	-	-	-	+	+	-	+	+	-	-	-	-	-	-	-	-	-	8.7	5500	52	40	6	2	0	412	1.4	MH	+	-	295	22	1.6	4.4	301	295	137	6.2	Reactive
24	Mahadevi	2119	32	F	+	-	+	-	-	+	+	-	+	-	-	-	+	-	-	-	BS	-	-	9.8	6200	62	36	2	0	0	501	2.8	DM	-	-	160	40	1.8	0.8	48	20	68	6.2	Reactive
25	pooja	19179	21	F	+	-	-	+	-	-	+	+	+	+	-	+	-	-	+	-	-	H	-	10.5	3100	84	15	1	0	0	81	3.1	MH	-	+	90	59	2.9	6.1	800	625	311	5.2	Reactive
26	Prakash	18652	32	M	+	-	-	-	+	-	+	-	-	-	-	+	-	-	-	-	-	-	-	13.1	5600	50	40	3	1	1	390	2.5	NN	-	-	109	23	1	0.9	21	18	105	6.3	Reactive
27	Dareppa	19490	40	M	+	+	-	-	+	+	+	-	+	+	-	-	-	+	-	NR	Crep	-	-	7.9	3000	73	20	6	0	0	176	0.7	MH	+	+	89	31	1.1	4.1	560	497	300	5.1	Reactive
28	Jakiya	19455	40	F	+	-	-	-	-	+	+	-	-	-	+	-	-	-	-	-	-	-	-	14	5700	49	40	8	2	0	351	1.9	NN	-	-	131	55	2.5	3.5	217	320	125	6	Reactive
29	Shivanand	19443	45	M	+	+	+	+	-	-	-	-	-	+	-	-	-	-	-	-	-	HS	-	13.1	2700	72	25	3	0	0	106	2.1	NN	-	+	111	21	1.1	0.9	21	30	90	6.5	Reactive
30	Ramakka	20034	35	F	+	-	+	+	-	-	-	+	+	-	-	-	+	+	+	-	-	-	-	10.1	6100	81	17	2	0	0	147	3	MH	-	-	71	20	1	1.1	27	28	44	5.1	Reactive
31	Basappa	18878	50	M	+	+	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	14	5500	45	45	3	1	0	238	2.5	NN	-	-	210	17	0.9	0.7	27	22	70	6.4	Reactive
32	Parvati	20240	40	F	+	+	-	-	+	+	+	+	-	-	+	-	-	-	+	-	BS	-	-	13.7	3100	58	38	4	0	0	125	1.9	NN	-	+	120	25	1.1	1.3	28	30	45	6.1	Reactive
33	Parvati B	20248	35	F	+	+	-	-	+	-	+	-	+	-	-	-	+	+	-	-	-	-	-	9.1	6900	50	40	6	2	1	380	2.1	MH	-	-	69	19	0.7	0.9	30	31	70	5.9	Reactive
34	Mallanagouda	19742	41	M	+	-	+	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	13.9	4100	35	49	5	1	0	475	3.9	NN	-	-	105	25	1	3.9	331	401	130	5.7	Reactive
35	Sahabgouda	20531	30	M	+	+	-	+	+	-	-	+	-	-	-	-	-	+	-	-	-	-	-	14	5500	58	35	6	1	0	223	2.7	NN	-	-	91	30	1.1	0.9	25	31	79	6.5	Reactive
36	Ramappa	20897	40	M	+	+	-	-	-	-	-	-	+	-	-	-	-	-	-	NR	-	-	-	10.5	6900	77	19	4	0	0	193	1.7	NN	-	-	230	27	1.2	1.5	31	34	75	6.2	Reactive
37	Kashibai	20781	55	F	+	+	-	-	-	-	-	+	+	+	-	-	-	-	+	-	-	H	-	9.3	4200	50	45	5	0	0	257	0.9	DM	+	-	84	30	1.1	4.3	409	511	170	5.8	Reactive
38	Hanamawwa	21290	30	F	+	-	+	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	16	6000	47	50	3	0	0	495	1.9	NN	-	-	120	18	0.9	0.9	22	25	44	6.7	Reactive
