A STUDY ON SERUM ALBUMIN LEVELS AND ITS CORRELATION WITH CD4 CELL COUNT IN HIV PATIENTS

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ABBREVIATIONS

AIDS: ACQUIRED IMMUNO DEFICIENCY SYDROME

ABC: ABACAVIR

ART: ANTI RETROVIRAL THERAPY

ARDS: ACUTE RESPIRATORY

DISTRESSSYNDROME

AKT: ANTI KOCH'S THERAPY

CDC: CENTER FOR DISEASE CONTROL

CMI: CELL MEDIATED IMMUNITY

CMV: CYTOMEGALOVIRUS

DTG: DOLTUGRAVIR

EFV: EFAVIRENZ

ELISA: ENZYME LINKED

IMMUNOSORBENT ASSAY.

HIV: HUMAN IMMUNODEFICIENCY VIRUS

HZV: HERPES ZOSTER VIRUS

HSV: HERPES SIMPLEX VIRUS

NAT: NUCLEIC ACID TESTING

NACO: NATIONAL AIDS CONTROL ORGANISATION

PML: PROGRESSIVE MULTIFOCAL LEUCOENCEPHALOPATHY

TDF: TENOFOVIR DISOPROXIL FUMARATE

NEF: NEGATIVE FACTOR

TAT: TRANS ACTIVATING GENE

VIF: VIRAL INFECTIVITY FACTOR

ZDV: ZIDOVUDINE

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ABSTRACT

BACKGROUND AND OBJECTIVES:

Prognostic markers of HIV disease progression include CD4+ cell counts and HIV rna levels, although their application is limited in underdeveloped countries due to THE HIGH EXPENSIVE AND AVAILABALITY cost constraints. as a result, it is important to find other indicators of immunosuppression's prognosis. recent research suggests that, regardless of CD4+ cell counts or RNA levels of HIV , low blood albumin levels are linked to rapid progression of the disease and aids-related mortality. the purpose of this research is to determine whether serum albumin levels can serve as a surrogate measure for cd4+cell counts in HIV/AIDS patients.

AIM OF THE STUDY

The purpose of this study is to track the absolute cd4+ cell counts & serum albuminof HIV-positive persons over time to see how they relate as an indicator of immunosuppression.

METHODS: Sixty five individuals with HIV/aids who admitted in shri b.m patil medical college during and research centre .

CD4+ T cell count and Albumin and HIV/aids individuals were correlated using descriptive and analytic statistics.

RESULTS:

The results showed that 70.8% of the cases were men and that 29.2% of the cases were women.

40 to 50 year age group were group were commonly involved.

Upper middle and lower middle class patients were commonly involved. Opportunistic lung disease TB was the most frequent disease .followed by candidiasis. Albumin levels in patients were directly proportional to cd4 cell counts. Albumin and cd4 count were found to have a linear relationship using regression analysis (p0.01). using spearman's rank correlation the rho value is 0.770.

CONCLUSION:

Regression analysis demonstrated a significant linear trend showing that albumin might be utilized as a surrogate marker for immunosuppression in HIV/aids patients, and there wasfound to be strong direct correlation between serum Albumin and CD4 count in the cases.

INTRODUCTION :

AIDS causes a person's immune system to gradually collapse, allowing life-threatening infections and cancers to develop. HIV is a lentivirus (a member of the retrovirus family).

In the summer of 1981, the U.S. Centres for Disease Control and Prevention (CDC) reported that twenty six previously in good health men having sexual relationship with men in New York and LA had developed Kaposi's sarcoma (KS) with or without Pneumocystis jiroveci (formerly P. carinii) pneumonia, as well as five young healthy homosexual men in Los Angeles who got infected with Pneumocystis jiroveci (formerly P. carinii).

The World Health Organization classifies human HIV infection as pandemic (WHO).

since its identification in 1981. More than 25 million people lost their lives to AIDS.

About 0.6% of the total population of the globe is infected with HIV.[3]

Over the next decade, there will be a rise in HIV infections as a result of COVID-19 system failures and a slow public health response to HIV. As a result, we will need to intensify our efforts to reach the UNAIDS-proposed worldwide 95-95-95 targets.

Having caused 40,1 million [33.6-48.6 million] fatalities to far, HIV remains a serious global public health concern..

In 2021, 1.1-2.0 million people contracted HIV, and 650 000 [510 000-860 000] people died from HIV-related causes.

HIV infection cannot be cured. HIV infection has evolved into a treatable chronic illness, enabling those who have it to lead more typical lives as more individuals have access to improved HIV prevention, diagnosis, medication, and care, especially for opportunistic infections..

HIV infects essential immune system cells, such as helper T cells (especially CD4+ T cells), macrophages, and dendritic cells. HIV infection reduces the number of CD4+ T cells by three

basic mechanisms: first, direct viral destruction of infected cells; second, increased rates of apoptosis in infected cells; and third, apoptosis of non-infected cells.

CD8 cytotoxic lymphocytes that recognise infected cells killing infected CD4+ T cells. If the number of CD4 cells falls less than a particular threshold, cell-mediated immunity is lost and the body becomes increasingly prone to opportunistic illnesses. [6]

The progression from HIV to AIDS dependent on virus, human, and environmental factors and interactions ; the majority of infected individuals get AIDS within ten years of illness. Antiretroviral therapy enhances the life expectancy of HIV-positive people. Even if HIV progresses to AIDS, the mean survival period with antiretroviral medication is expected to exceed 5 years. Without antiretroviral medication, AIDS patients frequently pass away in less than a year[7].

NEED FOR STUDY

CD4+cell counts and HIV RNA concentrations are largely recognised as the most accurate predictors of HIV disease progression.

In developed countries, the usage of these identifiers is ubiquitous, however in developing ones, they are difficult to obtain due to their expensive cost and technological limitations. While they continue to be used as key clinical markers, they do not entirely represent the prognosis of a patient. [9] It is crucial to identify and validate additional immunosuppressive prognostic indicators. There are several options, including Lymphocytosis, haemoglobin, Serum Albumin, Haematocrit, CRP, DHEAS, IgA, macroglobulin, p24 Antigen, CD8+ Cell Counts, Level Of CD38 On CD8+ Cells, and Platelet levels.[10]

Low levels of serum albumin in the serum have been linked to an increased risk of mortality in a wide range of chronic and acute diseases. [11.]

Independent of CD4 levels and RNA titre of HIV VIRUS , current research suggests that low albumin levels are connected with accelerated progression of the disease to AIDS, mortality related to AIDS, and overall survival. It is probable that the Albumin Level will out to be an incredibly useful, inexpensive, and readily available surrogate test. This test might be used to determine the severity of HIV infection, in addition to pre-treatment evaluation, clinical surveillance of the responsiveness to ART, and as a determinant of survival. In addition, this assay could be used to determine how long a person will live with HIV..

Within the context of CD4+ cell levels, the purpose of this study is to investigate whether or not the serum albumin level can serve as a surrogate marker of immunosuppression in HIV-positive individuals.

PURPOSE OF THE STUDY

As a method of determining immunosuppression, investigate the correlation in between serum levels of albumin and absolute CD4+ cell counts in HIV-positive individuals..

REVIEW OF LITERATURE:

HISTORICAL FACTORS

AIDS was originally identified in the United States in 1981, when homosexual males in New York and San Francisco were diagnosed with Pneumocystis jiroveci and KS, among other opportunistic illnesses.[16]

Within months, the condition was identified in IV Drug abusers and, shortly thereafter, in transfusion of blood products and blood in patients .

In 1983, the human immunodeficiency virus (HIV) was isolated from a patient with lymphadenopathy; by 1984, it had been proved conclusively to be the AIDS-causing agent. [2]

Approximately 10% of the patient population is comprised of heterosexual interactions with individuals with increased risk behaviours. mostly IV Drug addicts.[1]

The Indian Council of Medical Research began conducting surveillance for HIV infection in the country of India in the year 1985. Anti-HIV antibodies were discovered for the first time in 1986 among people who worked in the sex industry in Chennai, which is located in the southern part of India. In the same year, the first case of AIDS in India was reported from Mumbai.[17]

NACO was formed in 1990-1991. By mid-1986, the ICMR, under the direction of (Late) V. Ramalingaswami, had built HIV testing clinics in the capitals of every state. India is the first nation to use seroepidemiology to track the transmission of infection and estimate prevalence rates. [18]

The "3 by 5" campaign was launched by the World Health Organization (WHO) with goal of treating three million infected people in low- and middle-income countries by 2005.[19.]

EPIDEMIOLOGY

According to the most current HIV estimates report (2019) that was compiled by the Indian government, it is projected that there would be around 23,49,000 people living with HIV/AIDS (PLHIV) in India in 2019. The number of people who become newly infected with HIV in the country is predicted to Drop by 37% between the years 2010 and 2019, indicating that the HIV epidemic is on the decline overall in the country.

In India, HIV infection is primarily caused by high-risk behaviours. In India, the primary high-risk behaviours for HIV infection include unprotected heterosexual behaviour, unprotected homosexual behaviour, and unsafe injection Drug use behaviour.

There are no hospitals specialised to treating HIV/AIDS patients. As of July 2020, however, there are 570 Anti-retroviral treatment (ART) Centres and 1264 Link ART Centres under the National AIDS Control Programme of indian government.

GLOBAL HIV PREVALENCE DATA

In 2021, the people suffering HIV across the globe was estimated to be 38.4 million [33.9 million–43.8 million].

In 2021, approximately 1.5 million people were newly diagnosed with HIV.

The number of people who passed away as a result of AIDS-related illnesses was around 650 000 in 2021.

28.7 million persons worldwide have availability of antiretroviral medication in the year 2021.

Since the beginning of the epidemic, the number of people infected with HIV has ranged between 64.0 million and 113.0 million and is currently at 84.2 million.

Since the beginning of the pandemic, 40.1 million people have died as a result of AIDS-related illnesses. This number ranges from 33.6 million to 48.6 million.

In 2021, the number of HIV-positive individuals reached 38.4 million.

Females are accounted for 54% of all HIV-positive people infected with the virus.

In the year 2021, 85% (75–97%) of all HIV-positive people were aware of their situation. In 2021, around 5.9 million people remained unaware of their HIV-positive.

HIV-POSITIVE INDIVIDUALS RECEIVING ANTIRETROVIRAL MEDICATION

When compared to the number of people who had access to antiretroviral medication in 2010, there were 28.7 million people who did so at the end of December 2021.

In the year 2021, between 66 and 85 percent of all HIV-positive people had access to treatment.

NEW infections

Since its highest point in 1996, the number of people newly infected with HIV has Dropped by 54%.

The number of people who become newly infected with HIV in the year of 2021 was 1.1 million–2.0 million , which is a significant decrease from the 2.4 million–4.3 million in 1996.

In the year 2021, females accounted for about 49% of all newly acquired infections.

Since 2010, the number of people who have become newly infected with HIV has declined by 32%.

Since 2010, the number of new HIV cases in children has declined by 52 percent, falling from 320 thousand [220 thousand–480 thousand] in 2010 to 160 thousand [110 thousand–230 thousand] in 2021.

AIDS-related fatalities

AIDS-related mortality has dropped from 68% to 52% from 2004 to 2010.

As of 2021, there will be 510 000-860 000 AIDS-related deaths worldwide, significantly reduced from 2010.

Since 2010, AIDS-related deaths have fallen by 48% for boys and men and by 57% for women and girls.

"IMPORTANT POPULATIONS"

In 2021, key populations (sex workers and their clients, homosexual males and other men who have sex with men, Drug injectors, and transgender individuals) and their sexual partners accounted for 70% of HIV infections globally, including 94% of new HIV infections outside of sub-Saharan Africa.

In this region, 51% of new HIV infections in sub-Saharan Africa occur.

35 times reduced risk of HIV development in adults who do not engage in IV Drugs..

30 times greater than adult women for female sex workers.

28 times more prevalent among homosexual males.

14 times greater than adult women for transsexual women.

Approximately 4,900 female aged 15 to 24 become HIV-positive each week.

In sub-Saharan Africa, six out of seven new HIV infections among adolescents aged 15–19 are female. Females aged 15 to 24 are twice as likely to be infected with HIV than men in this population.

In sub-Saharan Africa, 63% of all new HIV infections in 2021 occurred in women and girls.

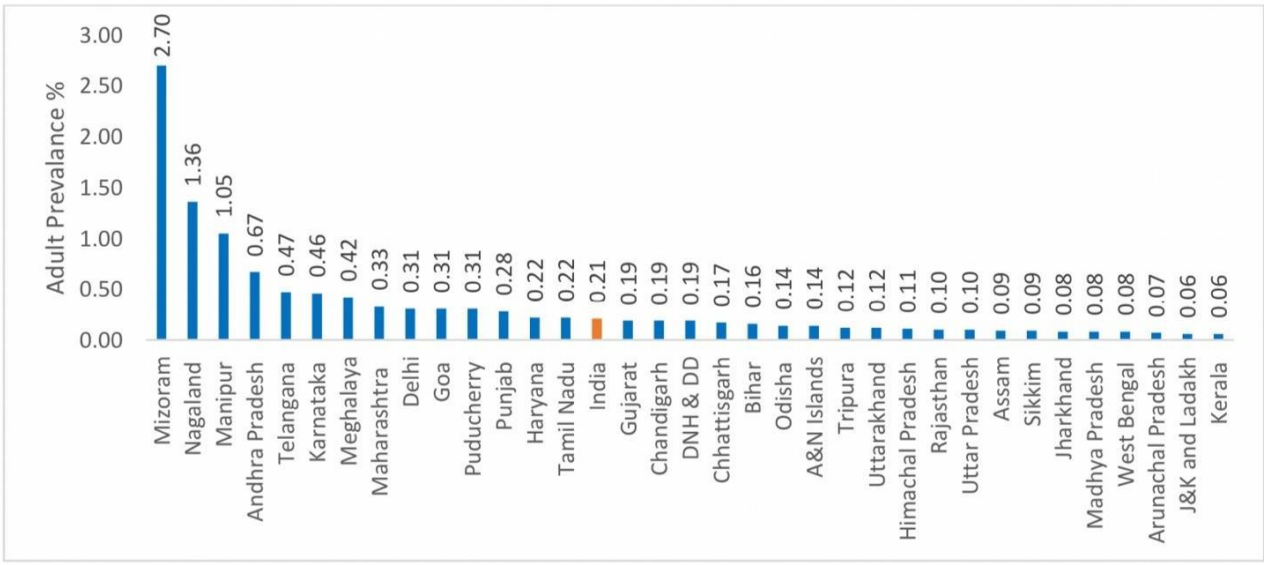
In 2021, 85 percent [75–97 percent] of HIV-positive individuals knew their HIV status.

88% [78– >98%] of those who knew their HIV status were receiving treatment.

And 92% [81– >98%] of those receiving therapy were virally suppressed.

INDIA AND HIV

Figure 1.State/UT-wise Adult HIV Prevalence (%), 2021



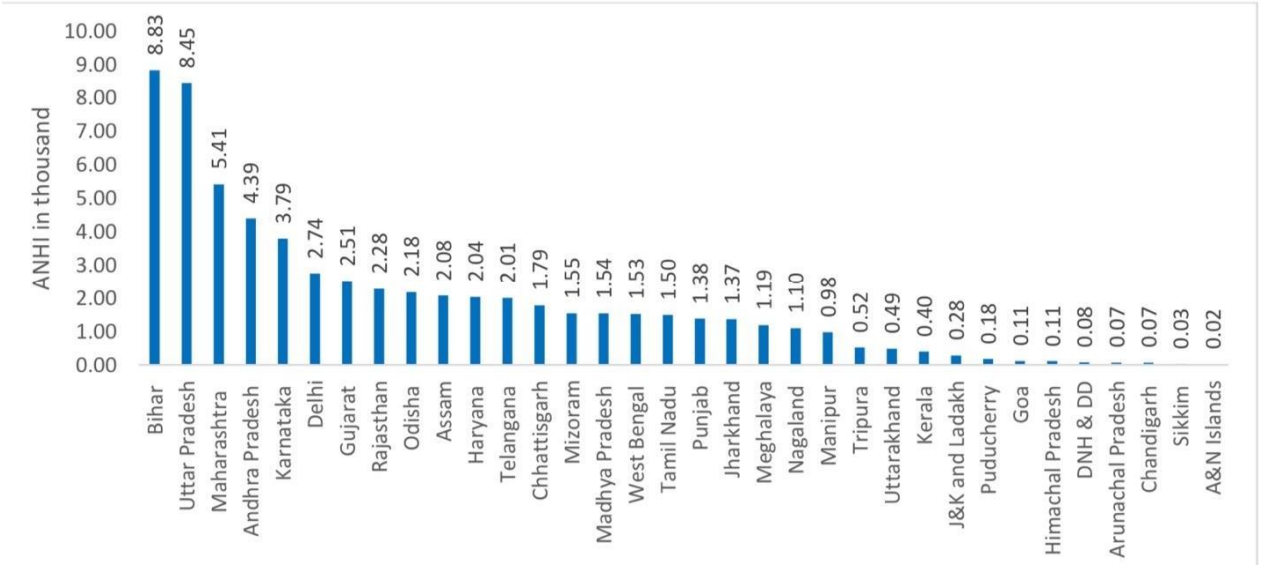
GRAPH 1 : STATE WISE HIV PREVELANCE

According to the India HIV Estimation 2019 report, the HIV prevalence trend among 15–49-year-olds in India has decreased and stabilised from the epidemic's peak in 2000. This indicator's anticipated value for 2019 was 0.17–0.22%. . In the same year, the prevalence of HIV among

males aged 15 to 49 years was estimated to be 0.18–0.32 percent and 0.15–0.2 percent among adult females.

Mizoram, Nagaland and Manipur standing at 2.32%, 1.40% and 1.18% respectively. These three subnational states in north-east india have the highest prevelance of HIV cases in adults..

Maharashtra (8,54 thousand) had the highest expected number of new HIV infections in 2019, followed by Bihar (8,04 thousand), Uttar Pradesh (6,72 thousand), West Bengal (3,97 thousand), Gujarat (3,37 thousand), and Delhi (3,37 thousand) (2.99 thousand).



GRAPH 2 : STATE WISE HIV NEW INFECTIONS

The state/UT with the greatest predicted number of AIDS-related deaths in 2019 is Andhra Pradesh (11.5 thousand), followed by Maharashtra (10 thousand), Karnataka (6.5thousand), Telangana (4.1 thousand), Uttar Pradesh (3.1 thousand), and Tamil Nadu (3.1 thousand).

An estimated 20,52 thousand pregnant women would need ART to prevent HIV transmission from mother to child at the national level. Maharashtra (14.66 percent), Bihar (12 percent), and Uttar Pradesh (10.8percent) had the greatest PMTCT requirements, followed by Karnataka (6.780

percent), Andhra Pradesh (6.8 percent), Telangana (5.0 percent), Gujarat (4.80 percent), Rajasthan (4.21 percent), Tamil Nadu (4.1 percent), and West Bengal (3.31 percent).

TRANSMISSION

1. Sexual transmission:

In underdeveloped nations, heterosexual transmission is by far the most prevalent route of pathogen transmission worldwide. The virus appears to concentrate in seminal fluid, especially with increased monocytes and lymphocytes in fluids, as in epididymites and urethritis, disorders strongly related with other STDs.

