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FROM DISCOVERY TO TREATMENT: A REVIEW OF HIV RESEARCH AND INTERVENTIONS

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ABSTRACT
The Human Immunodeficiency Virus (HIV) has remained a prominent global health concern. Presently, the introduction of viruses, reproductive mechanisms in host cells, genetic material, and the crucial difference between DNA and RNA viruses has been discussed. Then, detailed information on the HIV/AIDS epidemic's origins and quick spread worldwide, focusing on India has been given. A comprehensive review of current trends shows the global prevalence of HIV, new infections, and AIDS-related death, as well as regional variances and epidemic control success. The "HIV" virus's subtypes, structural components, and the antiretroviral medications that are the foundation of HIV treatment have been discussed. Highly active antiretroviral treatment (HAART) and gene therapy are highlighted in the HIV cure hunt. The opportunistic infections in HIV/AIDS patients explain the wide variety of illnesses that affect individuals with compromised immune systems and emphasize the vulnerability of those with low CD4 cell counts. These infections, ranging from tuberculosis to candidiasis, highlight the complexity of disease management and its complications. The extensive societal and economic consequences, exerted on both individuals and communities have been explained worldwide. Additionally, the paper explores the recent progress in HIV research and acknowledges the ongoing hurdles faced in the battle against this viral infection.

Keywords: *Virus, HIV, Disease, AIDS, Opportunistic infection, HAART*

INTRODUCTION

The word "virus" originates from the Latin word meaning “poison or sticky liquid”. They are extremely little organisms that are able to reproduce and spread solely within the cells of their host. In order to accomplish this, they make use of the machinery that is present within the host cell to produce their own building blocks, which they then utilize to self-assemble into new viral particles that are then discharged into the surrounding environment. In addition to having a protein coat that is enclosed in a lipid, protein, and carbohydrate envelope, a virus possesses either deoxyribonucleic acid (DNA) or ribonucleic acid (RNA) as its genetic material. RNA is the more common of the two. Both lytic and lysogenic stages are present in the viral replication cycle. The outer covering of a virus is known as the virion of that virus. Antibiotics are ineffective against viral infections and cannot treat them. Treatments such as antiviral drugs and vaccinations are efficient methods for preventing these illnesses. In order to be effective, these drugs either impede the process of DNA synthesis or get in the way of viral replication (Coffin *et al*., 1999).

Many diseases can be caused by viruses in humans. For instance, the Influenza virus causes influenza. Viruses cause immune response in the host, which kills the virus, but some viruses, such as HIV, are resistant to immune response and cause chronic infections that are difficult to treat. The white blood cells of the immune system provide protection against a variety of infections (Haynes *et al*.,1996). WBCs contain helper T cells, also known as CD4+ cells. HIV belongs to the genus *Lentivirus* within the family Retroviridae, subfamily Orthoretrovirinae. HIV assaults the immune system, resulting in a decrease in the number of CD4+ T lymphocytes circulating in the body. It also continues to replicate, which further reduces a person's resistance to a variety of infections and can lead to mortality from opportunistic infections and neoplasms. AIDS (Acquired Immune Deficiency Syndrome) is caused by the HIV infection (Pantaleo *et al*.,1996).

HISTORY

In the United States, the first incidence of immunodeficiency disease was identified in a gay man in 1981. Later in 1982, the same disease, referred as AIDS by the CDC in the United States and SIDA in France and Spain, spreads swiftly throughout Europe. In 1984, the United States and Europe reported 7,700 and 762 cases of AIDS, respectively (Greene, 2007).

In 1986, the first instance of HIV infection in India was identified among female sex workers in Chennai. Initially, India's southern states of Andhra Pradesh, Maharashtra, Karnataka, and Tamil Nadu, as well as the northeastern states of Nagaland and Manipur, had a high prevalence of infection (Paranjape and Challacombe, 2016). In 1988, the first World AIDS Day was observed on December

1. Worldwide, 8–10 million people in 1990, 14-15 million in 1993 and 23 million persons in 1996 were infected with HIV. In 2006, there were nearly 40 million HIV-positive individuals and over 25 million AIDS-related deaths (Greene, 2007).

CURRENT PATTERNS

Since the beginning of the epidemic, there have been 85.6 million new cases of HIV infection, and there have been 40.4 million deaths attributed to AIDS-related illnesses. The prevalence of HIV around the world is shown in Africa having the highest rate, followed by the United States of America and Southeast Asia Fig. 1. The estimated number of people living with HIV at the end of 2022 is 39 million, which represents a significant threat to public health. There are 37.5 million people and just 1.5 million children ages 0 to 14 in the country. In 2010, there were 2.1 million people who were infected with HIV; however, by the year 2022, this number had

