“STUDY OF CARDIAC MANIFESTATIONS IN PATIENTS OF HIV INFECTION - A ONE YEAR CROSS SECTIONAL STUDY AT KLES DR PRABHAKAR KORE HOSPITAL, BELGAUM”

REG NO. BG0112009

Dissertation

Submitted to the
KLE University, Belgaum, Karnataka

In Partial Fulfillment
of the requirements for the degree of

M. D.
in
GENERAL MEDICINE

DEPARTMENT OF MEDICINE,
JAWAHARLAL NEHRU MEDICAL COLLEGE,
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ENDORSEMENT

This is to certify that the dissertation entitled **"STUDY OF CARDIAC MANIFESTATIONS IN PATIENTS OF HIV INFECTION - A ONE YEAR CROSS SECTIONAL STUDY AT KLES DR PRABHAKAR KORE HOSPITAL, BELGAUM"** is a bonafide research work done by **CANDIDATE REG NO. BG0112009**.

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LIST OF ABBREVIATIONS USED

%	-	Percentage
µ	-	Micro
3TC	-	Lamivudine
AIDS	-	Acquired Immunodeficiency Syndrome
ART	-	Antiretroviral therapy
ARV	-	Antiretroviral
AZT	-	Zidovudine
CAD	-	Coronary Artery Disease
cART	-	Combination antiretroviral therapy
CCR	-	Chemokine receptor
CDC	-	Centers for Disease Control
CI	-	Confidence interval
cm	-	Centimeter
CMV	-	Cytomegalovirus
CNS	-	Central nervous system
CRP	-	C-reactive protein
CVD	-	Cardiovascular disease
DF	-	Degree of freedom
DHSS	-	Department of Health and Human Services
DNA	-	Deoxyribonucleic acid
ECG	-	Electrocardiography
EFV	-	Efavirenz
EIA	-	Enzyme immunoassay
ELISA	-	Enzyme-linked immunosorbent assay

FDA	-	Food and Drug Administration
FTC	-	Emtricitabine
HAART	-	Highly active antiretroviral therapy
HIV	-	Human Immunodeficiency Virus
HSV	-	Herpes simplex virus
KS	-	Kaposi sarcoma
L	-	Liter
LDL	-	Low density lipoprotein
LV	-	Left ventricle
mg	-	Milligrams
mg/dL	-	Milligrams per deciliter
min	-	Minute
ml	-	Milliliter
mmHg	-	Millimeters of mercury
mmol	-	Millimoles
MPAP	-	Mean pulmonary artery pressure
MTCT	-	Mother-to-Child transmission
NACO	-	National AIDS Control Organization
NHL	-	Non-Hodgkin lymphoma
NIH	-	National Institutes of Health
NK	-	Natural killer
NNRTIs	-	Non-nucleoside reverse-transcriptase inhibitors
NRTIs	-	Nucleoside reverse transcriptase inhibitors
NVP	-	Nevirapine
OR	-	Odds ratio

PAH	-	Pulmonary arterial hypertension
PCR	-	Polymerase chain reaction
PH	-	Pulmonary hypertension
PI	-	Protease inhibitor
PLHA	-	Person living with HIV and AIDS
POC	-	Point of care
RNA	-	Ribonucleic acid
SAT	-	Subcutaneous abdominal adipose tissue
SC	-	Subcutaneous
SD	-	Standard deviation
STD	-	Sexually transmitted disease
TB	-	Tuberculosis
TC	-	Total count
TDF	-	Tenofovir
TNF	-	Tumor necrosis factor
U.S.	-	United States
UNAIDS	-	United Nations Programme on HIV and AIDS
USPSTF	-	United States Preventive Services Task Force
VAT	-	Visceral adipose tissue
vs	-	Versus
WHO	-	World Health Organization
µg/min	-	Microgram per minute
µU/L	-	Microunit per litre

ABSTRACT

Background and objectives

The advances in diagnosis, treatment, monitoring of HIV infection and the availability of antiretroviral drugs have lead to improved survival of patients but this has resulted in manifestations of late stage disease including cardiac manifestations. This study was intended to find out the cardiac manifestations in HIV patients and to correlate them with CD4 count.

Methodology

This one year study was done from January 2013 to December 2014 in the Department of Medicine of a tertiary care centre in North Karnataka. Prior to the commencement, ethical clearance was obtained. A total of 100 consecutive patients presenting HIV infection with or without opportunistic infections were studied. Patients were subjected to complete blood count and lipid profile. Cardiac manifestations were assessed by electrocardiography and 2D echocardiography.

Results

Majority of the patients were males (76%) and the commonest age group was 31 to 40 years (36%). The CD4 count was found to be <50/cum in 43% of the patients. Cardiac manifestations were present in 57% of the patients. Sinus tachycardia was the commonest cardiac manifestation observed on ECG (25%). The other prominent cardiac manifestations included dilated cardiomyopathy (18%) and pericardial effusion (15%). The diastolic and systolic dysfunction was noted in 8% and pulmonary arterial hypertension in 3%. Few patients had

valvular heart disease and pulmonary embolism (2% each). Cardiac manifestations were significantly high in patients with CD4 count <50/cum (74.42%; p=0.002).

Conclusion and interpretation

Patients with HIV infection are at higher risk of developing cardiac manifestations and reduced CD4 count poses maximum risk.

Keywords

Acquired Immunodeficiency Syndrome; Cardiac manifestations; Human immunodeficiency virus;

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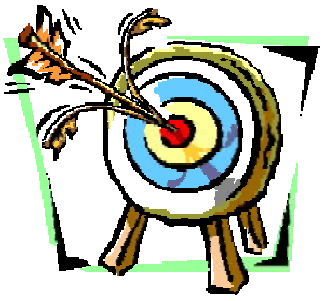

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INTRODUCTION

Acquired immunodeficiency syndrome (AIDS), resulting from human immunodeficiency virus (HIV) infection, was first recognized in 1981 when a common pattern of symptoms was observed among a small number of homosexual men in the United States of America (USA). Disease was soon reported in other groups, including intravenous drug users, haemophiliacs,[1] blood transfusion recipients female sexual partners of men with AIDS, infants born to mother with AIDS. At present HIV, infection is a global pandemic with cases reported from every country and presents serious public health problem in the developing countries, especially in India.[2]

HIV has claimed more than 36 million lives so far. There were approximately 35.3 [32.2–38.8] million people living with HIV in 2012. Sub-Saharan Africa is the most affected region, with nearly one in every twenty adults living with HIV. Sixty nine per cent of all people living with HIV are living in this region.[3] According to the latest (2012) UNAIDS estimates, 12 countries account for more than 90% of people living with HIV and more than 90% of new HIV infections in Asia and the Pacific: Cambodia, China, India, Indonesia, Malaysia, Myanmar, Nepal, Pakistan, Papua New Guinea, the Philippines, Thailand and Viet Nam. There were an estimated 350,000 (220,000–550,000) new HIV infections in Asia and the Pacific in 2012. India is estimated to have around 1.16 Lakh annual new cases among adults. Total number PLHA is estimated to be around 21 Lakhs in 2011 showing a steady decline from 23.6 lakh in 2006. Average prevalence rate in India is

about 0.9 % and it accounts for 10% of global HIV burden and 65% of that in Southeast Asia.[4]

AIDS is characterized by acquired profound, irreversible immune suppression that predisposes the individual to multiple opportunistic infection, malignant neoplasm and a progressive dysfunction of multiple organ system. AIDS can take from two to fifteen years to develop depending on the individual.[5]

HIV can be suppressed by combination ART. ART does not cure HIV infection but controls viral replication within a person's body and allows an individual's immune system to strengthen and regain the capacity to fight with infections. However, its prolonged usage has brought with it some metabolic abnormalities which need evaluation.[6] Treatment with potent ART has transformed HIV infection from a rapidly fatal disease into chronic illness.

In Asia alone, more people than ever are accessing treatment that is 1.25 million in 2012. Under the 2010 World Health Organization (WHO) guidelines, overall treatment coverage is 51% [43-63%] in Asia and the Pacific: a 46% increase since 2009. AIDS-related deaths across the region have declined 18% since 2005 to an estimated 270,000 [190,000–360,000] in 2012. With the availability of a large armamentarium of ART drugs and recent advances in the diagnosis, treatment and monitoring of persons living with HIV and AIDS (PLHA), there has been visible improved survival of such patients.[5]

Due to the longer survival of PLHA, the manifestations of late stage HIV infection are now being met with more commonly than before, which includes HIV related cardiac diseases.[7] Although not fully recognized in the early days of HIV

epidemic, cardiac involvement has been reported with increasing frequency in recent years.[5] The prevalence of cardiac involvement in AIDS patients have been reported to range between 28% and 73%.[5] The cardiac diseases in HIV infections include pericardial effusion, left ventricular dysfunction, myocarditis, dilated cardio-myopathy, endocarditis, pulmonary hypertension, malignant neoplasm, coronary artery disease and drug related cardiotoxicity.[5]

Patients with HIV/AIDS and symptoms suggestive of cardiac disease represent a diagnostic and therapeutic challenge in clinical practice; An algorithmic, anatomic approach to diagnosis, localizing disease to the endocardium, myocardium and pericardium can be useful. An intimate knowledge of opportunistic infections affecting the heart, effects of HAART therapy and therapy for opportunistic infections on the heart is needed to be able to formulate a differential diagnosis. Effects of HAART therapy, especially protease inhibitors on lipid and glucose metabolism, and their influence on progression to premature vascular disease require consideration.

Considering the above facts the present study was planned to assess the various cardiac manifestations in patients with HIV infection and to correlate them with CD4 count.

OBJECTIVES

The objectives of the present study were;

1. To study various cardiac manifestations in patients with HIV infection.

2. To study the correlation of cardiac manifestations with CD4 count.

REVIEW OF LITERATURE

Human immunodeficiency virus

HIV belongs to the family of retroviridae and sub family of lentivirus. HIV is a blood-borne, sexually transmissible virus. The virus is typically transmitted via sexual contact (both heterosexual and male to male), shared intravenous drug users, and mother-to-child transmission (MTCT), which can occur during the birth process (Intrapartum/ Perinatally) or via breast milk. After 30 years of scrutiny there is no evidence that HIV is transmitted by casual contact or virus can be spread by insects such as mosquito bites.[5]

Two distinct species of HIV (HIV-1 and HIV-2) have been identified, and each is composed of multiple subtypes, or clades. All clades of HIV-1 tend to cause similar disease, but the global distribution of the clades differs.[5]

HIV I is divided into subtypes designated A thorough K (Collectively referred to as group M with subtypes designation A, B, C, D, F, G, H, I, K & 15 circulating recombinant forms).[5]

Subtype O shows 55 to 70% homology with subtype M.[5]

Another group of viruses labeled N for 'new' was reported in 1998.[5]

Subtype C viruses (of the M group) are most common form worldwide accounting for ≈ 50% of prevalent infections worldwide. Subtype N viruses are predominant viruses seen in USA, Canada, Western Europe, Australia and account of 12 to 13% of global infection.[5]

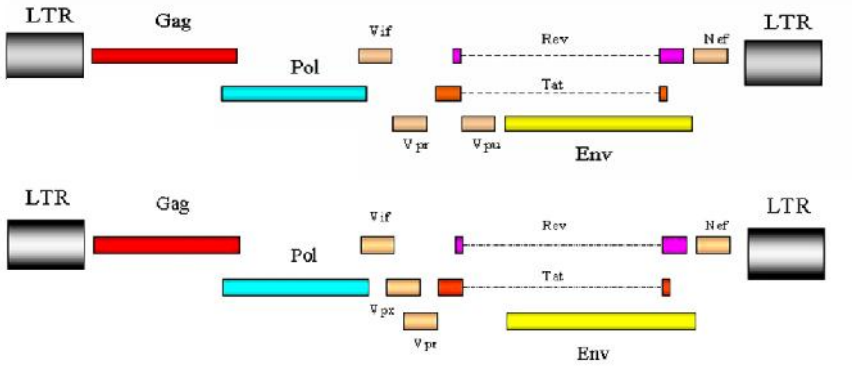


Figure 1. Genome layout of HIV–1 and HIV-2[9]

Various subtypes of HIV-1 have been found in specific geographic areas and in specific high-risk groups. A person can be coinfected with different subtypes. The following are HIV-1 subtypes and their geographic distributions:[9]

Subtype A: Central Africa, sub-Saharan Africa

Subtype B: South America, Brazil, United States, Thailand, Europe, Caribbean, India, Japan

Subtype C: Brazil, India, South Africa

Subtype D: Central Africa, sub-Saharan Africa

Subtype E: Thailand, Central African Republic, Southeast Asia

Subtype F: Brazil, Romania, Democratic Republic of Congo (Zaire)

Subtype G: Democratic Republic of Congo (Zaire), Gabon, Thailand, Russia, Central Africa

Subtype H: Democratic Republic of Congo (Zaire), Gabon, Russia, Central Africa

Subtype I: Cyprus

Subtype O: Cameroon, Gabon

HIV-2 is found primarily in West Africa. Compared with HIV I, HIV 2 infections are characterized by low viral loads, slow rates of clinical progression by low rates of transmission (vertically or sexually) and unique treatment recommendation due to intrinsic resistance to NNRTI's.[5]

Despite slow rates of progression mortality rates are similar when adjusted for viral load. There are no known subtypes of HIV-2.[5]

HIV 2 should be suspected in;[5]

- Patients of West African origin
- Patients having undetectable virus without therapy
- Patients epidemiologically linked to HIV infection
- In cases where HIV I Western blot is negative, indeterminate or atypical.

History

HIV-1 probably originated from one or more cross-species transferred from chimpanzees in central Africa.[10] HIV-2 is closely related to viruses that infect sooty mangabeys in western Africa.[11] Genetically, HIV-1 and HIV-2 are superficially similar, but each contains unique genes and its own distinct replication process.

Timeline of HIV

- *1959* - The first known case of HIV in a human occured in a person who died in Congo, and was later confirmed to have HIV infection from his preserved blood samples.[12] The authors of the study did not sequence a full virus from his samples, hence stated that "attempts to amplify HIV-1 fragments of >300 base pairs were unsuccessful ... However, after numerous

attempts, four shorter sequences were obtained"; these represented small portions of two of the six genes of the complete HIV genome.[13]

- June 28, in New York City, Ardouin Antonio, a 49-year-old Jamaican-American shipping clerk died of *Pneumocystis carinii* pneumonia, a disease closely associated with AIDS. Gordon Hennigar, who performed the postmortem examination of the man's body, found "the first reported instance of unassociated *Pneumocystis carinii* disease in an adult" to be so unusual that he preserved Ardouin's lungs for later study. The case was published in two medical journals at the time, and Hennigar has been quoted in numerous publications stating that he believed Ardouin probably had AIDS.[14]

- *1960s* – The HIV-2, a viral variant found in West Africa, was thought to have been transferred to people from sooty mangabey monkeys in Guinea-Bissau during that period.[14]

- *1964* - Jerome Horwitz of Barbara Ann Karmanos Cancer Institute and Wayne State University School of Medicine synthesized AZT under a grant from the US National Institutes of Health (NIH). AZT was originally intended as an anticancer drug.[14]

- *1966* - Genetic studies of the virus indicated that HIV first arrived in America, infecting one person in Haiti as many of the Haitians were working in Congo, providing the opportunity for infection.[14]

- *1968* - The disease spread from the 1966 American strand, but remained unrecognized for another 12 years.[14]

- *1969* - A St. Louis teenager, identified as Robert Rayford, died of an illness that baffles his doctors. Eighteen years later, molecular biologists at Tulane University in New Orleans test samples of his remains and find evidence of HIV.[14]

- *1975* - In the residents of Africa certain reports of wasting and other symptoms in patients were later seen who were later determined to have AIDS.[14]

- *1976* - Norwegian sailor Arvid Noe died and was later determined that he contracted HIV/AIDS in Africa during the early 1960s.[14]

- *1977* - Danish physician Grethe Rask died of AIDS contracted in Africa. A San Francisco prostitute gave birth to the first of three children who were later diagnosed to have AIDS. The children's blood was tested after their deaths and revealed an HIV infection. The mother died of AIDS in May 1987 and her test results showed HIV infection.[14]

- *1978* - A Portuguese man known as Senhor José dies; he was later confirmed as the first known person with HIV-2 infection. It is believed that he was exposed to the disease in Guinea-Bissau in 1966.[14]

- *1979* - An early case of AIDS in the United States was of a female baby born in New Jersey in 1973 or 1974. She was born to a sixteen-year-old girl, an identified drug-injector, who previously had multiple male sexual partners. The baby died in 1979 at the age of five. Subsequent testing on her stored tissues confirmed that she had contracted HIV-1.[14]

- *Gaetan Dugas* was a Canadian who worked for Air Canada as a flight attendant. In March 1984, a Centers for Disease Control and Prevention (CDC) study tracking the sexual liaisons and practices of gay, and bisexual men in California, New York, and some other states found Dugas to be the center of a network of sexual partners, and he was dubbed "patient zero".[15] After the study, mistaken assertions claimed he brought the HIV virus to the U.S., but Dugas was not the initial carrier of the infection to North America.

Epidemiology

Worldwide

According to recent World Health Organization statistics (WHO) HIV continues to be a major global public health issue, having claimed more than 36 million lives so far. There were approximately 35.3 [32.2–38.8] million people living with HIV in 2012. Sub-Saharan Africa is the most affected region, with nearly 1 in every 20 adults living with HIV.[3]

According to the latest (2012) UNAIDS estimates, 12 countries account for more than 90% of people living with HIV and more than 90% of new HIV infections in Asia and the Pacific: Cambodia, China, India, Indonesia, Malaysia, Myanmar, Nepal, Pakistan, Papua New Guinea, the Philippines, Thailand and Vietnam.[4]

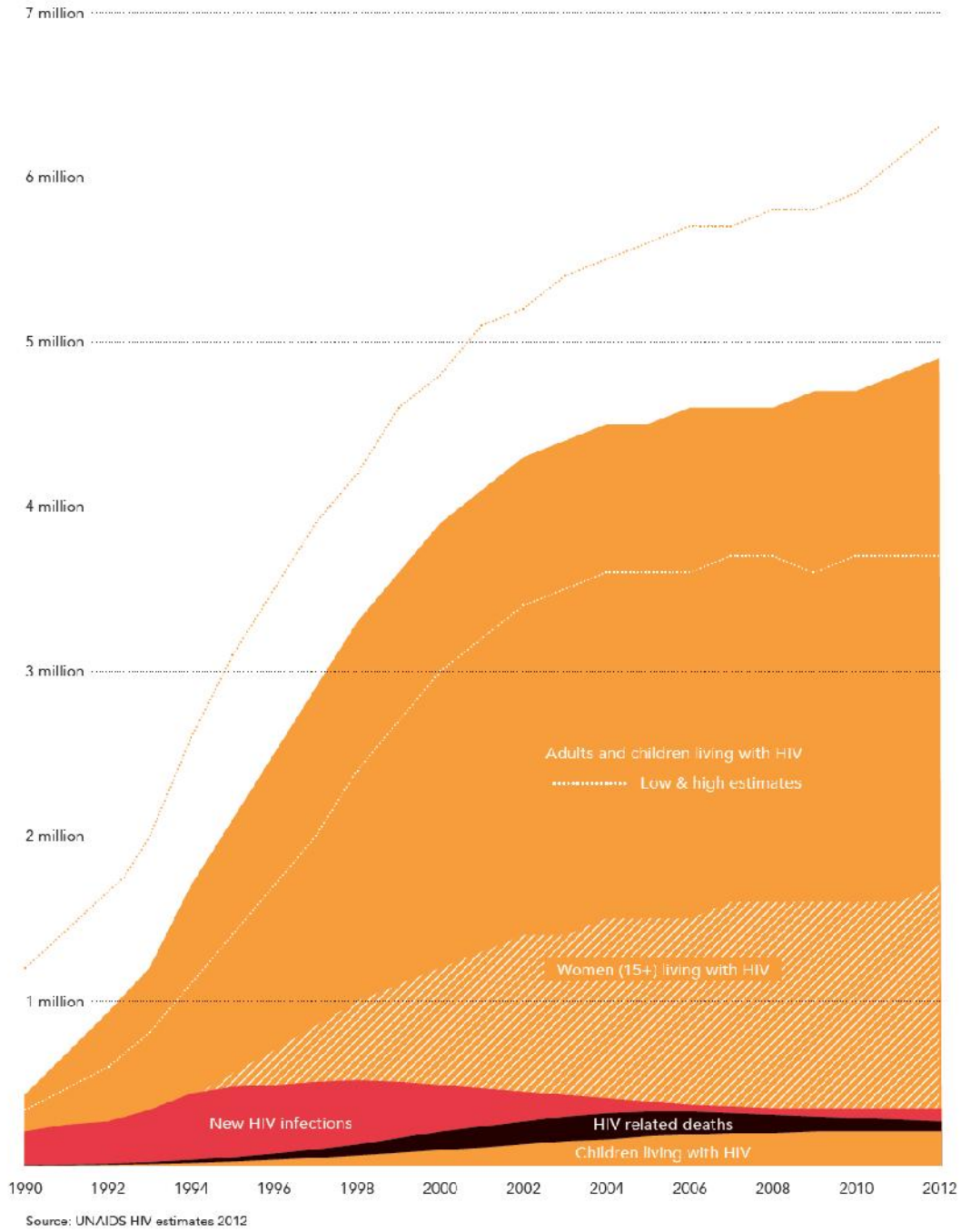


Figure 2. HIV in Asia and the Pacific, 1990 to 2012[4]

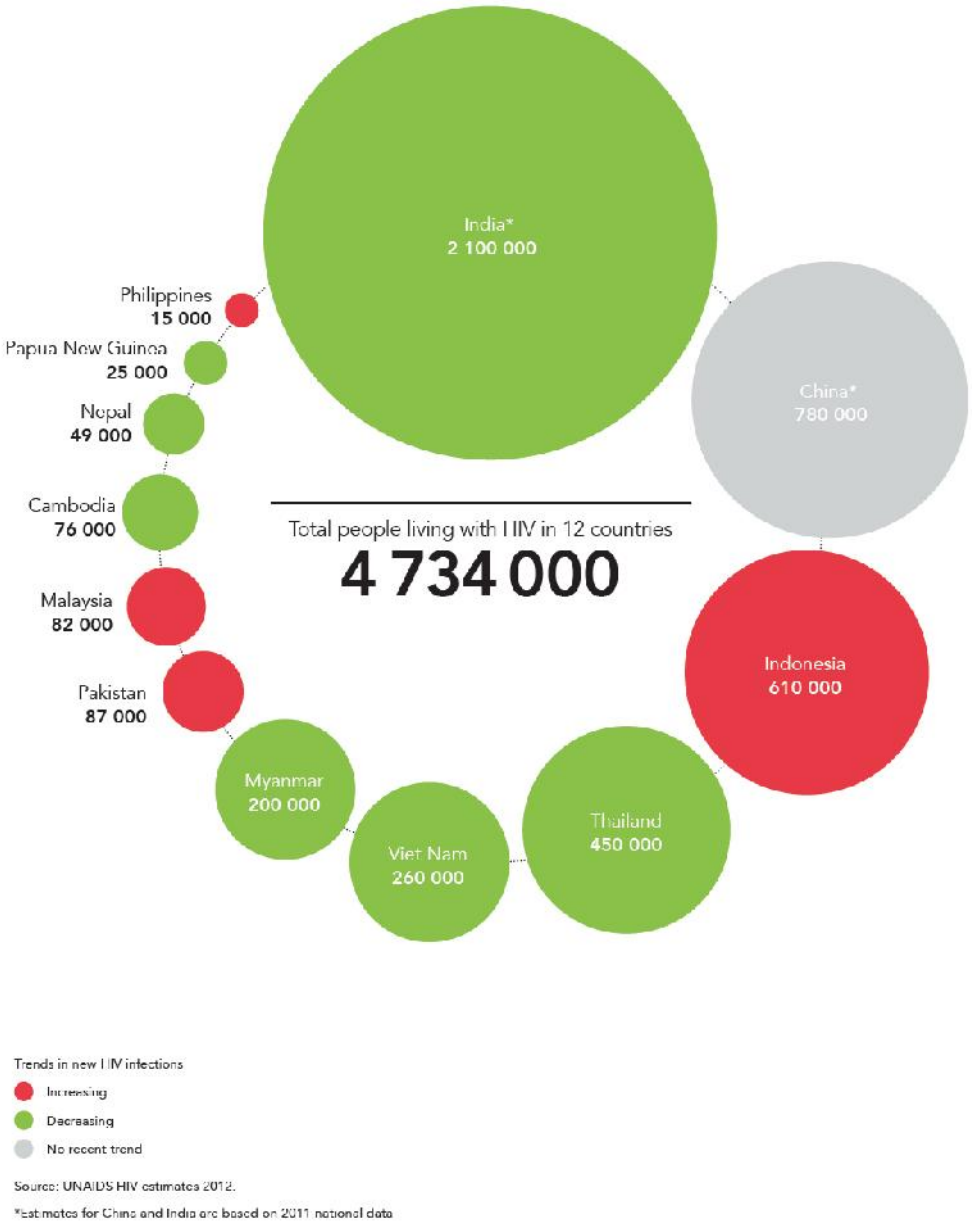


Figure 3. Twelve countries with highest HIV burden and new HIV infection trends[4]

The overall national prevalence of HIV in most countries in Asia and the Pacific remains low. However, the size of the regional population means low prevalence translates into large numbers of people living with HIV. Low national prevalence also masks higher HIV prevalence and incidence rates in certain geographical areas and among key populations at higher risk.[16]

There are significant variations in HIV epidemics between and within countries. New HIV infections are concentrated among key populations at higher risk, which include people who inject drugs, female and male sex workers and their clients, men who have sex with men and transgender people. Other vulnerable populations include migrants, prisoners, intimate partners of key populations at higher risk and people working in certain industries such as mining, construction, transport services.[16]

In 2012, there were an estimated 1.7 million [1.3–2.1 million] women living with HIV in Asia Pacific region. Women continue to account for about one third of people living with HIV, at 36% of the total, versus 35% in 2011.[4] There were 210,000 [180,000–280,000] children living with HIV in the region in 2012. New infections among children have declined by 28% to 23,000 [17,000– 34,000] since 2001.[4]

Racial, sexual, and age-related differences in incidence

In the United States, the rate of HIV infection is highest in blacks (83.7 cases per 100,000 population). The prevalence is also high among Hispanic persons (29.3 per 100,000 population). These increased rates are due to socioeconomic factors rather than genetic predisposition.[17]

In the developed world, HIV infection is much more common in males. In 2009, males accounted for about 76% of all diagnoses of HIV infection among adults and adolescents in the US.[18] Among heterosexuals, females are more likely to acquire HIV infection from an infected male than a male is from an infected female, but a large proportion of infections in males are due to homosexual contact, with or without injection drug use. Males are also more likely to acquire HIV infection from injection drug use alone.