Many factors, with the presence of STDs, the age and sex of the uninfected partner, the style of coitus, the level of sickness of the affected partner, and the severity of strain of Human immunodeficiency virus involved, influence the magnitude of the risk. [29]

2. "Transmission by means of blood and blood products" :

AIDS can also be transferred through blood transfusions containing contaminated RBC's, platelets, and factors IX and VIII obtained from plasma.

3.Transmission from mother to foetus or infant

The virus can be transmitted to the foetus in uterus, after child birth or through breastfeeding. priorly vertical transmission of HIV from mother to foetus with lack of treatment was approximately 25%. This risk, however, can be decreased to as low as 1%30 when antiretroviral medication combinations and caesarean sections are available.

By completely avoiding breastfeeding, postnatal mother-to-child transmission can be averted to a substantial extent; however, this comes with significant morbidity. Additionally, exclusive breast

feeding and extended antiretroviral treatment for the child are effective in preventing. transmission.

VIROLOGY

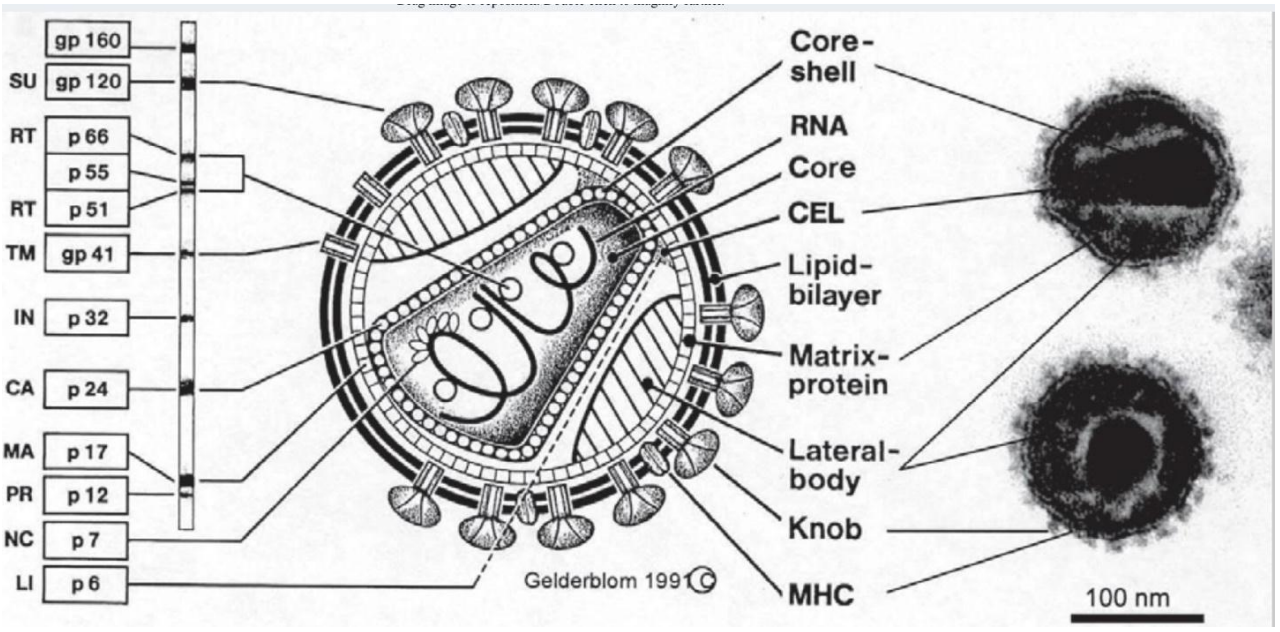


FIGURE 1 : STRUCTURE OF HIV

Schematic view of the HIV particle, corresponding electron micrograph (right) and immunoblot bands (left). Gp = Glycoprotein; p = protein; SU = surface protein; TM = transmembrane protein; gp120 (precursor of SU and TM); RT = reverse transcriptase; IN = integrase; CA = capsid protein; MA = matrix protein; PR = protease; NC = nucleic acid binding protein; LI = link protein. MHCs (major histocompatibility complexes) are HLA antigens

HIV has a different structure from other retroviruses. It is roughly spherical with a diameter of 120 nm, almost 60 times smaller than a red blood cell, and is composed of two copies of positive

single-stranded RNA encoding for the virus' nine genes and 2,000 copies of the viral protein p24 wrapped in a conical capsid. RNA is covalently bound to nucleocapsid proteins, p7, and enzymes.

This is then encased in the viral coat, which consists of 2 layers of phospholipid-containing lipid molecules extracted from the membrane of a cells, when a new-formed viron particle emerges. Host cell proteins and approximately 70 copies of a complex HIV protein protruding from the surface of the virus particle are encased within the viral envelope. [32]

Whenever a new virus particle emerges, it is enveloped in the viral membrane, which consists of two layer of phospholipid-containing lipid molecules derived from the membrane of a human cell. Within the viral envelope are host proteins and around 70 copies of a complex HIV protein projecting from the surface of the virus particle.[32]

ANTIGENS AND GENES

Coding genes for structural protein [33]

gag

this gene govern the shell and core of the virus.

It's formed as precursor protein to p^{55}. This is degraded into 3 viral core and shell proteins: p15, p18, and p24. The predominant core antigen is p24.

gp 160 is split into two envelope components: gp 120, which creates the surface spikes, and gp, the anchoring transmembrane protein. [41]

pol gene

viral enzymes and Polymerase reverse transcriptase, including endonuclease and proteases , are encoded to this gene.

Non-structural and administrative

Tat will Enhance devolopment of the gene particles.

nef gene prevents multiplication of virus.

vpu and vpx exclusive to HIV-1 and HIV-2 helps in formation and subsequent release of daughter viruses.

vpr aids in stimulation of promoter region in virus.

TROPISM :

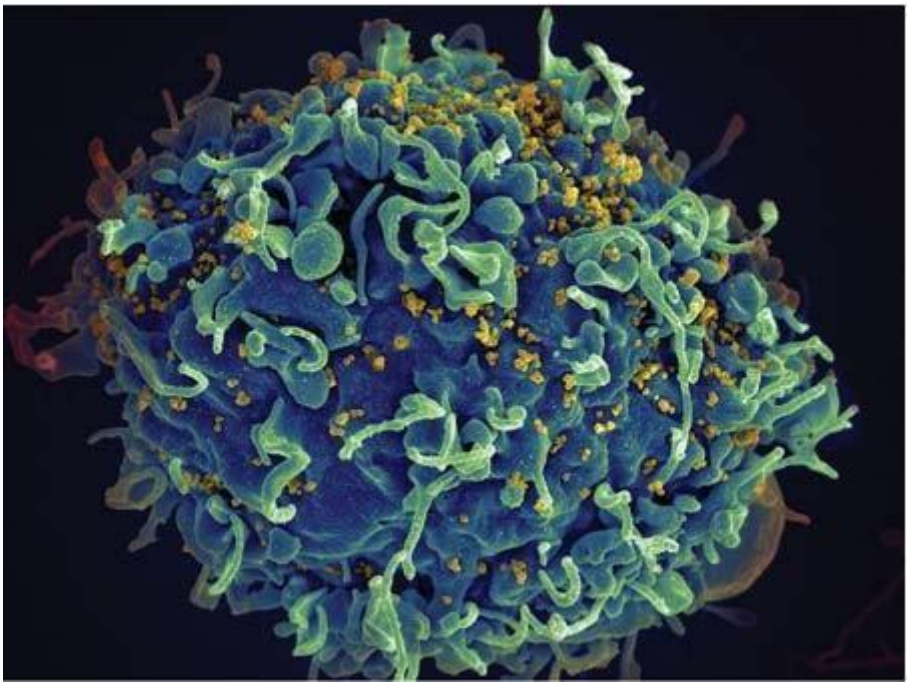


FIGURE 2: SEM image of HIV1 virions infecting a CD4+ T cell

Viral tropism refers to the cell types that are susceptible to infection by HIV. HIV is able to infect multiple types of cells, including, microglial cells and macrophages and CD4 T cells. The interaction of virion envelope glycoproteins (gp120) with theCD4molecule and chemokine coreceptors mediates the entry of HIV-1 into macrophages and CD4+ T cells. [34]

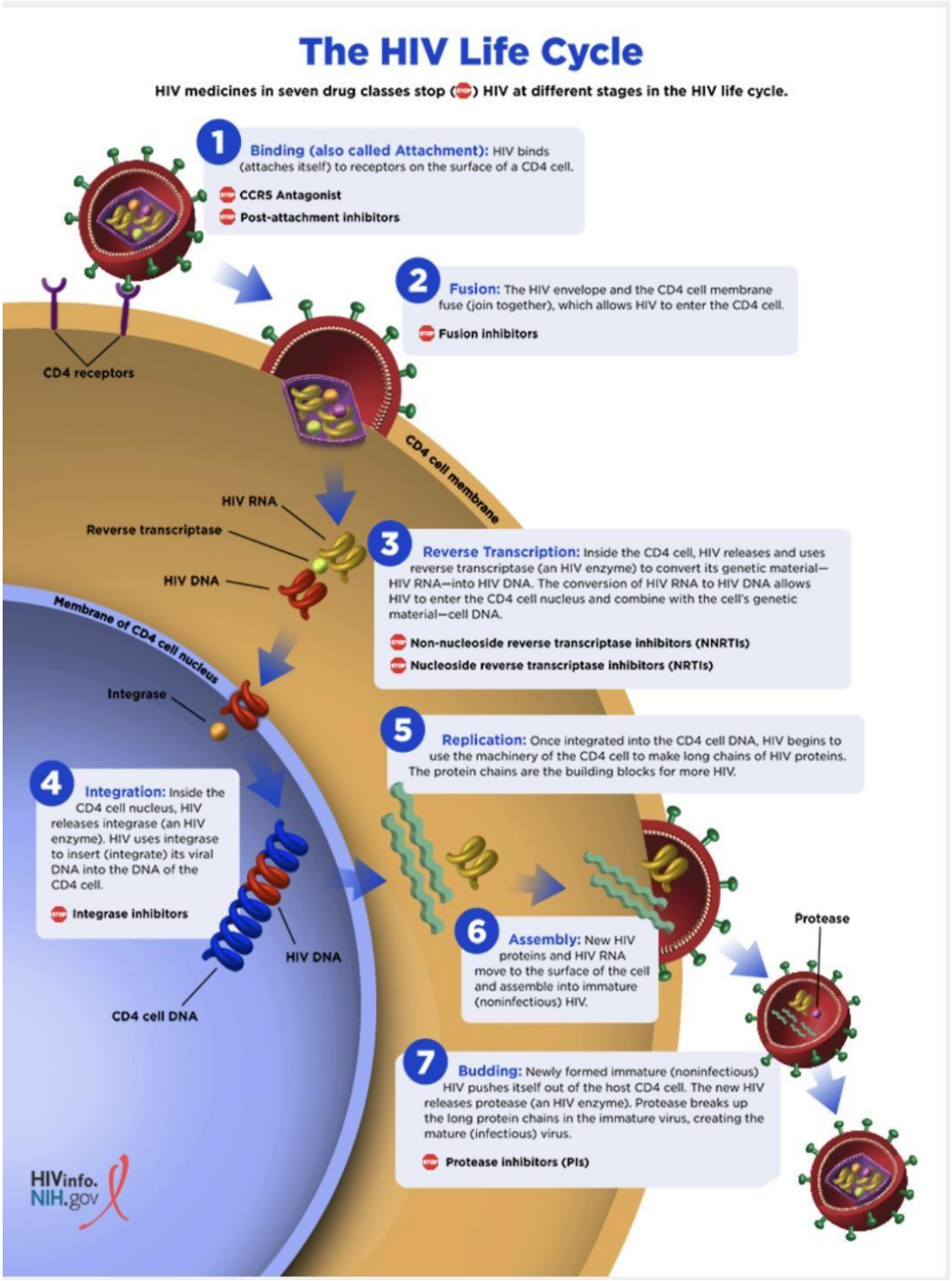
Non-syncytia-inducing (NSI) and macrophage-tropic HIV-1 strains utilise the -chemokine receptor CCR5 for entry and replication in macrophages.

Macrophages are first cells affected by HIV and they can be the basement for new HIV virus molecules. When CD4 cells are reduced. In HIV-infected patients' tonsils and adenoids, macrophages transform into multinucleated, virus-producing giant cells. [35]

T-tropic isolates, also known as syncitia-inducing (SI) strains, use the -chemokine receptor CXCR4 to enter CD4+ T cells and macrophages, where they grow. Dual-tropic HIV-1 strains are thought to be migratory HIV-1 strains since they can use both CXCR4 and CCR5 as viral entry co-receptors. [36]

Specific HIV strains are resistant to certain individuals. Individuals with the CCR5-32 mutation are resilient to R5 virus infection, for instance, since the mutation prevents HIV for interacting with coreceptor, hence limiting its capacity to invade target cells. [37]

HIV LIFE CYCLE :



" FIGURE 3: HIV LIFE CYCLE"

LIFE CYCLE OF HIV

The lifetime of HIV consists of eight distinct phases:

Stage 1: BINDING OF THE VIRUS TO CELL

Surface glycoproteins of HIV attach themselves to specific receptors on CD4+ T cells and macrophages , allowing the virus to penetrate these cell types., fusion of the viral envelope with the cell membrane, and release of the HIV capsid into the cell. [38]

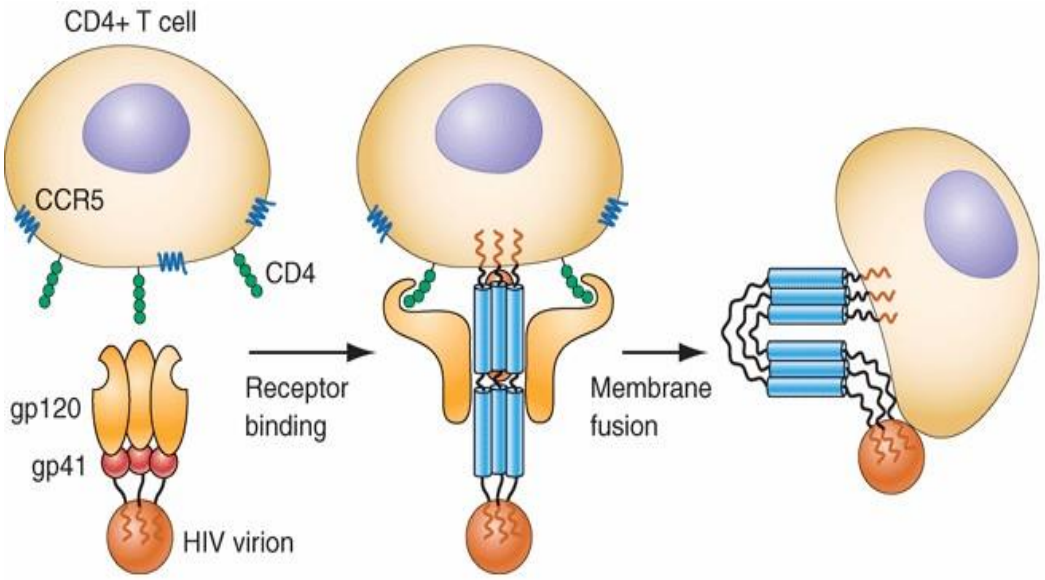


FIGURE 4 : Binding and fusion of HIV- 1 with its target cell. HIV- 1 binds to its target cell via theCD4molecule, leading to a conformational change in the gp120 molecule that allows it to bind to the co- receptor CCR5 (for R5- using cell adhesionoccurs as the transitional intermediateofgp41 wi**l** undergofurtherchangesto formhairpinstructurethat will DRaw thetwomembranes into closedistance.

"Stage 2: entry and uncoating"

After the virus attaches to a cell, its core and the RNA that goes with it enter the cell. In order for the virus's genetic material to be copied, the nucleocapsid, which protects the RNA, must be broken. Part of the nucleocapsid is not covered, so viral RNA can get into the host cell cytoplasm.[39]

Stage 3: Reverse transcription[40]

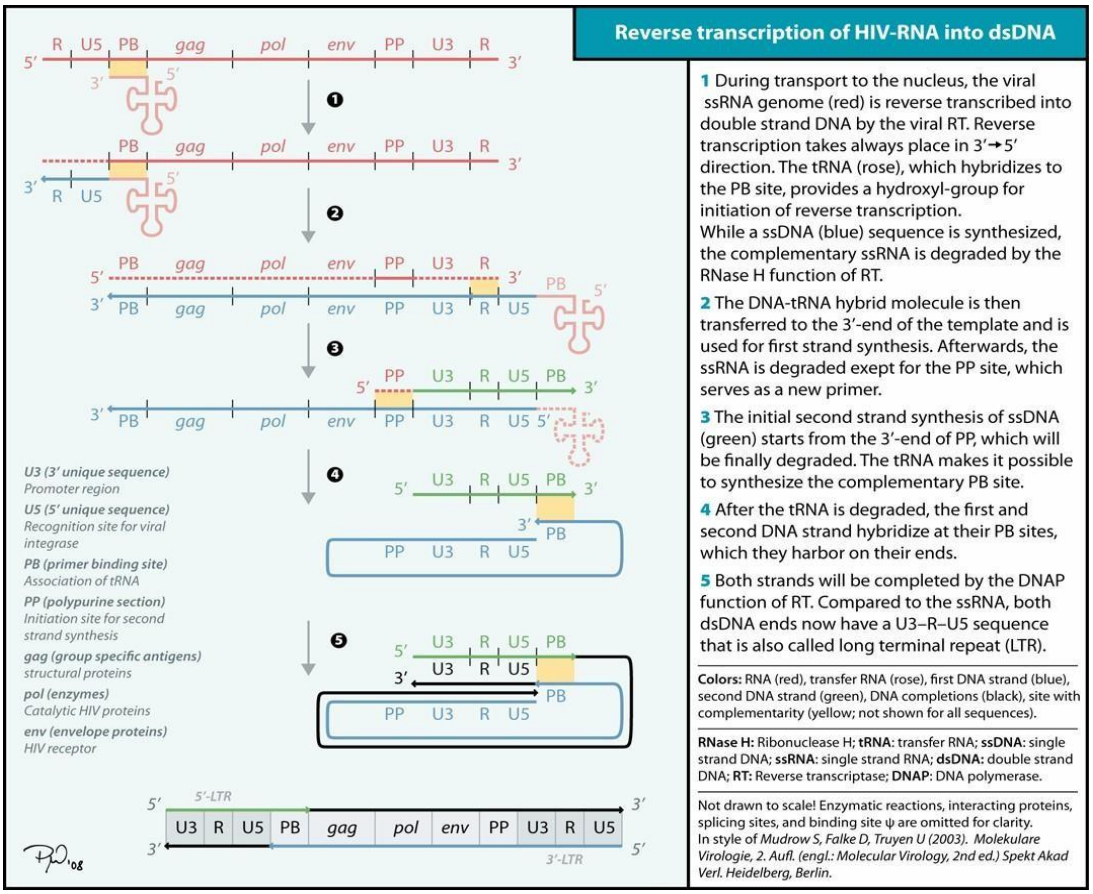


FIGURE 5: REVERSE TRANSCRIPTION

Reverse transcription is especially prone to mistakes, and the changes that happen as a result may make the virus resistant to treatment or help it hide from immune system.