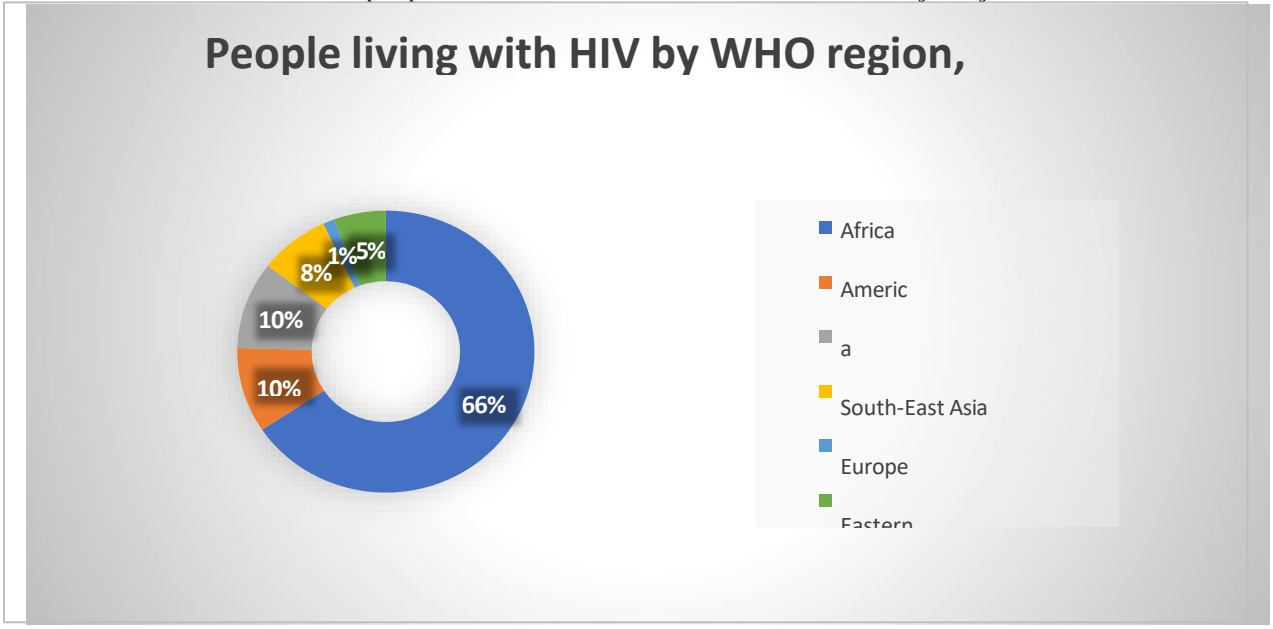

Figure 1: Percentage of People having HIV (WHO, 2022)

reduced to 1.3 million, representing a decrease of 38%. In the year 2022, there were 630 000 persons who passed away as a result of AIDS-related illnesses, while 29.8 million people were given antiretroviral treatment. According to UNAIDS, women and girls made up 53 percent of all people living with HIV in the world. Since the epidemic's height in 1995, the number of people newly diagnosed with HIV has dropped by 59%. Africa is the continent most severely impacted by the HIV epidemic, with roughly one in every 25 individuals (3.6% of the total population) living with the virus. Worldwide, more than two-thirds of the people living with HIV have been accounted (UNAIDS/WHO, 2023).

These statistics serve as a stark reminder that HIV is not just a medical issue but a deeply human one, where the numbers reflect countless personal stories, resilience, and the urgent need for continued global solidarity and commitment to ending the HIV epidemic. Global HIV epidemic in 2022 is summarized in Table-1.

In India, 24.01 lakh people are living with HIV. Among these, 23.31 lakh are adults and 0.70 lakh are children. According to NACO, 2021 people living with HIV are maximum in Maharashtra (3.94 lakh) followed by Andhra Pradesh (3.21) and Karnataka (2.76). Least people living with HIV reported in Arunachal Pradesh (0.01), Sikkim (0.005) and Andaman and Nicobar Islands (0.004) (NACO, 2023) (Fig. 2).

HIV (HUMAN IMMUNODEFICIENCY VIRUS)

HIV-1 and HIV-2 are the subtypes of Human Immunodeficiency Virus. Globally, HIV-1 is most prevalent, whereas HIV-2 primarily affects central and western Africa. (Faria *et al*., 2014). The HIV-1 and HIV-2 viruses are zoonotic infections (Gao *et al*., 1999). HIV-1 was first isolated in 1983 and evolved from non-human primate immunodeficiency viruses associated with AIDS in Central African chimpanzees in 1984 (Gallo *et al*., 1984). Subsequently, HIV-2 was discovered in West Africa in 1984 which has evolved from sooty mangabeys (Clavel *et al*., 1986).

HIV is an enclosed retrovirus composed of the lipid bilayer, single-stranded, positive-sense RNA virus. It uses reverse transcriptase enzyme to convert its genome from RNA to DNA and then uses integrase enzyme to integrate its genome into the host genome, becoming a part of it and replicating alongside it (Zhu *et al*., 2006).