Males were also more likely to acquire HIV infection through contaminated blood products for treatment of hemophilia before universal testing of the blood supply was instituted. The risk of HIV exposure from factor VIII concentrates has been virtually eliminated by viricidal treatment of plasma-derived factor VIII concentrates, as well as the introduction of recombinant factor VIII concentrates and the gradual elimination of albumin from the production process used for these products.

In the developing world, HIV infection is equally common in males and females. The primary route of HIV transmission in the developing world is heterosexual contact.

Young adults tend to be at a higher risk of acquiring HIV, typically through high-risk activities such as unprotected sexual intercourse or intravenous drug use. In 2009 in the US, the largest percentage (15% of all diagnoses) and the highest rate (36.9 per 100,000 population) were in person aged 20–24 years.[18]

Indian scenario

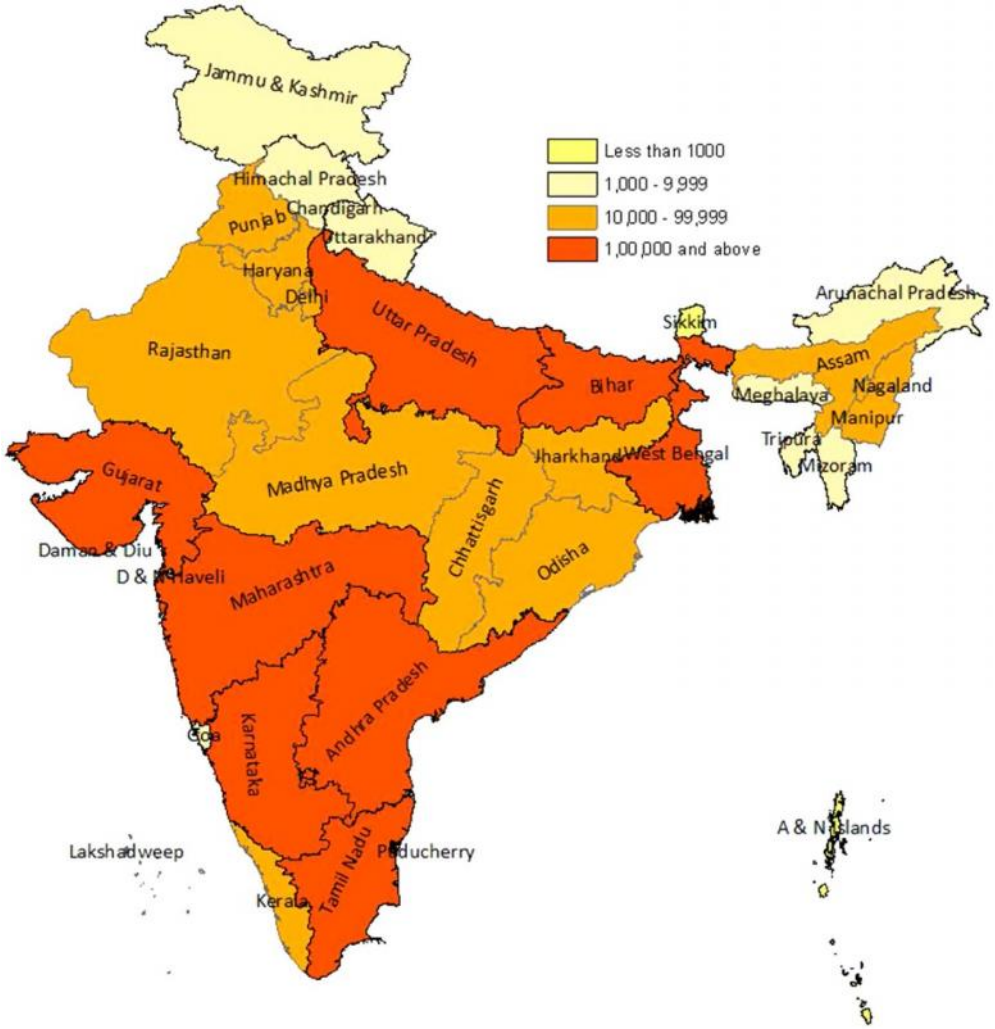


Figure 4. Estimated number of HIV infection by state, 2009[19]

The four high prevalence states of South India (Andhra Pradesh – 500,000, Maharashtra – 420,000, Karnataka – 250,000, Tamil Nadu – 150,000) account for about 55% of all HIV infections in the country. West Bengal, Gujarat, Bihar and Uttar Pradesh are estimated to have more than 100,000 PLHA each and together account for another 22% of HIV infections in India.[20]

Transmission

HIV infection can be transmitted through:

- Unprotected sexual intercourse with an infected partner;
- Injection or transfusion of contaminated blood or blood products;
- Sharing unsterilized injection equipment that has been previously used by someone who is infected;
- Maternofetal transmission (during pregnancy, at birth, and through breastfeeding).[21]

The risk of occupational HIV transmission from contaminated needles to healthcare workers was found to be 0.3% (in case series performed prior to the availability of potent anti retroviral therapy).[21]

Risk factors

Behaviours and conditions that put individuals at greater risk of contracting HIV include:[5]

- Having unprotected anal or vaginal sex;
- Having another sexually transmitted infection such as syphilis, herpes, chlamydia, gonorrhoea, and bacterial vaginosis;
- Sharing contaminated needles, syringes and other injecting equipment and drug solutions when injecting drugs;
- Receiving unsafe injections, blood transfusions, medical procedures that involve unsterile cutting or piercing; and

- Experiencing accidental needle stick injuries, including among health workers.

Pathophysiology

HIV produces cellular immune deficiency characterized by the depletion of helper T lymphocytes ($CD4^+$ cells). The loss of $CD4^+$ cells results in the development of opportunistic infections and neoplastic processes.[5]

Virology of HIV

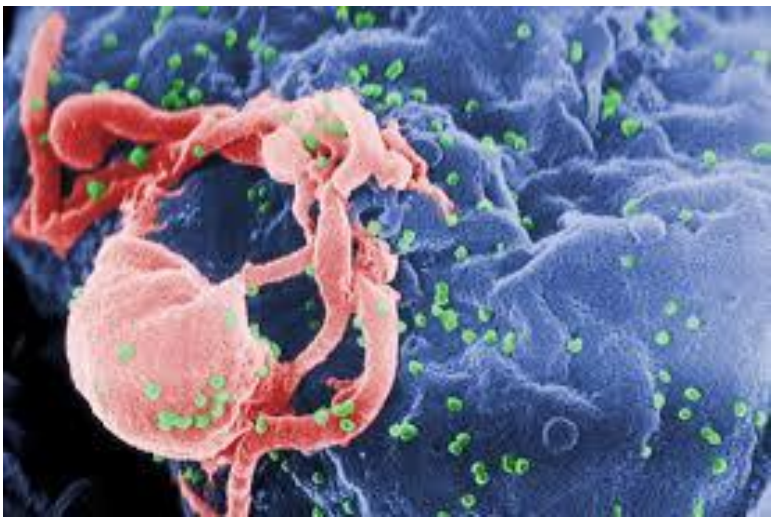


Figure 5. Scanning electron micrograph of HIV-1 budding (in green) from cultured lymphocyte[5]

HIV consists of a cylindrical center surrounded by a sphere-shaped lipid bilayer envelope. There are two major viral glycoproteins in this lipid bilayer, gp120 and gp41. The major function of these proteins is to mediate recognition of CD4+ cells and chemokine receptors, thereby enabling the virus to attach to and invade CD4+ cells. The inner sphere contains two single-stranded copies of the genomic

material, RNA, as well as multiple proteins and enzymes necessary for HIV replication and maturation: p24, p17, reverse transcriptase, integrase, and protease .[9]

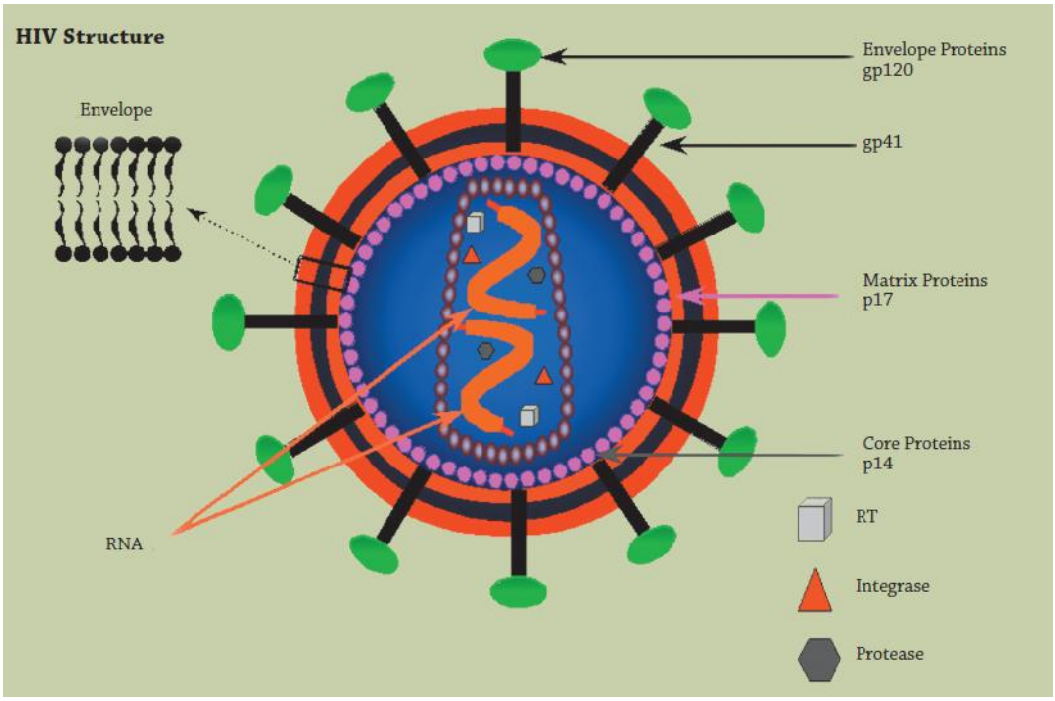


Figure 6. Human immunodeficiency virus anatomy[9]

Unlike other retroviruses, HIV uses nine genes to code for the necessary proteins and enzymes. The three principal genes are gag, pol, and env. The gag gene encodes core proteins. The pol gene encodes the enzymes reverse transcriptase, protease, and integrase. The env gene encodes the HIV structural components known as glycoproteins. The rest of the genes—rev, nef, vif, vpu, vpr, and tat—are important for viral replication and enhancing HIV's infectivity rate.[9]

HIV's Life Cycle

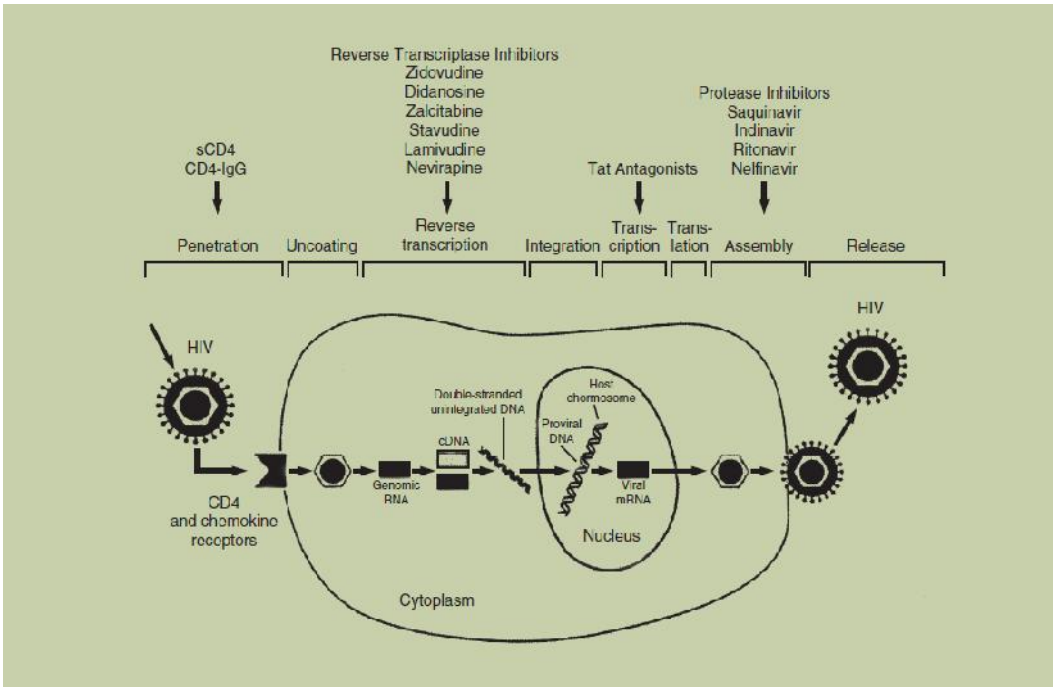


Figure 7. HIV life cycle and the sites of action of antiretroviral agents.[9]

Host cells infected with HIV have a shortened life span as a result of the virus's using them as "factories" to produce multiple copies of new HIV. Thus, HIV continuously uses new host cells to replicate itself. As many as 10 million to 10 billion virions (individual viruses) are produced daily. In the first 24 h after exposure, HIV attacks or is captured by dendritic cells in the mucous membranes and skin. Within 5 days after exposure, these infected cells make their way to the lymph nodes and eventually to the peripheral blood, where viral replication becomes rapid. CD4+ lymphocytes that are recruited to respond to viral antigen migrate to the lymph nodes. These become activated and then proliferate via complex interaction of cytokines released in the microenvironment of the lymph nodes.[9]

This sequence of events makes the CD4+ cells more susceptible to HIV infection, and it explains the generalized lymphadenopathy characteristic of the acute retroviral syndrome seen in adults and adolescents. In contrast, HIV-infected monocytes allow viral replication but resist killing. Thus, monocytes act as reservoirs of HIV and as effectors of tissue damage in organs such as the brain.[9]

The HIV life cycle includes six phases: binding and entry, reverse transcription, integration, replication, budding, and maturation.[9]

Binding and Entry

The envelope proteins gp120 and gp41 bind to CD4+ cell receptors and coreceptors on the outside of CD4+ cells and macrophages. The chemokine receptors CCR5 and CXCR4 facilitate viral entry. T-cell tropic viruses require CXCR4 to bind, and macrotropic strains of the virus require CCR5. R5 is the most common virus transmitted during acute infection, and later during infection X4 is the virus that is most common. The presence of a homozygous inactive mutation of the CCR5 allele has caused resistance to infection by the R5 virus.[9]

The joining of the proteins and the receptors and coreceptors fuses the HIV membrane with the CD4+ cell membrane, and the virus enters the CD4+ cell and macrophage. The HIV membrane and the envelope proteins remain outside of the CD4+ cell, whereas the core of the virus enters the CD4+ cell. CD4+ cell enzymes interact with the viral core and stimulate the release of viral RNA and the viral enzymes reverse transcriptase, integrase, and protease.[9]

Reverse Transcription

The HIV RNA must be converted to DNA before it can be incorporated into DNA of the CD4+ cell. This incorporation must occur for the virus to multiply. The conversion of HIV RNA to DNA is known as reverse transcription and is mediated by the HIV enzyme reverse transcriptase. The result is the production of a single strand of DNA from the viral RNA. The single strand of this new DNA then undergoes replication into double-stranded HIV DNA.[9]

Integration

Once reverse transcription has occurred, the viral DNA can enter the nucleus of the CD4+ cell. The viral enzyme integrase then inserts the viral DNA into the CD4+ cell's DNA. This process is known as integration. The CD4+ cell has now been changed into a factory used to produce more HIV.[9]

Replication

The new DNA, which has been formed by the integration of the viral DNA into the CD4+ cell, causes the production of messenger RNA that initiates the synthesis of HIV proteins.[9]

Budding

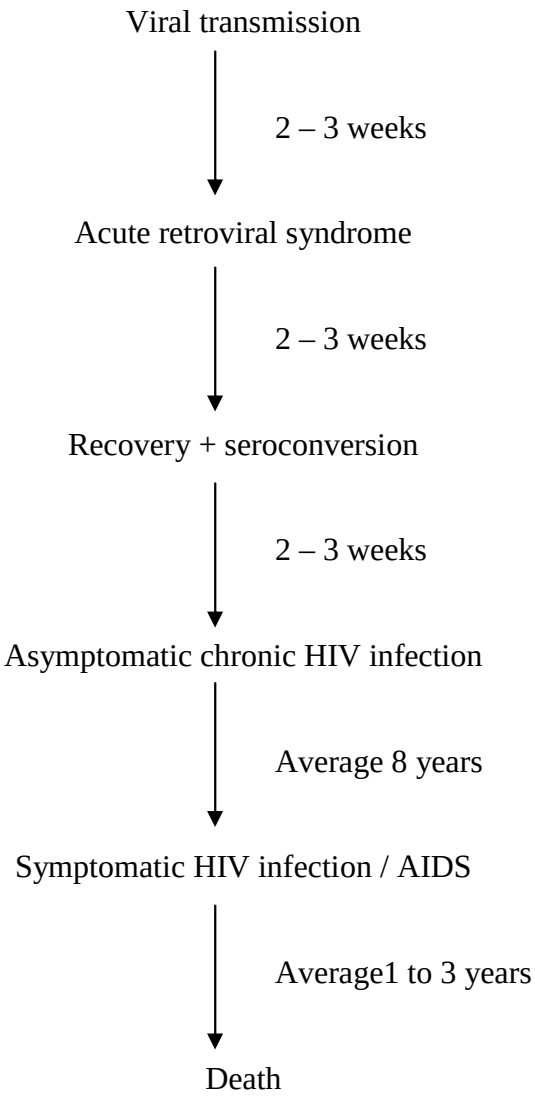
The HIV proteins and viral RNA, all the components needed to make a new virus, gather at the CD4+ cell membrane to form new viruses. These new viruses push through the different parts of the cell wall by budding. Many viruses can push through the wall of one CD4+ cell. These new viruses leave the CD4+ cell and contain all the components necessary to infect other CD4+ cells.[9]

Maturation

The new virus has all the components necessary to infect other CD4+ cells but cannot do so until it has matured. During this process, the HIV protease enzyme cuts the long HIV proteins of the virus into smaller functional units that then reassemble to form a mature virus. The virus is now ready to infect other cells.[9]

Natural history

The natural history of untreated HIV infection is divided into following stages.[5]



Effects on the Immune System

The pathogenesis of HIV is basically a struggle between HIV replication and the immune responses of the patient, via cell-mediated and immune-mediated reactions. The HIV viral burden directly and indirectly mediates CD4+ T-cell destruction. There is destruction of mature CD4+ cells; CD4+ progenitor cells in bone marrow, the thymus, and peripheral lymphoid organs; as well as CD4+ cells within the nervous system, such as microglia. The result of this destruction is failure of T-cell production and eventual immune suppression.[9]

There are many mechanisms of CD4+ cell depletion by HIV infection. Direct HIV-mediated cytopathic effects include single-cell killing as well as cell fusion, or syncytium formation. The syncytium is a fusion of multiple uninfected CD4+ cells with one HIV-infected CD4+ cell via CD4–gp120 interaction. This fusion results in a multinucleated syncytium, or giant cell, which may ultimately serve as a means to produce many virions. The host's natural immune responses also play a role in CD4+ cell depletion, mainly through cytotoxic CD8+ T-cells, antibody-dependent cellular cytotoxicity, and natural killer cells. Other mechanisms include autoimmune responses, anergy, superantigen-mediated activation of T cells, and programmed cell death (apoptosis).[9]

HIV can infect many types of cells. The spread of HIV outside lymphoid organs to the brain, spinal cord, lung, colon, liver, and kidney usually occurs late during illness.[9]

The immune systems of HIV-infected children undergo changes that are similar to those in adults. B-cell activation occurs in most children early in the

infection, evidenced by the presence of hypergammaglobulinemia (>1.750 g/L) with high levels of anti–HIV-1 antibody. This reflects both dysregulation of T-cell suppression of B-cell antibody synthesis as well as active CD4+ enhancement of B-lymphocyte humoral response. Also, as HIV disease progresses through more severe immunosuppression and depletion of CD4+ cells, the CD8+ count increases, yielding an overall decrease in the CD4+:CD8+ ratio.[9]

Cells Susceptible to HIV Infection[9]

- Hematopoietic - T-cells (CD4+ OR CD 8+); Macrophages/monocytes; Dendritic cells; Fetal thymocytes and thymic epithelium; B-cells; NK cells; Megakaryotic cells; Stem cells;
- Central nervous – Microglia; Capillary endothelial cells; Astrocytes; Oligodendrocytes;
- Large Intestine; Columnar epithelium
- Other - Kupffer cells; Synovial cells; Placental trophoblast cells

Clinical Categories of HIV Infection

Children infected with HIV often have severe disease when first evaluated, or they may develop AIDS over time, much like adults infected with HIV. Infants and young children normally have higher CD4+ counts than those of adults. The normal CD4+ count in children varies with age, but it is equal to the adult value by the time the child is 6 years old. Immunologic and clinical categories are used to evaluate the HIV disease status in children and to make treatment decisions.[9]

Primary Infection, or Acute Retroviral Syndrome

Primary infection refers to the time when HIV first enters the body. At the time of primary infection with HIV, a person's blood carries a high viral load, meaning that there are many individual viruses in the blood. The number of copies of virus per milliliter of plasma or blood can exceed 1 million. Newly infected adults often experience an acute retroviral syndrome. Signs and symptoms of acute retroviral syndrome include fever, myalgia (muscle pain), headache, nausea, vomiting, diarrhea, night sweats, weight loss, and rash. These signs and symptoms usually occur 2–3 weeks after infection, subside after a few days, and often are misdiagnosed as influenza or infectious mononucleosis. An important differentiating symptom that is often absent is the presence of a runny nose or nasal congestion.[9]