Reverse transcription is error-prone, so when the HIV genome is copied, it only makes a small number of changes. Because of this process, HIV is very different from one person to another. [41]

The reverse transcriptase also has ribonuclease activity, which destroys viral RNA during the making of cDNA, and DNA-dependent DNA polymerase activity, which makes sense DNA from anti-sense C-dna. [42]

Stage 4: Integration into the DNA of the host cell

Integrase, an additional viral enzyme, is responsible for integrating viral DNA into the genome of the host cell. [40]

During this phase, random pieces of viral DNA are added to the DNA of host cell. Because of this part of lifecycle, a new antiretroviral Drugs called "integrase inhibitors" has been made. Once the DNA of the virus is part of the host's DNA, it can lie dormant for many years. HIV's propensity to stay in this latent stage is a significant obstacle to eradicating or treating the virus. [43]

During the "latent" phase of an HIV infection, when the virus is already in the body, this DNA may stop working. For the virus to be made actively, it needs certain cellular transcription factors. The most important of these is NF-B (NF kappa B), which is made more when T-cells are activated. This means HIV is more likely to hurt cells that are already trying to fight infection.[44]

Step 4: Involves the production of viral DNA

During the process of viral replication, the DNA provirus is converted into messenger RNA, which is subsequently spliced into a series of shorter segments. Once in the cytoplasm, the components are translated in to gene products rev and tat after being transported from the nucleus.

The Tat Rev protein congregates, binds to, and facilitates translation of un-spliced mRNAs. It does this by attaching itself to HIV mRNAs.

The full-length mRNA is translated into the structural proteins Env and Gag at this step. The newly synthesised viral RNA acts as the genetic code for the next viral generation. Once produced, viral mRNA is transported from the nucleus into the cytoplasm of the host cell. [39]

Stage 6: Viral Protein Translation and Synthesis

The translation of viral mRNA leads to the production of polypeptide sequences. Each piece of mRNA is linked to enzyme or protein or enzyme that helps build new HIV particles.[39]

Stage 7: Budding and assembly

The plasma membrane of the host cell is the site where the final stage of the HIV-1 life cycle—the synthesis of new virus begins. gp41 and gp120 are glycoprotein in HIV. Synthesised from the Env polyprotein (gp160) that is shuttled from the endoplasmic reticulum to Golgi apparatus, where proteolysis occurs. These are taken to the infected cell's plasma membrane, where gp41 connects gp120 to the membrane. [45]

That HIV can kill infected CD4+ cells is well established. This cytotoxic effect is immune-mediated, so it probably prevents the thymus from regenerating new T cells Some of these immune cells, most notably CD4+ T-lymphocytes, have been shown to be reconstituted and become functionally efficient again[46].

Stage:8: Maturation

Both the separating bud and the immature virion undergo maturation processes. During development, proteases produced by HIV degrade polyproteins into active HIV proteins and enzymes. An HIV virion is formed when the various structural components come together. This cleavage can be blocked by using a protease inhibitor. In this way, cell 47 becomes infected with the virus.

Mechanism of HIV-Induced T-Cell Immunodeficiency

The majority of the reduction in CD4 cells is because of infection and intrinsic cytopathic consequences of the replicating virus [48].

Every day, around Hundred billion new virus particles are produced, whereas between One to two billion CD4+ T cells die.

The virus may directly destroy infected cells through an increase in plasma membrane permeability produced by the release of viral genomes from infected cells and by affecting the protein synthesis. In addition to the virus's direct destruction of cells, the loss of T cells may be caused by a number of other processes. [50]

By colonising lymphoid organs, HIV can cause gradual harm to the lymphoid organ's. Typically, this trait is unique to the T-tropic X4 subtype of HIV-1, also known as the syncytia-inducing (SI) virus.

Immune system is heavily involved due to declining numbers of CD4 T cells in the immune system.[51].

CELLS INVOLVED IN HIV:

The involvement of dendritic cells and macrophages plays a major role in HIV progression. [52] Even divisions of cells is required for the replication of most retroviruses, the HIV-1 vpr gene allows HIV-1 to infect and replicate in terminally differentiated, non-dividing macrophages. [53] Infected macrophages release a negligible amount of viral particles from the surface of the cells , but these cells has a vast quantity of virus particles, which are usually discovered in vacuoles within the cells .Macrophages have lot of resistance against cytological effects of HIV when compared to CD4 cells, yet nonetheless permit viral replication. As a result, macrophages may serve as infection reservoirs whose production is largely impervious to host defences. [53]

Even a modest number of infected blood monocytes can carry HIV to many body locations, including the nervous system. [54]

HIV requires follicular dendritic and mucosal cells for initiation and persistence.

The virus infects mucosal dendritic cells, which transmit it to lymph nodes of various regions. where CD4+ T cells get it. Additionally, dendritic cells have a lectin-like receptor that binds HIV and exposes it to T cells in infectious state, hence enhancing T cell infection. [54]

In lymph nodes, the dendritic follicular cells in germinal centre acts as reservoir for HIV. [54]

Furthermore, significant B-cell dysfunctional abnormalities is associated with AIDS. In paradoxical style, polyclonal stimulation of B lymphocytes causes germinal centre hyperplasia (primarily in the initial stages of the disease), and accumulation of circulating immune complexes. This activation may be the result of multiple factors: reinfection or reactivation with polyclonal B-cell activators cytomegalovirus and EBV; gp41's potential to promote growth of B cell and differentiation; and HIV-macrophages' raises the production of IL-6, which helps in proliferation

of B cells. AIDS patients are not able to create antibody responses to newly encountered antigens despite raised B-cell levels.

This may be partially attributable to a loss or reduced T-cell aid, but antibody responses against T-independent antigens are also suppressed, indicating that B cells may have additional intrinsic problems. Patients with compromised humoral immunity are prone to infections caused by encapsulated bacteria, such as a H. influenzae and S. pneumoniae, which require antibodies for efficient opsonization and clearance.[55]

NERVOUS SYSTEM INVOLVEMENT:

HIV infection also affects both peripheral and central nervous system. Therefore, the aetiology of symptoms needs further consideration Microglia cells and Macrophages, cells of the nervous system which belong to the macrophage line, are the brain cell types are commonly infected with HIV[56].

Infected monocytes are hypothesised to transfer HIV into the brain. Accordingly, most HIV isolates from the brain are M-tropic. However, the mechanism by which HIV promotes brain injury remains unknown. Since HIV does not infiltrate neurons and the magnitude of neuropathologic changes is often less than anticipated based on the intensity of neurologic symptoms, researchers believe that neurologic deficits are apparently caused by viral products and soluble factors generated by infected microglia. Typical offenders, including TNF, IL-1 and IL-6, are among the soluble factors. gp41-induced nitric oxide production in neuronal cells has also been implicated. Direct neuronal damage due to soluble gp120 is also postulated[56].

"Natural course of HIV Infection" -

The path of HIV from acute infection, is partially mediated by the adaptive immune response, into slowly progressive disease of periphery lymphoid tissues starts with acute infection. Viruses enter the body via the mucosal epithelium frequently. Many such phases can be differentiated between the ensuing etiopathogenesis and clinical features of an infection:

(1) an acute retroviral illness;

(2) chronic stage (the vast majority of patients experience no symptoms)

(3) clinical AIDS

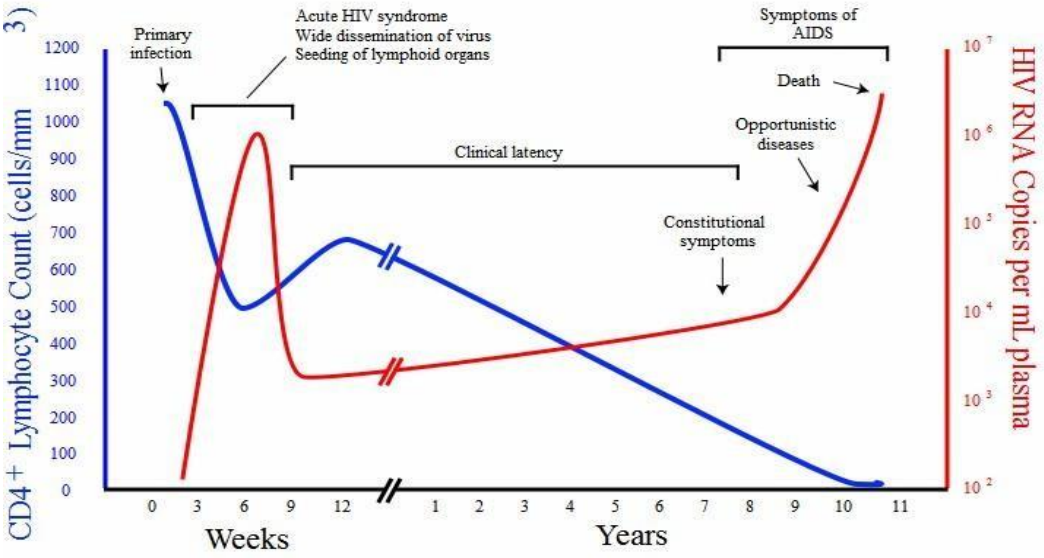


FIGURE 6: NATURAL COURSE OF HIV INFECTION

Acute Retroviral Syndrome, Primary Illness, and Virus Transmission [58]

Initially infection is distinguished first by invasion of memory CD4+ T cells into lymphoid tissues in mucosa and the demise of lot of infected cells.

Since mucosa are indeed the primary source of T cells and the primary area where memory T cells dwell, this local lymphocyte reduction has a significant impact.

There are few infectious cells identifiable in the circulation and other body tissues.

After mucosal infection, the virus infects and the host develops immunological responses. [59]

At the site of virus entry, dendritic cells in epithelia collect the virus before migrating to lymph nodes. In lymph nodes and spleen, dendritic cells can effectively spread The virus to cells via direct cell to cell interaction. The lymph nodes could detect viral replication within days of first HIV exposure. This replication results in viremia, characterised by an elevated HIV concentration. The virus attacks helper T cells, macrophages, and dendritic cells in peripheral lymphoid organs as it moves throughout the body.

Immune system creates humoral and CMI responses as the HIV infection progresses. [60]

Seroconversion (typically within three to seven weeks of putative exposure) and the development of specific cytotoxic CD8+ T cells are indicators of these responses. HIV-specific + T cells are present in the patient whenever virus titers have been at their peak.

Begin to decline that possibly account for the initial HIV control measures. 12 weeks following the initial contact, such immune responses partly restrict the infection and viral generation, as indicated by a quantitative but minor decrease in viremia.

Acute retroviral syndrome is the primary clinical state where there is transmission of virus and response of the hosts immune system to the virus.. [61]

40% to 90% of first-infection individuals are anticipated to develop the viral syndrome. This often occurs 3 to 6 weeks after infection and resolves on its own within two to four weeks. This is

clinically related with a self-limiting acute state characterised by vague symptoms, such as headache ,nausea ,sorethorat fever body pain and tiredness., which suggests influenza-like syndrome. Possible additional clinical signs include rash, lymphadenopathy of the cervical lymph nodes, diarrhoea, and vomiting.

The load of virus at the conclusion of the acute phase reflects the equilibrium between it virus and the immune system of the host, and it may remain relatively steady in a specific patient for several years. This constant viremia level, often known as the viral "set point," determines the rate of CD4+ T cell depletion and, consequently, the development of HIV illness.

Chronic Infection: Latency Clinical Phase.

In later phase of HIV infection, the lymph organs are specific sites for ongoing HIV replication and cell death. Throughout the phase of HIV infection, there are minimal or no symptoms. This stage of HIV infection is hence termed as clinical latency phase. The great majority of T cells in peripheral blood don't really maintain the virus, the death of CD4+ T cells inside spleen and lymph nodes proceeds. About 10^{12} T cells are normally located in lymph organs., and it is anticipated that HIV destroys between 1 x 10^9 and 2 x 10^9 CD4+ T cells daily.

Early in the evolution of the disease, the body may continue to manufacture new CD4+ T cells; hence, CD4+ T cells can also be replaced nearly as quickly as they are destroyed. At this stage, up to 10% of CD4+ T cells in lymphoid organs might well be infected, although less than 0.1% of all CD4+ T cells could be infected at any given time.

The constant cycle of virus infection, death of T cells, and exacerbation produces a progressive decline in CD4 cells in lymphoid tissues and the bloodstream[63].

In combination with the decline in CD4+ T cells, the host's defences start to weaken, and both the proportion of HIV-infected CD4+ cells that survive and the viral load per CD4+ cell rise. As

the host begins to lose the war with the virus, HIV RNA levels may begin to climb, as expected. It is not entirely clear how HIV circumvents immune regulation, but various hypotheses64 have been proposed.

On infected cells, antigenic diversity and downregulation of class I MHC molecules prevent CD8+ CTLs from identifying viral antigens. Throughout this time, the virus may adapt to enter its target cells via CXCR4 or both, as opposed to CCR5 alone. This change in coreceptors is associated with a faster decline in CD4+ T-cells, most likely as a result of a rise in T-cell infection. [64]

AIDS

The final phase of HIV infection is AIDS, which breaks down the host's immune system, a rapid rise in plasma viral levels, and life-threatening clinical illness.

Typically, the patient may present with a prolonged fever (more than one month), fatigue, loss of weight, and diarrhoea.

The patient is believed to have acquired AIDS subsequent to the development of major opportunistic infections, secondary neoplasms, or symptomatic neurologic disease .Most of patients with HIV infection acquire AIDS after a Seven to ten year chronic phase without treatment..

In situations of rapid progression, the intermediate, chronic phase following the first infection is reduced to two to three years.

Approximately 5% to 15% of infected individuals are protracted non-progressors, characterized as untreated HIV-1–infected individuals who have been symptom-free for at least 10 years.[65]

Elite controllers are the exceptional 1% of infected individuals whose plasma virus is undetectable (50–75 RNA copies per millilitre). People with such a unique clinical course have attracted a great deal of attention in the hope that their study would shed light on the host and viral determinants that influence illness progression.

Existing research reveals that this population is heterogeneous in terms of the characteristics that influence the progression of the disease. The lack of fundamental defects in the preponderance of viral isolates shows that illness progression could be attributable to a "weak" virus. Every patient demonstrates a significant anti-HIV immune response, however the immunological correlate of preservation remain unclear. It is hoped that subsequent study will provide solutions this and other important questions about disease progression. [65]

AIDS Clinical Features

The symptoms of HIV disease can be easily deduced from the preceding notes.

AIDS encompasses the ultimate phase of clinical symptoms. In fact, new antiretroviral medications have substantially altered the disease's progression, and several formerly lethal consequences are uncommon. In the United States resides the average adult.

A patient with AIDS would frequently demonstrate fever, weight loss, diarrhoea, extensive lymphadenopathy, numerous opportunistic infections, neurologic disease, and subsequent neoplasms.

Classification HIV disease staging and categorization systems are key for keeping track of the HIV epidemic and giving physicians and patients with crucial information about HIV stage of disease and clinical care.

There are now two primary classifications being used: the classification system of the Centres for Disease Control and Prevention (CDC) as well as the World Health Organization's Clinical Staging and Disease Classification System (WHO)

.

Classification system of the CDC [66]

HIV/AIDS is classified by the CDC according to the lowest recordedCD4cell level and previously confirmed HIV-related illnesses. Those in categories C1-C3,B3,A3 are diagnosed with "AIDS".

CD4 cell count categories	Clinical categories		
	A Asymptomatic, acute HIV, or PGL	B* Symptomatic conditions, not A or C	C# AIDS-indicator conditions
(1) ≥500 cells/µL	A1	B1	C1
(2) 200–499cells/µL	A2	B2	C2
(3) <200 cells/µL	A3	B3	C3

"TABLE 1: CDC HIV classification"

CATEGORY A:

Acute retroviral syndrome:

with Influenza like clinical presentation and infectious mononucleosis clinical picture.

Asymptomatic cases

CATEGORY B:

HIV infected individuals should satisfy at least one of the mentioned criteria:

a) Attributable to HIV infection or suggest a CMI deficiency.

b) Their clinical course or care is believed to be worsened by HIV infection.

Examples include, but are not limited to, the following-

Candidiasis of oropharyngeal system , vulvovaginal

Bacillary angiomatosis

Pelvic inflammatory disease (PID)

Moderate or severe Cervical dysplasia

Cervical carcinoma in situ Hairy leukoplakia, oral

ITP

Fever (>38.5°C) or diarrhea lasting >1 month

Peripheral neuropath

CATEGORY C

Pneumonia of bacterial origin , Recurrent Bacterial

pneumonia≥2 episodes in 12 months

Candidiasis – esophageal, trachea, bronchi, lungs.

Cervical carcinoma of cervix

Coccidioidomycosis,

Cryptococcosis,

Cryptosporidiosis, chronic intestinal (>1-month duration)

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

HIV-Encephalopathy

Herpes simplex: chronic ulcers (>1-month duration), or bronchitis, pneumonitis, or esophagitis

Histoplasmosis, disseminated or extrapulmonary

Isosporiasis, chronic intestinal (>1-month duration)

Kaposi sarcoma

Lymphoma, Burkitt, immunoblastic, or primary central nervous system

Mycobacterium tuberculosis ,

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

Pneumocystis jiroveci pneumonia

PML

The 2008 CDC Adult and Adolescent HIV Case Definition[67].

In 2008, the Centres for Disease Control and Prevention (CDC) modified the definition of HIV cases for adults and adolescents.

In 2008, the definitions for HIV cases for adolescents and adults replaced all prior HIV case definitions and classification systems.

In 2008, HIV confirmation test is required for the case definition of HIV infection.

The relevant laboratory diagnostic tests satisfy the diagnostic requirements:

A positive result of detectable HIV from a virologic test, specifically an HIV nucleic acid detection test,

HIV p24 antigen test (includes neutralization assay),

or HIV isolation test (viral culture).

It comprises four stages of HIV infection: stage 1, stage 2, stage 3 (AIDS), and unclassified stage.

This categorization excludes clinical categories A and B from the 1993 system, but maintains the 26 criteria that identify AIDS inside clinical category C.

The 2008 classification method classifies people as stage 3 (AIDS) if they possess aCD4count of < 200 cells/mm3, aCD4% of <14%, or an AIDS-defining clinical condition documentation at any time.

Like the 1993 method, HIV infection stage is defined by the patient's most advanced infection.

The 2008 CDC Adult and Adolescent HIV Case Definition[67].

In 2008, the HIV case definition for adolescents and adults replaced all prior case classification system and definitions.

A diagnosis of a condition defining AIDS without lab proof of HIV infection no more satisfies the

monitoring case definition.

The case classification for 2008 comprises four stages of HIV infection: stage 1, stage 2, stage 3 (AIDS), and unclassified stage.

This 2008 categorization excludes clinical categories A and B from the 1993 system, but maintains the 26 criteria that identify AIDS inside clinical category C.

The 2008 classification method classifies people as stage 3 (AIDS) if they possess aCD4count of less than 200 cells/mm3, aCD4% of less than 14%, or documentation of an AIDS-defining clinical condition at any time.