39	Gadageppa	21216	40	M	+	+	+	-	+	-	-	-	+	-	+	-	-	-	-	-	-	HS	-	8.2	4600	50	40	2	1	0	338	2.7	DM	-	-	79	60	2.4	1.7	39	40	100	6.1	Reactive
40	Chandrashaker	23565	45	M	+	-	-	+	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	14	5500	51	42	5	2	0	314	3.9	NN	-	-	107	19	0.5	1.9	33	37	55	6.8	Reactive
41	Shantappa	21913	33	M	+	-	-	+	-	+	+	-	-	-	-	-	+	-	+	-	Crep	-	-	12.7	12000	72	25	3	0	0	136	1.9	NN	-	-	111	27	0.9	0.9	27	30	97	6.3	Reactive

42	Duragappa	21914	25	M	+	+	-	+	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	10.1	3800	78	21	1	0	0	110	1.2	DM	+	+	200	31	1.1	2.9	130	127	110	6.1	Reactive
43	Parvatayya	22059	46	M	+	-	-	-	-	+	+	-	+	-	-	-	-	-	-	-	-	H	-	8	7000	45	45	3	1	0	222	2.1	NH	-	-	97	26	0.7	1	28	31	90	6.3	Reactive
44	Shivappa	22000	45	M	+	-	+	-	+	+	-	+	-	-	-	-	+	-	-	NR	BS	-	-	13.1	12500	65	30	4	1	0	115	3.1	NN	-	-	83	39	1.1	1.3	37	40	77	6.1	Reactive
45	Kadappa	23545	35	M	+	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	12	7000	72	25	3	0	0	108	2.9	NN	-	-	108	40	1.7	1.6	44	50	90	6.3	Reactive
46	Durgappa	25631	45	M	+	+	-	-	-	+	-	+	+	+	-	-	-	+	-	-	-	-	-	9.9	5000	55	43	2	0	0	267	2.6	NH	-	-	77	51	2.3	1.3	30	35	40	6.5	Reactive
47	Mallamma	24363	45	F	+	+	-	-	+	+	+	-	-	-	-	-	-	-	-	-	Crep	-	-	13	6000	71	26	3	0	0	106	1.9	NN	-	-	100	36	1.3	0.9	30	32	110	6.2	Reactive
48	Sangappa	25687	33	M	+	+	-	-	-	-	+	+	+	-	-	-	-	-	-	-	-	-	-	10.1	4100	55	42	2	1	0	231	1.3	NH	+	-	98	28	0.9	2.9	240	302	130	6.2	Reactive
49	Laxmibai	26143	33	F	+	-	-	-	-	+	+	-	-	+	-	-	-	-	-	-	-	H	-	14.1	5000	52	40	6	2	0	145	1.9	NN	-	-	79	31	1	1.7	28	35	90	7.1	Reactive
50	Rangamma	22682	35	F	+	+	-	-	-	-	+	-	+	+	-	-	-	+	-	-	-	-	-	6.7	2900	74	22	5	1	0	172	1.4	NH	+	+	104	60	2.7	4.6	309	411	160	5.9	Reactive
51	Suresh	25814	23	M	+	+	-	-	+	+	+	+	+	-	-	-	+	-	-	-	-	-	-	7.5	3100	88	10	2	0	0	81	1.1	DM	+	+	109	27	1.1	3.9	300	395	200	5.1	Reactive
52	Dodawwa	24208	35	F	+	+	+	-	-	-	+	-	+	-	-	-	-	+	-	NR	-	-	-	10.1	6000	60	30	5	1	0	234	2.3	NH	-	-	130	35	1.3	0.9	35	40	60	6.9	Reactive
53	Sandeep	5094	28	M	+	+	-	+	-	-	+	-	-	-	-	-	-	-	+	-	-	-	-	13.7	6200	65	25	6	3	0	222	0.8	NN	+	-	78	90	2.6	1.3	35	27	40	7.3	Reactive
54	Hanamawwa	21290	30	F	+	-	-	-	-	-	-	+	+	-	+	-	-	-	-	-	-	-	-	11	5000	60	35	4	1	0	687	1.9	NN	-	-	99	28	0.9	1.9	40	44	90	7.1	Reactive
55	Sharanappa	26342	36	M	+	-	-	-	+	-	-	-	-	-	-	-	-	+	-	-	-	HS	-	13.9	6200	55	40	1	4	0	436	2.1	NN	-	-	107	37	1.1	0.9	25	30	51	7.5	Reactive