During primary infection, the CD4+ count in the blood decreases remarkably but rarely drops to less than 200 cells/μL. The virus targets CD4+ cells in the lymph nodes and the thymus during this time, making the HIV-infected person vulnerable to opportunistic infections and limiting the thymus's ability to produce T lymphocytes. HIV antibody testing using an enzyme-linked immunosorbent assay or enzyme immunoassay may yield positive or negative results depending on the time of seroconversion. DNA PCR and RNA PCR will be positive, but confirmation with Western blot analysis may yield an indeterminate result because seroconversion can take up to 2–8 weeks to occur. The average time to seroconversion is 25 days.[9]

Chronic infection[32]

1. Chronic progressors

    a. Typical disease progression

b. Usually with V_L > 10000 c/mL and CD4 decline of 50 – 100 cells/mm^3/years

2. Chronic Non Progressors

   a. HIV infection without opportunistic infection and CD4 count > 500, >10 years

3. Slow progressors - Slow CD4 loss with VL 1000 – 10000 c/mL

4. ELITE controllers - V_L < 50 c/mL in absence of therapy make up < 0.5% of person with HIV infection

Clinical Latency/Asymptomatic Disease (Clinical Stage 1)

Although patients recently infected with HIV usually experience a "clinically latent" period of years between HIV infection and clinical signs and symptoms of AIDS, evidence of HIV replication and host immune system destruction exists from the onset of infection. Early during this time, referred to as Clinical Stage 1 , the immune system produces antibodies in an attempt to protect itself from HIV. This is when the "viral set point" is established. The viral load of the set point can be used to predict how quickly disease progression will occur. People with higher viral load set points tend to exhibit more rapid disease progression than those with lower viral load set points.[9]

During latency, HIV-infected patients may or may not have signs and symptoms of HIV infection though persistent lymphadenopathy is common. In HIV-infected adults, this phase may last 8–10 years. The HIV enzyme-linked

immunosorbent assay and Western blot or immunofluorescence assay will be positive. The CD4+ count is greater than 500 cells/μL.[9]

Mild Signs and Symptoms of HIV (Clinical Stage 2)

HIV-infected people may appear to be healthy for years, and then minor signs and symptoms of HIV infection begin to appear. They may develop candidiasis, lymphadenopathy, molluscom contagiosum, persistent hepatosplenomegaly, popular pruritic eruptions, herpes zoster, and/or peripheral neuropathy. The viral load increases, and the CD4+ count falls is between 350-499/uL. Once patients are in this stage they remain in stage 2. They can be reassigned stage 3 or 4 if a condition from one of those occurs, but they cannot be reassigned to Clinical Stage 1 or 2 if they become asymptomatic.[9]

Advanced Signs and Symptoms of HIV (Clinical Stage 3)

HIV-infected patients with weakened immune systems can develop life-threatening infections. The development of cryptosporidiosis, pulmonary and lymph node tuberculosis, wasting, persistent fever (longer than one month), persistent candidasis, recurrent bacterial pneumonia, and other opportunistic infections is common. These patients may present with wasting, or losing weight. Their viral load continues to increase, and the CD4+ count falls to less than 200-349 cells/μL.[9]

Clinical Stage 4

Patients with advanced HIV disease, or AIDS, can continue to develop new opportunistic infections, such as Pneumocystis jirovecii pneumonia (formerly Pneumocystis carinii pneumonia), cytomegalovirus infection, toxoplasmosis,

Mycobacterium avium complex, cryptococcal meningitis, progressive multifocal leukoencephalopathy, Kaposi sarcoma and other infections that commonly occur with a severely depressed immune system. The viral load is very high, and the CD4+ count is less than 200 cells/μL. At this point in the disease course death can be imminent.[9]

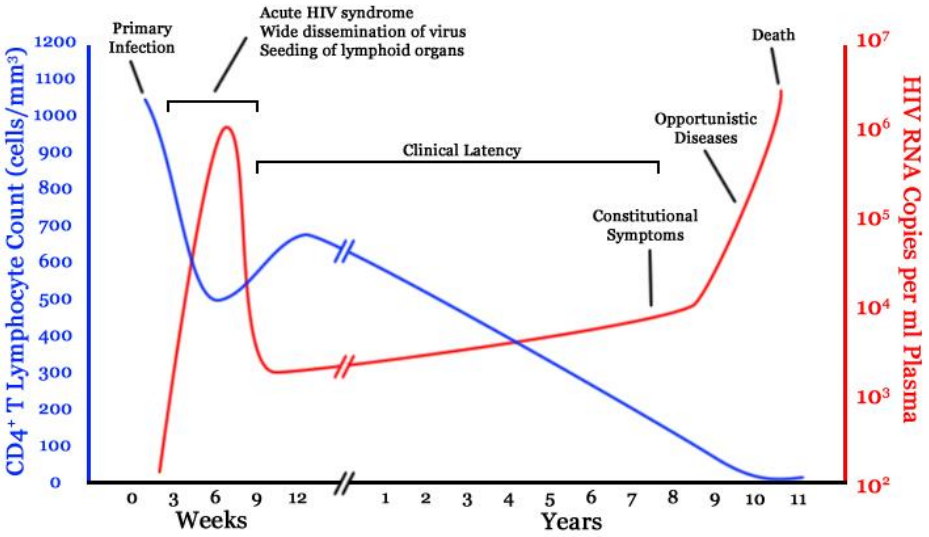


Figure 8. Timeline of CD4 T-cell and viral-load changes over time in untreated human immunodeficiency virus infection.[22]

Immunologic control of HIV

The primary mechanism for immunologic control of HIV appears to be CD8+ cytotoxic T-cells. T-cell responses are correlated with the steady-state of viral load and hence, the rate of progression.[23] Cellular immunity is apparently responsible for some multiple-exposed, but uninfected individuals.[24]

Although antibodies against HIV can be detected, it is clear that they are not sufficiently neutralizing to assist with immunologic control of the infection.

The role of NK (Natural Killer) cells may be important in the initial control of HIV. Escape mutations have been detected, implying that immunologic pressure on HIV exists from NK cells.[25]

WHO clinical staging system for HIV infection and HIV related disease

World Health Organization has developed a clinical staging system (originally for prognosis), based on clinical criteria. The definition of symptoms, signs and diseases is according to clinical judgement. Clinical condition or performance score, whichever is the higher, determines whether a patient is at clinical stage 1, 2, 3 or 4. Clinical stage is important as a criterion for starting antiretroviral (ARV) therapy.[26]

WHO clinical staging system for HIV infection[26]

Primary HIV Infection	• Asymptomatic • Acute retroviral syndrome
Stage 1	• Asymptomatic • Persistent generalized lymphadenopathy
Stage 2	• Moderate unexplained weight loss (<10% of presumed or measured body weight) • Recurrent respiratory tract infections sinusitis, tonsillitis, otitis media and pharyngitis) • Herpes zoster • Angular cheilitis • Recurrent oral ulceration • Papular pruritic eruptions • Seborrhoeic dermatitis • Fungal nail infections
Stage 3	• Unexplained severe weight loss (>10% of presumed or measured) • 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 • PulmonaryTB(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)
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) • Extrapulmonary tuberculosis • Kaposi's sarcoma • Cytomegalovirus infection (retinitis or infection of other organs) • Central nervous system toxoplasmosis • HIV encephalopathy • Extrapulmonary cryptococcosis including meningitis • Disseminated non-tuberculous mycobacterial infection • Progressive multifocal leukoencephalopathy • Chronic cryptosporidiosis (with diarrhoea) • 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

Diagnosis

Screening for HIV Infection

The U.S. Preventive Services Task Force (USPSTF) strongly recommends that clinicians should screen for HIV in all adolescents and adults at an increased risk for HIV infection, including all pregnant women.[27]

The Centers for Disease Control and Prevention (CDC) recommends HIV screening for patients in all health-care settings, after the patient is notified that testing will be performed unless the patient declines (opt-out screening). The CDC recommends that persons at high risk for HIV infection to be screened for HIV at least annually.[28]

Citing the benefits of early diagnosis and treatment and the failure of risk-based screening to identify a substantial proportion of HIV-infected patients early in the disease, the American College of Physicians recommends that clinicians shall adopt to routine screening for HIV and encourage all patients to be tested.[29]

HIV testing and counseling[36]

People access HIV treatment and prevention through the gateway of HIV testing and counseling. It is currently estimated globally that about half of the people living with HIV do not know of their HIV status.[36]

The people who do know often test late meaning that many people start treatment when they are already significantly immune compromised resulting in poor health outcomes and ongoing HIV transmission.[36]

WHO recommends all forms of HIV testing should be voluntarily and adhere to five C's. Consent, confidentiality, counseling, correct test results and connections to core treatment and prevention.[36]

Standard HIV Test[32]

- Standard serologic test consists of screening EIA (Enzyme linked immunoassay performed in lab with whole blood) done as a rapid test at point of care (POC).
- The EIA tests are screening test and require confirmatory western blot
- EIA screening for anti HIV requires a repeatedly reactive test which is the criterion for WB testing. Western blot detects antibodies to HIV I protein.
- WB should be coupled with EIA due to 2% rate of false positive EIA tests.
- Standard serologic assays (EIA and WB or 1FA) show sensitivity in patients with established disease (>3 months after transmission) of 99.5% and specificity of 99.994%.

Positive test should be confirmed with repeat testing or with collaborating clinical or laboratory data.

False negative results

- Window period
- Seroconversion
    - Infants
    - Patients treated prior to seroconversion
    - Patients with late stage disease
- Atypical host response
- Failure to mount immunologic response

- Rapid tests
- Technical or clinical error

False positive

Reported to range from 0.0004 to 0.0007%

- Autoantibodies
- Investigational HIV vaccines
- Factitious HIV infection
- False positive oral fluid ora Quick test
- Influenza vaccine
- False positive rapid screening tests
- Technical error

Alternate HIV serologic tests

- IFA
    - Possible advantage – Simple, less expensive, more rapid than WB
    - Disadvantages – Resource limited setting
- Home kits
- Saliva test
- Nucleic acid amplification testing
- Rapid test – Recommended for HIV screening as an alternative to EIA. Useful where rapid results are important
    - Occupational exposure
    - Pregnant women presenting in labour without testing
    - Outreach clinics

- In emergency rooms / STD clinics (Where patients are unlikely to return for test results)

CD4 cell count[32]

This is a standard test to assess

- Prognosis for progression to AIDS to death.
- Formulate differential diagnosis in a symptomatic patient
- To make therapeutic decision regarding antiretroviral treatment and prophylaxis for opportunistic infection

Technique

Standard technique uses flow cytology and hematology analyzers.

Normal values – Mean of 800 to 1050 with range of two standard deviation of approximately 500 – 1400 cell/mm3.

CD4 Slope – It refers to the rate of decline of CD4 counts. Sequentially collected data for 8729 untreated HIV infected patients from 20 cohorts in Cascade showed that median CD4 count at about 8 months post seroconversion was approximately 610 cells / mm3

With negative slope at 2 years of 130 cell/mm3 and a five year slope of 70 cells /mm3 /year.

Median baseline was about 40 cells/mm3 higher in women versus men and in persons (40 years versus 40 years).

Response to ART[30,32]

CD4 count typically increases by > 50 cells/mm3 at four to eight weeks after viral suppression with ART and then increases at a rate that correlates with time, baseline CD4 count and virologic suppression. With good virologic response the increase at one year averages 100 to 150 cells/mm3 at ≥ 5 years it averages 20 to 30 cells/mm3/year.

Treatment

Combination antiretroviral therapy (cART) also referred as highly active antiretroviral therapy (HAART) is the cornerstone of management of patients with HIV infection.[31,32]

Suppression of HIV replication is an important component in prolonging life as well as in improving the quality of life in patients with HIV infection.[31,32]

The continuing success of potent antiretroviral therapy (ART) has resulted in dramatic reductions in HIV-associated morbidity and mortality. HIV-infected individuals are now living longer.[33] Incidence of opportunistic infections has decreased in the HAART era in these patients and also the metabolic effects of the Highly Active Anti-Retroviral therapy (HAART), especially the protease inhibitors (PI) become more prevalent in this patient population. Patients with HIV/AIDS are not only on HAART therapy, but also on prophylaxis for opportunistic infections, depending on their level of immunity competence and prior infections, thereby complicating the picture.[8,34]

Treatment

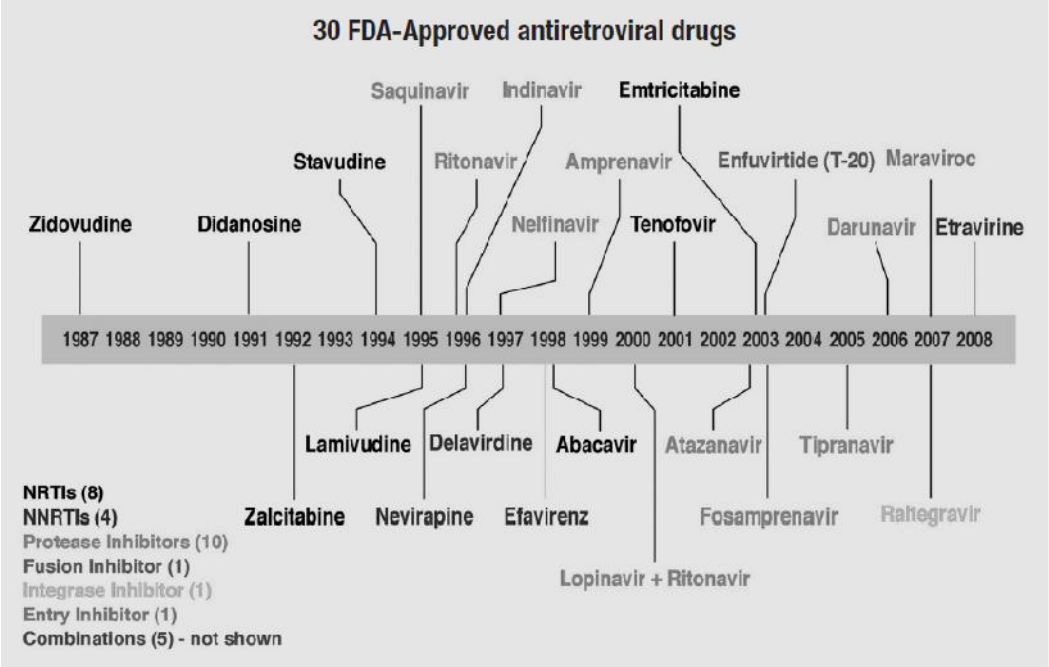


Figure 9. Antiretroviral drugs approved for HIV infection[35]

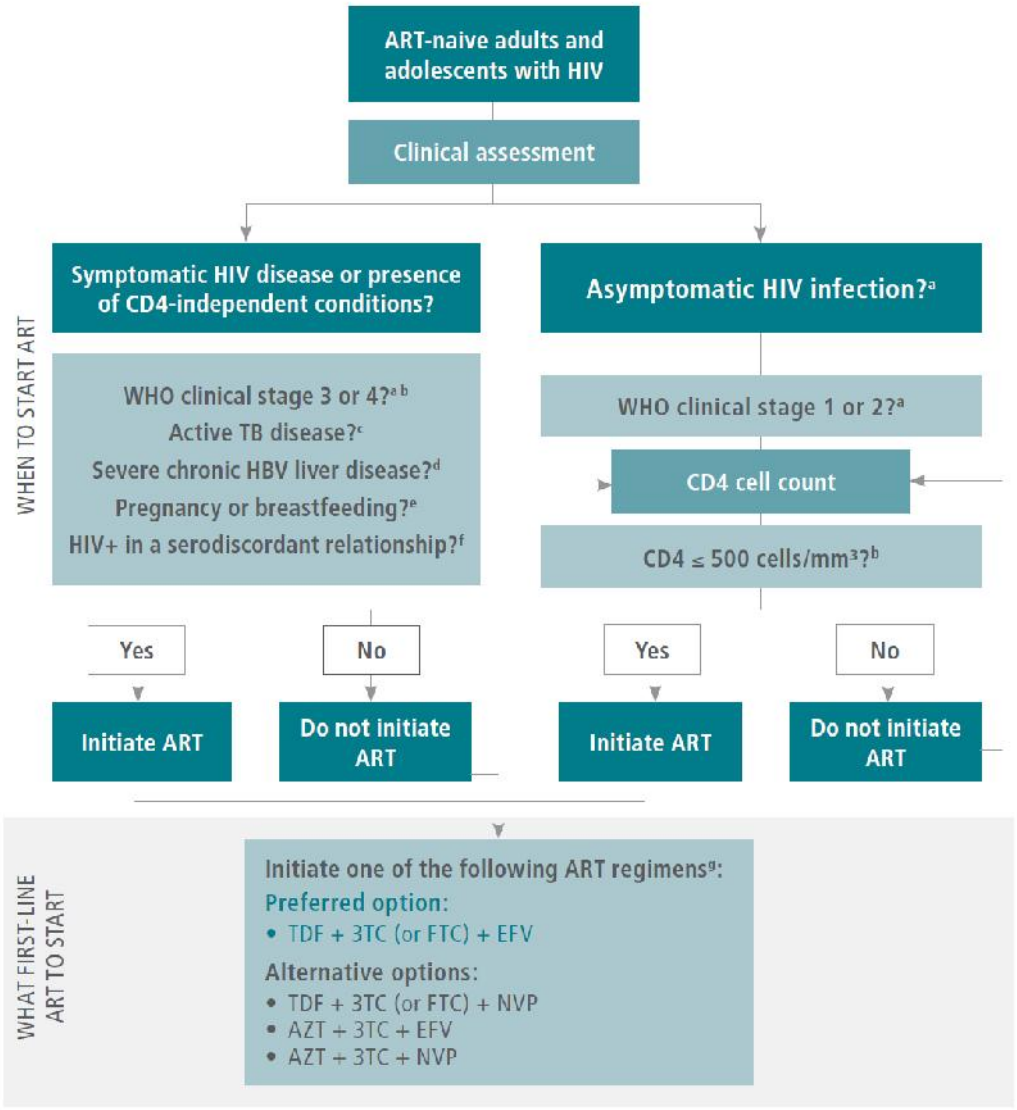


Figure 10. WHO 2013 guidelines to start ART in people living with HIV[36]

HIV-Related Cardiovascular Disease

It is increasingly common for HIV/AIDS patients to be seen by cardiologists, and cardiovascular disease in HIV/AIDS is becoming increasingly recognized in the developing world.[37,40,41] Despite this, heart disease can be overlooked in HIV-positive patients, because symptoms of breathlessness, fatigue, and poor exercise tolerance are frequently ascribed to other conditions associated with HIV infection.[38]

Cardiac complications of HIV infection tend to occur late in the disease or are associated with related therapies and are therefore becoming more prevalent as therapy and longevity improve. Complicated drug therapies for HIV infection have sustained life but may increase cardiovascular risk and accelerate atherosclerotic disease and events.[5,40,41]

A range of cardiac abnormalities associated with HIV infection has been suggested by studies; the conditions, in order of frequency, are pericardial effusion, lymphocytic interstitial myocarditis, dilated cardiomyopathy (frequently with myocarditis), infective endocarditis, and malignancy (myocardial Kaposi sarcoma and B-cell immune blastic lymphoma).[39,40,41]

Cardiac Manifestations of HIV/AIDS[40,41]

Pericardial effusion

- Idiopathic
- Infectious (viral, bacterial especially tuberculous, and fungal)
- Neoplastic (Kaposi sarcoma and non-Hodgkin lymphoma)

Heart muscle disease

- Myocarditis (idiopathic/lymphocytic, specific infections, toxins)
- Dilated cardiomyopathy and LV dysfunction

Endocarditis

- Marantic (nonbacterial thrombotic endocarditis)
- Infective

Tumors

- Kaposi sarcoma

- Lymphoma

Right ventricular dysfunction & pulmonary hypertension

- Primary
- Secondary (recurrent chest infections, thromboembolism)

Premature atherosclerosis and coronary artery disease

- Adverse drug effects
    - Hyperlipidemia
    - Proarrhythmia
- Vascular disease
- Autonomic dysfunction

HIV/AIDS and the Pericardium[40,41]

Pericardial effusion and pericarditis were the most common cardiac abnormalities found in early HIV/AIDS autopsy studies. HIV-infected patients with pericardial effusions generally have a lower CD4 count than those without effusions, indicating more advanced disease. Effusions are generally small and asymptomatic. Asymptomatic pericardial effusions are common in HIV-infected patients.

The incidence of pericardial effusion in those with AIDS was 11%/year. The prevalence of effusion in AIDS patients increases over time, reaching a mean in asymptomatic patients of about 22% after 25 months of follow-up.

Pericardial effusion may be related to an opportunistic infection, metabolic abnormality, or malignancy, but usually the cause is not clear.

Significant pericardial effusions are usually caused by viral or bacterial infection or malignant infiltration particularly with Kaposi sarcoma (KS) or non-Hodgkin lymphoma (NHL). In Africa, pericardial effusion itself is suggestive of HIV infection.

Pericarditis caused by Mycobacterium tuberculosis or Mycobacterium avium–intracellulare is a pressing problem and has been reported as the first manifestation of AIDS in mainland Europe and Asia.

Other unusual pathogens, including Nocardia asteroides and herpes simplex virus (HSV), should be considered along with CMV, which remains prevalent in the HIV population often without a definite anatomic site of infection. Other causes can include uremia from HIV-associated nephropathy or drug nephrotoxicity.

The effusion is often part of a generalized serous effusive process also involving pleural and peritoneal surfaces. This capillary leak syndrome may be related to enhanced cytokine production in the later stages of HIV disease.

Effusion markedly increases mortality. These may, however, resolve spontaneously in up to 42% of patients.

It is suggested that HIV should be considered as a differential in a young patient presenting with unexplained pericardial effusion or cardiac tamponade.

All HIV-infected patients with evidence of heart failure, Kaposi sarcoma, tuberculosis, or other pulmonary infections should undergo baseline echocardiography and electrocardiographic testing. Patients should undergo pericardiocentesis if they have pericardial effusion and clinical signs of tamponade

(e.g., elevated jugular venous pressure, dyspnea, hypotension, persistent tachycardia, pulsus paradoxus) or echocardiographic signs of tamponade (e.g., continuous-wave Doppler evidence of respiratory variation in valvular inflow, septal bounce, right ventricular diastolic collapse, a large effusion).

Patients with pericardial effusion without tamponade should be evaluated for treatable opportunistic infections, such as tuberculosis, and for malignancy. Highly active antiretroviral therapy (HAART) should be considered if therapy has not already been instituted. Repeated echocardiography is recommended after 1 month, or sooner if clinical symptoms direct.

It is pertinent to note that delay in initiation of antiretroviral therapy with anti tuberculous treatment because of the concern of IRIS did not confer any advantage as the randomized trial by Abdool Karim et al[42] recorded significant improvement in survival for patients with simultaneous treatment. Recurrence of TB may happen in HIV positive as compared with non-HIV patients even with successful initial therapy.[43]

<u>HIV/AIDS and the Myocardium</u>[40,41]

Diseases of the myocardium in patients with HIV/AIDS include cardiomyopathy, myocarditis, cardiac tumors and drug toxicity.

Myocarditis[40,41]

Numerous pathologic studies have confirmed the presence of varying histologic patterns of lymphocytic myocarditis in HIV patients. The apparent

difference in the prevalence of myocarditis in different studies can be related to clinical factors, sampling errors, and possibly the effect of HAART.

Estimates of the prevalence of myocarditis in HIV/AIDS varies from 53 percent in the pre-HAART era to much lower levels today in the developed world.

There are several hypotheses regarding the etiology of myocarditis in AIDS including:

a. Primary HIV myocarditis

b. Secondary HIV myocarditis,

c. Opportunistic infection

Autopsy has confirmed a variety of opportunistic infections of the myocardium in patients with AIDS. Infectious agents included Toxoplasma gondii in the hearts of both adults and children, Cryptococcus species, CMV, Candida species, Pneumocystis carinii, Microsporidium, Histoplasma capsulatum, atypical mycobacteria, and Aspergillus organisms involving the myocardium. The majority have been part of a disseminated infection and are infrequently associated with localized myocarditis.

d. Autoimmunity.

Myocarditis can be diagnosed clinically based on symptoms and physical findings, although this is often difficult in the HIV patient. The symptoms are protean and include fatigue, dyspnea, and pleuritic chest pain, which can wrongly be ascribed to other conditions. The finding of an unexplained tachycardia, third heart

sound, or a friction rub should alert the physician to the possibility of myocarditis and guide investigation.