Similar to the 1993 method, the HIV infection stage is defined by the patient's most advanced infection.

2008 CDC Case Definition for HIV Infection: Summary Table

Stage	Laboratory Evidence*	Clinical Evidence
Stage 1	Laboratory Confirmation of HIV *and* CD4 count >500 cells/mm^3 *or* CD4% ≥29	None required (but no AIDS-defining condition)
Stage 2	Laboratory Confirmation of HIV *and* CD4 count 200—499 cells/mm^3 *or* CD4% 14-28	None required (but No AIDS-defining condition)
Stage 3 (AIDS)	Laboratory Confirmation of HIV *and* CD4 count <200 cells/mm^3 *or* CD4% <14†	*or* Documentation of AIDS-defining condition (with laboratory confirmation of HIV infection)†
Stage unknown§	Laboratory Confirmation of HIV *and* No information on CD4 cell count or percentage	*and* No information on presence of AIDS-defining conditions

* The CD4+ T-lymphocyte percentage is the percentage of total lymphocytes. If the CD4+ T-lymphocyte count and percentage do not correspond to the same HIV infection stage, select the more severe stage.

† Documentation of an AIDS-defining condition supersedes a CD4+ T-lymphocyte count of >200 cells/mm^3 and CD4+ T-lymphocyte percentage of total lymphocytes of >14.

§ Every effort should be made to report CD4+ T-lymphocyte counts or percentages and the presence of AIDS-defining conditions at the time of diagnosis. Additional CD4+ T-lymphocyte counts or percentages and any identified AIDS-defining conditions can be reported as recommended.

FIGURE 7 : CDC CASE DEFINITION

WHO HIV/AIDS clinical staging [68]

The World Health Organization (WHO) developed the HIV clinical staging and case definition in 1990 for use in areas with limited resources, and it was revised in 2007. It is not necessary to have aCD4cell count in order to stage HIV/AIDS because the diagnosis, evaluation, and management of the disease are all guided by clinical symptoms. The initial HIV infection all the way up to the most severe stages of AIDS are represented by the numbers 1 through 4 in the clinical phases. Certain clinical issues or symptoms serve as indicators of having reached one of these stages.

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

FIGURE 8: WHO HIV CLINICAL STAGING

Clinical stage 3
Unexplained[i] severe weight loss (>10% of presumed or measured body weight)
Unexplained chronic diarrhoea for longer than one month
Unexplained persistent fever (above 37.6°C intermittent or constant, for longer than one month)
Persistent oral candidiasis
Oral hairy leukoplakia
Pulmonary tuberculosis (current)
Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis or bacteraemia)
Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
Unexplained anaemia (<8 g/dl), neutropaenia (<0.5 × 10^9 per litre) or chronic thrombocytopaenia (<50 × 10^9 per litre)
Clinical stage 4[ii]
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 diarrhoed)
Chronic isosporiasis
Disseminated mycosis (coccidiomycosis or histoplasmosis)
Recurrent non-typhoidal Salmonella bacteraemia
Lymphoma (cerebral or B-cell non-Hodgkin) or other solid HIV-associated tumours
Invasive cervical carcinoma
Atypical disseminated leishmaniasis
Symptomatic HIV-associated nephropathy or symptomatic HIV-associated cardiomyopathy

FIGURE 9: WHO HIV CLINICAL STAGING

“Effect of ART on the clinical course of HIV infection”:

The effect of antiretroviral treatment on the progression of HIV infection in clinical patients The clinical manifestations of AIDS have changed as a result of the development of innovative antiretroviral treatments that target reverse transcriptase, protease, and integrase. These treatment plans are also known as highly active antiretroviral therapy (HAART) or combination antiretroviral therapy. Both of these designations are used interchangeably. These Drugs are administered together in order to forestall the development of mutants that are resistant to any one of them individually.

There are currently over twenty-five antiretroviral Drugs available, and these treatments come from six different pharmacological classes. These medications are used to treat HIV infection. When 3 effective Drugs are given to a patient who is motivated and adherent, HIV virus multiplication will inevitably be reduced to below the level of and it will remain undetectable permanently when the patient sticks to appropriate therapy.

As soon as the virus is brought under control, the slow but steady loss of CD4+ T cells will stop. The number of CD4+ T cells found in the periphery steadily increases over the course of several years and frequently returns to normal levels.

Because to these treatments, the annual death rate from AIDS in the United States Dropped from its peak of 16 to 18 per 100,000 individuals in 1995–1996 to approximately 4 per 100,000 people in 2005. This decrease occurred during the time period in which the disease was at its most prevalent.

Numerous illnesses that are associated with AIDS, such as with P. jiroveci and KS, have become relatively uncommon in recent years. There has been a significant reduction in mortality, which has led to an increase in the number of people living with HIV; nevertheless, because these individuals do not have virus-free states, the danger of transmission is increased.

In spite of these impressive developments, a number of issues associated to HIV as well as treatment-related issues have surfaced. Some patients with terminal illness who are treated with antiretroviral medication experience a paradoxical worsening of their clinical condition during the time when their immune systems are getting better.

This is seen to be the case despite the fact that the number of CD4+ T cells is increasing and the viral load is decreasing. Immune reconstitution inflammatory syndrome is the name given to this medical disorder.[69]

It is uncertain what causes it; nevertheless, it is assumed that it is the outcome of an inadequately managed host response to a significant antigenic burden posed by persistent bacteria. The appearance of a string of long-term toxicity is one of the most severe issues that might arise from using HAART for an extended period of time. This included, but aren't restricted to, lipoatrophy (fat loss in the face), lipo-accumulation (central fat accumulation),with increased insulin resistance, and peripheral nerve damage, premature cardiovascular disease, renal disease, and hepatocyte dysfunction.

Lipoatrophy is characterized by a loss of fat in the face, while lipo-accumulation refers to the accumulation of fat in the body's central regions.

The mechanisms behind these harmful effects are not yet fully understood. Diseases of the liver, kidneys, and other organs, as well as cancer and accelerated cardiovascular disease, are some of the leading causes of morbidity. The mechanism that causes these outcomes that are unrelated to AIDS is unknown; however, chronic inflammation and/or T-cell dysfunction may play a role in their development.

In spite of the great progress, the long healthy survival for AIDS patients continues to be dismal. In spite of the fact that effective pharmacological treatment can help,

Although there has been a reduction in the number of fatalities, the lymphoid tissues of treated patients still carry viral DNA. As a result, the most important aspects of the fight against AIDS are still the prevention of the disease, the implementation of efficient health programmes, and the development of antiretroviral Drugs. [70]

DIAGNOSIS FOR HIV INFECTION

Human immunodeficiency virus (HIV), the cause AIDS, can be found in serum, saliva, or urine and can be detected with HIV testing. These tests may be able to identify RNA, antigens, and antibodies.

The window period is interval between an infection and the time at which a diagnostic can spot a change. The HIV-1 antibody assay window is approximately twenty five days long for B subtype. The period of window is reduced by antigen testing to about 16 days, while the window period is further decreased by NAT to 12 days[71].

Inappropriate replies can result in false-positive outcomes.

Having primary antibodies against other infectious illnesses that might have antigenic resemblances to HIV is known as hypergammaglobulinemia. Systemic lupus erythematosus and

other autoimmune diseases have rarely yielded false-positive results. The majority of false negatives are generated within the window period. High levels of specificity and sensitivity are required in the diagnostics used to identify HIV infection in an individual. [71]

In the US, it is achieved by combining two HIV antibody tests through the use of an algorithm. If antibodies can be detected using first test of diagnostics based on the ELISA method, a 2nd depending on the Western blot method that can determine the concentration.

Antibodies bind to antigens present in the test kit. This combination of two approaches is extremely exact.

In the United States, screening all patient for HIV in all contexts of health care is a becoming standard of treatment. [72]

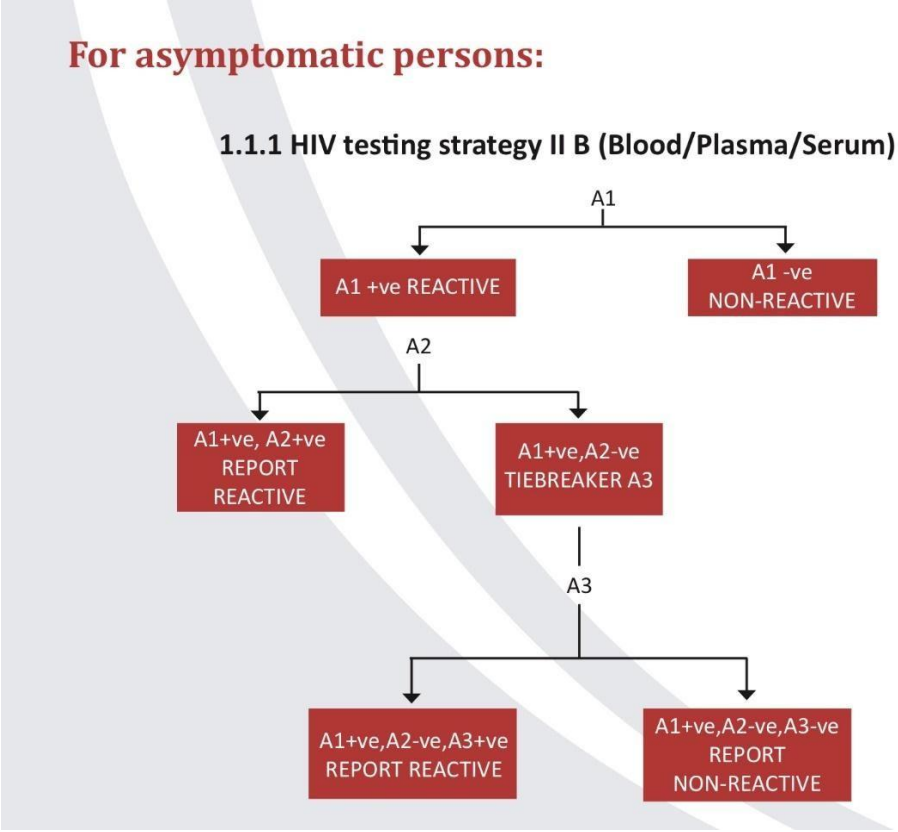


FIGURE 10: HIV TESTING FOR ASYMPTOMATIC PATIENT

ANTIBODY ANALYSES

Seventy-three cheap, highly accurate HIV antibody tests have been made especially for adult routine diagnostics.

Antibody testing may produce inaccurate results during the window of time of between three and six months between the time of HIV infection and the development of detectable antibodies against HIV seroconversion (no antibodies were detected despite the presence of HIV).

A person with HIV can transmit the virus while in the window period even though an antibody test may not show any signs of the virus.

ELISA

ELISA is often known as the enzyme immunoassay, was the first widely used HIV screening tool (EIA). It is quite fragile.

Inkblot analysis

Antibody detection is done using the western blot method.

Variability exists in the minimal number of viral bands. The outcome is negative if there are no detectable viral bands.

Positive findings are achieved if at least one band from each of the gene-product groups GAG, POL, and ENV is present.

The three-gene-product interpreting approach has not yet been adopted for use in clinical or public health practice.

Most of the HIV patients with inconclusive western blot findings will be testing +ve one month later; the six-month persistence of indeterminate results suggests that results are not due to HIV infection.

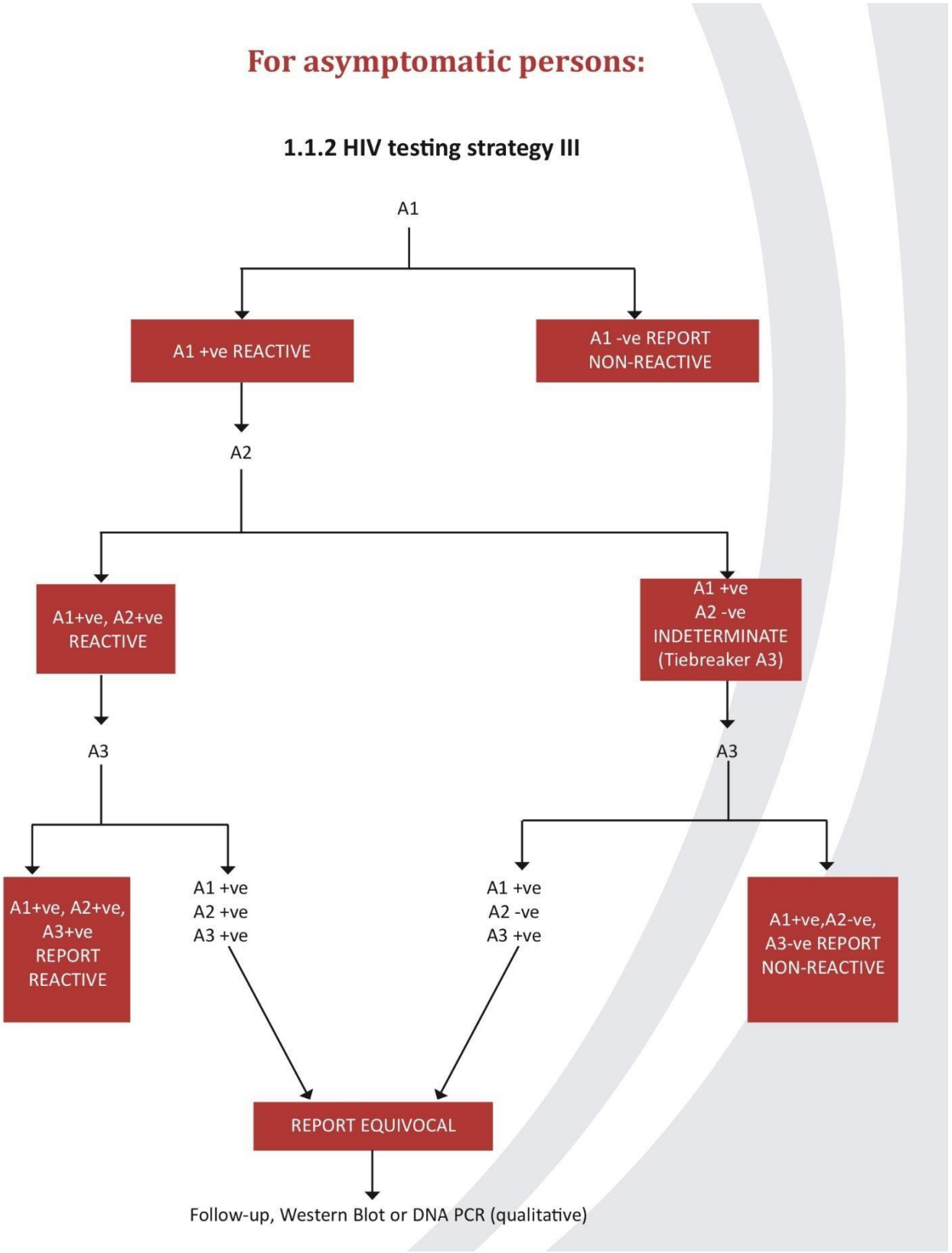


FIGURE 11: HIV TESTING FOR SYMPTOMATIC PATIENTS

IN-CLINIC OR RAPID DIAGNOSTICS:

Rapid antibody tests are high-quality immunoassays made to be utilized as HIV point-of-care diagnostics. Western blot analysis must be used to validate any significant test result. [73]

OraQuicK, Uni-Gold Complete, Clearview, and Orasure HIV/AIDS, urine test

HIV-1 and HIV-2 antibody testing

Tests to detect antigens The p24 antigen test determines if the HIV capsid protein p24 is present.

Nucleic acid-based assays (NAT) NATs are tests that use nucleic acids to amplify and identify a variety of target sequences found in certain HIV genes, such as the HIV-I GAG, HIV-II GAG, HIV-env, and HIV-pol.

The Quantiplex bDNA or branched DNA test was used in addition to the RT-PCR assay.

additional testing to diagnose HIV.

The CD4T-cell count is a technique for calculating the number of CD4T-cells in the blood, not an HIV test.

CD4 levels cannot be used to diagnose HIV infection. It is used to monitor people with HIV's immunological health.

Reductions in CD4T-cells are considered a precursor to the onset of HIV infection. HIV-positive individuals are formally identified as having AIDS when the CD4count falls < 250 cells/mL / even when opportunistic diseases appear.

Low CD4T-cell counts are linked to a variety of diseases, including numerous viral diseases, bacterial infections, parasitic illnesses, sepsis, TB, coccidioidomycosis, burn, trauma, IV immunosuppressant injections, and IV chemotherapy medicine injections..

Foreign proteins, starvation, excessive exercise, pregnancy, diurnal variation, psychological stress, and social withDRawal are all major risk factor for immunosuppression..

ROLE OF SURROGATE MARKERS:

RNA levels of HIV-1 is a diagnostic marker of disease progression and has clinical utility in the further evaluation and treatment of people living with HIV infection.

The Centre's for Disease Control and Prevention (CDC) separates people with HIV infection into three groups based on CD4+ T-cell counts since the lack of immunological function is related with diminishing CD4+ T-cell levels.CD4 cell numbers are like the dependable biomarker for the clinical treatment of disease progression. To identify whether to commence combination antiretroviral medication, the most essential clinical parameters are CD4+ cell counts.

In industrialized nations, the utilization of these markers is ubiquitous, whereas in underdeveloped ones, they are challenging to get due to their expense and technological limitations. While they remain the most significant clinical signs, they do not entirely explain the prognosis of a patient[9].

Regardless ofCD4cell counts and HIV RNA titre[12], recent data indicate that low albumin levels are linked to faster disease progression to Acquired Immunodeficiency syndrome, AIDS-related death, and mortality. Albumin serum level could be a very helpful, affordable, and easily available surrogate test for identifying the poor prognosis of HIV and for evaluation for treatment[14], medical surveillance of adherence and response to antiretroviral therapy, and survival prediction [16].

“HUMAN SERUM ALBUMIN”

FIGURE 12: ALBUMIN STRUCTURE

The protein with the highest concentration in human plasma is called albumin. It is a monomeric protein that is soluble and has a molecular mass of about 65 kD. It contains 584 different amino acids. [74]

Mutations in the albumin gene, which is found on chromosome 4, can result in the production of a wide array of proteins that do not function normally.

There are 17k nucleotides between the site of 'cap' and the 1st poly(A) addition site in the human albumin gene. This is the length of the gene. It is segmented into fifteen exons that are placed inside the three domains that are thought to have raised from the replication of a

primary domain. Each of these domains is named after a letter of the alphabet. [75]

Proteins are delivered from RER, Liver synthesizes albumin as pre-pro-albumin. This form of albumin has peptide of N-terminal peptide which is eliminated first and then nascent protein is released. Golgi vesicles are responsible for the cleavage of pro-albumin, which results in albumin being secreted.

Reference serum levels : 3.5-5.5 g/dl

Only the cells in the liver of a healthy person are capable of producing protein at a rate of about 15 g per day. Albumin degrades at a rate of around 4% each day and has a half-life of approximately 21 days.

It also binds calcium ions in a competitive manner, buffers pH, and maintains oncotic pressure, in addition to transporting unconjugated bilirubin, free fatty acids , hormones and medicines.

It is a -ve acute-phase reactant, has its expression decreased in situations of inflammation.