56	Hinagappa	27048	55	M	+	+	-	+	-	-	+	-	+	+	-	-	-	+	-	-	Crep	-	-	8	2100	82	16	2	0	0	34	3.9	NN	-	+	120	45	1.5	4.1	500	670	310	7.3	Reactive
57	Bhimashi	11927	43	M	+	+	+	-	-	+	+	-	+	-	-	-	-	-	-	-	BS	-	-	6.2	3200	73	20	5	1	1	175	3.1	DM	-	+	112	37	1.2	0.9	21	30	50	8	Reactive
58	Siddappa	108277	28	M	+	-	-	-	-	-	-	-	-	-	+	-	-	-	+	-	-	-	-	8.8	2400	55	40	4	1	0	125	2.5	NH	-	-	89	30	1.4	1.3	40	50	41	7.5	Reactive
59	Renuka	3911	30	F	+	+	+	+	+	-	-	+	-	-	-	+	-	-	NR	-	H	-	13	1800	47	45	6	2	0	262	3.1	NN	-	-	170	31	1.5	1.2	31	39	52	7.2	Reactive
60	Sanganna	27061	35	M	+	+	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	14.1	8000	60	35	4	1	0	295	0.9	NN	+	+	130	40	1.8	1.8	40	45	61	8	Reactive
61	Ankush	27033	38	M	+	-	+	+	-	+	-	-	+	+	-	-	-	-	-	-	Crep	S	-	10.1	4500	55	40	4	1	0	176	3.1	NN	-	-	99	28	1.1	5	800	1100	300	7.5	Reactive
62	Mallikarjuna	26352	38	M	+	+	-	-	+	+	-	+	+	-	-	-	+	-	-	-	-	-	-	9.7	3500	82	17	1	0	0	101	2.1	NH	-	-	106	21	1	1.3	31	42	51	7.9	Reactive
63	Gouramma	532	48	F	+	+	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	13.9	2100	80	18	2	0	0	49	3.9	NN	-	+	109	35	1.3	1.9	40	45	90	7.2	Reactive
64	Roopa	7675	45	F	+	-	-	+	-	+	-	-	+	+	-	-	-	-	+	-	BS	H	-	10.2	6000	60	35	4	1	0	234	2.5	NN	-	-	150	82	2.9	3.5	800	650	160	5.1	Reactive
65	Neelawwa	26472	35	F	+	+	-	-	-	+	+	+	-	-	-	-	-	+	-	-	-	-	-	12	1500	78	18	4	0	0	86	0.3	NN	+	+	171	28	1.1	0.7	27	25	49	8.1	Reactive
66	Ramesh	27039	28	M	+	-	+	-	+	-	+	-	+	-	-	-	+	-	-	-	-	-	-	8	5100	75	20	4	1	0	96	1.9	NN	-	-	110	40	2	1.5	40	49	90	8.2	Reactive
67	Adappa	26851	40	M	+	+	-	-	+	+	-	-	+	+	-	-	-	-	+	-	-	HS	-	9	3000	82	16	2	0	0	61	3.9	NN	-	+	137	35	1.5	3.1	600	710	210	5.1	Reactive
68	Dadapa	26659	47	M	+	-	-	+	-	+	+	-	-	+	+	-	-	-	-	-	-	-	-	14.1	5000	55	40	5	0	0	229	2.9	NN	-	-	211	38	1.3	0.9	52	61	115	8.3	Reactive
69	Basavaraj	27667	45	M	+	+	-	-	+	+	+	-	+	-	-	-	-	+	-	-	-	-	-	4.1	1800	83	14	3	0	0	87	4.7	DM	-	+	128	40	1.9	2	29	32	60	8.1	Reactive
70	Ramesh	27724	38	M	+	-	-	-	-	+	-	-	+	-	-	-	-	-	-	-	-	-	-	8.6	6000	70	25	5	0	0	125	1.9	MA	-	-	180	38	1.4	2	48	50	51	8	Reactive
71	Mallikarjuna	27433	53	M	+	+	-	-	-	-	-	+	+	-	-	-	-	-	-	NR	-	S	-	6.5	3500	87	12	1	0	0	81	0.9	MA	+	+	131	95	3.1	1.9	31	42	50	8.1	Reactive