Table 1: SUMMARY OF GLOBAL HIV EPIDEMIC, 2022

	People living with HIV	People acquiring HIV	People dying from HIV-related causes
TOTAL	39.0 million (33.1-45.7 million)	1.3 million (1.0-1.7 million)	630000 (480000-880000)
ADULTS (15+ years)	37.5 million (31.8-43.6 million)	1.2 million (900000-1.6 million)	540000 (410000-770000)
WOMEN (15+ years)	20.0 million (16.9-23.4 million)	540000 (400000-740000)	230000 (170000-340000)
MEN (15+ years)	17.4 million (14.7-20.4 million)	640000 (490000-850000)	310000 (230000-440000)
CHILDREN	1.5 million (1.2-2.1 million)	130000 (90000-210000)	84000 (56000-120000)

Source: UNAIDS/WHO estimates, 2023

STRUCTURE OF THE VIRION

HIV genome consists of two identical single-stranded RNA molecules enclosed within the core of virus particle. The virions are approximately 120nm in diameter with RNA genome 9750 nucleotides long (Wain-Hobson, 1989). The genome of this virus is known as pro-viral DNA which is formed by reverse transcription of viral RNA into DNA, degradation of RNA and integration of viral DNA into human genome by integrase enzyme. Recently by cryo-electron microscopy tomography, detailed 3-D structure of HIV-1 virus was studied which consists of envelope- glycoprotein spikes which help in infection of host cells (Zhu *et al*., 2006) (Fig. 3).

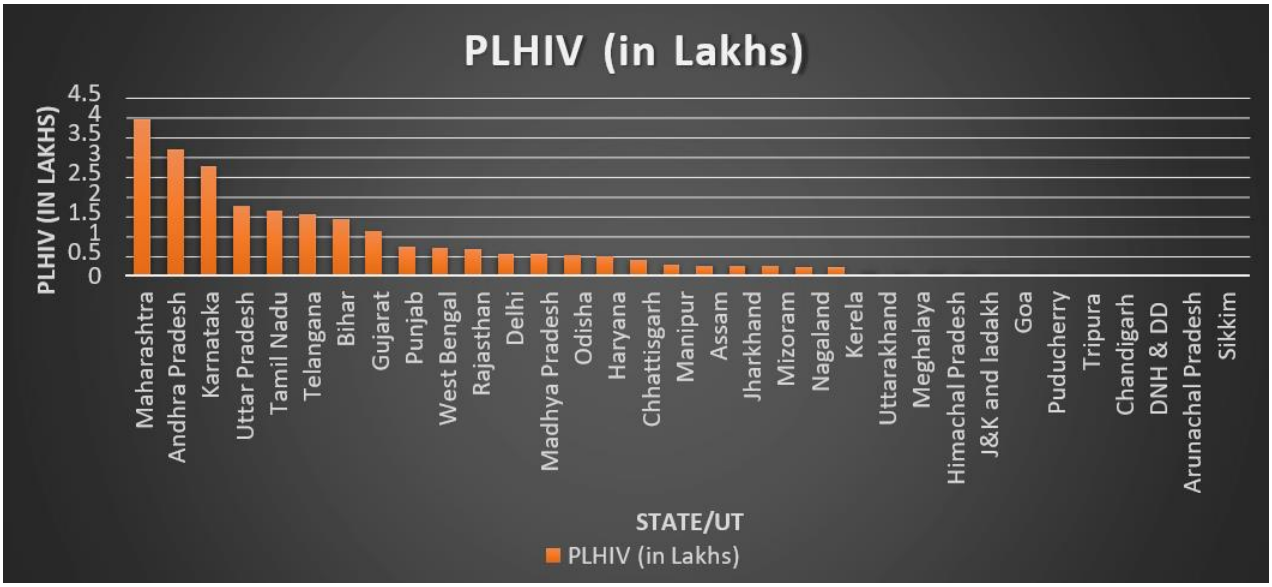

Figure 2: Graph showing PLHIV (People living with HIV) in different states of India