Dilated Cardiomyopathy and Left Ventricular Dysfunction in HIV/AIDS[40,41]

Dilated cardiomyopathy as a complication of HIV infection was first described in 1986 and was identified frequently thereafter. The differential diagnosis of HIV-related cardiomyopathy includes LV dysfunction secondary to ischemic heart disease, diabetes or hypertension, hypersensitivity reactions to drugs, or foreign injected material and coronary spasm secondary to cocaine use.

Isolated LV dysfunction in HIV-positive patients can resolve spontaneously, suggesting a self-limiting myocarditis, and reflects current thinking on the pathogenesis of non-HIV dilated cardiomyopathy.

The presence of dilated cardiomyopathy is ominous and associated with poor survival compared to patients with structurally normal hearts. This poor outlook remained true, even after correcting for CD4 counts.

Mortality in HIV-infected patients with cardiomyopathy is increased, independently of CD4 count, age, gender, and HIV risk group. The median survival to AIDS-related death was 101 days in patients with LV dysfunction and 472 days in patients with a normal heart at a similar stage of infection before HAART. Isolated right ventricular dysfunction or borderline LV dysfunction did not place patients at risk.

The mechanisms for the development of LV dysfunction, cardiomyopathy, in AIDS remain unclear. In addition to the role of HIV, lymphocytic myocarditis, and

cytokines, the contributions of autoimmune responses, illicit and prescribed medications, nutritional deficiencies, and other factors also appear to be pathogenetically or pathophysiologically important.

Drug-Induced Heart Muscle Disease[40,41]

Drug toxicity can cause clinically significant myocardial dysfunction; drugs specific to the HIV/AIDS patients that can cause heart failure include zidovudine,[44] interferon alpha, foscarnet, doxorubicin, pentamidine and amphotericin B.

The exact role of zidovudine in the pathogenesis of HIV-related heart muscle disease in humans remains unclear, and evidence for its existence is limited, however, small numbers of HIV-positive patients who have developed cardiac dysfunction while taking the drug were seen to improve following its discontinuation. It seems reasonable to discontinue zidovudine therapy for 1 month in those patients who develop cardiac dysfunction while receiving the drug. However, this should be followed by reassessment and possible reintroduction of zidovudine if no improvement in cardiac function is noted. The cardiac and other side effects of NRTIs can become more common through improved AIDS survival and increasing cumulative doses of HAART.

Cardiovascular Actions and Interactions of Drugs Commonly Used in HIV Therapy*

Class	Cardiac drug interactions	Cardiac side effects
Antiretroviral		
Nucleoside reverse transcriptase inhibitors	Zidovudine, dipyridamole	Rare—lactic acidosis, hypotension; Accelerated risk with cardiopulmonary bypass; Zidovudine—skeletal muscle myopathy, myocarditis
Non-nucleoside reverse transcriptase inhibitors	Calcium channel blockers, warfarin, beta blockers, nifedipine, quinidine, steroids, theophylline; Delavirdine—can cause serious toxic effects if given with antiarrhythmic drugs and calcium channel blockers	
Protease inhibitors	Metabolized by cytochrome P-450 and interact with other drugs metabolized through this pathway, such as selected antimicrobials, antidepressant, and antihistamine agents; cisapride, HMG-CoA reductase inhibitors (lovastatin, simvastatin), sildenafil; Potentially dangerous interactions that require close monitoring or dose adjustment; can occur with amiodarone, disopyramide, flecainide, lidocaine, mexiletine, propafenone, quinidine; Ritonavir—most potent cytochrome activator (CYP3A) and P-glycoprotein inhibitor; most likely to interact; Indinavir, amprenavir, and nelfinavir—moderate; Saquinavir—lowest probability to interact; Indinavir, amprenavir, and nelfinavir—moderate; Calcium channel blockers, prednisone, quinine, beta blockers (1.5- to 3-fold increase); Decrease theophylline concentrations	Implicated in premature atherosclerosis, dyslipidemia, insulin resistance, diabetes mellitus, fat wasting and redistribution

Anti-infective		
Antibiotics	Rifampin—reduces therapeutic effect of digoxin by inducing intestinal P-glycoprotein, reduces protease inhibitor concentration and effect; Erythromycin—cytochrome P-450 metabolism and drug interactions; Trimethoprim-sulfamethoxazole (Bactrim)—increases warfarin effects	Erythromycin—orthostatic hypotension, ventricular tachycardia, bradycardia, torsades (with drug interactions); Clarithromycin—QT prolongation and torsades de pointes; Trimethoprim-sulfamethoxazole—orthostatic hypotension, anaphylaxis, QT prolongation, torsades de pointes, hypokalemia; Sparfloxacin (fluoroquinolones)— QT prolongation
Antifungal agents	Amphotericin B—digoxin toxicity; Ketoconazole or itraconazole—cytochrome P-450 metabolism and drug interactions; increases levels of sildenafil, warfarin, HMG-CoA reductase inhibitors, nifedipine, digoxin	Amphotericin B—hypertension, arrhythmia, renal failure, hypokalemia, thrombophlebitis, bradycardia, angioedema, dilated cardiomyopathy; liposomal formulations still have potential for electrolyte imbalance and QT prolongation; Ketoconazole, fluconazole, itraconazole—QT prolongation, torsades de pointes
Antiviral	Ganciclovir—zidovudine	Foscarnet—reversible cardiac failure, electrolyte abnormalities; Ganciclovir—ventricular tachycardia, hypotension.

Nutritional Deficiencies and Cardiac Dysfunction in HIV/AIDS[40,41]

Nutritional deficiencies are common in HIV infection, particularly in those with late-stage disease. Poor absorption and diarrhea both lead to electrolyte imbalances and deficiencies in elemental nutrients. Deficiencies of trace elements have been associated with cardiomyopathy. For example, selenium deficiency increases the virulence of coxsackie virus to cardiac tissue. Selenium replacement reverses cardiomyopathy and restores LV function in nutritionally depleted patients.

Levels of vitamin B12, carnitine, and growth and thyroid hormone can also be altered in HIV disease; all have been associated with LV dysfunction. Experimentally, carnitine administration reversed myopathic changes induced by zidovudine (AZT) in vitro, but the clinical effects have yet to be established.

Endocardial Disease in HIV/AIDS

Endocardial/ valvular disease in patients with HIV/AIDS can be secondary to bacterial or non-bacterial (marantic) endocarditis.[45] Bacterial endocarditis is usually secondary to intravenous drug abuse in this patient population,[46] making Staphylococcus aureus and Streptococcus viridans the most common organisms and the tricuspid valve, the most common valve involved. Unlike in the myocardium, the HIV virus does not affect the endocardium directly. Non-bacterial (marantic) endocarditis is usually clinically silent, affects the tricuspid valve and can lead to embolism into the pulmonary artery, which is also clinically silent. The CD4 count has implications on the risk of developing heart disease, as well as on the prognosis. Patients with lower CD4 count, especially less than 200, have a higher risk of endocarditis, and more importantly, patients with endocarditis and lower CD4 counts have a much poorer prognosis.[47] Treatment of infective endocarditis in HIV-infected patients does not differ from those who are HIV-negative.[8]

Valvular heart disease happens mainly as either bacterial or fungal endocarditis. HIV disease generally does not seem to predispose to increased incidence of endocarditis. Further, patients with HIV have averagely similar manifestations and outcome (85% vs 93%) as compared with HIV-negative patients.[48] However, salmonellal endocarditis is more prevalent as compared with immunocompetent individuals.[49]

In addition intravenous drug users with advanced immunosuppression are more prone to develop IE. However, sustained valvular damage is less likely due to impaired immune response.

Gebo et al[50] noted decreased rates of endocarditis in a review of periods of pre-HAART versus post-HAART eras. They found a decrease in incidence from 20.5 to 6.6 per 1000 persons-years. Generally, mortality is higher in those with CD4 counts of below 200/mm3. Right-sided valves are most commonly affected with the predominant organism being Staphylococcus aureus in up to three-quarter of cases.[51]

Gram negative organisms and fungi also demonstrate higher incidence with mortality higher than in non-HIV patients if left valve is affected and CD4 count is less than 200 cells/mL.[51]

Bacterial pathogens isolated include *Salmonella species*, *Strepto-coccus pneumoniae* and *Haemophilus influenzae*. Organisms such as *Aspergillus species*, *Candida species* and *Cryptococcus neoformans* are fungal causes of endoarditis recorded in both IV and non-IV drug abusers in HIV patients.[51]

Further, Losa et al[52] had also re-ported eight cases of infective endocarditis from *Enterococus faecalis*, Staphylococci, *Salmonella enteritidis* and *Coxiella burnetii* in non-IV drug abusing HIV patients in a series over a period of twenty years.

Symptoms and signs of infective endocarditis include fever, lethargy and heart murmurs which were documented in one-third of patients. Repeated blood cultures and transoesophageal echocardiography are essential in reaching diagnosis. Immediate and appropriate empirical therapy should be started promptly. Once sensitivity of the blood culture is available then therapy should be directed towards the result. Valve replacement surgery should be considered in patients with hemodynamic instability, antibiotic failure and profound valvular destruction.

Prophylaxis for endocarditis in patients for dental surgery should be as per recommendation of established guidelines.[51]

Cardiac Tumors in HIV/AIDS[40,41]

Cardiac tumors affecting the heart in patients with HIV/AIDS are more frequently secondary than primary, as in the general population.

Kaposi sarcoma (KS) is the most common AIDS-related neoplasia, and in contrast to the classic dermatologic form of the disease, there is often widespread and potentially fatal visceral involvement in HIV-positive individuals

Kaposi's sarcoma is usually a part of disseminated mucocutaneous involvement, only rarely is the heart the sole site of involvement. Lesions are frequently asymptomatic.

It affects up to 35% of AIDS patients, particularly homosexuals, with an incidence inversely related to the CD4 count. Autopsy studies have found that 28% of HIV-infected patients with widespread Kaposi sarcoma had cardiac involvement and rarely described it as a primary cardiac tumor.

Primary cardiac malignancy associated with HIV infection is generally caused by cardiac lymphoma. Non-Hodgkin lymphomas are 25 to 60 times more common in HIV-infected individuals. They are the first manifestation of AIDS in up to 4% of new cases. Patients with primary cardiac lymphoma can present with dyspnea, right-sided heart failure, biventricular failure, chest pain, or arrhythmias. Cardiac lymphoma is associated with rapid progression to cardiac tamponade,

symptoms of congestive heart failure, myocardial infarction (MI), tachyarrhythmias, conduction abnormalities, or superior vena cava syndrome.

HAART has not substantially affected the incidence of HIV-related non-Hodgkin lymphomas, but cumulative viremia has been associated, even during HAART therapy. An intracardiac mass in late-stage HIV infection is associated with a uniformly poor prognosis.

Right Ventricular Dysfunction and Pulmonary Hypertension in HIV/AIDS[40,41]

Patients with HIV/AIDS can develop pulmonary hypertension that is believed to be secondary to a combination of inflammation and genetic factors. Plexogenic arteriopathy has been described in this patient population.[8]

Primary pulmonary hypertension, occurs in less than 0.5% of patients with HIV infection,[53] the prognosis is usually poor. Echocardiography is useful for the diagnosis of pulmonary hypertension and to rule out secondary forms. Right heart catheterization remains the gold standard for diagnosis. Histologically, plexogenic arteriopathy is found most commonly, similar to the findings in immunocompetent patients.[8,53]

Thrombotic arterial lesions and venoocclusive disease occur far more rarely. Intravenous drug users are prone to the development of pulmonary hypertension, which may be related to intravenous injection of foreign material. This pulmonary hypertension is usually worsened by poor compliance. Treatment of pulmonary hypertension includes calcium-channel blockers, diuretics, anticoagulation, and prostacyclin analogues. The latter, specifically epoprostenol, efficiently reduces

pulmonary artery pressure both acutely and in the long term in patients with HIV infection.[8]

The effect of HAART therapy on slowing the progression of pulmonary hypertension is a topic of current research. A study showed improvement of pulmonary arterial pressures with long term HAART therapy.[53] Pulmonary hypertension, associated with HIV/AIDS, differs from idiopathic/ primary pulmonary hypertension in terms of rapidity of progression, is unrelated to CD4 count and is associated with a worse prognosis compared to non- AIDS patients. Bosentan/ PDE inhibitors and heart-lung transplant are usually the only treatment options that work in these sub-groups of patients.[53]

It has been shown that pulmonary hypertension (PH) is commoner in HIV patients as compared with the general population. Further another study had shown similar incidences despite the access to antiretroviral therapy. It is defined as a mean pulmonary artery pressure (mPAP) >25mmHg at rest with a mean pulmonary capillary wedge pressure ≤15 mmHg or an mPAP with exercise >30mmHg.[51]

Causative factors implicated include lung infections, venous thromboembolism and left ventricular dysfunction. Animal model had shown that immune response to Pneumocystis jirovicei may be disturbed and prolonged with potential development of chronic disorder like pulmonary hypertension.[54] This novel finding should be evaluated by designing prospective, cohort study on patients who survive Pneumocystis pneumonia in humans. HIV-related PAH is mostly seen in young and male patients with major symptom being progressive shortness of breath,

followed by non-productive cough, fatigue, syncope or near syncope and chest pain.[51]

Diagnostic tools employed include chest x-ray, electrocardiography and echocardiography, however, cardiac catheterization is mandatory to definitively diagnose the disease and exclude any underlying cardiac shunt. Modalities of treatment include individualized assessment for anticoagulation, vasodilator agents as tolerated, diuretics, oxygen as required and endothelin antagonists.[51]

A review of the HIV-PAH cases reported in the literature over a twenty-two year period showed a more favorable outcome in patients treated with PAH-specific therapy than in those treated with antiretroviral therapy only.[55] Nevertheless, HAART could delay the development of PAH in HIV-infected patients and is recom-mended independent of the CD4 counts.[51]

Disorders of Rhythm Associated with HIV Infection[40,41]

Sudden death and rhythm abnormalities are common in HIV infection and account for up to 20 percent of cardiac-related deaths in this group of patients. These can be secondary to other cardiac pathology, or be a consequence of some forms of treatment.

Concomitant electrolyte disturbance can be important in the development of cardiac arrhythmia, and careful evaluation of the QT interval and magnesium concentration should be used as a guide to cardiac toxicity. ECG abnormalities and rhythm disturbances are not uncommon findings in HIV-positive patients with myocarditis or heart muscle disease, and ectopic beats, ventricular tachycardia, and sudden death have all been reported.

Accelerated Atherosclerosis and Coronary Heart Disease in HIV/AIDS

On one hand, although HAART therapy slows the progression to HIV-associated cardiomyopathy, HAART therapy, especially the protease inhibitors, have clinically significant effects on metabolism; causing hyperlipidemia, insulin resistance, lipodystrophy and hyperglycemia. Different classes of HAART appear to have varying effects on the lipid profile, notably, PIs raising low density lipoproteins (LDL) and NNRTIs raising HDL cholesterol. Accelerated atherosclerosis appears to be one of the unexpected side-effects of HAART. The relationship between anti-retroviral therapy and coronary artery disease is a topic of much debate and uncertainty. Suffice, to say, the current literature suggests that HAART therapy decreases cardiovascular risk in the short term, but prolonged use of HAART therapy, especially protease inhibitors has been shown to be associated with increased risk of CAD/ MI.[8]

Patients on HAART therapy have a 26% increased relative risk of a myocardial infarction, per year of treatment.[56] More recently, it has also been shown that NNRTIs have a low to no increased risk of myocardial infarction compared to protease inhibitors.[57]

It has also been shown that Ritonavir, protease inhibitors, is associated with increase in carotid intimal wall thickness. The incidence of peripheral arterial disease appears to be increased in this patient population, independent of traditional cardiovascular risk factors.[8]

There is substantial clinical evidence for the development of vascular disease in HIV infected patients. The large vessel vasculitis involving the aorta and its major

branches is increasingly being recognized in young Africans who have no evidence of atherosclerosis, syphilis or any other cause of vascular disease.[51]

The vascular disease shows similar histology to the intracranial variant, HIV-associated intracranial aneurysmal vasculopathy, first described in children in the 1980s and over the last decade has been increasingly reported in adult patients.[51]

The typical pathologic process has been described as either an idiopathic focal necrotizing vasculitis with aneurysmal dilatation or a granulomatous vasculitis with fibro proliferative occlusion. Interestingly, vasculopathy is also observed in simian immunodeficiency virus-infected rhesus monkeys and in a mouse model of HIV vasculopathy using a defective HIV pro-virus. The transgenic mice develop a diffuse vasculopathy with intimal hypertrophy, primarily a result of smooth-muscle proliferation, disruption of the elastic lamina and fibrosis of the media and adventitia – findings similar to those seen in HIV-associated vasculopathy.[51]

Clinical approach to heart disease in HIV/AIDS patients[40,41]

The history and physical examination must be used to detect symptoms and signs of cardiovascular disease in patients with HIV/AIDS. The history must include details of previous opportunistic infections, traditional risk factors for atherosclerosis, details regarding present and prior anti-retroviral therapy. One of the important questions clinicians should ask themselves is whether an HIV-positive individual is immunocompetent or immunodeficient- on the basis of a recent CD4 count and if not available, this would be necessary for further diagnostic evaluation and decisions regarding treatment and prognosis.

If the patient is not already on anti-retroviral therapy and presents with cardiac symptoms, this may require referral to an infectious disease specialist for decision making regarding anti-retroviral therapy. Co-ordination of care between infectious disease and cardiology can improve the quality of care and aid in developing an individualized treatment plan based on all of the above factors. Routine use of electrocardiography or echocardiography in these patients is discouraged, especially because of the lack of evidence for finding sub-clinical disease. Shortness of breath is a common complaint, and in patients with HIV/AIDS, requires consideration of cardiomyopathy and pulmonary hypertension as possible etiologies. Transthoracic echocardiography is required for further evaluation.

Drug therapy of for heart failure is not different from HIV-negative individuals, except for consideration of drug-drug interactions, especially with anti-retroviral therapy. Endomyocardial biopsy may be needed in HIV/AIDS patients

with ventricular dysfunction on echocardiography to identify potentially treatable causes of myocarditis/cardiomyopathy.

Lastly, cardiotoxic medications may need to be stopped in patients who have pre-existing or those who have developed significant cardiovascular disease. Management of pericardial disease, especially tuberculous effusions, is different in this patient population: addition of steroids is indicated and pericardiocentesis is needed even in the absence of tamponade.

Treatment of endocarditis does not differ from HIV negative individuals. In this new era of significantly improved prognosis in patients with HIV/AIDS, both cardiac procedures and cardiovascular surgery, including valve replacement and coronary artery bypass grafting should be done in these patients, except in the setting of advanced immunosuppression or high risk of mortality from AIDS-related complications. Increased incidence of coronary artery disease, peripheral vascular disease and deep venous thrombosis has been shown in this patient population and requires careful consideration of the adverse effects of the different classes of anti-retroviral therapy.

A patient with HIV/AIDS and symptoms suggestive of cardiac disease, a growing problem, represents a diagnostic and therapeutic challenge in clinical practice. An intimate knowledge of opportunistic infections affecting the heart, effects of HAART therapy and therapy for opportunistic infections on the heart need to be considered in the differential diagnosis. Effects of HAART therapy, especially protease inhibitors on lipid and glucose metabolism, and their influence on progression to premature vascular disease require consideration. Finally,

management of these patients can vary from non-infected patients, based on drug interactions, differences in responsiveness, and other factors; and this area requires further research.

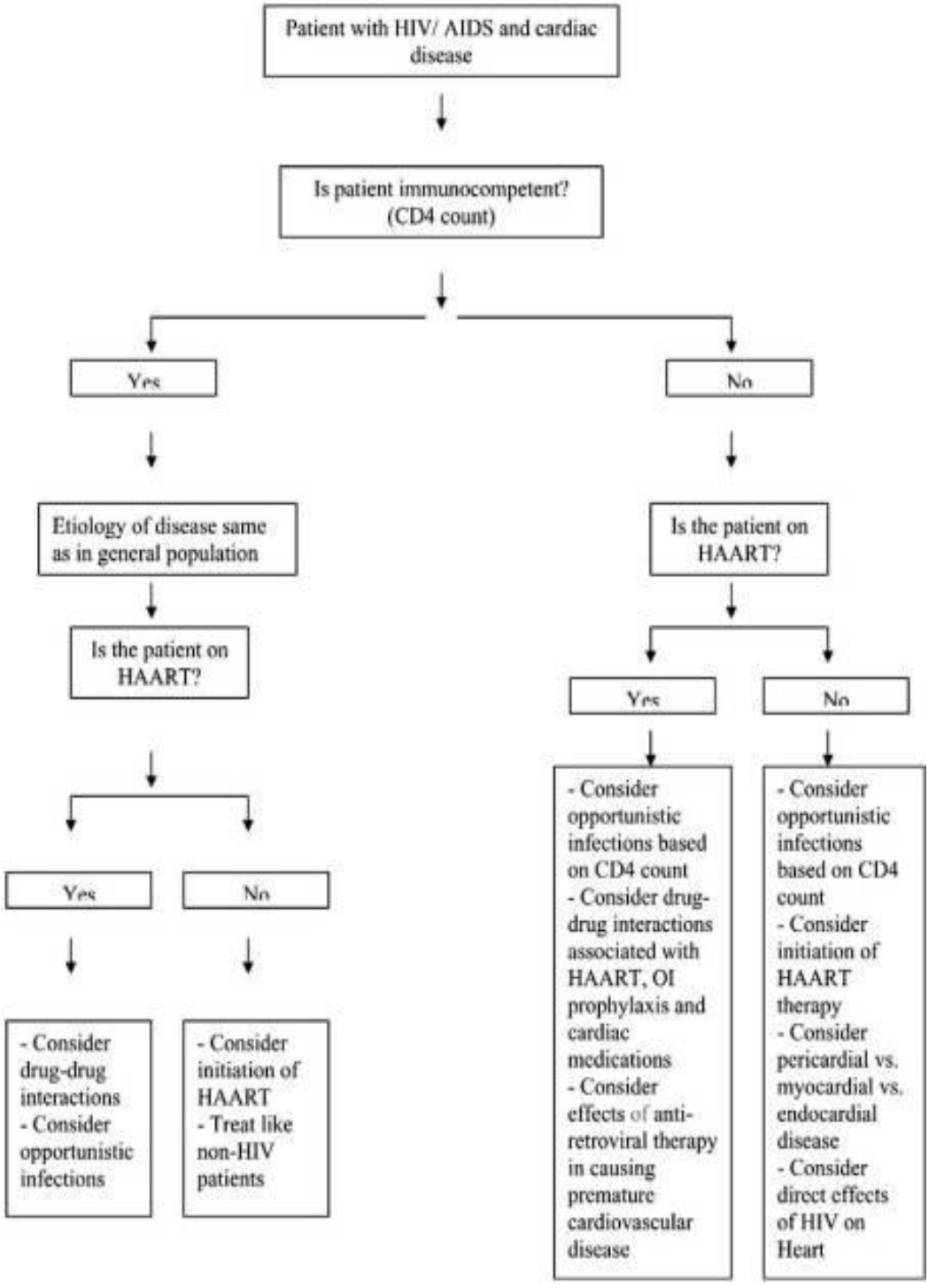


Figure 11. An algorithmic approach to cardiac problems in HIV/AIDS

METHODOLOGY

The present study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on HIV infected patients during the period of January 2013 to December 2013.

Study design

The study design was one year cross sectional study.

Study period and duration

The present one year study was conducted during the period of January 2013 to December 2013.

Place

The present study was conducted in Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum a teaching tertiary care hospital attached to Jawaharlal Nehru Medical College, Belgaum.

Source of Data

HIV infected patients admitted in the wards of Medicine Department or attending the Medicine OPD were enrolled.

Sample size

A total of 100 HIV positive patients were enrolled for the study.

Sampling procedure

Based on the convenient Sample method, the sample size was calculated using the following formula

$n = 4 p q / d^2$

Where, p = Prevalence

q = 100-p (%)

d = Absolute error considered as 10%

Considering the above formula the sample size was calculated as 100 patients. Every consecutive patient fulfilling the selection criteria was enrolled.