In a wide variety of groups, including healthy persons as well as those with acute and chronic diseases, reduced serum albumin levels are associated with higher mortality. This is true even when the levels are measured within the normal range. There is no break in this reverse association between albumin concentrations and mortality across a broad range of serum albumin concentrations. [12]

It has been observed that there is a 24–56% increase in the chance of passing away for every 25 g/l falls in serum albumin content.

The association allows for the prediction of mortality rates for both overall and individual causes. The beneficial effect of high albumin levels is unaffected by the inclusion or exclusion of other recognized risk factors, including previous illness and early mortality.

Numerous research has pointed to a connection between low levels of serum albumin and

an increased risk of death.

After the treatment, albumin levels coincided with CD 4cell count, making it a valuable instrument for assessing how well therapy is working.

The projected specificity was just forty percent, however, the sensitivity against CD 4 was ninety-one-point five percent.[13]

Graham et al. conducted a study in which it was found that low albumin sped up the progression of the disease. Furthermore, the researchers found that a Drop of 1 g/dl in albumin raised the probability of progressing to cd4+ cell counts 200 by 13%. In patients with CD200 per mm3 progression, a 10% Drop in albumin is correlated with a 3.5-fold greater risk of advancement.

Albumin has a substantial correlation with both the progression of HIV disease and short-term mortality 14, making it a useful measure of the evolution of HIV disease.

Baseline Albumin was found out to be to be an independent predicting indicator of death in HIV-infected females in Feldman and colleagues' WIHS-15.1 research. This research was carried out by the Women's Interagency HIV Collaboration. The category with the lowest serum albumin level, which was 3.4 gm/dl, had a three year death rate of 49%, whereas the segment with the higher serum albumin level, which was 4.2 gm/dl, had a mortality rate of 11%, which resulted in a p value of 0.001 for the comparison.

In a continuation of the WIHS trial, serial serum albumin measurements were utilized to create a survival prediction in connection to HAART.

“Studies was out in India by Vajpayee et al. [76] and Sundaram et al. at YRGCARE in Chennai[78] produced results that were consistent with one another”.

According to the findings of a study that was carried out at CMC Vellore[10], albumin may serve as a predictive biomarker for antiretroviral therapy in HIV infection.

Multiple factors are involved in the development of hypoalbuminemia in HIV infection.

1. Insufficient food intake
2. Anorexia
3. The control of cytokines
4. Inflammatory state
5. Abnormal immunological activation, characterized by high levels of gamma globulin and a reversed A/G ratio.
6. Autoantibodies against serum albumin
7. The breakdown of the barrier of endothelium caused by HIV-1 Tat1, which also contributes to the spread of the virus [51]
8. Hepatic involvement
9. HIV associated nephropathy

EFFECTS OF HYPOALBUMINEMIA ON PATHOPHYSIOLOGY:

It has been discovered that the proinflammatory cytokine IL6 promotes HIV-1 replication in vitro and has a strong inverse relationship with albumin levels. [76]

Albumin is a negative acute phase reactant associated with excessive cytokines in HIV infection , such as TNF and IL 1, which are upregulated and cause its level to decrease[77.]

Due to a relative lack of Pyridoxal 5'-Phosphate78, CD4+ cells become more susceptible to gp120-mediated viral binding.

Negatively charged albumin fraction's succinylated, malonylated have inherent antiviral activity.[79]

Loss of the protective effects of normal albumin, which serves as a vasodilator, anti-haemostatic, antioxidant, and platelet-modifying agent. [80]

The therapeutic efficiency of anti-HIV medications in combination therapy is reliant on the mutual interactions of bonding equilibria with plasma proteins and, in particular, with HAS, a crucial factor regulating the distribution and the free, active concentration of many given pharmaceuticals [81].

MATERIALS AND METHOD:

1. METHOD OF COLLECTION OF DATA:

This is **observational cross-sectional study** includes 65 HIV/AIDS patients who got admitted to **Shri B.M Patil medical college hospital and research centre** during the period of January 2021 to July 2022. Descriptive and Analytical Statistics was done to find correlation of albumin with CD4+ T lymphocyte count in HIV/AIDS patients. Study was carried out after taking ethical clearance from the institution.

A detailed history, clinical examination and laboratory investigations including Hb, TLC, DLC, Haematocrit, LFT with serum albumin level, RFT, CD4+Cell Counts, HIV test was done.

2. INCLUSION CRITERIA

- HIV-infected patients > 18 years of age irrespective of sex.

3. EXCLUSION CRITERIA

- Patients with gastroenteritis, Crohn's disease, and ulcerative colitis.
- Patients with renal disease.
- Patients with hepatobiliary disorders.
- Patients with congestive cardiac failure.
- Any h/o burns in last 21 days
- Any clinical evidence of shock.

In all cases, a comprehensive clinical examination will be performed. Under aseptic biosafety precautions, peripheral blood will be extracted from all study subjects.

Albumin is measured in serum (tube with a yellow cap) using the bromocresol green Olympus AU2700 analyser.

FIGURE 13: BD FACS CD4 COUNTER FLOW CYTOMETER

CD4+ T lymphocytes will be counted on an automated four color BD – two laser FACS Calibur with multiset software instrument utilizing single-platform flow cytometry technology.

4. <u>TYPE OF STUDY</u>: CROSS-SECTIONAL STUDY

<u>STATISTICAL ANALYSIS</u>

SAMPLE SIZE CALCULATION: With anticipated Mean ± SD of Albumin level in HIV/AIDS patients 2.98±0.6[(ref)], the study would require a sample size of 65 patients [(ref)] with 95% level of confidence and a precision of 0.15

Formula used

$$n=\frac{z^2S^2}{d^2}$$

Z= Z statistic at α level of significance

d^2= Absolute error S

S=standard deviation.

- The data obtained will be obtained and entered in a Microsoft Excel sheet, and statistical analysis

  will be performed using statistical package for the social sciences (Verson 20).

- Results will be presented as Mean (Median) ±SD, counts and percentages and diagrams.
- . Categorical variables will be compared using Chi square test.
- For normally distributed continuous variables will be compared using Independent t test. For not normally distributed variables Mann Whitney U test will be used.
- Correlation between variables will be calculated by Person's/ Spearman's Correlation.

- $p<0.05$ will be considered statistically significant. All statistical tests will perform two tailed.

RESULTS:

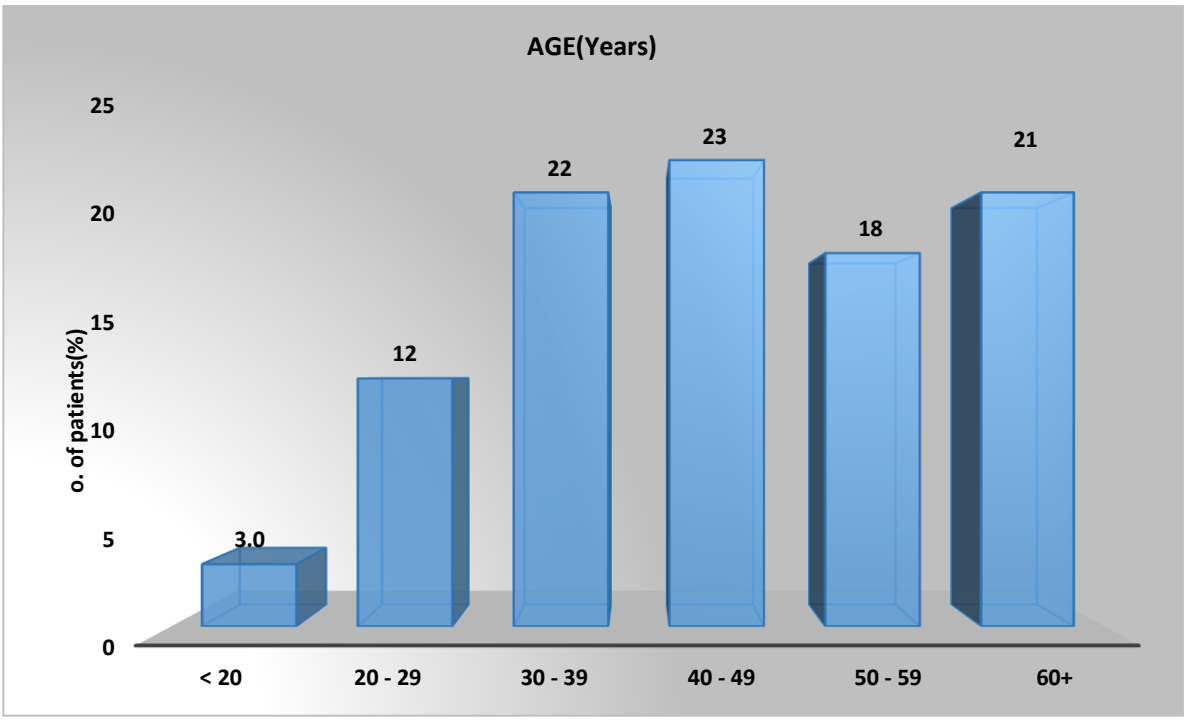
In the current study, absolute CD4cell count and albumin levels were correlated to assess the current status of HIV in a possibility to check of alternative cheap surrogative marker in HIV patients who were admitted in Shri B M Patil Medical College And Research Centre, Vijayapura, results are as follows.

AGE DISTRIBUTION:

In our study on 65 patients, the age of patients were classified as between18-20 years had 2 patients (3.1%), 20-29 year had 8 patients (12.3%), 30-39 years 14 patients had (21.5%), 40 – 49 years had 15 patients (23.1%), 50-59 years had 12 patients (18.5%) and 60+ had 14 patients (21.5%).

Age (Years)	No. of patients	Percentage
18 - 20	2	3.1
20 - 29	8	12.3
30 - 39	14	21.5
40 - 49	15	23.1
50 - 59	12	18.5
60+	14	21.5
Total	**65**	**100.0**

TABLE 2: AGE DISTRIBUTION



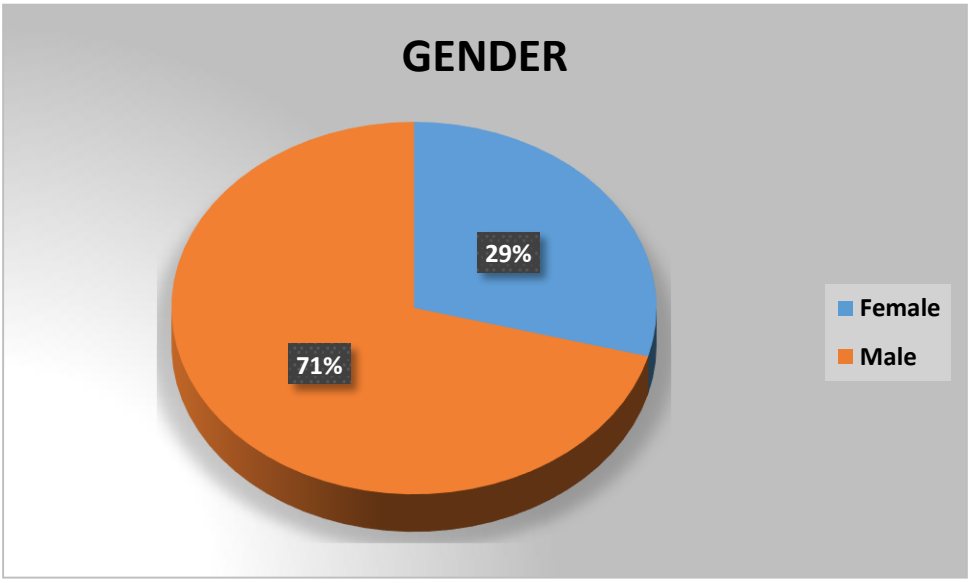
GRAPH 3 : AGE DISTRIBUTION

SEX DISTRIBUTION:

In our study on 65 patients, majority of patients were Male having 46 patients constituting 70.8% and Females were 19 (29.2%). Males are predominantly affected in this population.

Gender	No. of patients	Percentage
Female	19	29.2
Male	46	70.8
Total	**65**	**100.0**

TABLE 3 : SEX DISTRIBUTION



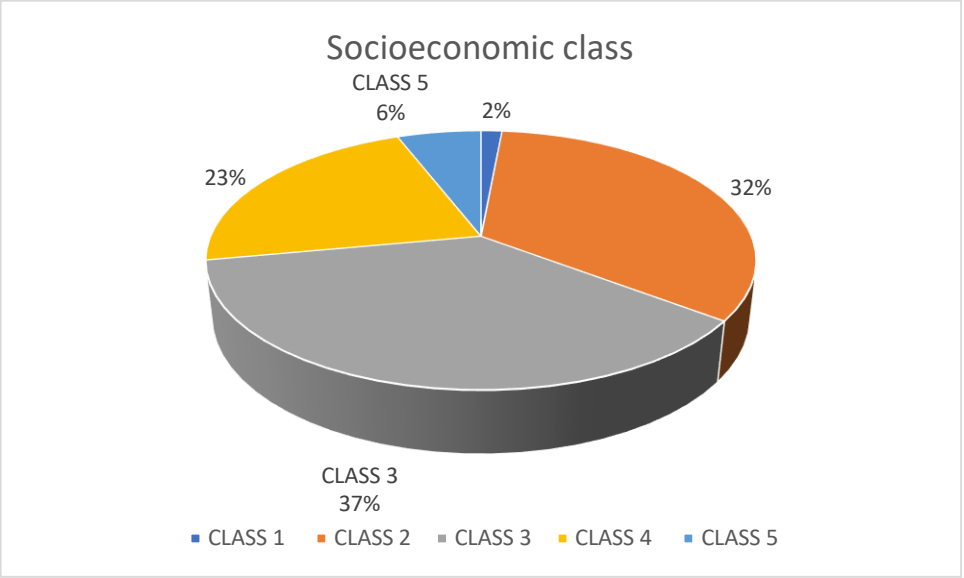
GRAPH 4: SEX DISTRIBUTION PIE CHART

SOCIOECONOMIC STATUS:

In our study on 65 patients, socioeconomical status of the oatets were evaluated and classified accordig to the modified kuppuswamy scale which consist of 5 classes. Under class 1 we had 1 (2%), under class 2, cass 3, class 4 and class 5 had 21 (32%), 24 (37%), 15 (23%), 4 (6%) respectively. Lower middle and upper middle classess were more affected in this study.

Modified kuppuswamy scale	Categrorie	No of patients	Percentage
Class 1	Upper	1	2
Class 2	Upper Middle	21	32
Class 3	Lower Middle	24	37
Class 4	Upper Lower	15	23
Class 5	Lower	4	6
Total		**65**	**100**

TABLE 4: SOCIOECONOMIC STATUS ACCORDING TO MODIFIED KUPPUSWAMY SOCIO-ECONOMIC SCALE:



GRAPH 5: SOCIOECONOMIC CLASS PIE CHART

PRESENTING COMPLAINTS:

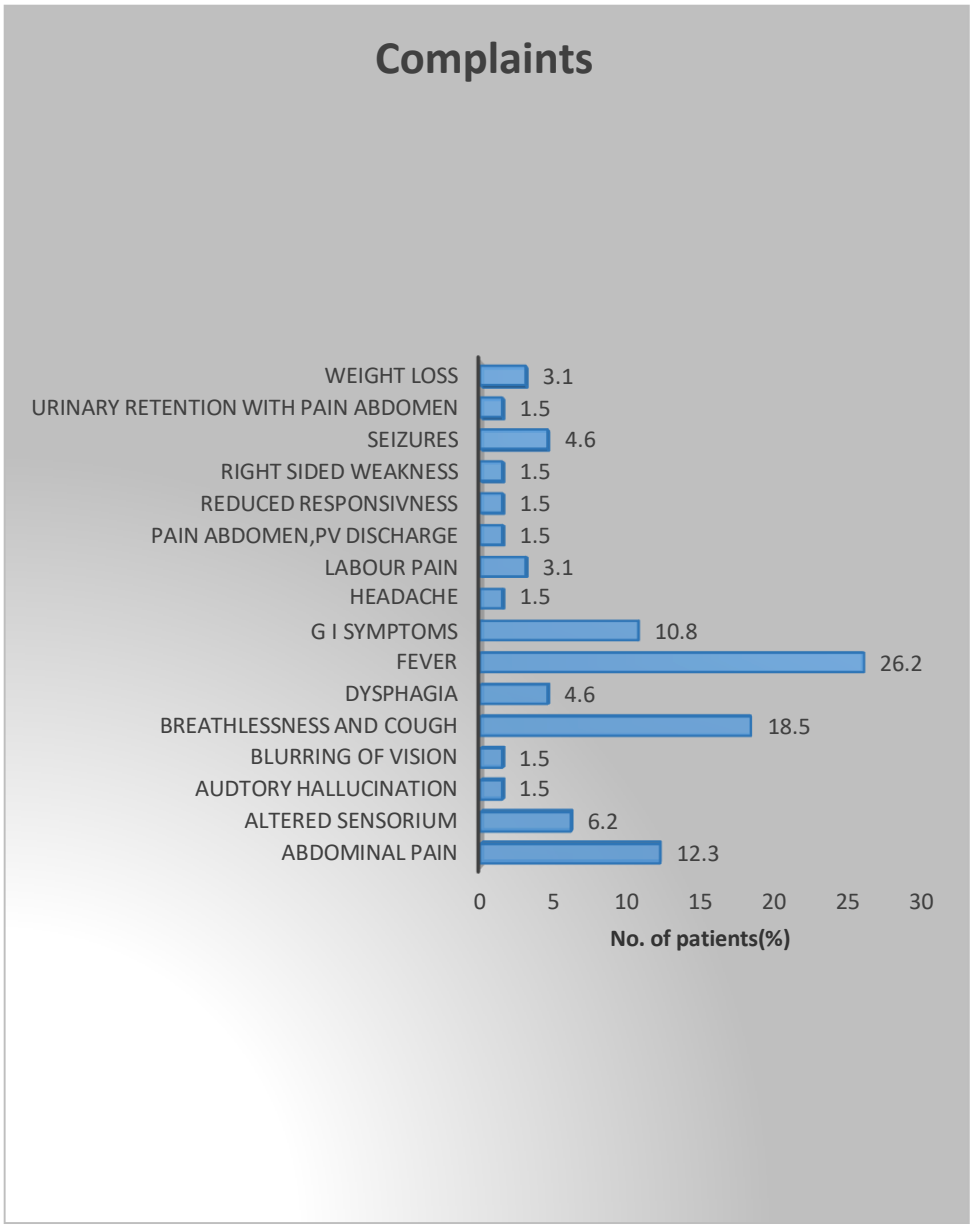
Fever was the main presenting complaint in this study population i.e. in 17 patients (26.2%) followed by cough and breathlessness.