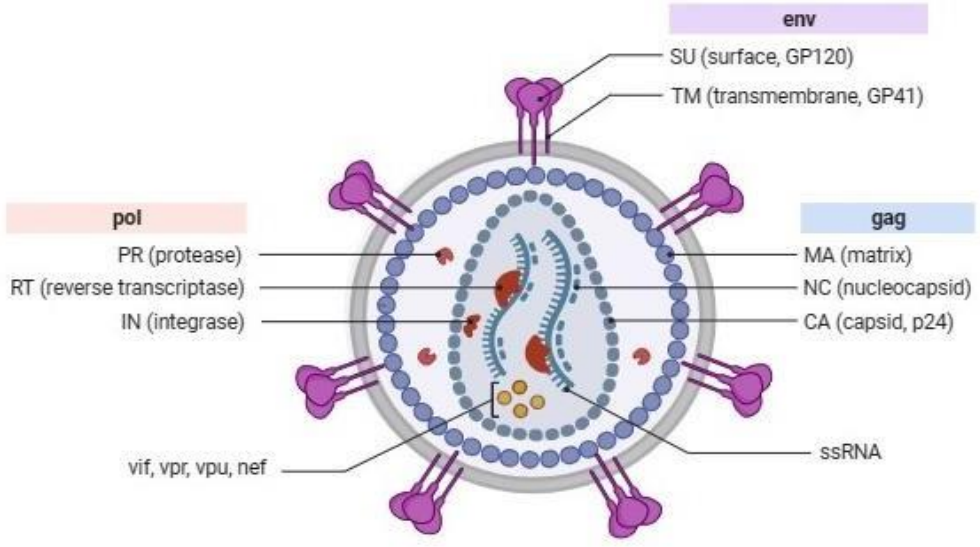

Figure 3: HIV structure

HIV-1

Long terminal repetitions flank the virus's genomic DNA on both ends. The 5' LTR encodes the promotor region, which initiates viral gene transcription. Following this is the gag gene reading frame, which encodes p6 and p7 (nucleocapsid proteins), p24 (viral capsid protein), and p17 (matrix protein). Following the gag gene comes the pol reading frame, which codes for P51 (reverse transcriptase), P12 (protease), P15 (RNase H), and P32 (Integrase) (Bukrinskaya, 2004). The env reading frame is located next to the pol gene and encodes gp120 (Surface Protein) and gp41 (Transmembrane Protein). Additionally, HIV encodes regulatory genes in addition to these genes. HIV replication requires the proteins tat (transactivator protein) and rev (RNA splicing-regulator). Whereas nef (negative regulatory factor), vif (viral infectivity factor), vpr (virus protein r), and vpu (virus protein unique) are required for viral budding, replication, and pathogenicity (Levy *et al*., 2007, Sauter *et al*., 2021). The HIV-1 gene Nef has fewer amino acids and has a greater capacity to promote the pathogenicity of HIV-1 than HIV-2. (Kumarasamy *et al*., 2005)

HIV-2

HIV-2 is more closely related to SIV-2 of mangabey monkeys in West Africa. HIV-1 and HIV-2 are morphologically indistinguishable, but their genomic structure and antigenicity are unique. As a result, specific tools are necessary to diagnose HIV-2. HIV-2 has a lower pathogenicity than HIV-1 because it codes for vpx (virus protein x) rather than vpu, which is responsible for the lower pathogenicity (Vicenzi and Poli, 2013)

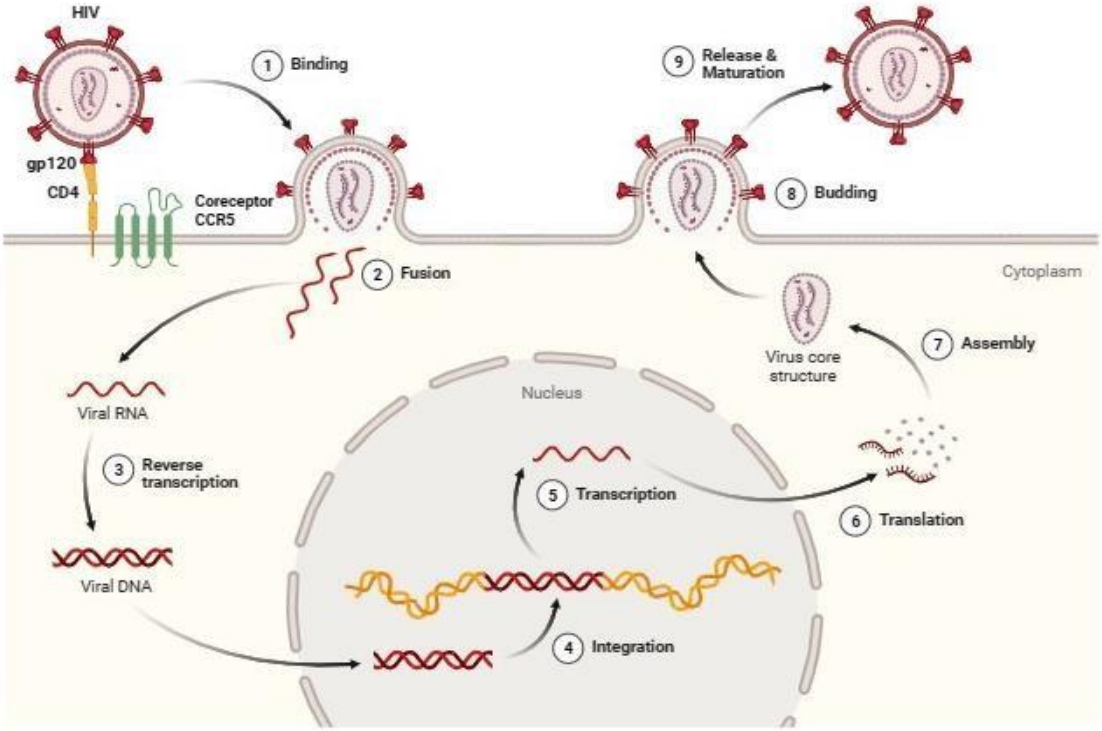

Figure 4: Life cycle of HIV virus- *1. HIV envelope gp120 glycoprotein binding to CCR5/CXCR4 (coreceptor) and CD4 (receptor) cell surfaces. 2. Fusion of viral and cell membranes, allowing viral proteins to enter the cytoplasm. 3. HIV is a retrovirus, and viral RNA is transcribed into double-stranded DNA by the enzyme reverse transcriptase. 4. Following reverse transcription, viral double-stranded DNA is carried to the nucleus and integrated into the host genome by the integrase enzyme. 5. The transcription of infectious virions into viral RNAs, which are then exported to the cytoplasm.*
6. Translation of RNAs in the cytoplasm to generate viral protein. 7. Viral RNA and viral protein packaging and assembly into virions for budding. 8. Packaged virion budding. 9. Infectious virion release and maturation (Ramdas et al., 2020)