72	Channu	28490	40	M	+	+	-	-	-	+	+	-	-	-	-	-	-	-	-	-	Crep	-	-	13.7	3000	65	25	7	2	0	82	4.1	NN	-	+	99	40	1.9	2	28	27	50	8.1	Reactive
73	Ashok	27961	45	M	+	+	-	-	-	+	+	-	+	+	-	-	-	+	-	-	-	-	-	11	2800	53	40	6	0	0	107	4.5	NN	-	+	195	40	1.9	4.2	950	1000	200	5.4	Reactive
74	Eranna	28181	38	M	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	10.1	8000	50	40	6	1	0	205	1.9	DM	-	-	200	35	1.3	2	40	37	77	6.3	Reactive
75	Shivappa	28692	60	M	+	+	+	+	+	+	-	+	+	-	-	-	-	-	-	NR	BS	HS	-	8.6	5000	67	25	6	1	0	258	0.81	NH	+	-	110	41	1.9	2	50	47	61	6.8	Reactive
76	Anand	23556	42	M	+	+	-	+	+	-	+	-	-	+	-	-	-	-	-	NR	-	-	-	14.7	5600	50	43	6	1	0	501	3.9	NN	-	-	96	22	0.9	0.8	25	30	66	6.1	Reactive
77	Hanamant	25537	45	M	+	-	+	+	+	+	+	-	+	-	-	-	-	-	-	-	Crep	-	-	8.7	6100	55	43	2	0	0	247	2.8	NH	-	-	110	31	1.1	2	40	51	90	6.2	Reactive
78	Bapugouda	25279	25	M	+	+	-	-	-	+	+	-	+	-	-	-	-	+	-	-	-	-	-	9.1	4800	68	28	4	0	0	170	2	DM	-	-	120	59	2.9	1.3	35	40	66	6.4	Reactive
79	Pandu	27954	35	M	+	+	-	-	-	-	-	+	-	+	-	-	-	+	-	-	-	S	-	10.5	3010	72	25	3	0	0	171	1.1	NH	+	+	99	31	0.9	1.8	33	35	70	7.1	Reactive
80	Ramappa	24000	39	M	+	-	+	-	-	+	+	+	-	-	-	-	+	-	-	-	-	-	-	13.1	6500	47	45	6	1	0	420	2.7	NN	-	-	85	25	0.9	0.9	25	27	65	7.4	Reactive
81	Ramanna	23923	40	M	+	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	14	7000	40	50	8	2	0	205	3.1	NN	-	-	109	30	1.1	1.2	33	38	90	8.1	Reactive
82	Yallappa	25377	65	M	+	+	-	-	+	+	+	-	+	-	+	-	-	+	+	-	BS	H	-	9.1	8000	50	45	5	0	0	224	2.7	NH	-	-	130	40	1.6	1.7	35	39	88	7	Reactive
83	Sattewwa	27796	30	F	+	-	-	-	+	-	+	-	+	+	-	-	-	-	-	-	-	-	-	13.8	2100	65	35	0	0	0	95	2.1	NN	-	+	175	39	1.4	0.9	25	29	60	6.5	Reactive
84	Ragavendra	21939	68	M	+	+	-	+	-	-	+	+	+	-	-	-	+	-	+	-	-	-	-	14.6	5500	55	40	5	0	0	700	3	NN	-	-	151	70	3.1	2	40	41	100	6.1	Reactive
85	Ningamma	21418	30	F	+	+	-	+	+	+	-	-	+	-	-	-	-	+	-	-	-	-	-	13.8	4000	58	40	2	0	0	172	2.7	NN	-	-	99	25	0.7	0.9	30	35	68	6.9	Reactive
86	Shantappa	14312	30	M	+	-	+	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	10	5100	49	40	8	2	0	169	0.9	NN	+	-	150	35	0.9	1.8	35	40	55	7.2	Reactive
87	Gourabai	28468	55	F	+	+	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	10.1	4100	63	25	8	2	1	120	1.7	NH	-	-	98	21	0.8	0.9	25	27	47	6.8	Reactive
88	Sharanappa	23967	55	M	+	+	+	-	-	-	-	+	+	+	-	-	-	+	-	-	Crep	-	-	9.8	5500	67	27	5	1	0	104	2	DM	-	-	141	95	3.9	3.5	200	250	130	5.9	Reactive