Abdominal pain was in 8 patients (12.3%), Altered sensorium 4 patients (6.2%), Auditory hallucination in 1 patient (1.5%), Blurring of vision in 1 patient (1.5%), Breathlessness and cough in 12 patients (18.5%), Dysphagia in 3 patients (4.6%), Fever in 17 patients (26.2%), G I symptoms in 7 patients (10.8%), seizures in 3 patients (4.6%), Labour pain and weight loss was in 2 patients (3.1%), headache, pain abdomen with per vaginal discharge, reduced response , right sided weakness, urinary retention with pain abdomen was in in 1 patient (1.5%).

complaints	No. of patients	Percentage
Abdominal pain	8	12.3
Altered sensorium	4	6.2
Auditory hallucination	1	1.5
Blurring of vision	1	1.5
Breathlessness and cough	12	18.5
Dysphagia	3	4.6
Fever	17	26.2
G i symptoms	7	10.8
headache	1	1.5

Labor pain	2	3.1
pain abdomen, per vaginal discharge	1	1.5
reduced response	1	1.5
right sided weakness	1	1.5
seizures	3	4.6
urinary retention with pain abdomen	1	1.5
weight loss	2	3.1
Total	**65**	**100.0**

TABLE 5: PRESENTING COMPLAINTS



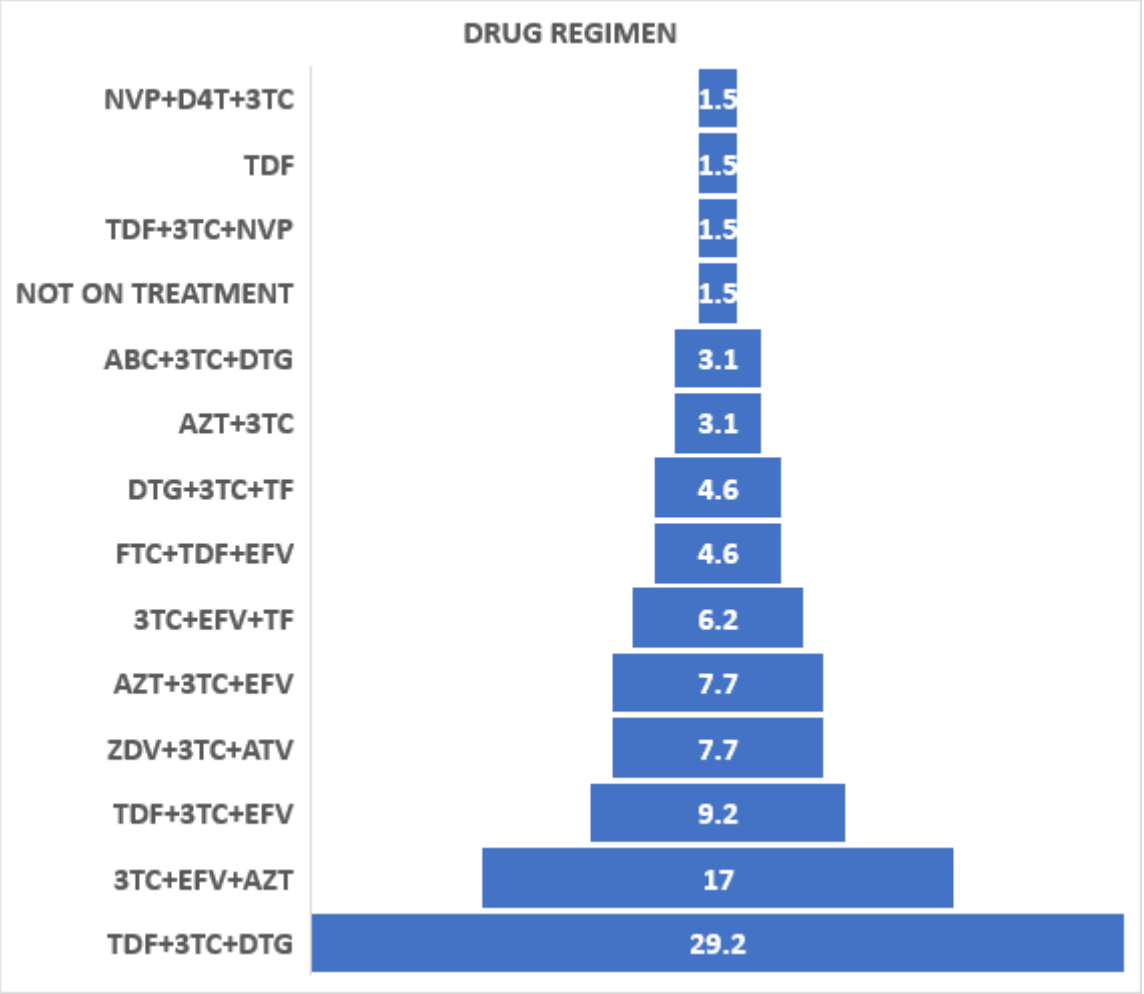
GRAPH 6: PRESENTING COMPLAINTS HISTOGRAM

DRUG REGIMEN:

In our study,65 patients were found to be on different regimens which are as stated in the table and the commonest was **TDF+3TC+DTG (**Tenofovir +lamivudine+dolutegravir) constituted 29.2%

TABLE 6: DRUG REGIMEN

Drug regimen	Frequency	Percent
TDF+3TC+DTG	19	29.2
3TC+EFV+AZT	11	17
TDF+3TC+EFV	6	9.2
AZT+3TC+EFV	5	7.7
ZDV+3TC+ATV	5	7.7
3TC+EFV+TF	4	6.2
DTG+3TC+TF	3	4.6
FTC+TDF+EFV	3	4.6
ABC+3TC+DTG	2	3.1
AZT+3TC	2	3.1
NVP+D4T+3TC	1	1.5
TDF	1	1.5
TDF+3TC+NVP	1	1.5
NOT ON TREATMENT	1	1.5



GRAPH 7: DRUG REGIMEN

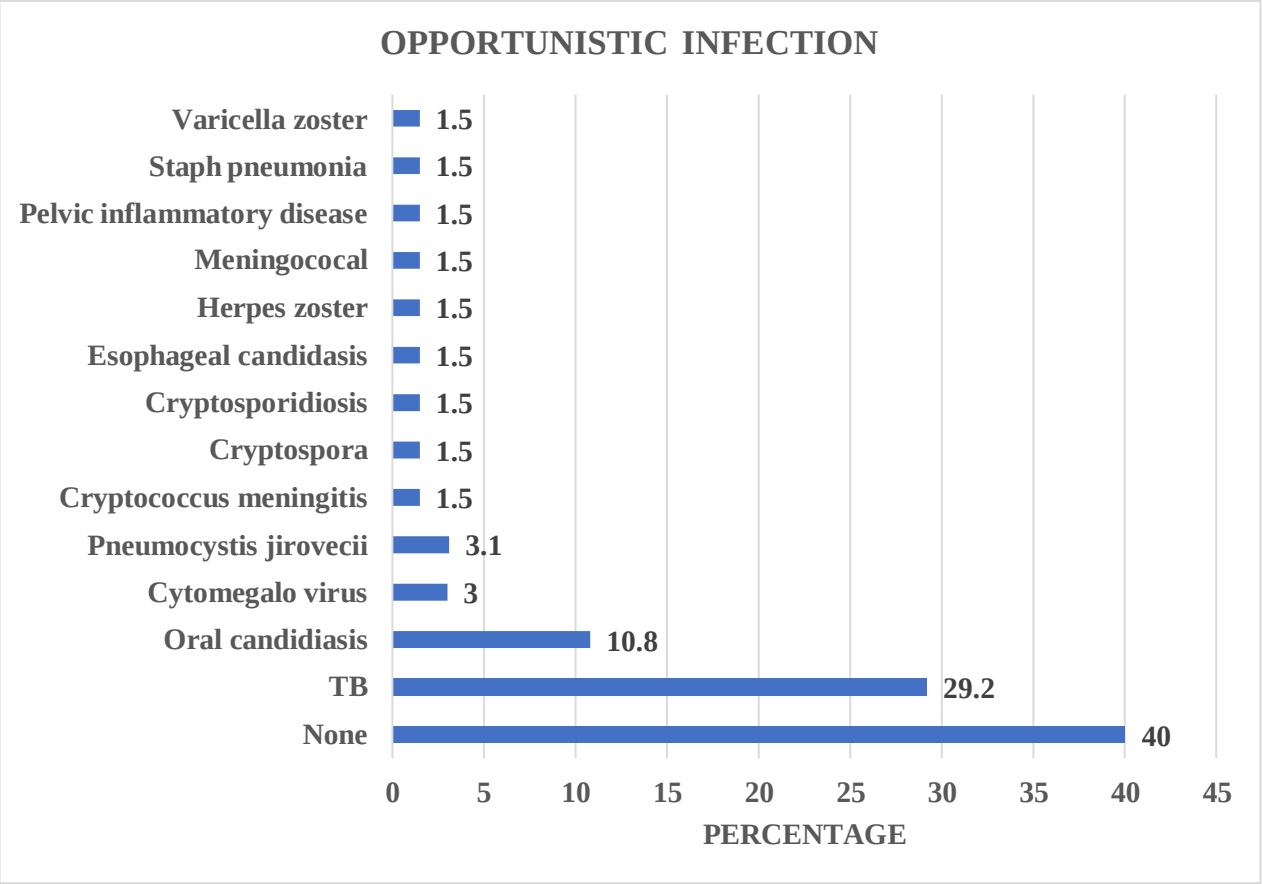
OPPORTUNISTIC INFECTIONS:

In our study on 65 patients, it was found 26 patients (40%) had no any opportunistic infection, Tuberculosis (TB) was the most common infection seen in 19 patients (29.2%), oral candidiasis was in 7 patients (10.8%), cytomegalo virus and Pneumocystis jirovecii was in 2 patients (3.1%), Cryptococcus meningitis, Cryptospora, Cryptosporidiosis, Esophageal candidiasis, Herpes zoster,

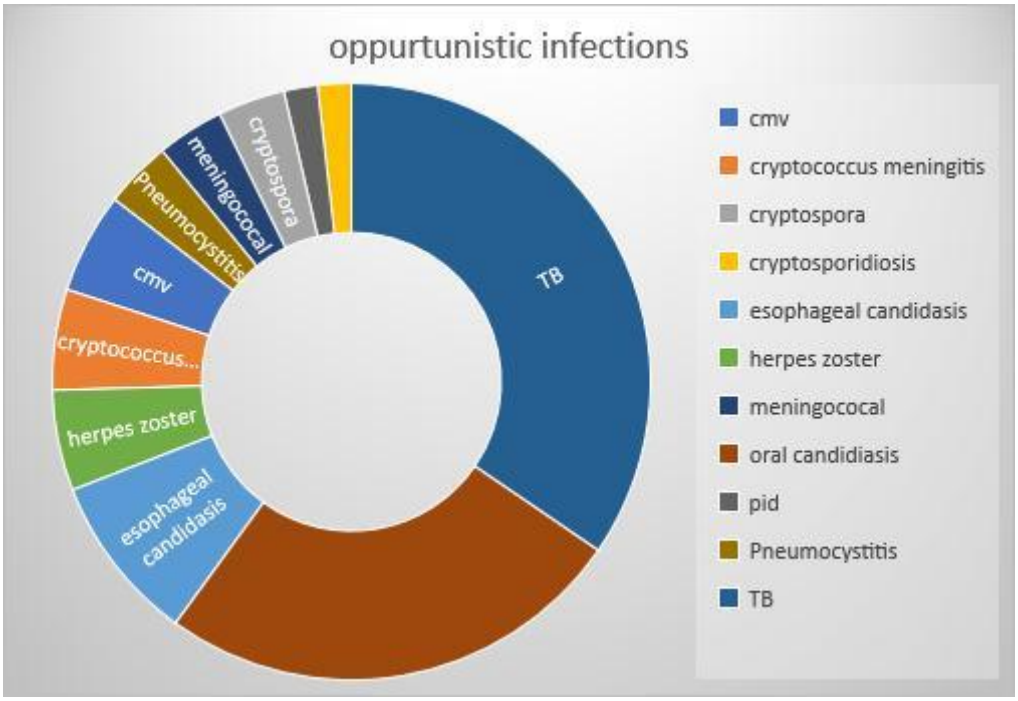
Meningococal, Pelvic inflammatory disease, Staph pneumonia and Varicella zoster was in 1 patient each 1.5%.

TABLE 7: OPPORTUNISTIC INFECTIONS

OPPORTUNISTIC INFECTIONS	FREQUENCY	PERCENTAGE
None	26	40
TB	19	29.2
Oral candidiasis	7	10.8
Cytomegalo virus	2	3
Pneumocystis jirovecii	2	3.1
Cryptococcus meningitis	1	1.5
Cryptospora	1	1.5
Cryptosporidiosis	1	1.5
Esophageal candidasis	1	1.5
Herpes zoster	1	1.5
Meningococal	1	1.5
Pelvic inflammatory disease	1	1.5
Staph pneumonia	1	1.5
Varicella zoster	1	1.5
Total	**65**	**100.0**



GRAPH 8: OPPURTUNISTIC INFECTIONS BAR DIAGRAM



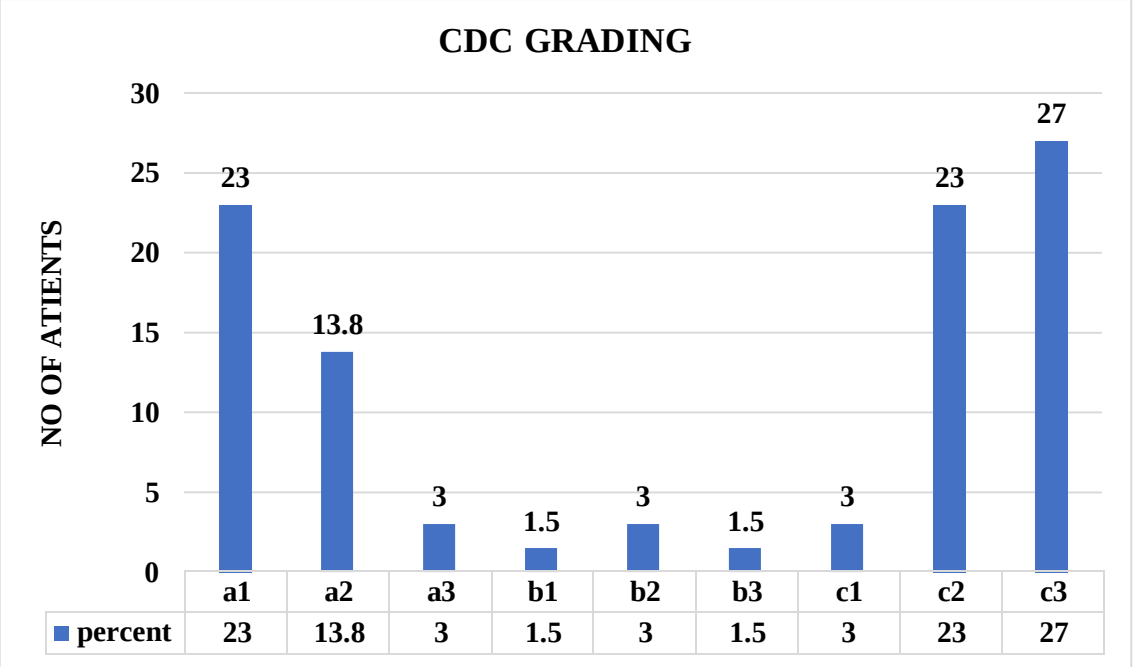
GRAPH 9: OPPURTUNISTIC INFECTION PIE CHART

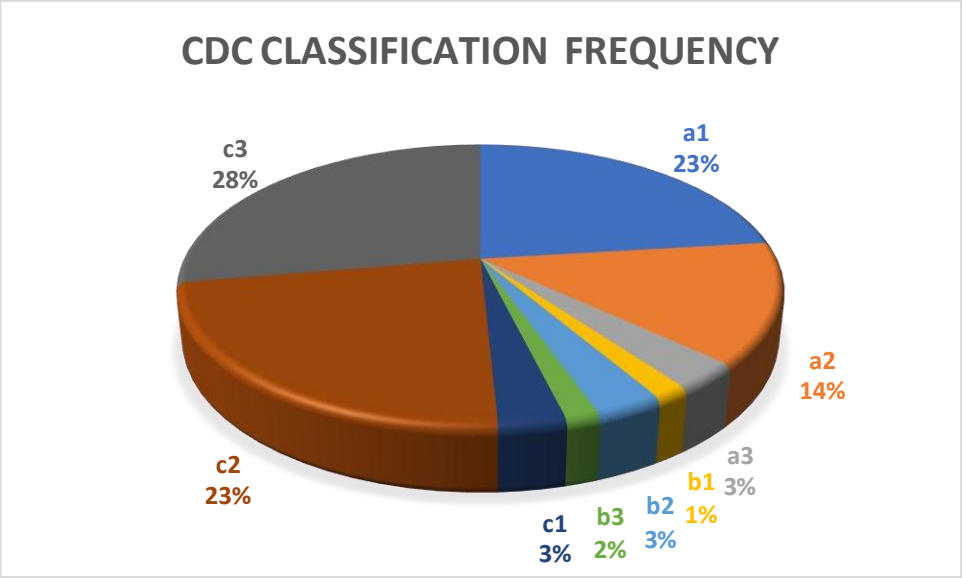
CDC GRADING AND FREQUENCY:

In our study on 65 patients, all patients were graded according to the CDC grading system, and it was found under **a1** 15 patients (23%), under **a2** 9 patients (13.8%), under **a3** 2 patients (3%), under **b1** 1 patient (1.5%), under **b2** 2 patients (3%), under **b3** 1 patient (1.5%), under **c1** 2patients (3%), under **c2** 15 patients (23%) and under **c3** 18 patients (27%). And this is been plotted in the graph.

CDC grade	No of patients	percentage
a1	15	23
a2	9	13.8
a3	2	3
b1	1	1.5
b2	2	3
b3	1	1.5
c1	2	3
c2	15	23
c3	18	27
total	65	100

TABLE 8 :CD4 RANGE WITH NUMBER OF PATIENTS





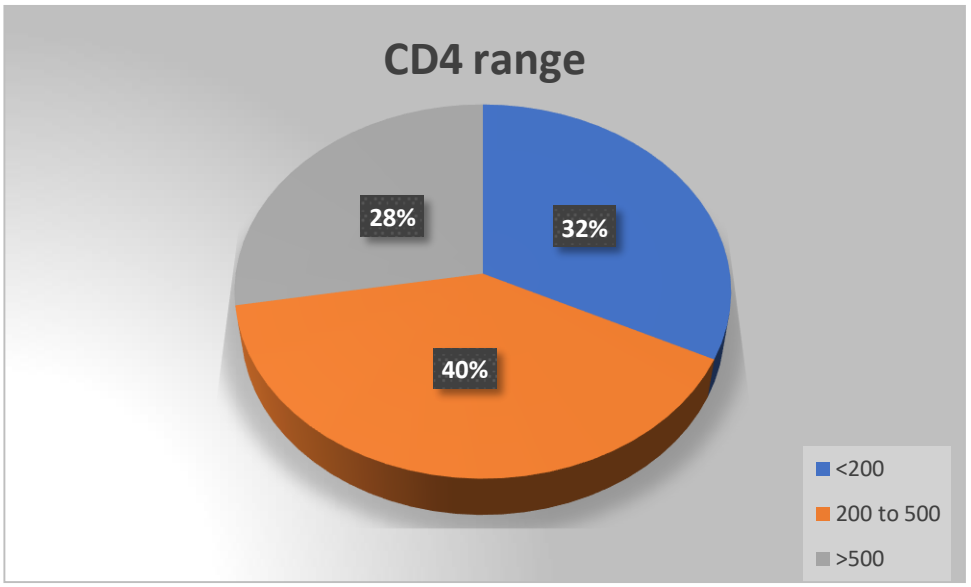
GRAPH 11: CD4 GRADING WITH THE NUMBER OF PATIENTS

CD4 range

In our study, it was observed that 21 patients (32%) were havingCD4< 200, 26 patients (40%) hadCD4200 – 500 and 18 patients (28%) hadCD4>500. And the same has been plotted.