HIV REPLICATION CELL CYCLE

It is clear from the data that individuals show variability to the infection caused by HIV-1, their viral control and progression to AIDS. Even in the absence of ART, small subset of HIV infected persons does not progress to AIDS because of homozygous 32-bp deletion in the CCR5 gene (Liu *et al*, 1996). This gene codes a HIV-1 coreceptor which is nonfunctional. Initial resistance to HIV-1 is associated with the genetic variant CCR5Δ32. Genetic determinants of host also affect severity of disease progression and the rate at which virus is controlled. HLAs also play major role in rapid progression to AIDS and death (Carrington *et al*, 1999) (Fig. 4).

SIGNS AND SYMPTOMS DEPENDING ON THE PHASE OF INFECTION

Acute HIV (Primary infection)

HIV symptoms differ according to infection stage. Within three to six weeks of exposure, plasma viraemia increases rapidly, accompanied by a decrease in CD4 cell count (Valencia *et al*., 2007). In the first few weeks after infection, people may experience no symptoms or a flu-like illness, including fever, hoarse throat, skin rash, lymphadenopathy, splenomegaly, myalgia, arthritis, and, less frequently, meningitis. However, many individuals are unaware of their circumstances until it is too late. Currently, these symptoms are moderate, but the virus load is quite significant. During primary infection, infection spreads more readily (Portillo *et al*., 2007).

Clinical latent infection (Chronic HIV)

The acute phase of HIV is followed by the chronic phase, characterized by a progressive decline in CD4 count and low viral replication. In this stage, patients can remain asymptomatic for several months to years. In one study of HIV patients from Mumbai, the median interval between HIV infection and the onset of AIDS was 7.9 years (Valencia *et al*., 2007).

Progression to AIDS

During the later stages, when immune system has been severely damaged, many opportunistic infections develop. People with HIV are diagnosed with AIDS if they have a CD4 count of less than 200 cells/mm3 or if they have certain opportunistic infections. Once a person is diagnosed with AIDS, they can have a high viral load and are able to transmit HIV to others very easily. Without treatment, people with AIDS typically survive about 3 years (Fauci *et al*., 1996).

TRANSMISSION OF HIV

Infected person can transmit the disease through: Semen, Blood, Vaginal secretions, cervical secretions and Breast milk. Activities that allow transmission are direct blood contact, unprotected
sexual contact, blood transfusions and by sharing injection drug needles. HIV can enter the body through mucous membranes that line vagina, urethra, rectum and on rare occasions the mouth. Damage to mucus membrane can increase the risk of transmission (Castilla *et al*., 2005).
Mainly, HIV is transmitted in three ways:

1. By sexual contact
2. By mother to child
3. By blood through transfusion blood products or contaminated needles.

By sexual contact

Homosexual and heterosexual contact is the major source of HIV transmission. Since the early years of epidemic, it has been well documented that HIV-1 is transmitted through unprotected oral or vaginal intercourse from woman to man and man to woman. During the pre-HAART period (1991-95). HIV-1 was more prevalent (10.3%) which later declined to 1.9% in late HAART period (1999-2003) (Castilla *et al*., 2005). The increased risk of HIV-1 transmission in men to men is due to anal intercourse (Butler *et al*., 2008). Oral sex is also associated with HIV-1 transmission (Richters *et al*., 2003).

By mother to child

Around 30% pregnant women infected with HIV will pass the infection to their babies which can occur before as well as during birth. Infected mothers breast milk also contains the virus. Vertical transmission is also there that

is, from infected mother to foetus and from mother to infant via breast milk. Three possible routes are there which can transmit HIV from infected mother to their offspring: to foetus in utero through maternal circulation, by inoculation of blood and other infected fluids during labour and delivery and through infected breast milk shortly after birth. During pregnancy, labour, delivery and breastfeeding about 1800 new HIV-1 infections are transmitted daily from mother to infants (Kourtis *et al*., 2006) (UNICEF, http://www.unicef.org/media/files/RegionalSummary.doc)

By blood through transfusion blood products or contaminated needles

Intravenous drug users who share narcotics, infected blood, and needles are also key carriers. Infected blood can transmit HIV directly through intramuscular and intravenous injections. Transfusing infected blood and blood products to recipients results in blood-to-blood transmission by passing around unsterile hypodermic needles and syringes (Friedland and Klein, 1987). HIV can be transmitted through whole blood, plasma, blood cellular components, and clotting factors, however blood products such as immunoglobulin, albumin, and plasma protein cannot transmit it (IRAC, 1996).