Selection criteria

Inclusion

- All HIV infected individuals with/without opportunistic infection

Exclusion

- HIV patients suffering from;
    - Congenital heart disease;
    - Rheumatic heart disease;
    - Hypertension;
    - Diabetes Mellitus
    - Ischaemic heart disease

Ethical clearance

Prior to the commencement, the ethical clearance was obtained from Institutional Ethics Committee, Jawaharlal Nehru Medical College, Belgaum.

Informed Consent

All the patients fulfilling selection criteria were explained about the nature of study and a written informed consent was obtained before enrollment (Annexure I).

Method of collection of data

Demographic data such as age and sex were recorded. Patients were interviewed for chief complaints and physical examination was done. These findings were recorded on a predesigned and pretested proforma (Annexure II).

Investigations

The selected patients underwent the following investigations.

- HIV testing
- CD4 count
- Complete blood count
- Lipid profile – Total cholesterol, HDL, LDL and triglycerides.
- Electrocardiography
- 2D Echocardiography
- Coronary Angiography, Cardiac enzymes wherever feasible

Procedure

CD4 count was done for all patients using flowcytometry using a BD FACS Count system. The CD4 count was done using kits supplied by the National AIDS Control Organisation of India (NACO) to anti Retroviral Therapy (ART) Centre.

The ECG was done on 12 lead surface ECG machine. All the patients were evaluated using M Mode and Two dimensional transthoracic echocardiography and colour flow doppler examination. Each two dimensional study consist of parasternal long and short axis, and apical two and four chamber views.

Outcome variables

The ECG findings were noted. The 2D echocardiography findings were evaluated as for pericardial effusion, dilated cardiomyopathy, systolic / diastolic dysfunction, regional wall motion abnormalities, clot, vegetation and ejection fraction.

Statistical analysis

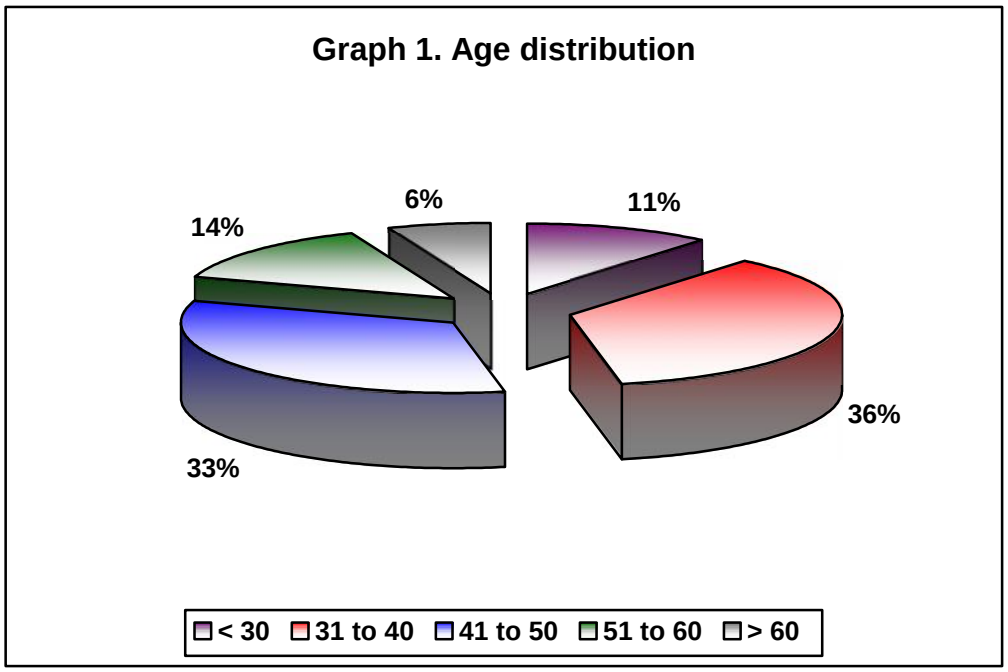
The data obtained was coded and entered into Microsoft Excel Worksheet (Annexure III). The categorical data was expressed as rates, ratios and proportions and comparison was done using chi-square test. The continuous data was expressed as mean ± standard deviation (SD) and comparison was done using independent sample ‘t’ test. A probability value (‘p’ value) of less than or equal to 0.05 was considered as statistically significant.

RESULTS

The present one year cross-sectional study titled “Study of Cardiac Manifestations in Patients of HIV Infection” was carried out in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. During the study period from January 2013 to December 2013, a total of 100 HIV positive patients were studied. The findings/observations and final results are tabulated as below.

Table 1. Age distribution

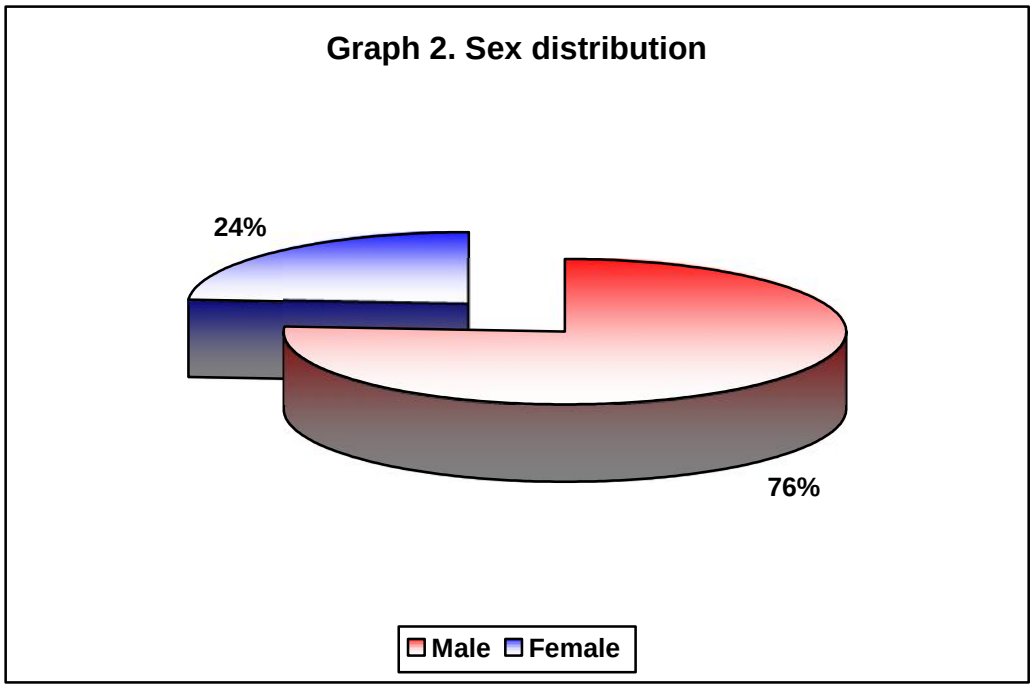
Age group (Years)	Distribution (n=100)	
	Number	**Percentage**
<30	11	11.00
31 to 40	36	36.00
41 to 50	33	33.00
51 to 60	14	14.00
> 60	6	6.00
Total	**100**	**100.00**



Patients age ranged from 18 to 73 years, maximum number of cases were in the age group of 31 to 40 that is 36 patients (36%), between 41-50 years 33 patients (33%), between 51-60 years 14 patients (14%), below 30 years 11 patients (11%) and more than 60 years 6 patients (6%). The mean age of the study population was 42.97 ± 11.07 years.

Table 2. Sex distribution

Sex	Distribution (n=100)	
	Number	**Percentage**
Male	76	76.00
Female	24	24.00
Total	**100**	**100.00**

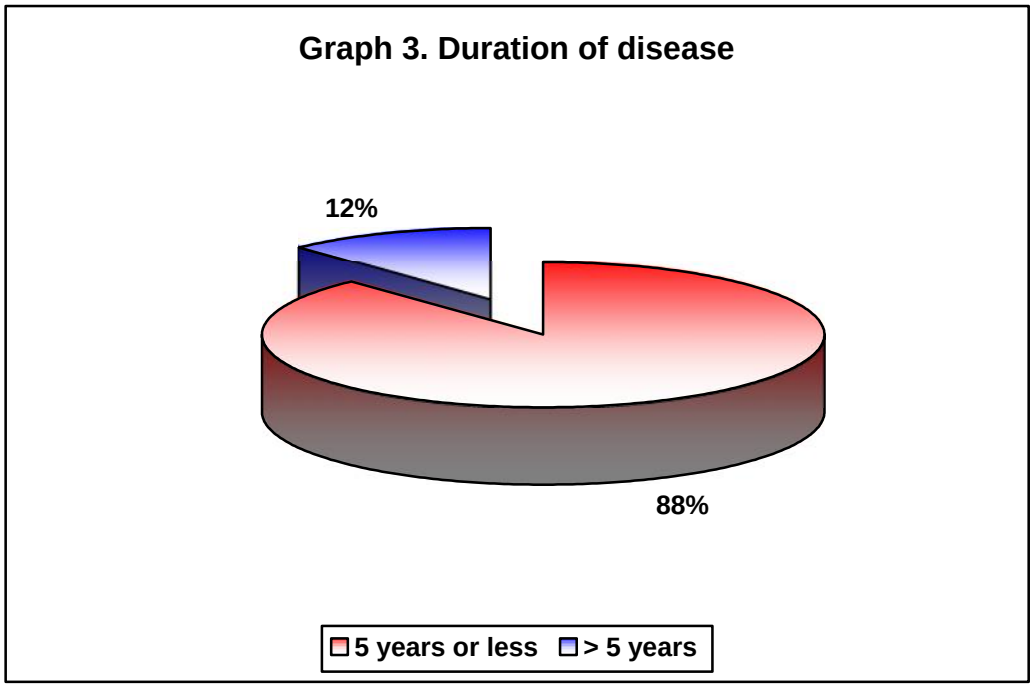


Out of 100 patients 76 (76%) were males and 24 patients (24%) were females, accounting a ratio of male to female 3.16:1.

Inference ***:*** Male preponderance was observed.

Table 3. Duration of HIV infection

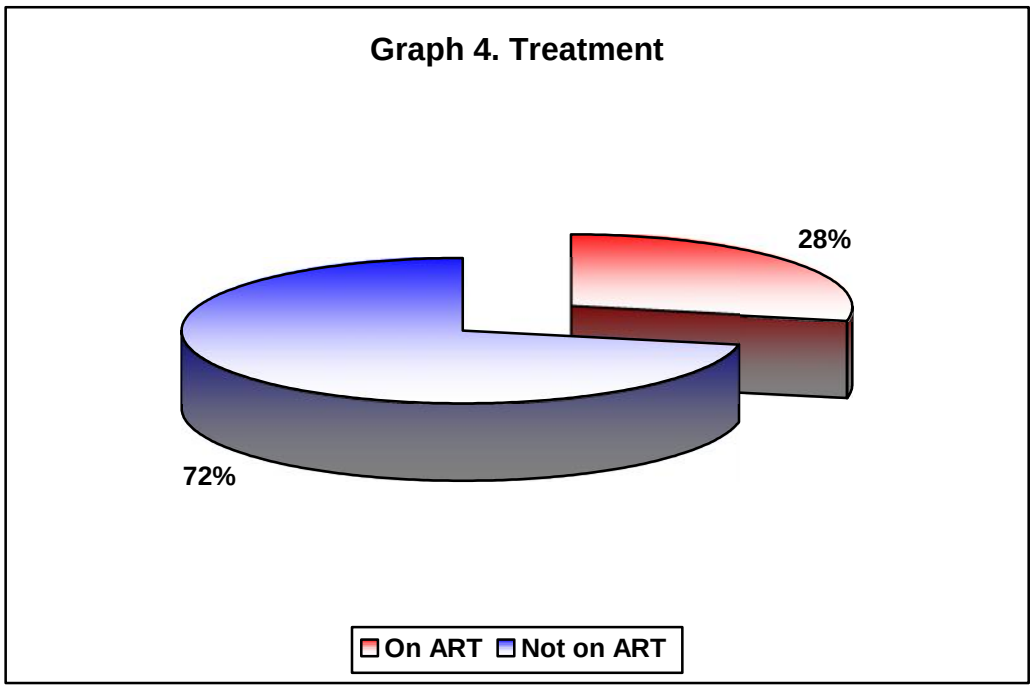
Duration	Distribution (n=100)	
	Number	Percentage
5 years or less	88	88.00
> 5 years	12	12.00
Total	**100**	**100.00**



In the present study, we observed the duration of HIV infection varied from 1 month to 9 years. In 88 patients (88%) duration was either 5 or less than 5 years. In 12 patients (12%) it was more than 5 years .

Table 4. Treatment (ART)

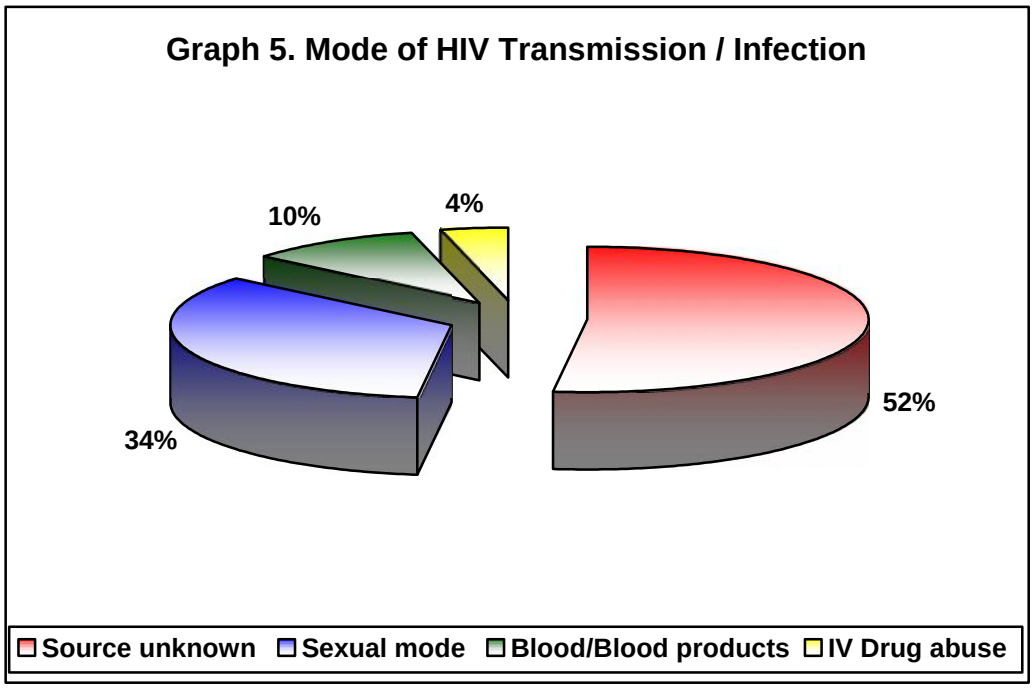
Treatment (ART)	Distribution (n=100)	
	Number	Percentage
On ART	28	28.00
Not on ART	72	72.00
Total	**100**	**100.00**



We observed 28 patients (28%) were on the treatment with Anti-Retroviral drugs, remaining 72 patients (72%) were not on ART.

Table 5. Mode of HIV Transmission / Infection

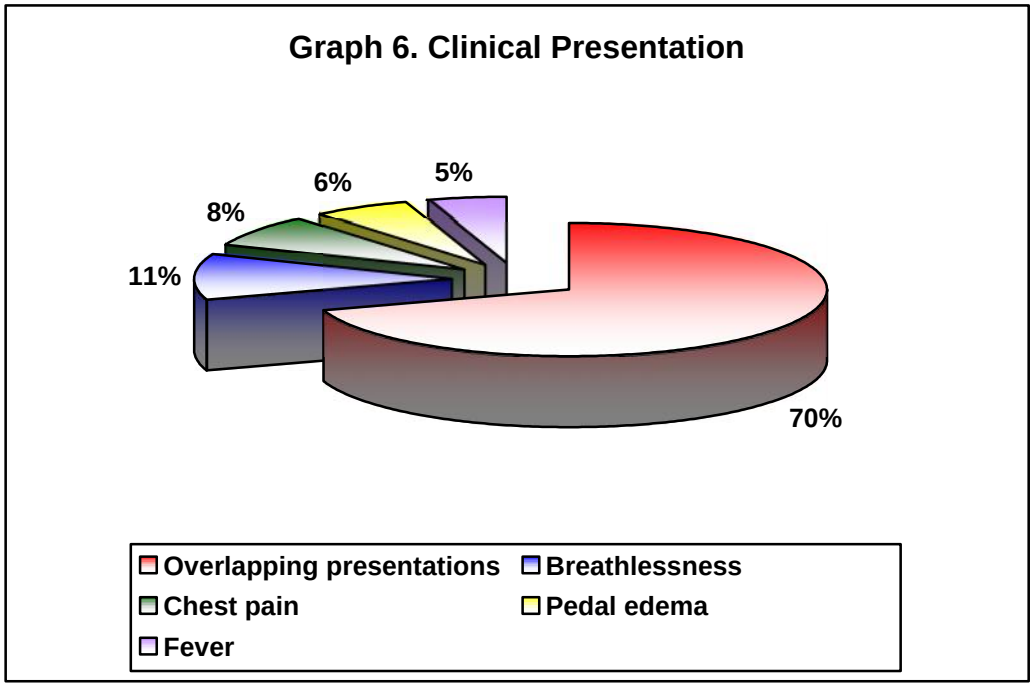
Mode	Distribution (n=100)	
	Number	**Percentage**
Source unknown	52	52.00
Sexual mode	34	34.00
Blood/Blood products	10	10.00
IV drug abuse	4	4.00
Total	**100**	**100.00**



In majority of our patients that is 52 (52%) the mode of transmission / infection was not ascertained, In 34 patients (34%) the mode of transmission was sexual (all heterosexuals), In 10 patients (10%) it was by blood or blood products and in only 4 patients (4%) it was by intravenous drug abuse.

Table 6. Clinical Presentation

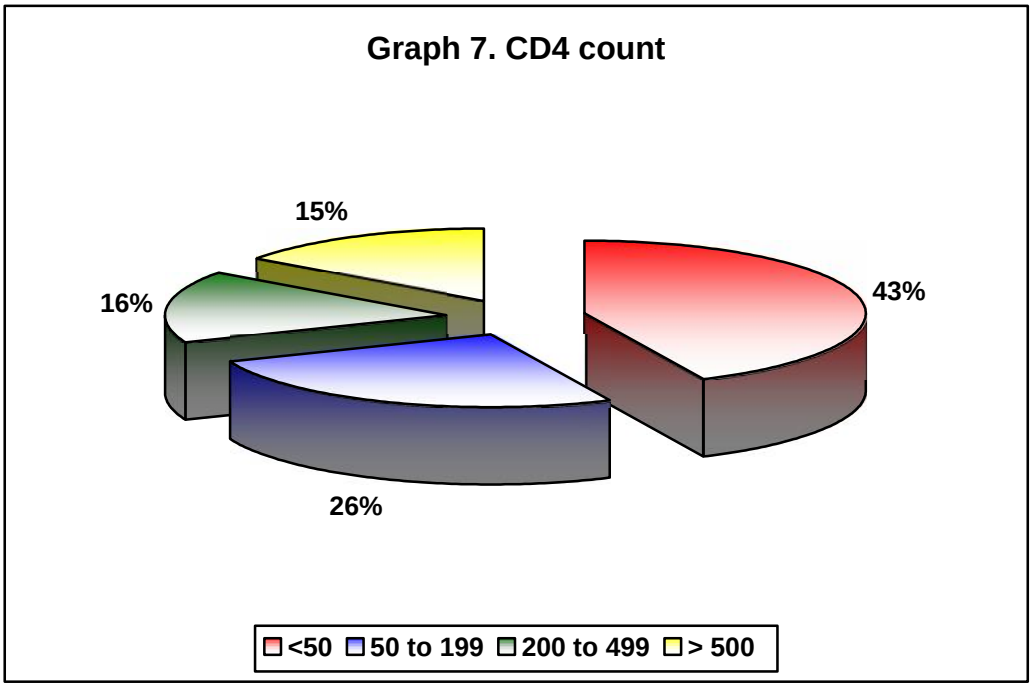
Complaints	Distribution (n=100)	
	Number	**Percentage**
Overlapping Presentations (Symptoms)	70	70.00
Breathlessness	11	11.00
Chest pain	8	8.00
Pedal edema	6	6.00
Fever	5	5.00
Total	100	100.00



In our study majority of patients that is 70 (70%) presented with overlapping symptoms (like breathlessness, chest pain, edema, fever), 11 patients (11%) presented only with breathlessness, followed by chest pain 8 patients (8%), pedal edema 6 patients (6%) and fever 5 patients (5%).

Table 7. CD4 count

CD4 count (/cumm)	Distribution (n=100)	
	Number	**Percentage**
< 50	43	43.00
50 to 199	26	26.00
200 to 499	16	16.00
>500	15	15.00
Total	**100**	**100.00**

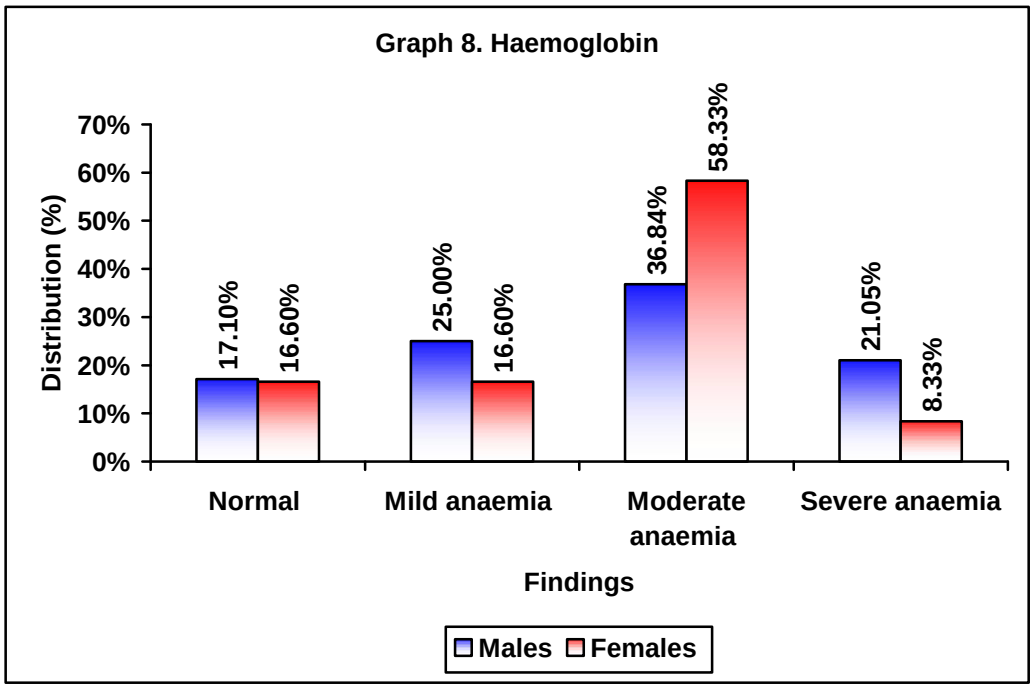


Most of our patients who had presented had CD4 count of less than 50 that is 43 patients (43%), followed by 26 patients (26%) count of more than 50 but less than 200, 16 patients (16%) had CD4 count of more than 200 and less than 500. Only 15 patients (15%) had count of more than 500.