CD4 range	No. of patients	percentage
<200	21	32%
200 to 500	26	40%
>500	18	28%

TABLE 9 :CD4 CELL COUNT FREQUNCE.



GRAPH 12: CD4 CELL COUNT DISTRIBUTION PIE CHART

CD4 & ALBUMIN LEVEL IN COMPARISON WITH GRADING

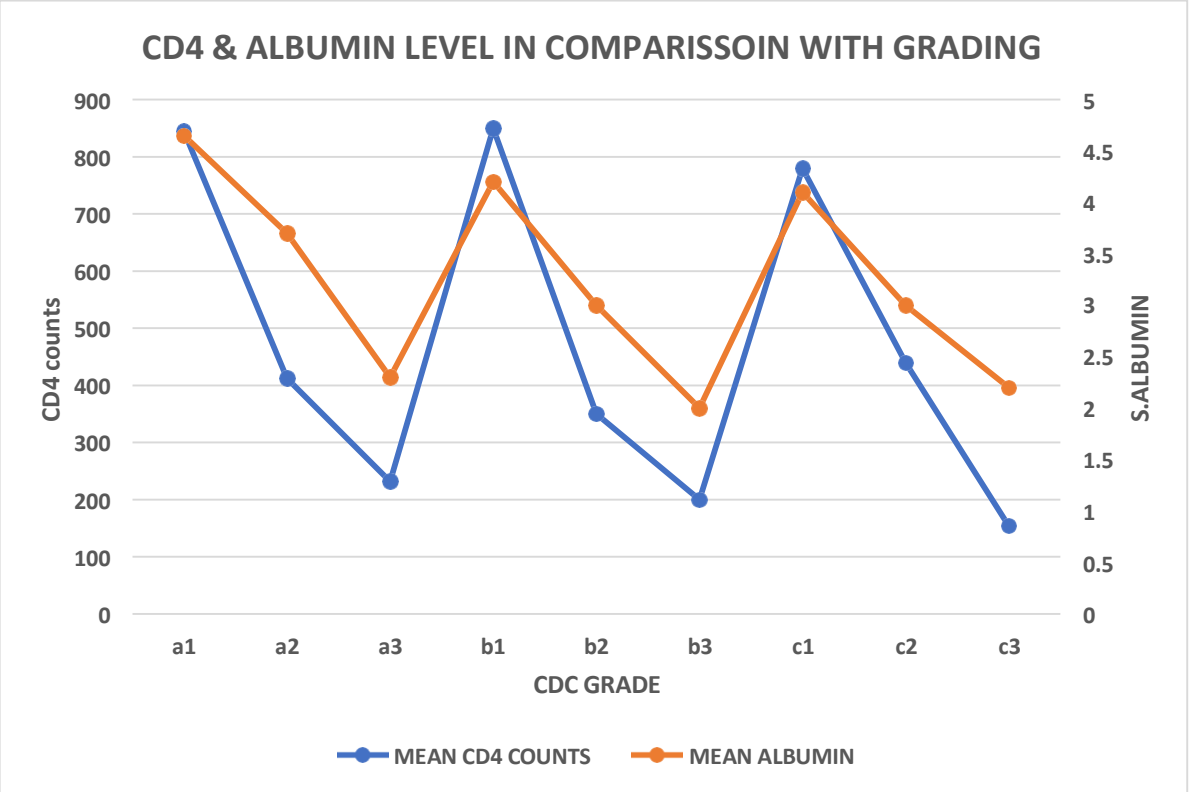
In our study, the comparison of serum albumin andCD4counts with CDC grading was done, results were. Serum albumin and CD4 counts showed linear changes, i.e., the higher the CD4counts higher is the serum albumin value and vice versa.

The correlation between CD4 counts and serum albumin, had a P-value < 0.0001 which is statically significant and SPERSON'S CORRELATION COEFFIENT was **r=0.770** which signifies the moderate correlation.

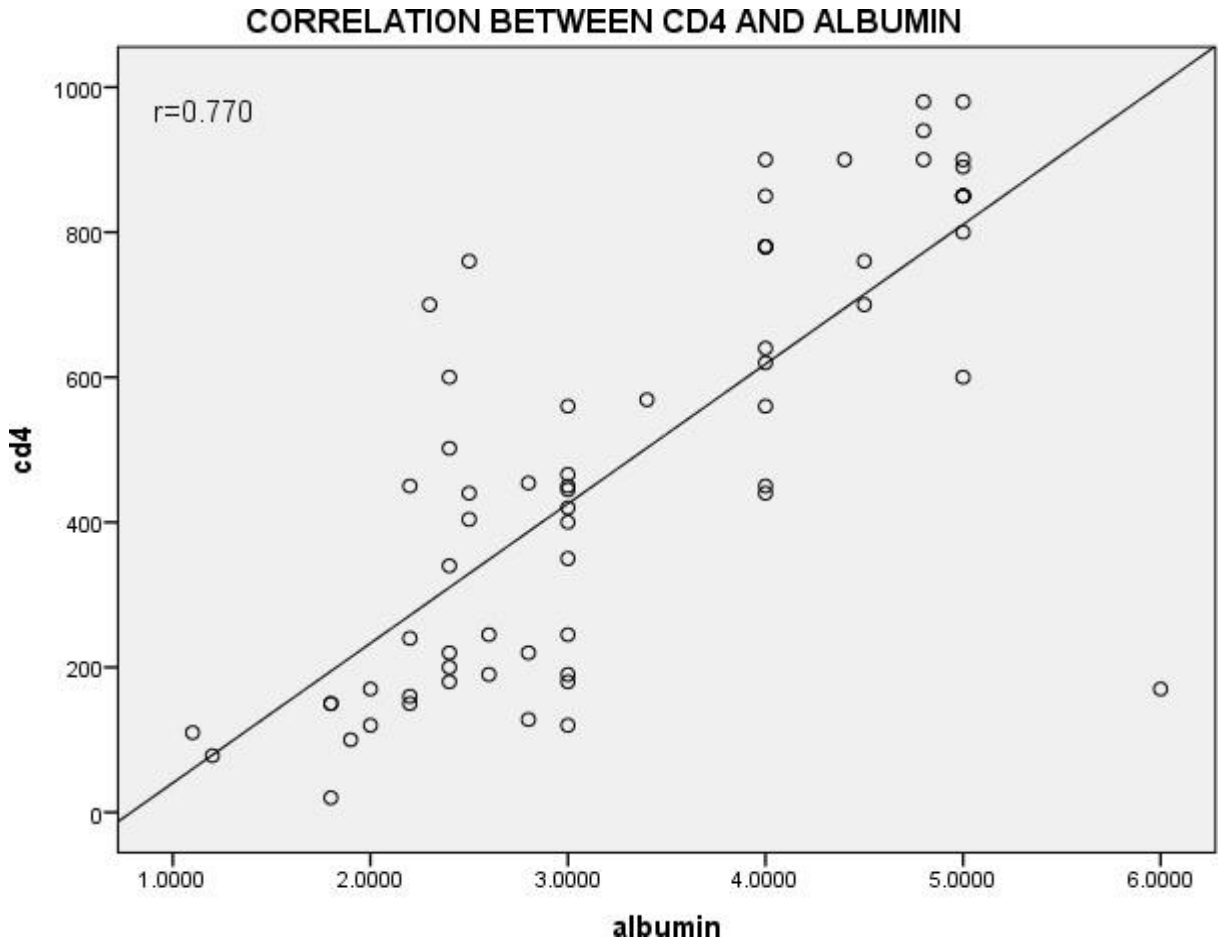
CDC grade	MEAN CD4 COUNTS	MEAN ALBUMIN
a1	844	4.65
a2	412	3.7
a3	232	2.3
b1	850	4.2
b2	350	3
b3	200	2
c1	780	4.1
c2	440	3
c3	154	2.2

TABLE: 9 CD4 & ALBUMIN LEVEL IN COMPARISON WITH GRADING

GRAPH 12: CD4 & ALBUMIN LEVEL IN COMPARISON WITH CDC GRADING



As the graph 10 suggests in A3, B3, C3 grades the albumin levels are also in declining trend when compared with CD4 cell count.



GRAPH 13: CD4 CELL COUNT & ALBUMIN LEVEL CORRELATION SCATTER PLOT

In the above scatter plot rho factor shows moderate co-relation according to SPEARSON"S CORRELATON COEFFICIENT.

CORRELATION BETWEEN	SPEARSON'S CORRELATION COEFFIENT	P VALUE	REMARK
CD4 COUNTS AND SERUM ALBUMIN	r=0.770	P=0.0001*	MODERATE CORRELATION & SIGNIFICANT
*:STATISTICALLY SIGNIFICANT			

TABLE 11: correlation between cd4 cell count and serum albumin.

p VALUE IS 0.001 which indicates significant correlation between CD4 cell count and Serum albumin.

DISCUSSION

Many studies have been conducted for cheaper surrogate markers in HIV patients ascd4cell count and HIV viral load are very expensive and is not feasible in developing countries and in as such as our country. so in this current study, Correlation between absolute CD4 cell count and serum albumin was done. many other studies have been proposed to compare albumin andcd4cell count as albumin is cheaper and readily available.

albumin was suggested to be useful as HIV progression marker and mortality predictor in resource-limited settings.

In addition to descriptive analysis, a correlation between CD4 count and serum albumin levels was performed. In this study, albumin and esr were also correlated.

1.AGE

In this study the most common age group was 41 to 50 similarly, in a study done by Kannangai et al[10] in 2008.Another study conducted by Jasmeet dingra et al[65] in 2011 the most common age group was 40 to 50. The reason could be a lack of education, unprotected intercourse iv Drug abuse and lack of awareness in 20th century.

Study	Year	Mean age(yrs)
Mehta et al[12]	2006	39.9 ± 11.3
Oluwami et al[13]	2006	37 ± 10.0
Shah et al [9]	2007	38.3 ± 7.9
Kannangai et al[10]	2008	40 ± 9.3
Present study	2020	43 ± 9.2

TABLE 12:Comparison of age distribution: patients

1.2 GENDER DISTRIBUTION

The majority were male, with 46 male patients and 19 female patients. Similarly study conducted by Jasmeet Dhingra et al[65] in 2011 of 60 patients, 18 were females (30%) and 42 males(70%). Males are at more risk for exposure of HIV virus as they are outgoing and work different jobs in developing nations.

STUDY	YEAR	male	female
PRESENT STUDY	2020	46	19
Jasmeet Dhingra et al	2011	42	18

1.3 PRESENTING COMPLAINTS:

Fever was the main presenting complaint in this study population i.e. in 17 patients (26.2%) followed by cough and breathlessness. Similarly study conducted by Jasmeet Dhingra et al[65] fever was the most common presenting complaints i.e seen in 30% of the study population followed by cough in 3.8% of the study population.

Fever is most common symptom of acute HIV infection as well as due to other infection due to immunocompromised status.

1.4 OPPURTUNISTIC INFECTIONS

In our study on 65 patients, it was found 26 patients (40%) had no opportunistic infection, Tuberculosis (TB) was the most common infection seen in 19 patients (29.2%), oral candidiasis was in 7 patients (10.8%), cytomegalovirus and Pneumocystis jirovecii was in 2 patients (3.1%), Cryptococcus meningitis, Cystospore, Cryptosporidiosis, Oesophageal candidiasis, Herpes zoster, Meningococcal, Pelvic inflammatory disease, Staph pneumonia and Varicella zoster was in 1 patient each 1.5%. Similarly study conducted by Jasmeet Dhingra et al[65] in 2011 TB was the

main presenting opportunistic infection that is seen in 48% of patients followed by oral candidiasis at 23%.In a study conducted by s.yogesh et al[66] TB was the most common presenting opportunistic infection i.e. 51% followed by candidiasis in 40% of patients.

1.5 CD4 RANGE:

In our study, it was observed that 21 patients (32%) were havingCD4< 200, 26 patients (40%) hadCD4200 – 500 and 18 patients (28%) hadCD4>500. In study conducted by Dhingra et al[65], 30(50%) patients had CD4<200, 23(38%) people hadCD4between 200 to 500 and 7 people(12%) hadCD4of more than 500.CD4cell count is a direct prognostication indicator of HIV progression and as a mortality indicator. In both study a3, b3,c3grades of CDC HIV classification patients had lowCD4cell count as well.

1.6 CD4 CELL COUNT AND ALBUMIN COMPARISON

In the current study CD4cell count and albumin had a strong positive correlation.

Following are the similar studies which showed same correlation

STUDY	YEAR
JASMEET DHINGRA et al[65]	2011
YOGESH et al[66]	2018
OUR STUDY	2020

CONCLUSIONS:

- 40 to 50 years were the most prevalent population affected
- Males were more prevalent, and the Decompensated Stage (C3) was the most common presentation.c2 and a1 had 15 patients each.
- males were more prevalent in all the classes.
- Fever was the most common presentation followed by cough and dyspnea.
- TDF+3TC+DTG (Tenofovir +lamivudine dolutegravir) was the most common Drug regimen being used in this population.
- Pulmonary TB is the most prevalent opportunistic infection in this population followed by candidiasis.
- 40 to 50 years were the most prevalent population affected.
- Albumin could be employed as a surrogate measure for immunosuppression in HIV/AIDS patients, as there was a potent direct correlation between theCD4count and albumin at both baseline and follow-up.
- Regression analysis revealed a significant linear trend, indicating that albumin is a significant factor influencing the change inCD4count (p 0.01)
- Albumin and ESR was also correlated and found strong co-relation between them. indicating efficiency of albumin in using it as a surrogate marker for assessment of HIV prognosis and as a mortality indicator.
- The present study conducted to CORRELATE Albumin levels and CD4+ T lymphocyte.
- There was a significant positive connection between albumin andCD4count (p0.001).

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ANNEXURE I

INSTITUTIONAL ETHICAL CLEARENCE CERTIFICATE.

BLDE

(DEEMED TO BE UNIVERSITY)

Declared as Deemed to be University u/s 3 of UGC Act, 1956

Accredited with 'A' Grade by NAAC (Cycle-2)

The Constituent College

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA

BLDE (DU)/IEC/ 807/2022-23 21/10/2022

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this University met on **Friday, 21st October, 2022 at 11.00 a.m. in the CAL Laboratory, Dept. of Pharmacology,** scrutinizes the Synopsis/ Research Projects of Post Graduate Student / Under Graduate Student /Faculty members of this University /Ph.D. Student College from ethical clearance point of view. After scrutiny, the following original/ corrected and revised version synopsis of the thesis/ research projects has been accorded ethical clearance.

Title: "A STUDY ON SERUM ALBUMIN LEVELS AND ITS CORRELATION WITH CD4 CELL COUNT IN HIV PATIENTS".

Name of the Principal Investigator: Dr.Sujay V,PG student, Dept. of General Medicine.

Dr. Santoshkumar Jeevangi
Chairperson
IEC, BLDE (DU),
VIJAYAPURA

Chairman,
Institutional Ethical Committee,
BLDE (Deemed to be University)
Vijayapura

Dr.Akram A. Naikwadi
Member Secretary
IEC, BLDE (DU),
VIJAYAPURA

MEMBER SECRETARY
Institutional Ethics Committee
BLDE (Deemed to be University)
Vijayapura-586103. Karnataka

Following documents were placed before Ethical Committee for Scrutinization.

- Copy of Synopsis/Research Projects
- Copy of inform consent form
- Any other relevant document

Smt. Bangaramma Sajjan Campus, B. M. Patil Road (Sholapur Road), Vijayapura - 586103, Karnataka, India.
BLDE (DU): Phone: +918352-262770, Fax: +918352-263303, Website: www.bldedu.ac.in, E-mail:office@bldedu.ac.in
College: Phone: +918352-262770, Fax: +918352-263019, E-mail: bmpmc.principal@bldedu.ac.in

ANNEXURE II

SHRI B.M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE.VIJAYAPURA-586 103

RESEARCH INFORMED CONSENT FORM

TITLE OF THE PROJECT :" A STUDY ON SERUM ALBUMIN LEVELS AND ITS CORRELATION WITHCD4CELL COUNT IN HIV PATIENTS")"

PG GUIDE : DR. S N BENTOOR

PG STUDENT : DR. SUJAY V

PURPOSE OF RESEARCH: I have been informed about this study. I have also been given a free choice of participation in this study.

BENEFITS:-

I understand that my participation in this study will help the investigator to diagnose the disease better and will help in the management of the disease.

PROCEDURE:-

I understand that relevant history will be taken and I will undergo detailed clinical examination after which necessary investigations will be done and accordingly treatment will be given.

RISK AND DISCOMFORTS:-

I understand there is no risk involved and I will experience no pain during the procedures performed.

CONFIDENTIALITY:-

I understand that medical information produced by this study will become a part of my hospital records and will be subjected to the confidentiality and privacy regulation of the said hospital. Information of a sensitive personal nature will not be a part of the medical records, but will be stored in the investigator's research file.

If the data are used for publication in the medical literature or for teaching purposes no names will be used and other identifiers such as photographs and audio or videotapes will be

used only with my special written permission. I understand I may see the photographs, videotapes and hear the audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION:-

I understand that I may ask more questions about the study at any time Concerned. The researcher is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study, which may influence my continued participation.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:-

I understand that my participation is voluntary and I may refuse to participate or may withDRaw consent and discontinue participation in this study at any time without prejudice. I also understand that the researcher may terminate my participation in this study at any time after he has explained the reasons for doing so and has helped arrange for my continued care by my own physician, if this is appropriate.

INJURY STATEMENT:-

I understand that in the unlikely event of injury to me resulting directly from my participation in this study and if such injury were reported promptly, then medical treatment will be available to me, but no further compensation will be provided. I understand that by my agreement for my participation in this study, I am not waiving any of my legal rights.

I have explained to (patient's / relevant guardian's name) the purpose of the research, the procedures required, and the possible risks and benefits to the best of my ability in patient's own language.

_____ _____

Investigator / P. G. Guide Date

I confirm that …….(Name of the PG guide / chief researcher) has explained to me the research, the study procedures that I undergo and the possible risks and discomforts as well as benefits that I may experience. I have read and I understand this consent form. Therefore, I agree to give my consent for my participation as a subject in this research project.

_____	_____
Participant / guardian	Date
_____	_____
Witness to signature	Date

ANNEXURE III

B.L.D.E. (DU) SHRI B.M. PATIL MEDICAL COLLEGE,

HOSPITAL AND RESEARCH

CENTRE, VIJAYAPURA - 583106. KARNATAKA

A STUDY ON SERUM ALBUMIN LEVELS AND ITS CORRELATION

WITH

CD4 CELL COUNT IN HIV PATIENTS

Name: CASE NO:

Age: IP NO:

Sex:

DOA:

Religion:

DOD:

Occupation:

Residence:

Presenting complaints with duration:

History of present complaints:

Past History:

Family History:

Personal History:

Diet/a

ppetit

e

Sleep

Bladder and bowel habits:

Addictions

Drug allergy

Treatment History:

General Physical Examination
Height:

Weight:

Body

Mass

Index

:

Vitals

PR:

BP:

RR:

Temp:

Neck:

Upper Limbs:

Chest:

Abdomen:

Lower Limbs:

Skin:

SYSTEMIC EXAMINATION.