The risk of HIV transmission is determined by the concentration of HIV in contaminated fluid, the quality of fluid delivered into the body, and the ability of infected fluid to reach T4 cells. Semen, blood and blood components, menstrual flow, vaginal secretions, pre-ejaculatory fluid, and breast milk are all high in HIV concentrations. HIV concentrations are low in pus, saliva, tears, urine, faeces, vomiting, and nasal mucosa (Friedland and Klein, 1987).

The isolation of a virus from a bodily fluid does not always imply that the fluid is transmittable. The virus has been isolated from semen, blood, vaginal secretions, saliva, breast milk, tears, urine, serum, CSF, and alveolar fluids, but only semen and blood have been directly linked to transmission. The virus cannot be communicated by the faecal-oral pathway, aerosols, insects, or casual contact such as sharing household items, kissing, hugging, shaking hands, sharing personal belongings, food, and water (Curran *et al*., 1984).

DIAGNOSIS AND TREATMENT

The treatment for HIV is called antiretroviral therapy (ART). ART involves taking a combination of HIV medicines called an HIV treatment regimen every day. ART cannot cure HIV, but HIV medicines help people with HIV live longer, healthier lives. ART also reduces the risk of HIV transmission. HIV medications can help lower the viral load and fight infections. The goals of these medicines are to control the growth of the virus, to slow down the symptoms, to prevent further transmission and to control the growth of the virus. The drugs are organized into six different classes based largely on the stage of the life cycle they inhibit (Parekh *et al*., 2018). Since 2022, FDA has approved 26 individual drugs and 22 fixed-dosed combination (FDC) drugs comprised of two or more antiretrovirals. The first antiretroviral drug regimen, called Cabenuva, which requires a once-a-month or once-every-two-months injection rather than having to take an oral dose every day. ART is quickly changing, with newer drug agents offering fewer side effects, greater durability, and a decreased risk of drug resistance.

While several new antiretroviral drugs have been added to the treatment arsenal since 2010, older ones like Crixivan (indinavir), Invirase (saquinavir), Rescriptor (delavirdine), Videx (didanosine), Viracept (nelfinavir), and Zerit (stavudine) have been discontinued and are no longer in use. Since 2010, with addition to new antiretroviral drugs, older ones like Crixivan, Invirase, Rescriptor, Videx, Viracept, and Zerit are no longer in use.

Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs)

The first class of antiretroviral drugs are NRTIs. In order to replicate, HIV uses an enzyme reverse transcriptase to translate its RNA into double stranded DNA which is than integrated inti the host cell nucleus to "hijack" its genetic machinery and make its own multiple copies. Intracellularly the NRTIs are phosphorylated to their active di or triphosphate metabolites, which inhibit the action of reverse transcriptase enzyme. Later it halts the conversion of viral RNA into dsDNA. In 1987, Zidovudine was approved for patients with AIDS and with individuals with <200 cells per cubic mm CD4 count for the first time. Eg. abacavir, emtricitabine, lamivudine, tenofovir alafenamide and tenofovir disoproxil fumarate (Arts and Hazuda, 2012).

Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

These inhibitors are different from NRTIs and they do not require intracellular phosphorylation. These inhibitors also block reverse transcriptase but in a different way. Rather than attaching to viral DNA like NRTIs do, NNRTIs bind directly to the enzyme, blocking its action. NNRTIs are noncompetitive inhibitors of RT. These are also called "non-nukes." Eg. doravirine, efavirenz, etravirine, nevirapine and rilpivirine (Béthune, 2010)

Protease Inhibitors (PIs)

These inhibitors block the proteolytic activities of an enzyme known as HIV protease. This blockage leads to inability to form infectious mature virion. Once HIV takes over the genetic machinery of the host cell, it produces long-chain proteins that must be cut into smaller pieces (by protease) in order to be assembled into a new viral particle. By binding to protease, the long-chain proteins cannot be cut and new viral particles cannot be produced. Eg. atazanavir, darunavir, lopinavir + ritonavir and ritonavir (Ananworanich and Robb, 2014).

Integrase Inhibitors

Integrase inhibitors block the incorporation of HIV's DNA into the host cell's DNA by inhibiting a viral enzyme integrase. A process known as integration. They are also called integrase strand transfer inhibitors (INSTIs). Eg. bictegravir, cabotegravir and rilpivirine, dolutegravir, elvitegravir and raltegravir (Arts and Hazuda, 2012).

Fusion Inhibitors

Unlike NRTIs, NNRTIs, PIs, and INSTIs, fusion inhibitor binds to HR1 (first heptad-repeat) in the envelope of viral glycoprotein gp41, which prevent confirmational changes required for fusion of viral and cell membrane. Eg. enfuvirtide (Ananworanich and Robb, 2014).