LABORATORY PARAMETERS

Table 8. Haemoglobin

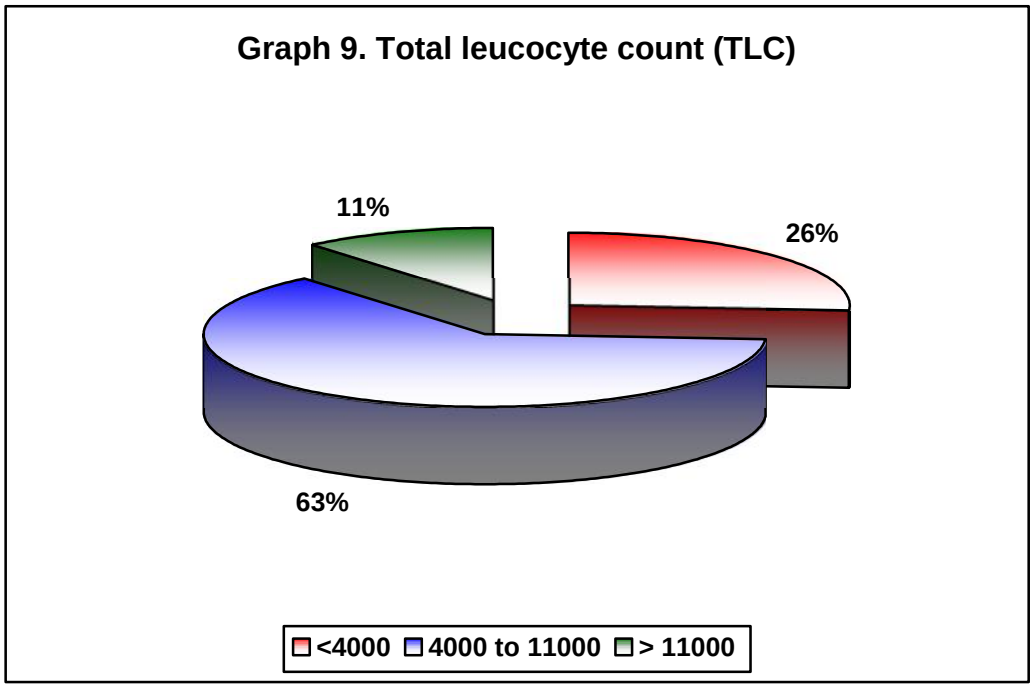
Findings	Males		Females	
	Number	Percentage	Number	Percentage
Normal	13	17.10	4	16.60
Mild anaemia	19	25.00	4	16.60
Moderate anaemia	28	36.84	14	58.33
Severe anaemia	16	21.05	2	8.33
Total	**76**	**100.00**	**24**	**100.00**



We observed 17 patients (17%) had hemoglobin in normal range (M- 13; F-4), 23 patients (23%) had mild anemia (M-19; F-4), followed by 42 patients (42%) who had moderate anemia (M-28; F-14), 18 patients (18%) had severe anemia (M-16; F-2).

Table 9. Total leucocyte count (TLC)

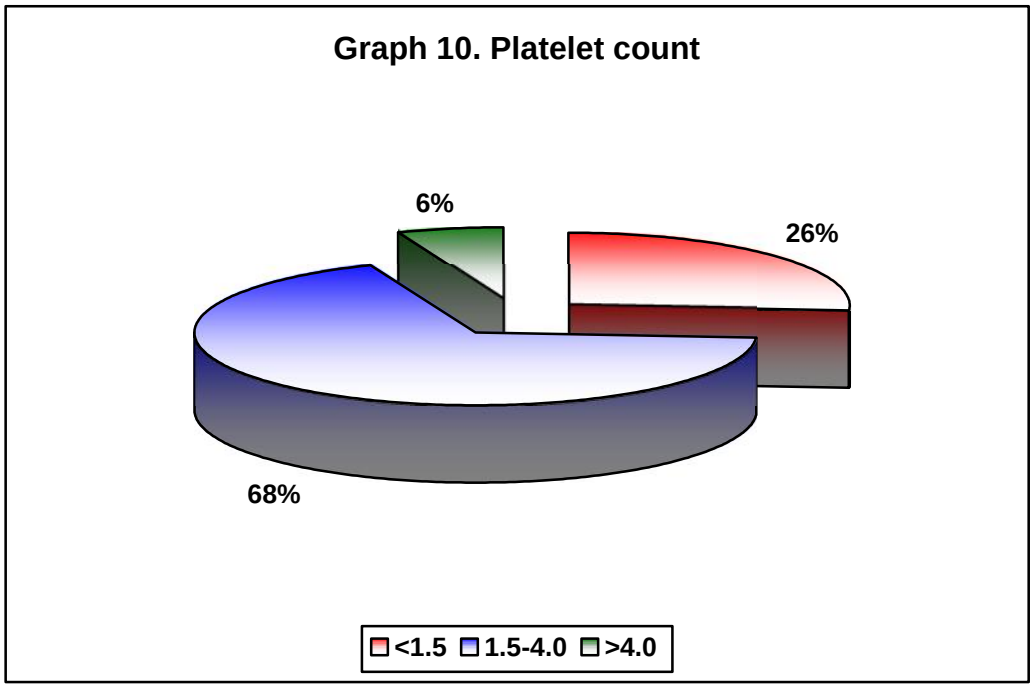
TLC (/cumm)	Distribution (n=100)	
	Number	**Percentage**
<4000	26	26.00
4000 - 11000	63	63.00
>11000	11	11.00
Total	**100**	**100.00**



26 patients (26%) the Total leucocyte count was below 4000 cells/cumm, In 63 patients (63%) the count varied between 4000 to 11000 cells/cumm and in only 11 patients (11%) the count was more than 11000 cells/cumm.

Table 10. Platelet count

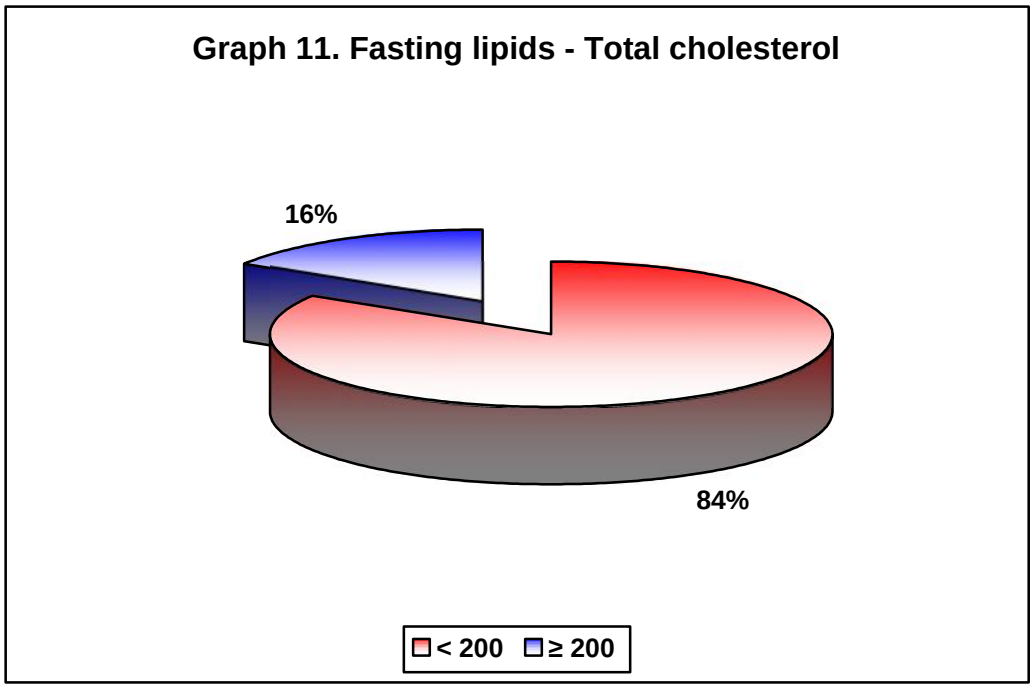
Platelet count (Lakhs/cumm)	Distribution (n=100)	
	Number	Percentage
<1.5	26	26.00
1.5 - 4.0	68	68.00
>4.0	6	6.00
Total	**100**	**100.00**



In 26 patients (26%) the platelet count was below 1.5 lakhs/cumm, 68 patients (68%) had counts ranging between 1.5 to 4.0 lakhs/cumm and in 6 patients (6%) it was more than 4 lakhs/cumm.

Table 11. Fasting lipids - Total cholesterol

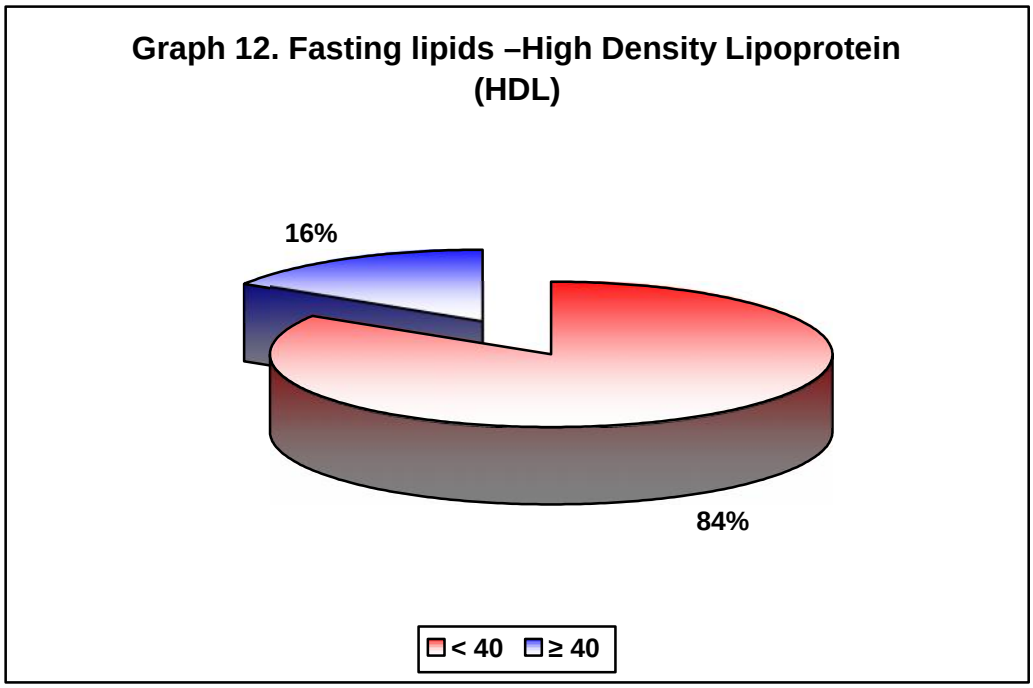
Total cholesterol (mg/dL)	Distribution (n=100)	
	Number	**Percentage**
< 200 mg/dl	84	84.00
≥200 mg/dl	16	16.00
Total	**100**	**100.00**



84 patients (84%) had cholesterol of less than 200 mg/dl and in 16 patients (16%) was more than 200 mg/dl.

Table 12. Fasting lipids –High Density Lipoprotein (HDL)

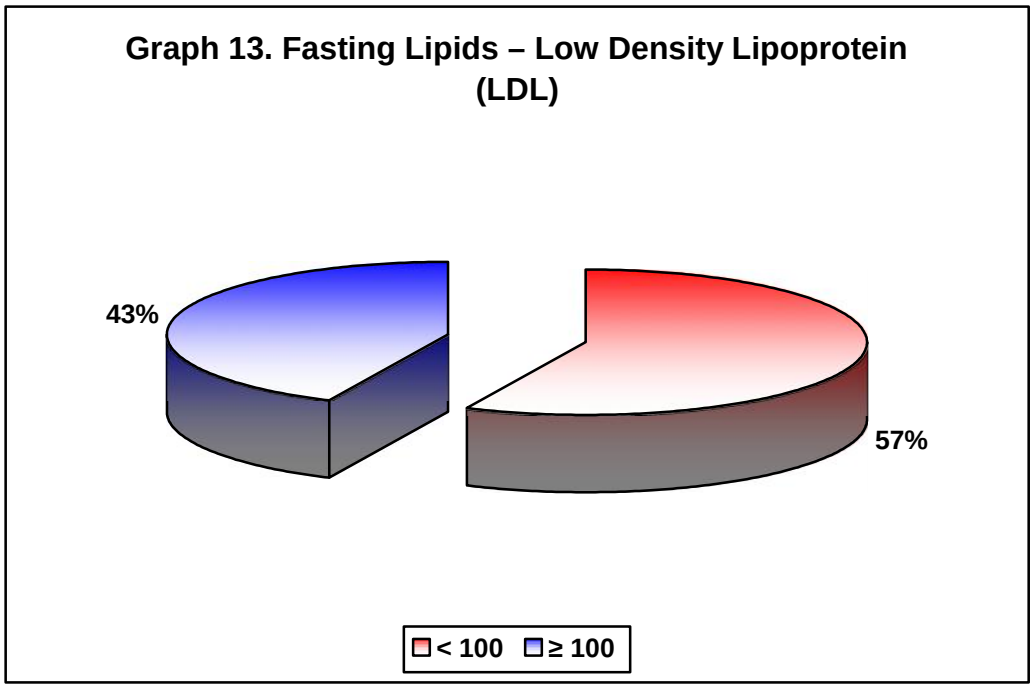
HDL (mg/dL)	Distribution (n=100)	
	Number	**Percentage**
<40 mg/dl	84	84.00
≥40mg/dl	16	16.00
Total	**100**	**100.00**



Majority of our patients that is 84 patients (84%) had HDL of less than 40 mg/dl, 16 patients (16%) had levels more than 40 mg/dl.

Table 13. Fasting Lipids – Low Density Lipoprotein (LDL)

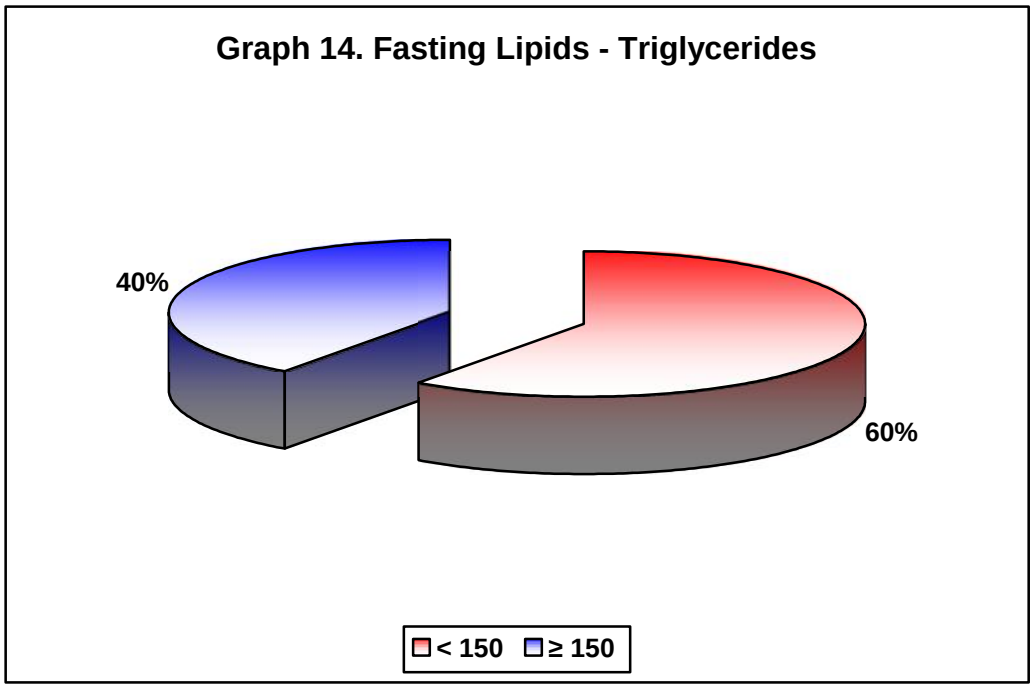
LDL (mg/dL)	Distribution (n=100)	
	Number	**Percentage**
< 100 mg/dl	57	57.00
≥ 100 mg/dl	43	43.00
Total	**100**	**100.00**



It was observed in 57 patients (57%) the LDL was less than 100 mg/dL and in remaining 43 patients (43%) it was equal to or more than 100 mg/dl.

Table 14. Fasting Lipids - Triglycerides

Triglycerides (mg/ dL)	Distribution (n=100)	
	Number	**Percentage**
< 150 mg/dl	60	60.00
≥ 150 mg/dl	40	40.00
Total	**100**	**100.00**

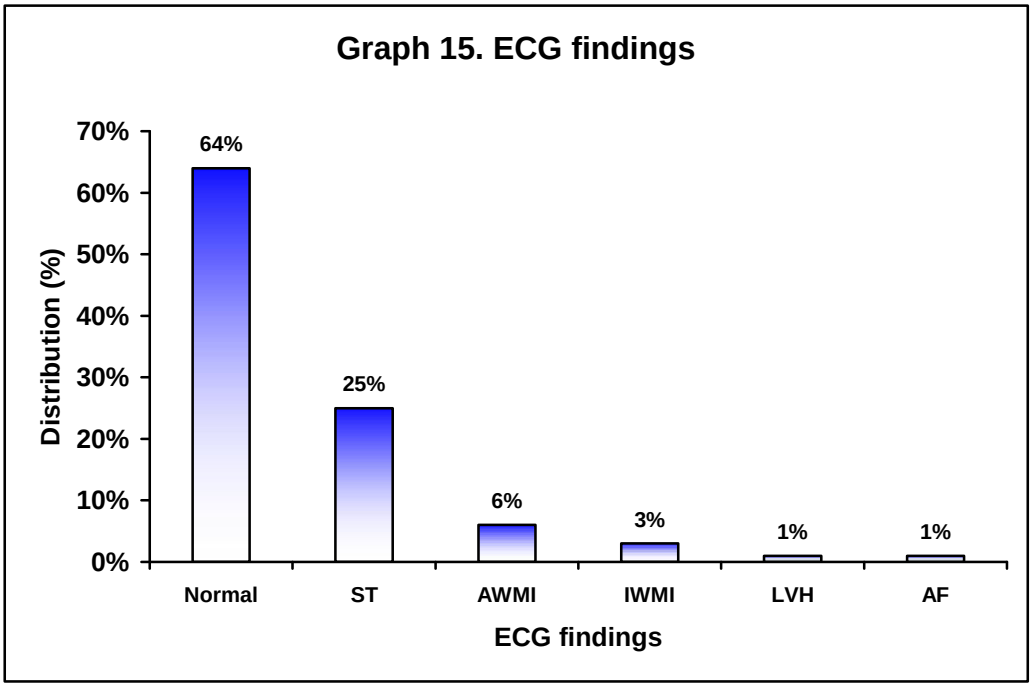


60 patients (60%) had Triglycerides below 150 mg/dl, 40 patients (40%) had equal to or more than 150 mg/dl.

CARDIAC EVALUATION

Table 15. ECG findings

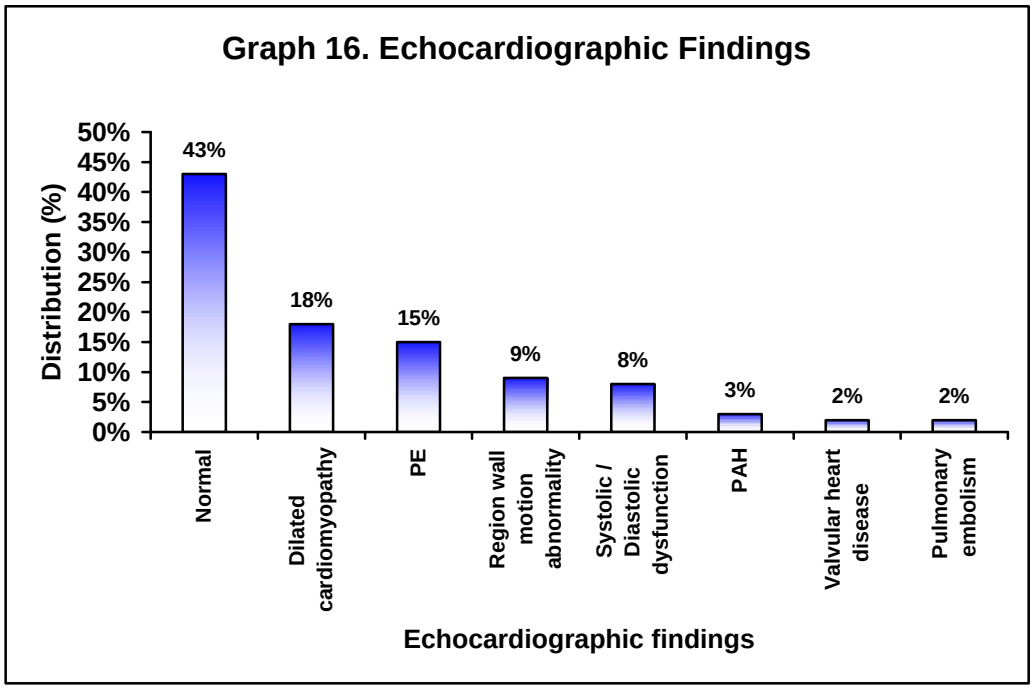
ECG Findings	Distribution (n=100)	
	Number	**Percentage**
Normal	64	64.00 %
Sinus tachycardia	25	25.00 %
Myocardial Infarction Anterior wall	6	6.00 %
Inferior wall MI	3	3.00 %
Left ventricular hypertrophy	1	1.00 %
Atrial fibrillation	1	1.00 %
Total	**100**	**100%**



In 64 patients (64%) ECG tracing was normal, 25 patients (25%) had sinus tachycardia, 9 patients (9%) had evidence of Myocardial Infarction (6 patients- Anterior wall MI, 3 patients- Inferior wall MI), 2 patients (2%) 1 had left ventricular hypertrophy and other patient atrial fibrillation.

Table 16. Echocardiographic Findings

Cardiac Manifestation	Distribution (n=100)	
	Number	**Percentage**
Normal	43	43.00
Dilated cardiomyopathy	18	18.00
Pericardial effusion	15	15.00
Regional wall motion abnormality	9	9.00
Systolic/diastolic dysfunction	8	8.00
Pulmonary Hypertension	3	3.00
Valvular Heart Disease	2	2.00
Pulmonary Embolism	2	2.00
Total	**100**	**100.00**



Most of our patients 43 patients(43%) had normal study, however 57 patients (57%) had various cardiac abnormalities – Dilated cardiomyopathy-18, Pericardial effusion- 15, Regional wall motion abnormality-9, Systolic/diastolic dysfunction-8, Isolated Pulmonary hypertension-2, Valvular pathology-2, Pulmonary embolism-2.

FURTHER EVALUATION WHEREVER FEASIBLE

Table 17. Cardiac Enzymes

Cardiac enzymes	Distribution (n = 9)	
	Normal	**Elevated**
CK-MB	1 (11.11%)	8 (88.89%)
Troponin I	0 (0.00%)	9 (100.00%)

In 9 patients who had presented with Myocardial Infarction, CK-MB was elevated in 8 patients and in 1 patients it was normal. All 9 patients had elevated levels of Troponin I.

Table 18. Coronary Angiography (Number = 9; in MI patients)

Vessel Involvement	Distribution (n = 9)	
	Number	**Percentage**
Single Vessel Disease	5	55.55
Double Vessel Disease	3	33.33
Triple Vessel Disease	1	1.11
Total	**100**	**100.00**

All 9 patients of myocardial infarction were subjected to Coronary Angiography, and found to have in all 9 patients the abnormalities of coronary arteries, 5 patients had single vessel disease, 3 had double vessel disease and 1 had triple vessel disease.

Table 19. CT Pulmonary Angiogram (In 2 patients)

Vessel Involved	Distribution (n = 2)	
	Number	**Percentage**
Right/Left Pulmonary artery	2	100.00
Total	**2**	**100**

In 2 of our patients, who had clinical suspicion of pulmonary embolism, were subjected to CT pulmonary angiogram and both were found to have right as well as left pulmonary artery thrombosis.

Table 20. Correlation of cardiac manifestations with duration of HIV infection and treatment with ART

Duration	Cardiac manifestations (n=28)				Total
	Present		Absent		
	No	**%**	**No**	**%**	**No**
5 years or less	15	68.18	7	31.82	22
> 5	4	66.67	2	33.33	6
Total	**19**	**67.86**	**9**	**32.14**	**28**

p=0.944

We observed 22 patients who had infection of 5 years or less on treatment, 15 had cardiac abnormalities, 7 patients did not. Whereas 6 patients who had infection of >5 years on treatment, 4 patients showed cardiac abnormalities, 2 patients did not. (p-value = 0.944 being statistically insignificant)

Table 21. Correlation of cardiac manifestations with duration of HIV infection without treatment (ART)

Duration	Cardiac manifestations (n=72)				Total	
	Present		Absent			
	No	%	No	%	No	%
5 years or less	34	51.52	32	48.48	66	100.00
> 5	4	66.67	2	33.33	6	100.00
Total	**38**	**52.78**	**34**	**47.22**	**72**	**100.00**

p=0.477

In patients with infection of 5 years or less without treatment (ART), 34 patients showed cardiac abnormalities, 32 patients did not. Similarly in patients with duration of infection >5 years, 4 patients had cardiac abnormalities, 2 did not. (p-value = 0.477 being statistically insignificant)

Table 22. Correlation of Cardiac manifestations with CD4 count

CD4 count (/Cumm)	Cardiac manifestations					
	Present (n=57)		Absent (n=43)		Total (n=100)	
	No.	%	No.	%	No.	%
< 50	32	74.42	11	25.58	43	100.00
50 to 199	14	53.85	12	46.15	26	100.00
200 to 499	3	18.75	13	81.25	16	100.00
>500	8	53.33	7	46.67	15	100.00
Total	**57**	**57.00**	**43**	**43.00**	**100**	**100.00**

p = 0.002

Cardiac manifestation were compared with CD4 counts. In patients less than 50 count abnormalities were found in 32 patients and in 11 patients no abnormalities.