89	Jayashree	29887	45	F	+	-	-	+	-	+	-	-	-	-	-	-	-	-	-	BS	-	-	13.7	2000	50	45	4	1	0	196	3.1	NN	-	+	170	21	0.9	1.4	27	30	50	6.8	Reactive
90	Parvati	27813	30	F	+	+	-	-	+	+	-	-	+	+	-	-	-	-	-	-	-	-	6.3	5000	67	28	5	0	0	223	2.5	NH	-	-	105	30	1.1	4.1	350	400	150	5.5	Reactive
91	Ashok	27961	45	M	+	+	-	-	-	-	-	-	+	-	-	-	-	+	-	-	-	-	8.7	3100	63	35	2	0	0	174	0.7	DM	+	+	113	25	0.9	0.9	27	30	115	6.3	Reactive
92	Shivappa	28692	60	M	+	-	+	-	+	-	+	+	+	-	-	-	-	-	-	-	-	-	14.1	6000	60	35	4	1	0	297	2.1	NN	-	-	85	31	1.2	1.3	31	35	45	7	Reactive
93	Tukaram	30300	30	M	+	+	-	+	-	-	+	-	-	-	-	-	-	-	-	-	-	-	13.7	5100	50	40	7	3	0	221	0.9	NN	+	-	120	40	1.8	1.5	25	30	47	7.3	Reactive
94	Ambreesh	392	21	M	+	-	-	-	-	+	-	+	-	-	+	-	-	+	+	-	Crep	-	-	15	6000	49	45	5	0	0	210	1.9	NN	-	-	105	31	1.1	0.9	31	37	50	6.8	Reactive
95	Vijaykumar	712	38	M	+	+	+	+	+	-	-	-	+	-	-	-	-	-	-	-	-	-	7.1	31100	70	22	6	1	0	136	2	NH	-	+	112	40	1.9	1.8	40	42	100	7	Reactive
96	Renuka	4754	30	F	+	-	+	-	-	+	+	+	+	-	-	-	-	-	-	-	BS	-	-	8.9	11000	65	30	4	1	0	108	1.9	MA	-	-	170	39	1.7	2.1	50	45	99	5.9	Reactive
97	Mahadevi	3544	22	F	+	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	14	6000	50	40	8	1	0	390	3.8	NN	-	-	99	27	1.1	0.8	27	30	41	7.8	Reactive
98	Laxmibai	5826	30	F	+	+	-	-	-	-	+	+	+	-	-	-	-	-	-	-	-	-	-	11	3800	65	25	8	2	0	156	1.8	NH	-	+	100	90	3.3	1.9	47	45	70	6.3	Reactive
99	Vilas	4653	23	M	+	-	-	+	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	10.3	12600	55	43	2	0	0	351	0.7	NN	+	-	105	27	0.9	1.1	37	40	78	6.9	Reactive
100	kashinath	4918	45	F	+	+	+	+	-	-	-	-	+	+	+	-	-	-	-	-	-	-	-	7.1	2300	57	40	3	0	0	95	2.3	DM	-	+	89	30	1.3	4.9	300	350	200	5.6	Reactive
101	Nagamma	12228	42	F	+	+	-	-	+	+	+	-	+	+	-	-	-	+	+	NR	Crep	-	-	9.2	3100	62	33	3	1	1	112	3.7	DM	-	+	105	37	2	4.5	300	150	100	6.5	Reactive
102	Kallappa	16232	42	M	+	+	-	+	-	-	+	-	-	-	-	-	-	+	-	-	-	-	-	13.7	6100	33	25	10	1	0	232	0.8	NN	+	-	72	90	2.6	1.3	35	27	40	7.3	Reactive
103	Chandrashaker	18054	40	M	+	+	-	-	-	+	+	-	+	+	-	-	-	+	-	-	-	-	-	11	3000	27	43	6	1	0	107	4.5	NN	-	+	195	40	1.9	4.2	950	1000	200	5.4	Reactive
104	Basappa	18878	55	M	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	10.1	8500	50	40	1	1	0	204	1.9	DM	-	-	200	35	1.3	2	40	37	77	6.3	Reactive