Capsid Inhibitor

This is a new class of drugs that works by blocking the HIV-1 virus' protein shell known as the capsid. Lenacapavir has a starting dose as oral tablets and subcutaneous injections, followed by maintenance injections every six months. It is given in combination with other antiretroviral(s) and is used by adults with HIV that is not adequately controlled by their current treatment regimen (Arts and Hazuda, 2012).

1. gp120 Attachment Inhibitor

This is a new class of drug with just one medication, fostemsavir. It targets the glycoprotein 120 on the surface of the virus, stopping it from being able to attach itself to the CD4 T-cells of your body's immune system. It is for adults who have tried multiple HIV medications and whose HIV has been resistant to other therapies (Volberding, 2008).

2. **CCR5 Antagonists**

Maraviroc (CCR5 antagonists) binds with CCR5 coreceptors on the surface of cell membrane. Interaction of HIV gp120 and CCR5 cell membrane receptor is blocked (Pau *et al*., 2014).

HAART (HIGHLY ACTIVE ANTIRETROVIRAL THERAPY)

HAART It is highly active antiretroviral therapy. HIV can also be treated by HAART. It is a combination of three drugs. Currently, there is no effective cure for HIV infection. As we discussed about ARTs, which can only suppress viral replication, as long as antiviral drugs are taken. HIV targets the immune system of the host and can establish a long-lived viral reservoir, which can be edited and targeted through gene therapy (Lu *et al*., 2018).

CRISPR-Cas9 (Clustered regularly interspersed palindromic repeats-CRISPR associated 9) system for gene editing has been recognized as propitious tool in development of gene therapy for HIV infections. CRISPR-Cas9, derived from prokaryotes, is a potent DNA editing technique. It involves Cas9, the "molecular scissors," and engineered single-guide RNA (sgRNA). Cas9 targets and precisely cuts DNA at specific sites, with guidance from sgRNA (Ebina *et al*., 2013). The sgRNA is a synthetic molecule combining CRISPR elements with a customizable sequence that directs Cas9 to the desired DNA location (Mao *et al*., 2016). Once sgRNA identifies a target DNA sequence, usually adjacent to a Protospacer Adjacent Motif (PAM) sequence, it guides Cas9 to create a double-strand DNA break. The cell's repair mechanisms can then be utilized for precise genetic modifications. Depending on the type of CRISPR-Cas system, Cas binds to short CRISPR RNA (crRNA) that

target complementary viral DNA or RNA sequences. Endonucleases Cas9 and Cas12 cleave DNA and Cas13 cleaves RNA (Hussein *et al*., 2023).

OPPORTUNISTIC INFECTIONS IN HIV/AIDS PATIENTS

Different opportunistic infections are prevalent in different geographical regions (Ayyagiri *et al*., 1999). According to the National AIDS Control Organization (NACO), tuberculosis is the most prevalent opportunistic infection among AIDS patients, followed by candidiasis, cryptosporidiosis, and other infections. In India, opportunistic infections such as Mycobacterium avium complex (MAC) and Kaposi's sarcoma are not as prevalent as they are in the developed world (Patel *et al*., 2011). In India, pulmonary tuberculosis is the most prevalent opportunistic infection among individuals with HIV infection. Patients with CD4 counts below 200 cells/l are highly susceptible to opportunistic infections (Tan *et al*., 2012). Opportunistic infections that take advantage of weakened immune defences, are more prevalent and severe in HIV-positive individuals. Most of these infections are typically abbreviated as "OI" and are caused by microorganisms. HIV-Human immunodeficiency virus first identified in 1981, is one of the deadliest and most persistent pandemics. This virus attacks the cells that aid the immune system in fighting off infections. This virus increases an individual's susceptibility to other infections and maladies (Chang *et al*., 2013).

Every person living with HIV/AIDS will have at least one episode of candidiasis during illness. HIV infected persons represents cardiovascular risk factor and inversely the cumulative CVD burden among aging people with HIV constitutes a major cause of mortality and morbidity (Fragkou *et al*., 2023).

As the virus continues to proliferate and destroy immune cells, the cells in your body fight against the virus and develop symptoms such as swollen lymph nodes, often one of the first indications of HIV infection, diarrhoea, weight loss, oral candidiasis (thrush), shingles (herpes zoster), and pneumonia (Kumarasamy *et al*., 2005) As the infection progresses, the immune system is weakened. Other signs and symptoms include weight loss, fever, diarrhoea, congestion, and lymph node enlargement. The virus is present in white blood cells at this stage. This stage can last for many years if patients are receiving ART (antiretroviral therapy). Without treatment, life- threatening conditions such as cryptococcal meningitis, severe bacterial infections, tuberculosis, and cancers such as lymphomas and Kaposi's sarcoma (Patel *et al*., 2011).