Counts between 50-199, 14 had manifestation and 12 did not have.

Counts between 200-499, 3 had manifestation and 13 did not have.

And in patients >500 counts, 8 had manifestation, 7 did not have.

Correlation of cardiac manifestation with CD4 count had a significant p value (p value=0.002)

Table 23. Comparison of mean CD4 count with cardiac manifestations

Cardiac manifestations	CD4 Count (/cumm)	
	Mean	**SD**
Present	152.14	191.90
Absent	274.28	250.62

p = 0.009

Attempt to compare mean CD4 count with cardiac manifestation showed cardiac abnormalities present in 152.14 ± 191.90, absent in 274.28 ± 250.62. Statistically p value was significant (p=0.009).

DISCUSSION

In the present study of 100 patients with HIV infection, different cardiac manifestations were observed and same was compared with various factors.

In our study patients age ranged from 18 to 73 years, maximum number of cases were in the age group of 31 to 40 that is 36 patients (36%), between 41-50 years 33 patients (33%), between 51-60 years 14 patients (14%), below 30 years 11 patients (11%) and more than 60 years 6 patients (6%). HIV infection was more common in younger age group, same was observed by NACO annual report 2012-2013.[31] Similar observations were made by Das S et al[58] and Currie et al.[38]

Taking sex into consideration we observed in our study males were more affected (76 patients-76%) as compared to females (24 patients -24%).Same sex difference was observed by NACO annual report (2012-2013).[31] Same conclusion was drawn by Das et al[58] and Aggarwal et al.[59]

The duration of HIV infection varied from 1 month to 9 years. Maximum number of patients were 88 (88%) with a duration, either five years or less than five years. Only 12 patients (12%) duration was more than 5 years. It is difficult to state whether duration of HIV infection has direct bearing on cardiac manifestations owing to small sample size of 100 in our study. One study by Giradi E et al[60] has found a definite correlation between CD4 count and duration of HIV infection, but not with duration of HIV infection alone and cardiac manifestations. As we know CD4 count is dependent on duration of infection, age of patient, virological features and host genetic characteristics.

In our study most of patients were not on treatment with ART. Only 28 patients (28%) were on ART. Similar observation was made by NACO annual report (2012-2013).[31] they found 6.04 lakh people on treatment in India among people of 20.89 lakh infected with HIV.

We made an attempt to find out mode of infection (transmission) in our study population. To our surprise majority of patients (52%) source of infection was not known, next common source was by sexual means i.e. 34% (all heterosexuals). 10% was due to blood and blood products and In only 4% it was due to intravenous drug abuse.

This is in sharp contrast to west where in 75% affected males were homosexuals, 14% heterosexuals, 8% IV drug abusers and in 3% source was unknown. The reason for this difference in India and West is owing to sexual practice (behavior), in west homosexuality is more common as compared to India, wherein heterosexuality is more common in India owing to sociocultural reasons. One study by Hakim et al[61] similar observations as ours were made.

The clinical presentations in our patients, majority i.e. 70 patients (70%) had one or the other overlapping symptoms (like breathlessness, chest pain, edema, fever) followed by isolated symptoms of breathlessness 11 patients (11%) chest pain 8 patients (8%), pedal edema 6 patients (6%) and fever 5 patients (5%).

This is in sharp contrast to studies done by Das et al[58] and Anita et al[62] who found symptoms pertaining to pulmonary infections.

When attempt was made to compare our study with various lab parameters, we observed following factors- In majority of our patients CD4 count was less than

50 i.e. 43 patients (43%), CD4 count between 50-199 had 26 patients (26%), 16 patients (16%) had CD4 count of more than 200 and less than 500, and in only 15 patients (15%) count was more than 500. Similar observation was made by Das et al.[58] The low CD4 count in our study was probably due to advanced disease state as all our patients were admitted cases in hospital.

The Hemoglobin estimation in our patients revealed normal in 17 patients (M- 13; F-4), mild anemia 23 patients (23%) (M-19; F-4), moderate anemia 42 patients (42%) (M-28; F-14) and severe anemia 18 patients (18%) (M-16; F-2).

In study by Sullivan et al,[63] (sample size >32000 patients infected with HIV) observed incidence of anemia increased with disease progression.

Next observed parameter was total leukocyte count. In 26 patients (26%) the Total leucocyte count was below 4000 cells/cumm, In 63 patients (63%) the count varied between 4000 to 11000 cells/cumm and in only 11 patients (11%) the count was more than 11000 cells/cumm. As it is known due to continued immunosuppression because of HIV infection the CD4 count would decrease as well as lymphocyte count. Similarly total count may be affected either per se because of immunosuppression, overwhelming infection or could be due to drugs. One study by Robert wood et al[64] used total leucocyte count to monitor ART (TLC count <1250 /cumm correlates well with CD4 count <200, TLC<1800 with CD4 <350).

Platelet count in 26 % patients was less than 1.5 lakhs/cumm, in majority i.e. 68 patients (68%) the count was between 1.5 to 4.0 lakhs/cumm and in only 6 patients (6%) it was more than 4 lakhs/cumm. This is similar to study done by Sloand et al.[65] It is observed that frequency of thrombocytopenia is less observed in

heterosexual people and thrombocytopenia is a known complication of HIV infection. To know the consequences of thrombocytopenia in these patients detail study is required with large sample size.

The fasting lipid studies – Total cholesterol, 84 patients (84%) had cholesterol of less than 200 mg/dl and in only 16 patients (16%) it was more than 200 mg/dl. HDL was less than 40 mg/dl in 84 patients (84%), more than 40 mg/dl in 16 patients (16%).In 57 patients (57%) the LDL was less than 100 mg/dl and in remaining 43 patients (43%) it was equal to or more than 100 mg/dl. 60 patients (60%) had Triglycerides below 150 mg/dl and 40 patients (40%) had equal to or more than 150 mg/dl.

When compared to studies by Baker et al,[66] El- Sadr et al[67] they found low CD4 count associated with lower LDL-C, HDL-C. Another study by Riddler et al[68] in patients of HIV seroconversion was associated with decreased triglycerides, LDL-C, HDL-C levels. In our study majority i.e. 84 % had total cholesterol less than 200 this difference is little difficult to explain owing to our small sample size.

ECG findings revealed normal tracing in 64 patients (64%), 25 patients (25%) had sinus tachycardia, 9 patients (9%) had evidence of Myocardial Infarction (6 patients-Anterior wall MI, 3 patients- Inferior wall MI), 2 patients (2%) 1 had left ventricular hypertrophy and other patient atrial fibrillation.

A study by Anita B et al[62] in their patients sinus tachycardia was observed in 72%; Study by Herdy GV et al[69] had normal tracing in 33% and ST-T changes in 37%: Study by Hadadi et al[70] observed 9.7 % ST-T changes.

Echocardiographic evaluation of these 100 patients, normal study was observed in 43%. In remaining 57% of patients various cardiac abnormalities were observed. Dilated cardiomyopathy-18, pericardial effusion- 15, Regional wall motion abnormality-9, Systolic/diastolic dysfunction-8, Isolated Pulmonary hypertension-2, Valvular pathology-2, pulmonary embolism-2.

Various studies done by Das et al,[58] Aggarwal et al[59] (India) and Hakim et al[61] in Zimbabwe, similar cardiac abnormalities were observed with varying percentage related to cardiac abnormalities.

Studies done by different workers, pulmonary embolism is less reported. One study done by Howling et al[71] reported incidence of 0.26%. We observed in 2 of our patients pulmonary embolism which was confirmed by gold standard investigation-pulmonary angiography. Reason for this in these HIV patients is little difficult to explain and needs further evaluation in our patients.

As it is known number of abnormalities of coagulation have been described in patients of HIV infection the most common is caused by lupus anticoagulant which is found in almost 60% of patients and may be associated with major thromboembolic phenomena. Other coagulation abnormalities that can occur in patients of HIV infection include anticardiolipin antibodies and reduced levels of active protein S. Some opportunistic infections particularly Cytomegalovirus and Herpes simplex virus may be responsible for the prothrombotic states by converting vascular endothelial cells from a noncoagulative to a procoagulative phenotype leading to expression to procoagulant phospholipids.

In all our 9 patients of Ischemic heart disease (Anterior wall MI-6, Inferior wall MI-3) had cardiac enzyme abnormalities

Mary-Krause M, et al.[72] and Klein D et al.[73] observed an increased incidence of myocardial infarction in their patients. Also noted it is more common with patients on treatment with protease inhibitors, in our study none of our patients were on protease inhibitors. All 9 patients in our study were subjected to Coronary Angiography, and all 9 patients had abnormalities of coronary arteries, 5 patients had single vessel disease, 3 had double vessel disease and 1 had triple vessel disease. Similar observation was made by Hsue PY et al[74] who also observed coronary artery abnormalities (blocks). In his study most of the patients had single vessel disease.

In 22 patients with duration of HIV infection less than 5 years on treatment with ART, 15 patients had cardiac abnormalities whereas 7 patients did not have. In patients with more than 5 years duration of HIV infection on treatment (ART) 4 patients had cardiac abnormalities and 2 patients did not have.In patients without treatment (ART), duration of HIV infection less than 5 years 34 patients had cardiac manifestations and 32 patients did not have.Patients with duration of more than 5 years, 4 patients had cardiac manifestations and 2 did not reveal.

We observed taking into consideration duration and treatment with or without ART, in both these groups there were patients with cardiac involvement and without cardiac abnormalities. It is difficult to state the facts observed in these patients. This may be owing to small sample size, duration being less than 5 years or more than 5 years of HIV infection, with or without treatment.

Finally comparison of cardiac manifestations with CD4 count was attempted. In patients less than 50 count abnormalities were found in 32 patients and in 11 patients no abnormalities. Counts between 50-199, 14 patients had manifestation and 12 patients did not have. Counts between 200-499, 3 patients had manifestation and 13 did not have. And in patients >500 counts, 8 patients had manifestation, 7 patients did not have. (p value=0.002; statistically significant)

When mean CD4 count was considered there was a positive correlation between mean CD4 count and cardiac manifestation. (p=0.009;statistically significant) Similar observation was made by Aggarwal et al.[59]

The comparison of CD4 count by various authors has shown cardiac abnormalities increase with the level of immunosuppression and low CD4 count which is also observed in our study.

It has become easier in the recent years to find various cardiac abnormalities in patients with HIV infection because of availability of sophisticated investigations routinely in most of hospitals/centers.

The various cardiac abnormalities observed in our small sample size of 100 patients is little difficult to explain, it could be direct HIV infection, may be opportunistic infection, progressive disease state or may be ART drug toxicity, needs to be addressed by detailed study and large sample size.

CONCLUSION

In present study of 100 patients with HIV infection, we observed various cardiac abnormalities and same was compared to various factors. There was a positive correlation with low CD4 count and mean CD4 count.(p value being statistically significant) In patients with other variables like duration of infection, treatment with ART we found no correlation (p value being statistically insignificant).

In our study, found to have different cardiac manifestations to the tune of 57%. This was possible because of availability of 2D echocardiography.

It is necessary to evaluate further these patients to find out exact reasons for various cardiac abnormalities.

We feel it is worth to study by adjusting the co-morbid conditions/ confounding factors and comparing the cardiac abnormalities by detailed studies including histopathological which may reflect whether these abnormalities per se are because of HIV infection or may be affected by factors like age, sex, duration of HIV or treatment with ART.

Owing to our small sample size (100 patients) large sample size, may be required to overcome these bias.

SUMMARY

The present study of 100 patients with HIV infection admitted in Department of Medicine, KLE Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum during the study period of Jan 2013 to December 2013, to find out the various cardiac manifestations and its correlation with CD4 count.

The results observed were significant correlation of cardiac abnormalities with low CD4 count and mean CD4 count.

However we did not find significant correlation with variable factors – age, sex, duration of infection, treatment with ART.

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ANNEXURE I – CONSENT FORM

"Study of Cardiac Manifestations in Patients of HIV Infection- A One Year Cross Sectional Study at KLES Dr. Prabhakar Kore Hospital, Belgaum"

Objective and purpose of the study:

This research is intended to study various cardiac manifestations in patients with HIV infection and to study the correlation of cardiac manifestations with CD4 count. The principal investigator of the study is Dr. **** ****** under the guidance of Dr.**** ********

Procedure:

If you agree to be part of the research study you will be asked the relevant history and will be subjected to relevant clinical examination and investigations. You will also have to give blood sample for the study.

Risk and Benefits:

The only risk and possible discomfort you might get is while taking blood from your arm for the investigations. It may cause swelling, pain, redness, bruising or infection (rarely happens) at the site from where the blood is drawn.

Alternatives

Taking part in this study is voluntary. You may choose not to take part in this study, or if you decide to take part you can later change your mind and withdraw from the study. Your decision will not change the present or future health care or

other services that you receive. The study doctor may stop your participation in this study any time. If you choose not to take part in the study you will receive the standard treatment for patients with your condition.

Voluntary participation/ withdrawal: Your participation in this study is entirely voluntary and you may withdraw from the study at any time.

Privacy and Confidentiality

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you in this research record. Information from this study may be published but your identity will be confidential in any publication.

Institution / Sponsor's policy

Does not apply to this research

Financial incentives for participation

You will not be paid / offered any gifts /incentives for participating in the study.

Authorization to publish the results

The results of the study would be forwarded to the KLE University, Belgaum as part of requirement towards the completion of MD degree, review and publishing.

If you have any questions about your rights as participant you may call:

1) Dr. **** ******
Investigator,
Postgraduate Student,
Department of Medicine,
JNMC, Belgaum.
Phone- ***** ******

2) Dr. ***** **********
Guide/Chief Investigator,
Professor of Medicine,
JNMC, Belgaum.
Phone- **** *******

3) Dr. **** *********
Professor and Head,
Department of Medicine,
JNMC, Belgaum.
Phone- ***** ******
Extn-***** *****

4) Dr. ***** *******
Professor and Head, Chairman IEC,
Department of Pathology,
JNMC, Belgaum
Phone- ***** *******

CONSENT FORM

I voluntarily agree to take part in this study by signing on the line below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicated that I have read this entire consent form or it has been read to me, and has been explained to me in my vernacular language and had all my questions answered. I will be given a copy of this consent form.

Signature /Left Thumb print of the Participant or legally authorized representative.

Participant's Name/ : …….

Signature/ Left Thumb

Impression of the participant's : …….

Name of the legally : …….

authorised representative/ Guardian

Signature/ Left Thumb Impression. : …….

Witness's Name : …….

Signature/ Left Thumb Impression. :…….

Investigators name and Signature : …….

Date and Place : …….

Dr. **** **********
Professor,
Dept. of Medicine, J. N. Medical College,
K.L.E. University, Belgaum 10.
Ph. No. ***** ******
Ext. *******

Dr. **** *******
Post-Graduate,
Department of Medicine,
J.N. Medical College,
Belgaum
Ph. No. **** **** Ext. *****

ANNEXURE II – PROFORMA

Case Number:

Name Age/Sex

IP Number

Address

Occupation

History of HIV infection

When diagnosed

CD4 count

Whether on anti retroviral therapy Yes/No

If yes,

Type of drugs

Since when

Whether presence of opportunistic infection Yes/No

If yes

What kind of infection

When diagnosed

Treatment offered

Whether patient fulfills inclusion criteria

HIV infected individual with/without opportunistic infection Yes/No

Whether patient has any of the exclusion criteria

Congenital heart disease Yes/No

Rheumatic heart disease Yes/No

Hypertension Yes/No

Diabetes mellitus Yes/No

Ischemic heart disease Yes/No

History suggestive of cardiovascular involvement

Fever

Cough

Breathlessness

Chest pain

Odema

Others

General physical examination

Systemic examination

Cardiovascular system

Respiratory system

Per abdomen

CNS examination

Investigations

Haemoglobin -

TLC -

Differential count -

Neutrophils -

Lymphocytes -

Monocytes -

Eosinophils -

Basophils -

Platelet count -

Lipid profile

Total cholestrol _____

LDL _____

HDL _____

Trigycerides _____

CD4 count _____

ECG

2D echocardiography

Ejection fraction

Systolic/diastolic dysfunction

Pulmonary hypertension

Dilated cardiomyopathy

Pericardial effusion

Valvular lesion

Calcification

Clot

Vegetation

Regional wall motion abnormality

Miscellaneous

ANNEXURE III – KEY TO MASTER CHART

-	-	Absent
+	-	Present
AF	-	Atrial fibrillation
AML	-	Anterior mitral leaflet
AR	-	Aortic regurgitation
AWMI	-	Anterior wall myocardial infarction
CD4	-	Cluster of differentiation 4
CF	-	Circumferential
CK-MB	-	Creatine Kinase-MB
CT	-	Computed tomography
cumm	-	Cubic millimeter
DVD	-	Double vessel disease
ECG	-	Electrocardiography
F	-	Female
gm	-	Gram
HDL	-	High density lipoprotein
INC	-	Increased
IWMI	-	Inferior wall myocardial infarction
LDL	-	Low density lipoprotein
LV	-	Left ventricle
LVH	-	Left ventricular hypertrophy
M	-	Male
m	-	Month

MA	-	Mitral annular
MD	-	Moderate
mg/dL	-	Milligram per deciliter
ML	-	Mild
MR	-	Mitral regurgitation
MS	-	Mitral stenosis
N	-	Normal
ND	-	Not done
NSR	-	Normal sinus rhythm
PAH	-	Pulmonary arterial hypertension
PE	-	Pericardial effusion
PL	-	Postero-lateral
PS	-	Posterior
RBC	-	Red blood cell
RWMA	-	Regional wall motion abnormality
ST	-	Sinus tachycardia
SV	-	Severe
SVD	-	Single vessel disease
TR	-	Tricuspid regurgitation
TVD	-	Triple vessel disease
y	-	Years

ANNEXURE III - MASTER CHART

Serial Number	In / Out patient number	Age (Years)	Sex	Duration of disease	Treatment	Mode of transmission				Presentation					Investigations															
																Haemogram										Lipids				
						Source unknown	Sexual mode	Blood / Blood products	IV drug abuse	Breathlessness	Chest pain	Oedema	Fever	Cough	CD4 count	Haemoglobin (gm%)	Total count (/cum)	Platelet count (/cum)	RBC (/cum)	Neutrophils	Lymphocytes	Monocytes	Eosionophils	Basophils	Cholesterol (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	Triglycerides (mg/dL)	ECG findings
1	2068117	38	F	1y	-	+	-	-	-	+	-	+	+	+	148	11.8	7700	2.56	4.00	61	27	10	2	0	134	34	77	119	ST
2	881996	36	M	4y	+	-	+	-	-	+	-	-	-	-	155	15.0	6400	1.97	4.36	72	21	1	6	0	94	14	58	112	NSR
3	519369	41	M	2y	-	-	-	+	-	-	-	-	+	+	141	10.6	8900	2.19	3.06	90	10	0	0	0	116	31	92	148	ST
4	519675	37	M	8y	+	+	-	-	-	+	-	-	+	+	40	13.3	6300	1.97	4.11	75	23	2	0	0	80	12	48	103	ST
5	519747	22	M	1y	+	-	+	-	-	+	-	-	-	-	144	12.6	2800	0.90	2.56	48	40	8	4	0	182	29	164	206	NSR
6	529552	49	M	6y	+	+	-	-	-	-	-	+	-	-	559	10.8	5900	2.73	3.22	52	43	3	2	0	76	35	87	134	NSR
7	531762	42	M	1m	+	+	-	-	-	+	-	+	-	+	645	12.5	5500	1.85	4.09	63	33	2	2	0	90	43	102	127	ST
8	538178	38	M	3m	-	-	+	-	-	+	+	-	-	-	512	12.7	7100	4.06	5.76	70	22	6	2	0	156	40	89	89	AWMI
9	538797	67	F	8y	+	+	-	-	-	+	+	+	-	+	29	10.0	6100	2.16	3.73	76	17	5	2	0	168	35	68	126	AF
10	540462	46	M	5m	-	+	-	-	-	+	+	-	-	-	48	7.9	7100	3.65	4.17	71	19	7	3	0	216	30	186	308	IWMI
11	540251	43	M	9y	+	-	+	-	-	+	-	-	+	-	42	7.7	3010	1.82	3.08	83	12	3	2	0	218	29	141	256	ST
12	539806	45	F	2y	+	+	-	-	-	+	-	-	-	+	46	9.5	4450	2.65	3.95	80	16	2	2	0	86	34	90	110	NSR
13	543547	42	M	4y	-	+	-	-	-	-	-	-	+	+	32	7.7	8000	0.11	2.61	68	22	10	0	0	163	36	87	202	ST
14	545019	60	M	7y	-	-	+	-	-	+	-	-	+	+	412	10.3	33100	2.19	3.59	79	12	7	2	0	133	34	97	188	NSR
15	549634	46	F	3y	+	-	-	+	-	+	-	+	-	-	43	10.4	4600	2.49	3.11	72	20	8	0	0	176	34	99	216	ST
16	563735	54	M	1y	-	-	+	-	-	+	-	-	-	+	527	12.1	8800	2.93	3.24	72	26	2	0	0	79	18	86	106	NSR
17	544975	41	M	4y	+	+	-	-	-	+	+	-	-	-	47	10.6	5520	2.07	3.24	58	30	4	8	0	88	20	62	113	AWMI
18	545788	38	F	10m	-	-	-	-	+	+	-	-	-	-	39	7.2	3800	1.02	3.81	68	25	7	0	0	133	30	62	104	NSR
19	545566	72	M	3y	+	-	+	-	-	+	-	+	-	-	137	11.8	3000	1.51	2.90	49	44	5	2	0	216	32	124	190	NSR
20	546213	40	M	4y	+	+	-	-	-	+	-	-	+	-	32	10.9	5600	1.63	3.65	41	32	7	0	0	246	39	140	319	ST
21	556491	40	M	8y	+	-	+	-	-	+	-	-	-	+	86	9.8	3300	2.14	3.03	60	38	1	1	0	134	30	86	171	NSR
22	555610	44	M	2y	-	+	-	-	-	-	-	-	+	+	560	12.3	3600	2.49	4.36	57	39	2	2	0	156	31	106	148	NSR

ANNEXURE III - MASTER CHART

Serial Number	In / Out patient number	Investigations																										
		2D Echocardiography																								Cardiac enzymes		Coronary angiography	CT Pulmonary Angiogram
		PE		Dilated cardiomyopathy	ysfunctio		PAH	H/Akinesia								Valvular lesion						Clot	Vegetation	Ejection fraction				
									Akinesia																				
		Finding	Type		Systolic	Diastolic		Global	Anterior wall	Apical septum	Apex	RWMA	Inferior wall	LV	Lateral wall	MR	TR	AR	MS	Calcification				CK-MB	Troponin I		
1	2068117	-	-	+	+	-	MD	+	-	-	-	-	-	-	-	3	2	-	-	-	-	-	30%	ND	ND	ND	ND
2	881996	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	AML	-	-	60%	ND	ND	ND	ND
3	519369	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	MA	-	-	60%	ND	ND	ND	ND
4	519675	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	55%	ND	ND	ND	ND
5	519747	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
6	529552	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
7	531762	+	PL	-	+	-	ML	+	-	-	-	-	-	-	-	2	1	-	-	-	-	-	35%	ND	ND	ND	ND
8	538178	-	-	-	-	-	-	-	+	+	+	-	-	-	-	3	-	-	-	-	+	-	40%	N	INC	SVD	ND
9	538797	-	-	-	-	-	SV	-	-	-	-	-	-	-	-	3	3	-	2	-	-	-	40%	ND	ND	ND	ND
10	540462	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	50%	INC	INC	DVD	ND
11	540251	-	-	+	+	-	MD	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	35%	ND	ND	ND	ND
12	539806	+	PS	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
13	543547	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	50%	ND	ND	ND	ND
14	545019	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
15	549634	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
16	563735	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	55%	ND	ND	ND	ND
17	544975	-	-	-	-	-	-	-	-	+	+	+	-	-	-	-	-	-	-	-	-	-	45%	INC	INC	TVD	ND
18	545788	+	PS	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	40%	ND	ND	ND	ND
19	545566	-	-	+	+	-	MD	+	-	-	-	-	-	-	-	-	-	1	-	-	-	-	35%	ND	ND	ND	ND
20	546213	-	-	+	+	-	MD	+	-	-	-	-	-	-	-	3	-	-	-	-	-	--	30%	ND	ND	ND	ND
21	556491	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
22	555610	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND

ANNEXURE III - MASTER CHART

Serial Number	In / Out patient number	Age (Years)	Sex	Duration of disease	Treatment	Mode of transmission				Presentation					Investigations															
																Haemogram										Lipids				
						Source unknown	Sexual mode	Blood / Blood products	IV drug abuse	Breathlessness	Chest pain	Oedema	Fever	Cough	CD4 count	Haemoglobin (gm%)	Total count (/cum)	Platelet count (/cum)	RBC (/cum)	Neutrophils	Lymphocytes	Monocytes	Eosionophils	Basophils	Cholesterol (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	Triglycerides (mg/dL)	ECG findings
23	557342	53	M	6y	-	+	-	-	-	+	-	+	-	+	48	7.3	5000	0.83	2.70	85	10	4	1	0	110	38	43.4	143	ST
24	549967	40	M	1y	-	-	+	-	-	-	-	-	+	+	256	10.0	12800	7.57	4.21	83	10	6	1	0	88	32	78	98	NSR
25	551289	40	M	2y	-	+	-	-	-	-	-	-	+	+	456	14.2	6400	1.88	4.64	76	14	8	2	0	167	25	132	238	NSR
26	509940	35	M	1y	-	-	-	+	-	+	-	+	-	-	26	12.9	8400	3.33	4.07	92	6	2	0	0	133	48	102	146	ST
27	503023	73	M	1y	-	-	+	-	-	+	-	+	+	-	63	12.2	5300	4.14	3.43	54	36	10	0	0	93	40	68	86	NSR
28	507892	34	F	2y	-	+	-	-	-	+	-	-	+	-	43	7.1	3300	2.04	2.42	79	18	2	1	0	154	39	86	189	NSR
29	502291	39	M	1y	-	-	+	-	-	-	+	-	-	-	584	13.2	4500	0.53	5.36	33	54	10	3	0	216	29	136	319	AWMI
30	500286	29	F	1y	-	+	-	-	-	+	-	-	-	-	189	9.5	8100	1.84	3.59	84	13	3	0	0	116	39	76	149	NSR
31	536934	45	M	2y	-	+	-	-	-	+	-	+	-	+	88	13.2	10800	2.64	4.81	79	14	3	4	0	122	23	90	44	NSR
32	557883	66	M	4y	-	-	+	-	-	+	-	+	+	+	37	6.8	6000	0.77	2.06	58	26	10	4	2	38	7	0	58	ST
33	516621	36	M	3y	-	-	-	+	-	+	-	+	-	-	29	7.1	7300	0.05	2.54	42	40	8	10	0	76	29	65	89	NSR
34	556319	34	M	5m	-	+	-	-	-	+	-	-	-	+	81	12.1	11030	1.70	4.10	85	10	3	2	0	159	32	125	119	IWMI
35	550357	52	M	1y	-	-	+	-	-	-	-	-	+	+	481	7.4	1700	0.51	2.69	54	41	2	3	0	77	24	53	89	NSR
36	559018	40	M	6m	-	+	-	-	-	+	-	+	-	+	40	10.0	6600	4.17	3.20	75	17	8	0	0	148	22	106	98	ST
37	559905	42	M	5m	-	-	+	-	-	+	-	+	+	+	42	8.9	6400	3.54	3.88	71	26	2	1	0	182	44	108	229	NSR
38	559725	51	M	1y	-	+	-	-	-	-	-	-	+	+	411	13.3	3900	0.89	4.21	79	12	8	1	0	88	19	54	86	NSR
39	559218	60	M	1y	-	-	+	-	-	+	-	-	+	-	25	10.5	3200	0.90	4.25	54	41	5	0	0	145	19	111	104	NSR
40	557787	53	M	2y	-	+	-	-	-	-	-	-	+	+	167	6.7	1600	0.76	2.16	74	14	9	3	0	169	34	112	192	NSR
41	560063	60	M	2y	+	+	-	-	-	+	-	+	-	+	47	11.9	2900	1.43	3.13	63	29	7	1	0	98	28	72	104	NSR
42	560373	52	M	7y	+	-	+	-	-	-	+	-	-	-	38	10.0	4000	0.78	3.36	90	8	0	2	0	82	14	58	91	AWMI
43	559993	32	F	4y	+	+	-	-	-	-	-	-	+	+	1048	8.5	8520	2.47	2.56	60	35	4	1	0	149	45	112	237	NSR
44	560298	35	F	6y	-	-	+	-	-	+	-	+	-	+	121	13.2	11500	2.08	3.96	85	10	5	0	0	155	28	110	83	NSR

ANNEXURE III - MASTER CHART

Serial Number	In / Out patient number	Investigations																										
		2D Echocardiography																								Cardiac enzymes		Coronary angiography	CT Pulmonary Angiogram
		PE		Dilated cardiomyopathy	ysfunctio		PAH	H/Akinesia								Valvular lesion							Ejection fraction				
									Akinesia																			
		Finding	Type		Systolic	Diastolic		Global	Anterior wall	Apical septum	Apex	RWMA	Inferior wall	LV	Lateral wall	MR	TR	AR	MS	Calcification	Clot	Vegetation		CK-MB	Troponin I		
23	557342	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	55%	ND	ND	ND	ND
24	549967	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
25	551289	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	65%	ND	ND	ND	ND
26	509940	+	PL	-	+	-	ML	-	-	-	-	-	-	-	-	2	-	-	-	-	-	-	40%	ND	ND	ND	ND
27	503023	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	58%	ND	ND	ND	ND
28	507892	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	73%	ND	ND	ND	ND
29	502291	-	-	-	-	-	-	-	-	+	-	-	-	-	+	-	-	-	-	-	-	-	56%	INC	INC	SVD	ND
30	500286	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
31	536934	-	-	+	+	-	ML	-	-	-	-	-	-	+	-	2	-	-	-	-	-	-	40%	ND	ND	ND	ND
32	557883	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	52%	ND	ND	ND	ND
33	516621	+	PS	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	40%	ND	ND	ND	ND
34	556319	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	50%	INC	INC	DVD	ND
35	550357	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
36	559018	+	CF	-	+	-	-	-	-	-	-	-	-	-	-	-	1	-	-	-	-	--	40%	ND	ND	ND	ND
37	559905	-	-	+	+	-	-	+	-	-	-	-	-	-	-	1	1	-	-	-	-	-	40%	ND	ND	ND	ND
38	559725	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
39	559218	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		40%	ND	ND	ND	ND
40	557787	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	55%	ND	ND	ND	ND
41	560063	+	PS	-	-	+	ML	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	50%	ND	ND	ND	ND
42	560373	-	-	-	+	-	-	-	+	+	-	-	-	-	+	1	-	-	-	-	-	-	45%	INC	INC	DVD	ND
43	559993	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
44	560298	+	CF	-	+	-	ML	+	-	-	-	-	-	-	-	2	-	-	-	-	-	-	30%	ND	ND	ND	ND

ANNEXURE III - MASTER CHART

Serial Number	In / Out patient number	Age (Years)	Sex	Duration of disease	Treatment	Mode of transmission				Presentation					Investigations															
																Haemogram									Lipids				
						Source unknown	Sexual mode	Blood / Blood products	IV drug abuse	Breathlessness	Chest pain	Oedema	Fever	Cough	CD4 count	Haemoglobin (gm%)	Total count (/cum)	Platelet count (/cum)	RBC (/cum)	Neutrophils	Lymphocytes	Monocytes	Eosionophils	Basophils	Cholesterol (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	Triglycerides (mg/dL)	ECG findings
45	561189	46	M	1y	+	+	-	-	-	-	-	-	+	+	161	6.4	11300	2.32	1.83	47	43	8	2	0	89	27	58	86	NSR
46	561471	48	M	8y	-	-	-	+	-	+	-	-	-	-	47	12.8	29000	1.64	4.01	64	33	2	1	0	122	14	37	354	NSR
47	564127	26	M	4y	+	+	-	-	-	-	+	-	-	-	44	11.7	3900	2.36	3.78	57	28	10	5	0	246	20	189	185	AWMI
48	558570	25	F	3m	-	-	+	-	-	+	-	-	+	-	167	12.4	13500	1.51	4.01	55	39	4	2	0	289	29	156	356	NSR
49	555986	40	M	6m	-	+	-	-	-	-	-	+	-	-	382	14.5	3300	0.51	4.23	38	60	0	2	0	132	37	96	140	NSR
50	559839	52	M	9m	-	+	-	-	-	-	+	-	-	-	82	14.9	9100	3.37	5.25	68	30	0	2	0	278	27	139	306	AWMI
51	561882	50	M	3m	-	+	-	-	-	+	-	+	-	+	42	6.5	10500	1.80	1.65	65	28	7	0	0	175	35	129	148	ST
52	561952	50	M	1y	+	-	+	-	-	-	-	+	-	-	667	9.6	3800	0.51	3.90	54	44	1	1	0	156	23	129	206	NSR
53	562359	64	M	1y	-	-	+	-	-	+	-	+	-	+	42	9.4	9800	2.97	3.93	85	8	7	0	0	152	21	103	143	NSR
54	562472	36	F	5y	+	-	-	-	+	+	-	-	+	-	397	9.2	10300	2.92	2.93	76	14	4	4	2	120	46	90	136	ST
55	562183	35	F	5y	+	+	-	-	-	-	-	-	+	+	212	11.7	5500	2.31	4.28	79	14	5	2	0	103	23	71	109	NSR
56	562197	32	M	1y	-	+	-	-	-	+	-	+	-	+	40	11.2	1900	1.63	3.97	60	25	8	7	0	136	19	84	167	NSR
57	562870	30	M	1y	-	-	-	+	-	+	-	+	+	+	5	13.0	7300	2.27	4.45	86	9	5	0	0	237	20	136	289	NSR
58	560979	50	F	1y	-	-	+	-	-	+	-	-	-	-	168	9.6	3800	0.51	3.90	54	44	1	1	0	156	23	129	206	NSR
59	562760	36	F	1m	-	+	-	-	-	+	-	+	-	+	433	10.7	5200	2.65	4.03	60	30	8	2	0	83	18	79	64	NSR
60	563252	24	F	3m	-	+	-	-	-	-	-	+	-	-	969	10.0	5630	1.96	3.07	71	27	0	2	0	134	41	87	97	NSR
61	562691	46	M	4m	-	+	-	-	-	+	-	-	-	+	45	8.9	4860	0.91	3.57	78	20	0	2	0	208	36	115	259	NSR
62	562330	48	M	4m	-	+	-	-	-	-	-	-	+	-	567	12.4	3800	1.91	3.58	66	30	0	4	0	107	18	73	114	ST
63	563397	18	F	6m	-	-	+	-	-	+	-	+	-	-	42	8.7	4900	3.02	3.17	87	9	1	3	0	149	31	120	138	NSR
64	562937	49	M	5m	-	+	-	-	-	-	-	-	+	+	442	11.4	8600	0.97	3.89	59	28	7	6	0	251	28	181	239	NSR
65	563745	29	M	6m	+	+	-	-	-	+	-	+	-	-	40	10.1	3400	0.46	3.87	70	24	6	0	0	230	36	131	257	NSR
66	562691	46	M	4y	+	+	-	-	-	+	-	-	-	+	45	9.0	4010	1.89	3.73	55	40	3	2	0	208	36	115	259	NSR

ANNEXURE III - MASTER CHART

Serial Number	In / Out patient number	Investigations																										
		2D Echocardiography																								Cardiac enzymes		Coronary angiography	CT Pulmonary Angiogram
		PE		Dilated cardiomyopathy	ysfunctic		PAH	H/Akinesia								Valvular lesion						Clot	Vegetation	Ejection fraction				
									Akinesia																				
		Finding	Type		Systolic	Diastolic		Global	Anterior wall	Apical septum	Apex	RWMA	Inferior wall	LV	Lateral wall	MR	TR	AR	MS	Calcification				CK-MB	Troponin I		
45	561189	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
46	561471	-	-	+	+	-	ML	+	-	-	-	-	-	-	-	1	1	-	-	-	-	-	40%	ND	ND	ND	ND
47	564127	-	-	-	-	-	-	-	+	+	-	-	-	-	+	-	-	-	-	-	-	-	55%	INC	INC	SVD	ND
48	558570	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	55%	ND	ND	ND	ND
49	555986	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
50	559839	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	INC	INC	SVD	ND
51	561882	-	-	-	+	-	MD	-	-	-	-	-	-	-	-	-	2	-	-	-	-	-	45%	ND	ND	ND	+
52	561952	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
53	562359	+	PS	-	+	-	ML	+	-	-	-	-	-	-	-	1	1	-	-	-	-	-	30%	ND	ND	ND	ND
54	562472	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
55	562183	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	62%	ND	ND	ND	ND
56	562197	+	PS	-	+	-	MD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	45%	ND	ND	ND	ND
57	562870	-	-	+	+	-	ML	+	-	-	-	-	-	-	-	2	2	-	-	-	-	-	35%	ND	ND	ND	ND
58	560979	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
59	562760	+	PS	-	-	+	ML	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
60	563252	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
61	562691	+	CF	-	+	-	MD	+	-	-	-	-	-	-	-	2	2	-	-	-	-	-	30%	ND	ND	ND	ND
62	562330	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	65%	ND	ND	ND	ND
63	563397	-	-	+	+	-	MD	-	-	-	-	-	-	-	-	2	-	-	-	-	-	-	35%	ND	ND	ND	ND
64	562937	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
65	563745	-	-	+	+	-	ML	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	40%	ND	ND	ND	ND
66	562691	+	CF	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	40%	ND	ND	ND	ND

ANNEXURE III - MASTER CHART

Serial Number	In / Out patient number	Age (Years)	Sex	Duration of disease	Treatment	Mode of transmission				Presentation					Investigations															
																Haemogram									Lipids				
						Source unknown	Sexual mode	Blood / Blood products	IV drug abuse	Breathlessness	Chest pain	Oedema	Fever	Cough	CD4 count	Haemoglobin (gm%)	Total count (/cum)	Platelet count (/cum)	RBC (/cum)	Neutrophils	Lymphocytes	Monocytes	Eosionophils	Basophils	Cholesterol (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	Triglycerides (mg/dL)	ECG findings
67	564203	30	F	2y	-	-	+	-	-	-	-	-	+	-	416	8.2	4300	1.31	2.23	48	40	4	8	0	142	42	110	148	NSR
68	562029	43	M	3y	-	-	-	+	-	+	-	-	-	+	42	13.2	6300	1.97	4.11	75	23	2	0	0	98	23	60	88	NSR
69	564358	38	M	1y	-	+	-	-	-	-	+	-	-	-	29	9.4	5500	1.31	3.16	86	8	6	0	0	192	35	125	276	IWMI
70	564038	36	M	2y	-	+	-	-	-	-	-	-	+	-	35	9.3	8900	2.05	3.08	85	15	0	0	0	92	14	46	73	NSR
71	565352	40	F	2y	-	-	+	-	-	+	-	-	-	-	86	11.0	9900	3.54	2.65	76	16	8	0	0	212	47	131	168	ST
72	564889	35	F	1y	-	+	-	-	-	-	-	-	-	+	537	11.4	4900	3.41	3.61	70	20	8	2	0	103	26	95	119	NSR
73	558451	38	F	4y	-	+	-	-	-	-	+	+	-	-	326	10.6	3000	1.68	4.06	56	33	10	1	0	132	26	103	179	NSR
74	564974	49	M	3y	-	-	+	-	-	+	-	+	-	+	47	11.4	8600	0.97	3.89	59	28	7	6	0	251	28	181	239	NSR
75	548784	48	M	4y	-	+	-	-	-	-	+	-	-	-	147	10.2	7900	2.21	3.59	82	10	4	4	0	112	28	63	119	ST
76	565440	48	F	3y	-	-	+	-	-	+	-	+	+	-	672	12.6	8400	2.81	3.90	76	16	6	2	0	192	45	87	138	NSR
77	565785	36	F	4y	+	+	-	-	-	-	-	+	-	-	46	10.9	4030	2.08	4.21	60	38	1	1	0	98	31	67	134	NSR
78	565078	50	M	9y	-	+	-	-	-	+	-	-	-	-	177	9.4	13110	4.22	3.74	80	16	2	2	0	124	21	95	147	ST
79	566215	42	M	4y	+	-	+	-	-	-	+	-	-	-	48	7.8	21200	3.76	2.09	90	7	2	1	0	131	48	90	156	NSR
80	566043	35	M	2m	-	-	-	-	+	-	-	-	+	-	43	17.7	5300	2.83	6.52	56	36	5	3	0	145	35	112	169	ST
81	561760	59	M	8m	-	-	-	+	-	+	-	-	-	-	34	9.7	7200	4.76	4.75	58	36	4	2	0	161	30	134	203	NSR
82	566375	47	M	10m	-	+	-	-	-	-	-	+	-	-	325	13.4	8300	2.31	4.23	48	40	4	8	0	86	10	44	73	NSR
83	566678	31	M	1y	-	-	+	-	-	-	-	-	+	-	29	10.4	2100	0.31	2.23	88	10	0	2	0	142	43	87	96	ST
84	564869	36	F	1y	-	+	-	-	-	-	+	-	-	-	105	12.6	4950	1.98	4.20	70	23	5	2	0	112	36	90	143	NSR
85	572699	40	M	2y	-	-	+	-	-	+	-	+	+	+	148	4.8	6600	1.41	1.68	87	6	7	0	0	74	19	35	98	NSR
86	572521	28	M	3y	-	+	-	-	-	+	-	-	-	-	155	9.6	4900	1.61	3.13	80	10	8	2	0	94	14	58	112	LVH
87	572472	60	M	2y	-	-	+	-	-	+	-	-	+	+	141	12.2	9700	3.58	4.52	56	33	8	3	0	116	31	92	148	NSR
88	553183	45	F	4y	-	+	-	-	-	+	-	-	+	+	40	10.8	3500	1.20	3.53	60	19	7	14	0	80	12	48	103	ST

ANNEXURE III - MASTER CHART

Serial Number	In / Out patient number	Investigations																										
		2D Echocardiography																								Cardiac enzymes		Coronary angiography	CT Pulmonary Angiogram
		PE		Dilated cardiomyopathy	ysfunctio		PAH	H/Akinesia								Valvular lesion						Clot	Vegetation	Ejection fraction				
									Akinesia																				
		Finding	Type		Systolic	Diastolic		Global	Anterior wall	Apical septum	Apex	RWMA	Inferior wall	LV	Lateral wall	MR	TR	AR	MS	Calcification				CK-MB	Troponin I		
67	564203	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	55%	ND	ND	ND	ND
68	562029	+	PL	-	-	-	ML	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	55%	ND	ND	ND	ND
69	564358	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	60%	INC	INC	SVD	ND
70	564038	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
71	565352	-	-	-	+	-	ML	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	35%	ND	ND	ND	+
72	564889	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	65%	ND	ND	ND	ND
73	558451	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	55%	ND	ND	ND	ND
74	564974	-	-	+	+	-	MD	+	-	-	-	-	-	-	-	2	2	-	-	-	-	-	25%	ND	ND	ND	ND
75	548784	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
76	565440	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	50%	ND	ND	ND	ND
77	565785	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
78	565078	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	65%	ND	ND	ND	ND
79	566215	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
80	566043	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	55%	ND	ND	ND	ND
81	561760	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
82	566375	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
83	566678	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
84	564869	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
85	572699	-	-	+	+	-	MD	+	-	-	-	-	-	-	-	3	2	-	-	-	-	-	30%	ND	ND	ND	ND
86	572521	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	AML	-	-	60%	ND	ND	ND	ND
87	572472	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	MA	-	-	35%	ND	ND	ND	ND
88	553183	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	55%	ND	ND	ND	ND

ANNEXURE III - MASTER CHART

Serial Number	In / Out patient number	Age (Years)	Sex	Duration of disease	Treatment	Mode of transmission				Presentation					Investigations															
																Haemogram										Lipids				
						Source unknown	Sexual mode	Blood / Blood products	IV drug abuse	Breathlessness	Chest pain	Oedema	Fever	Cough	CD4 count	Haemoglobin (gm%)	Total count (/cum)	Platelet count (/cum)	RBC (/cum)	Neutrophils	Lymphocytes	Monocytes	Eosionophils	Basophils	Cholesterol (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	Triglycerides (mg/dL)	ECG findings
89	572930	50	M	2y	-	+	-	-	-	+	-	-	+	-	548	10.0	9000	1.51	4.34	84	6	10	0	0	182	29	164	206	NSR
90	571944	47	M	6y	-	-	+	-	-	+	-	-	-	-	559	10.8	8400	2.72	3.52	50	42	4	4	0	76	35	87	134	NSR
91	573637	42	M	1y	+	+	-	-	-	+	-	+	+	+	145	5.4	19900	0.09	1.79	52	30	0	5	0	90	43	102	127	NSR
92	573854	38	M	4y	+	+	-	-	-	+	+	-	-	-	601	7.9	14700	2.40	2.02	85	7	8	0	0	156	40	89	89	ST
93	574174	37	M	2m	-	-	+	-	-	+	-	+	-	+	209	14.3	7900	1.60	5.08	90	4	6	0	0	168	35	68	126	ST
94	572389	58	M	7m	+	-	-	+	-	+	-	+	-	-	43	9.0	3900	1.95	2.82	60	36	2	2	0	218	29	141	256	NSR
95	573596	52	M	9m	-	+	-	-	-	-	-	-	+	+	256	7.0	1400	1.84	3.17	36	56	4	4	0	88	32	78	98	NSR
96	568501	30	M	4m	-	-	+	-	-	-	-	-	+	+	456	9.3	3400	2.07	3.07	58	38	2	2	0	167	25	132	238	ST
97	568923	41	M	1m	-	-	-	-	+	+	-	-	+	+	63	7.6	8200	1.84	2.80	78	20	0	2	0	93	40	68	86	ST
98	570279	38	M	1y	-	-	-	+	-	+	-	-	+	-	43	11.4	7900	2.82	4.24	88	10	1	1	0	154	39	86	189	ST
99	574170	32	M	2y	-	-	+	-	-	+	-	-	+	+	86	9.9	3900	1.75	3.59	69	21	10	0	0	145	35	112	169	NSR
100	572915	72	M	1y	-	+	-	-	-	+	-	+	+	+	46	11.1	4900	2.08	4.09	60	35	3	2	0	161	30	134	203	NSR

ANNEXURE III - MASTER CHART

Serial Number	In / Out patient number	Investigations																										
		2D Echocardiography																								Cardiac enzymes		Coronary angiography	CT Pulmonary Angiogram
		PE		Dilated cardiomyopathy	ysfunctio		PAH	H/Akinesia								Valvular lesion						Clot	Vegetation	Ejection fraction				
									Akinesia																				
		Finding	Type		Systolic	Diastolic		Global	Anterior wall	Apical septum	Apex	RWMA	Inferior wall	LV	Lateral wall	MR	TR	AR	MS	Calcification				CK-MB	Troponin I		
89	572930	-	-	+	+	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	40%	ND	ND	ND	ND
90	571944	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
91	573637	+	PL	-	+	-	ML	+	-	-	-	-	-	-	-	2	1	-	-	-	-	-	35%	ND	ND	ND	ND
92	573854	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
93	574174	-	-	-	-	-	SV	-	-	-	-	-	-	-	-	3	-	-	-	-	-	-	60%	ND	ND	ND	ND
94	572389	-	-	+	+	-	MD	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	35%	ND	ND	ND	ND
95	573596	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60%	ND	ND	ND	ND
96	568501	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	65%	ND	ND	ND	ND
97	568923	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	58%	ND	ND	ND	ND
98	570279	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	73%	ND	ND	ND	ND
99	574170	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	55%	ND	ND	ND	ND
100	572915	-	-	+	+	-	MD	+	-	-	-	-	-	-	-	-	1	-	-	-	-	-	30%	ND	ND	ND	ND