105	Gous	19674	30	M	+	+	+	-	-	-	-	+	+	+	-	-	-	+	-	-	Crep	-	-	9.8	5500	67	27	5	1	0	112	2	DM	-	-	141	95	3.9	3.5	200	250	130	5.9	Reactive
106	Rangamma	22682	35	F	+	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	BS	-	-	13.7	2000	55	40	4	1	0	196	3.1	NN	-	+	170	21	0.9	1.4	27	30	50	6.8	Reactive
107	Jayashree	24150	25	F	+	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	13.9	2100	80	18	2	0	0	52	3.9	NN	-	+	109	35	1.3	1.9	40	45	90	7.2	Reactive
108	Surya	24219	30	M	+	-	-	+	-	+	-	-	+	+	-	-	-	-	+	-	BS	H	-	10.2	6000	70	25	4	1	0	234	2.5	NN	-	-	150	82	2.9	3.5	800	650	160	5.1	Reactive
109	Mahadevi	21471	48	M	+	+	-	-	-	+	+	+	-	-	-	-	+	-	-	-	-	-	-	12	1700	78	18	4	0	0	94	0.3	NN	+	+	171	28	1.1	0.7	27	25	49	8.1	Reactive
110	Dodawwa	24208	35	F	+	+	-	-	+	-	+	+	+	-	-	-	-	+	-	NR	-	-	-	9.2	3500	55	37	8	0	0	384	2.1	DM	-	-	94	26	0.7	0.8	18	20	112	6	Reactive
111	Mahadevi	1054	36	F	+	+	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	10.3	5100	68	30	1	1	0	386	8.5	NH	-	-	86	23	0.7	0.7	37	40	90	6.9	Reactive
112	Mallanna	24623	66	M	+	+	+	-	-	-	-	-	-	+	-	-	+	-	-	-	-	-	-	14.5	29000	74	19	1	1	0	322	5.4	NN	-	-	70	53	0.9	5.1	200	305	110	6.1	Reactive
113	Parvati	27727	35	F	+	-	-	+	-	-	+	+	-	-	+	-	-	+	-	-	-	-	-	13	2500	75	21	2	2	0	121	1	NN	+	-	80	40	2.2	2	25	35	80	5.8	Reactive
114	Anand	23556	42	F	+	+	-	-	+	-	-	-	+	+	-	-	-	-	-	-	-	H	-	8	4000	53	35	6	2	1	234	2.5	NH	-	+	90	35	1.5	3.5	230	310	150	6	Reactive
115	Siddayya	26247	35	M	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	9.9	9500	60	34	4	2	0	132	3	MH	-	-	11	27	1.8	2.1	39	40	100	6.2	Reactive
116	Shanker	27628	37	M	+	+	-	+	-	-	-	-	+	-	-	-	+	-	-	-	-	-	-	7.5	8500	72	26	2	0	0	131	2.7	NH	-	-	75	60	2.5	1.9	40	41	80	6	Reactive
117	Mahaveer	28263	40	M	+	+	-	-	+	+	+	-	+	+	-	-	-	+	+	NR	Crep	-	-	10.2	3200	70	22	6	1	1	115	3.7	DM	-	+	10	37	2	4.5	300	150	100	6.5	Reactive
118	Irrappa	29149	44	M	+	-	+	+	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	11	4900	70	26	4	0	0	377	0.9	NH	+	-	99	45	2.2	0.7	25	30	105	5.9	Reactive
119	Basappa	29139	45	M	+	+	-	-	-	-	+	+	+	-	-	-	+	-	-	-	-	-	-	9.3	5300	49	48	2	1	0	402	1.7	DM	-	-	120	40	1.7	1.2	50	45	80	6	Reactive
120	Ashok	29505	30	M	+	+	+	-	-	-	-	+	+	+	-	-	-	+	-	-	Crep	-	-	9.8	5500	67	27	5	1	0	99	2	DM	-	-	141	95	3.9	3.5	200	250	130	5.9	Reactive