- Respiratory System

- Cardiovascular System

- Central Nervous System

- Per abdomen

INVESTIGATIONS:

PATHOLOGY: **CBC:**		
Total Count		
Differential counts	Neutrophils	
	Lymphocytes	
	Eosinophils	
	Monocytes	
HB		
Platelets		
ESR		
PT,INR		
BT,CT		
BIOCHEMISTRY		
LFT:	Total S. Bilirubin	
	Conjugated S.Bilirubin	
	Unconjugated S.Bilirubin	
	SGOT	
	SGPT	
	ALP	

S.Protein	
S.Albumin	
S.AGR	
RFT:	
B.Urea	
S.Uric Acid	
S.Creatinine	
CD4+ CELL COUNT:	
ECG:	
CHEST X RAY:	

FINAL DIAGNOSIS:

SIGNATURE OF INVESTIGATOR

DR SUJAY V

9

NAME	AGE	SEX	IP/MRD NO	ses score	complaints	oppurtunistic infectio	drug regimen	clinical findings	cdc	cd4	ESR	albun	bilirubin t	conjugated	unconjugate	protie	sgot	sgpt	alp	hb	tc	nutrophil	lymphocytes	creati	DIAGNOSIS
bibi ayesha	58	female	118768	16	G I SYMPTOMS	no	tdf+3tc+dtg	dry skin	c2	450	40	4	0.8	0.4	0.4	5.8	40	40	52	11	4500	40	30	1	acute ge with rvd with hep b
basappa g m	51	male	142911	19	fever	no	tdf+3tc+dtg	bilateral rhonchi	a3	220	56	2.4	0.6	0.1	0.5	4.9	62	27	77	9.3	11000	76.5	12.5	0.8	bacterial pneumonia with oral candidiasis with rvd
basavraj b	46	male	93481	14	fever	TB	tdf+3tc+efv	ascities	b2	400	90	3	3	2.4	0.6	3	100	104	112	8	10000	80	12	1.1	alcholic liover diseasde with rvd with anemia
somaning m	25	male	49972	15	abdominal pain	no	tdf+3tc+dtg		a3	245	12	2.2	4	2.3	0.4	5.4	80	38	124	9.8	29.25	95.3	1.3	2.8	retroviral disease with acute gastroenteritits
jyoti ph	32	female	71111	16	fever	no	tdf+3tc+efv	bilateral rhonchi	c3	110	50	1.1	2	1.1	0.9	3	77	30	105	8.5	7000	81	12.6	1.1	rvd with tb
parshuram s	22	male	365483	14	fever	herpes zoster	tdf+3tc+dtg	multiple vesicles	b2	300	24	3	1.3	0.8	0.5	6	40	48	100	10	20000	88	6.9	0.6	rvdwith herpes zoster infection
janabai	62	female	342906	10	abdominal pain	pelvic inflammatory c	tdf+3tc+dtg	abdomnal tenderness	c3	150	20	1.8	1.8	0.8	1	5	60	40	89	10	4500	90	6	1.8	pid rvd with aki
chandru	38	male	148998	11	dysphagia	cytomegalovirus	tdf	dry skin	c3	190	10	3	2	1.4	0.6	6	40	40	90	11	6000	74	22	0.8	cmv oesophagitis with rvd
bouramma	40	female	50107	20	breathlessness and cough	TB	tdf+3tc+dtg	decreased air entry to rigl	c2	200	40	2.4	0.4	0.3	0.1	7	40	18	114	8.5	7000	80	15	0.4	tb effusion with rvd
mallikarjun	63	male	212800	17	fever	no	tdf+3tc+efv	none	a1	850	6	5	0.8	0.4	0.4	6	40	20	80	12	5000	60	30	0.4	viral fever with rvd
ravi kumar	40	male	50100	18	weight loss	oral candidiasis	tdf+3tc+efv	oral thrush	c2	400	10	3	1.2	0.8	0.4	5	20	20	100	10	6000	80	50	1	oral candidiasis with rvd
sadik pasha	50	male	32040	10	breathlessness and cough	no	azt+3tc	rhonchi+	a1	800	6	5	0.6	0.4	0.2	8	40	40	30	11	2000	80	40	0.4	pneumonia with rvd
shrishail	54	male	197596	8	breathlessness and cough	TB	3tc+efv+azt	rhonci+	c2	245	36	2.6	1.8	0.8	1	6	60	40	40	12	9000	80	30	0.1	prurigo with tenia cruris with rvd
mallamma b	45	female	179440	7	fever	no	tdf+3tc+dtg	blanching	a1	900	6	4	0.6	0.4	0.2	6	16	6	10	12	9000	83	9	0.7	dengue fever witrh rvd
santosh	26	male	2022-601	17	G I SYMPTOMS	cryptospora	zdv+3tc+atv	rhonchi+	c2	420	12	3	0.8	0.4	0.2	6	18	20	34	11	6800	30	48	1	ccryptosporiodiosis with rvd
nagarathmm	35	female	70810	12	fever	oral candidiasis	tdf+3tc+dtg	oral thrush	a1	850	14	5	1.2	0.8	0.4	6.2	34	32	28	10	7000	45	45	0.8	oral candidiasis with rvd
mallikarjun	50	male	19216	16	breathlessness and cough	TB	zdv+3tc+atv	rhonchi+	c2	404	48	2.5	1	0.5	0.5	6	43	34	53	13	3800	20	70	1.2	pulmonary tb with rvd
gurupadapp	38	male	21108	13	altered sensorium	oral candidiasis	azt+3tc	neck rigidity	c3	128	24	2.8	0.7	0.4	0.3	5.6	70	60	66	11	3600	20	78	1	hiv induced encephalopathy
bilal mulla	24	male	31221	23	reduced responsivness	varicella zoster	3tc+efv+azt		c3	100	34	1.9	5	0.6	0.5	0.3	45	34	23	10	18000	80	16	1.8	varicella zoster with septic shock with rvd
parvati hipp	65	female	140945	8	seizures	cryptococcus meningi	tdf+3tc+dtg		c3	78	50	1.2	1	0.2	0.8	4	21	24	31	9	12000	32	63	1.5	cryptococcalmeninigtis with aids
mahadevi sh	60	female	116175	12	fever	TB	3tc+efg+azt		a1	940	5	4.8	1	0.8	0.2	6	21	25	44	13	5000	40	40	1	viral fever with rvd
prakash jh	32	female	72650	14	weight loss	no	tdf+3tc+dtg	no	a1	780	34	4	1	0.6	0.4	6	34	24	78	12	4200	60	40	0.5	rvd
suryakanth	70	male	157907	9	breathlessness and cough	TB	tdf+3tc+dtg	rhonci+	c2	502	56	2.4	1	0.4	0.6	5.6	24	222	40	13	5400	46	44	0.8	piulmonary tb with rvd
hanmanth k	62	male	362938	21	right sided weakness	no	3tc+efg+azt	umn lesion	a1	900	10	5	0.8	0.6	0.2	6	20	18	28	14	5000	32	44	0.9	cerebrovascular accident with rvd
ramesh g	25	male	268474	20	fever	TB	tdf+3tc+efv	no	a2	330	12	4.5	1	0.8	0.6	5.6	20	18	40	13	6000	60	20	0.8	rvd
pandu c	45	male	29219	14	fever	oral candidiasis	tdf+3tc+dtg	no	b1	850	18	4.2	0.8	0.6	0.2	6	16	14	67	12	5000	78	24	0.4	oral candidiasis with rvd
mahadev ko	16	male	282008	32	fever	TB	3tc+efv+azt	no	c1	800	10	5	1	0.7	0.3	6.5	18	12	22	11	9800	90	10	0.6	rvd
siddappa cr	48	male	372108	23	breathlessness and cough	TB	azt+3tc+efv	rhonci+	c3	170	65	2	0.8	0.6	0.2	5.6	24	20	40	9.1	3400	30	66	0.4	pulmonary tb with anemia
holeppa s b	66	male	57194	26	abdominal pain	TB	azt+3tc+efv	tender abdomen	c3	150	66	2.2	1	0.4	0.6	6	20	40	120	8	5000	20	75	0.8	abdominal tuberculosis with anemia with rvd
subhas	50	male	197139	15	audtory hallucination	no	tdf+3tc+dtg	no	c3	180	5	3	0.8	0.2	0.6	6.5	12	21	40	11	4500	40	60	0.9	rvd with htn with hand (delusion of infedility)
basaiyya gm	42	male	142901	17	fever	oral candidiasis	azt+3tc+efv	oral thrush	a1	600	10	5	0.9	0.5	0.4	6	16	18	40	13	12000	70	25	1	pneumonia with oral candidiasis with rvd
sunanda cha	58	female	58001	14	breathlessness and cough	TB	azt+3tc+efv	rhonci+	c3	160	54	2.2	1.8	0.8	1	5.5	20	14	60	13	15000	70	30	1.8	relapsing tb with covid 19 pnemonia with rvd
ramappa sh	52	male	34435	8	breathlessness and cough	no	zdv+3tc+atv	rhonchi+	a2	440	14	2.5	1.2	0.8	0.6	5.5	30	34	100	7.5	2400	32	57	1	Lrti with rvd
sidddappa c	48	male	35957	15	G I SYMPTOMS	TB	nvp+d4t+3tc	tender abdomen	c1	760	10	3.3	0.5	0.3	0.2	5.2	23	9	65	13	5920	71	19	1.6	acute ge with ca rectum with rvd

NAME	AGE	SEX	IP/MRD NO	ses score	complaints	oppurtunistic infectio	drug regimen	clinical findings	cdc	cd4	ESR	albur	bilirubin t	conjugated	unconjugate	protie	sgot	sgpt	alp	hb	tc	nutrophil	lymphocytes	creati	DIAGNOSIS
holeppa s b	66	male	57194	26	abdominal pain	TB	azt+3tc+efv	tender abdomen	c3	150	66	2.2	1	0.4	0.6	6	20	40	120	8	5000	20	75	0.8	abdominal tuberculosis with anemia with rvd
subhas	50	male	197139	15	audtory hallucination	no	tdf+3tc+dtg	no	c3	180	5	3	0.8	0.2	0.6	6.5	12	21	40	11	4500	40	60	0.9	rvd with htn with hand (delusion of infedility)
basaiyya gn	42	male	142901	17	fever	oral candidiasis	azt+3tc+efv	oral thrush	a1	600	10	5	0.9	0.5	0.4	6	16	18	40	13	12000	70	25	1	pneumonia with oral candidiasis with rvd
sunanda ch	58	female	58001	14	breathlessness and cough	TB	azt+3tc+efv	rhonci+	c3	160	54	2.2	1.8	0.8	1	5.5	20	14	60	13	15000	70	30	1.8	relapsing tb with covid 19 pnemonia with rvd
ramappa sh	52	male	34435	8	breathlessness and cough	no	zdv+3tc+atv	rhonchi+	a2	440	14	2.5	1.2	0.8	0.6	5.5	30	34	100	7.5	2400	32	57	1	Lrti with rvd
sidddappa c	48	male	35957	15	G I SYMPTOMS	TB	nvp+d4t+3tc	tender abdomen	c1	760	10	3.3	0.5	0.3	0.2	5.2	23	9	65	13	5920	71	19	1.6	acute ge with ca rectum with rvd
renuka ak	55	female	55121	22	G I SYMPTOMS	oral candidiasis	dtg+3tc+tf	oral thrush	c2	640	6	4	0.8	0.5	0.3	6	20	16	50	12	5940	58	35	1	rvd with type 2 dm with oral candidasis
chandra l c	37	male	66249	9	fever	oral candidiasis	ftc+tdf+efv	oral white patch	c2	560	4	4	1	0.6	0.4	5	14	15	40	11	4800	14	51	1	oral candidasis with rvd
ashwathapp	52	male	172165	22	seizures	no	azt+3tc+efv	no	c2	240	8	2.2	0.8	0.6	0.4	6	20	18	40	14	7050	40	50	1	hiv encephalopathy with miliary tb
parvati sind	34	female	15888	8	abdominal pain	TB	abc+3tc+dtg	no	a2	450	12	3	0.9	0.7	0.2	6.6	12	13	21	9	5600	40	45	0.9	acute gastritis with anemia with rvd
ramesh kam	18	male	49310	21	fever	cryptosporidiosis	3tc+efv+tf	tender abdomen	c3	120	12	3	0.7	0.3	0.4	10	21	13	180	8	6000	58	34	1.4	cryptospordiasis with hiv with anemia
neelabai rat	44	female	31782	15	abdominal pain	no	3tc+efv+tf	old prolapse	a1	980	6	4.8	0.8	0.6	0.2	6	20	18	38	13	8000	35	65	0.8	third degree uterine wall prolapse with rvd
vasanth pati	35	male	39042	23	altered sensorium	meningococal	abc+3tc+dtg	neck rigidity	c3	170	10	6	0.6	0.3	0.3	5	50	40	116	7.8	11000	35	65	2.8	streptococal meningitis with aki with rvd
jayalakhmi	28	female	220188	6	labour pain	no	3tc+efv+tf		a1	900	10	4.8	0.7	0.3	0.4	8	21	13	100	9.8	9500	74	16	1.3	ftvd with rvd
gangabai b	37	male	133645	14	fever	staph pneumonia	tdf+3tc+dtg	rhonchi+	a2	466	20	3	0.8	0.4	0.4	5.8	50	40	50	9	12000	94	4	0.4	b/l pneumonia with anemia with rvd
srivedevi	48	female	313685	4	altered sensorium	no	zdv+3tc+atv	agitated	c2	454	40	2.8	1.6	1	0.6	4.6	58	46	70	11	20000	88	6	2.2	aki with hiv encephalopathy
lakshmi bira	42	female	133642	12	fever	no	tdf+3tc+nvp	rhonchi	c2	350	50	3	1.6	0.8	0.6	6	50	40	54	9	3500	24	74	1.1	pulmonary tb with anemia with rvd
mallappa k	70	male	35766	10	dysphagia	cmv	dtg+3tc+tf	ringed lesions in esophag	c2	220	5	2.4	0.8	0.6	0.2	7	46	50	54	8.5	12400	87	20	0.9	cmv esophagitis with rvd
shoba l g	34	female	131962	7	fever	TB	ftc+tdf+efv	rhonchi	c3	340	56	2.4	0.8	0.6	0.2	6	30	45	34	10	4300	74	14	0.9	pulmonary tb with anemia with rvd
rachappa	60	male	382660	5	abdominal pain	no	tdf+3tc+dtg	no	a1	780	4	4	1.8	1.6	0.2	5.5	43	34	34	10	5380	69	12	2.2	pre renal aki with acute ge with rvd
haleppa har	65	male	221304	14	abdominal pain	no	tdf+3tc+efv	lmn lesion	a2	445	14	3	1	0.6	0.4	7	12	21	44	13	9800	66	14	0.8	lumbar compressive myeolopathy with rvd
mallikarjun	56	male	105343	8	altered sensorium	TB	3tc+efg+azt	pigementation	c3	20	10	1.8	0.9	0.7	0.3	6.5	23	18	19	9	6000	20	70	1.1	progressive multifocal leukoencephalopathy with rvd
chandrappa	40	male	86292	7	abdominal pain	no	3tc+efv+azt	tender abdomen	a1	780	23	4	0.9	0.6	0.3	6	18	16	20	10	14000	60	25	1	acute apppicitis with rvd
santosh b	20	male	6218	12	G I SYMPTOMS	no	tdf+3tc+dtg	no	a1	850	3	5	0.6	0.2	0.4	7	14	12	20	13	5600	40	40	0.9	acute diarrhea with rvd
surya birad	29	male	25329	21	breathlessness and cough	TB	3tc+efv+tf	rhonchi	c3	190	56	2.6	0.9	0.7	0.2	6	20	18	24	11	5000	20	70	1	pulmonary tb with rvd
ningappa	60	male	45592	20	urinary retention with pair	no	ftc+tdf+efv	colickey pain	a2	440	5	4	0.9	0.7	0.5	6.5	10	12	24	12	4500	40	45	1.8	renal calculi with htn, type 2 dm with rvd
pooja	32	male	294771	19	labour pain	no	tdf+3tc+dtg	fetal heart sound+	a1	900	8	4.4	0.8	0.6	0.2	7	20	18	28	14	11000	60	38	1	ftvd with rvd
jayalaxmi	65	male	220188	16	pain abdomen,pv discharg	TB	dtg+3tc+tf	pv discharge,mucopurule	c3	220	28	2.8	0.9	0.8	0.1	5.6	22	12	16	14	12000	20	70	1.8	pelvic inflammatory disease with rvd
vijaylakshm	36	male	91138	7	seizures	no	3tc+dtg+tdg	post ictal phase	a2	400	12	4	0.9	0.7	0.2	6	8	10	10	10	6500	40	48	1	status epilepticus with anemia with rvd
pintu rathoc	32	male	382562	12	G I SYMPTOMS	no	no	no	a1	850	14	5	1	0.2	0.8	7	14	20	20	14	5700	50	40	1.6	acute diarrhea with rvd
mallappa	44	male	12495	9	dysphagia	esophageal candidas	3tc+efg+azt	npne	c2	569	24	3.4	1.6	0.8	0.6	6.5	16	14	13	15	9890	40	54	1.4	oesophageal cndidiasis with rvd
veena ashok	48	female	273076	25	breathlessness and cough	TB	3tc+efv+azt	rhonchi	c3	180	58	2.4	0.9	0.7	0.2	24	22	18	14	11	4600	20	75	1.1	relapsing pulmonary tb with rvd
bapugowda	64	male	169018	20	blurring of vision	no	3tc+efg+azt	opacified lens	a2	420	26	4.5	1	0.6	0.2	12	14	24	40	14	5400	45	45	1	b/l senile cataract with rvd
sandya kulk	34	female	133064	16	headache	no	tdf+3tc+dtg	sinus tenderness	a2	320	5	5	2	1.5	0.5	6	12	9	20	10	6500	30	55	0.8	maxillary sinusitis with rvd
chandappa l	65	male	261997	10	breathlessness and cough	TB	3tc+efv+azt	rhonchi	c2	560	76	3	1	0.8	0.6	5	21	8	18	12	3400	25	70	1.6	pneumocystits jiroveci with rvd
manjunath	45	male	200643	5	G I SYMPTOMS	pneumocystitis	tdf+3tc+dtg	pain abdomen	c3	120	25	2	0.9	0.7	0.2	5	12	10	16	14	7800	45	50	0.7	pulmonary tb with rvd
shivananad	52	male	58001	15	breathlessness and cough	pneumocystitis	zdv+3tc+atv	rhonchi	c3	150	34	1.8	1.8	0.8	1	4	3	5	18	12	12000	30	40	1.2	pneumocystits jiroveci with rvd