HIV patients may get yeast oral or vaginal infections, frequent and severe herpes infections which cause mouth, genital or anal sores, herpes zoster, other pulmonary infections, pelvic inflammatory disease in women. Virus may attack nervous system which produce variety of symptoms like tingling in feet and trouble walking to memory disturbances (Shahapur and Bidri, 2014)

COVID-19 is a global medical emergency with socioeconomic effects. Due to immunosuppression and HIV stigma, people with HIV (PWH) are vulnerable and high-risk. PWH have risk factors for severe COVID-19, including age and comorbidities, but virological and immunological state also matters. Opportunistic infections can mimic COVID-19, but clinical presentation is similar (Basoulis *et al*., 2023). Patients who are HIV-positive and also co-infected with COVID-19 have a significantly increased risk of developing hypertension and diabetes mellitus. The possibility that HIV and COVID-19 co-infection had a negative impact on HIV treatment and diagnosis highlights the importance of performing routine screenings of HIV patients during the COVID-19 pandemic (Heidary *et al*., 2023)

SOCIAL AND ECONOMIC IMPACT OF HIV

SOCIAL IMPACT

Stigma and Discrimination: HIV-related stigma is a deeply embedded societal problem. People living with HIV frequently face prejudice in a variety of situations, including their families, communities, workplaces, and healthcare settings. This stigma can take the form of social exclusion, verbal abuse, loss of social support, and even violence. Fear of prejudice and rejection causes many people to conceal their HIV status, limiting their access to testing and therapy. Stigma not only hurts the mental and emotional well-being of those affected, but it also contributes to the virus's transmission by preventing people from seeking medical assistance and following treatment programs.

Psychological and Emotional Impact: In addition to external stigma, people living with HIV frequently experience internalized stigma, which leads to emotions of shame, guilt, and low self-esteem. Depression,

anxiety, and other mental health issues can follow. Furthermore, the fear of admitting their status can lead to social isolation and strained relationships, which can have a negative influence on mental health and quality of life.

Effect on Relationships and Families: HIV can strain relationships and families, producing emotional turbulence and communication failures. The disclosure of an HIV-positive status can be a stressful event for both the individual and their loved ones. Families may learn to manage with the problems, and relationships can grow over time, with adequate education and support (Barnett *et al*., 1995).

ECONOMIC IMPACT

Healthcare Costs: The financial burden of HIV includes the substantial costs associated with healthcare. These expenses encompass antiretroviral therapy (ART), regular medical check- ups, specialized care for opportunistic infections, and hospitalizations. These costs can be particularly burdensome for individuals and families, especially those without adequate health insurance or access to affordable care (Bonnel, 2000).

Loss of Productivity: HIV can lead to a loss of productivity, both at the individual and societal levels. As the virus progresses, individuals may face illness and reduced capacity to work. Furthermore, discrimination in the workplace can lead to job loss or reduced job opportunities for people living with HIV. Collectively, these factors contribute to a significant economic burden.

Burden on Healthcare Systems: The management of HIV places a substantial burden on healthcare systems, especially in regions with high prevalence rates. Healthcare facilities must allocate resources for HIV testing, treatment, counselling, and support services. The growing demand for healthcare services related to HIV can strain healthcare infrastructures, impacting the availability and quality of care for all patients (Poudel *et al*., 2017).

Long-Term Economic Consequences: Beyond the immediate costs, HIV can have long- term economic consequences for communities and countries. A productive workforce is vital for economic growth, and the loss of individuals in their prime working years can hamper development. Investments in HIV prevention, treatment, and support services can help mitigate these long-term economic impacts by allowing individuals to remain healthy and engaged in the workforce (Taraphdar *et al*., 2011).

It is concluded that, the social and economic impact of HIV is profound and multifaceted. Addressing these challenges requires comprehensive efforts that include combating stigma, providing accessible healthcare, and promoting inclusive workplaces. By reducing the social and economic burdens associated with HIV and HIV individuals are treated with dignity, have access to proper care, and can lead fulfilling lives (Kleinman, 1997).

CONCLUSION

HIV, which stands for Human Immunodeficiency Virus, is widely believed to have its origins in the Simian Immunodeficiency Virus (SIV), a virus found in non-human primates. The striking similarities observed in the epidemiological, phylogenetic, and genomic characteristics of HIV and SIV strongly support the theory of cross-species transmission, underlining the zoonotic nature of this virus. One pivotal development in the fight against HIV has been the advent of Antiretroviral Therapy (ART). ART has had a profound impact on the global landscape of HIV epidemiology. In the early days of treatment, antiviral drugs were often administered as monotherapy. However, the field of HIV treatment evolved significantly with the introduction of combination therapy, which is commonly known as Highly Active Antiretroviral Therapy (HAART). HAART has shown remarkable potential in reducing both mortality and morbidity associated with HIV-1 infection. This multi-pronged approach to treatment has been a game-changer in managing the virus. It's essential to note that while we've made significant strides in HIV treatment, there is no definitive cure for the virus. Nonetheless, the relentless efforts of researchers have yielded promising results, and one of the most exciting recent developments is the emergence of CRISPR/Cas9 technology. This ground breaking genetic editing tool has opened up new possibilities for the development of more effective therapeutic strategies in the ongoing battle against HIV.

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