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Overview Of The HIV/AIDS

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ABSTRACT
One of the most extensively global diseases has always been AIDS/HIV. AIDS and HIV infection are caused by the transferred virus known as HIV (human immunodeficiency virus). The immune response gradually fails in people with AIDS, promoting the growth of potentially fatal malignancies and infections. HIV can be passed through the interaction of vaginal fluids, sperm, blood, as well as breast milk. HIV can be found in these bodily fluids as unbound virus particles as well as a pathogen inside infected immune cells. Important immune system components including helper CD4 T cells and macrophages are infected by HIV. HIV infection leads to a reduced number of T cells via a variety of processes, including pyroptosis of afflicted T cells. Most AIDS-related symptoms are brought on by infections that do not commonly affect persons with robust immune systems. The majority of these diseases are caused by opportunistic infections caused by parasites, viruses, bacteria, and other microbes that are frequently regulated by defense parts of the system that HIV impairs. The yearly rate for HIV infection is a little less than 1% when a pair with one affected member consistently wears condoms. According to certain research, female condoms may provide comparable protection.

Keywords: Disease; human immunodeficiency virus; Acquired immunodeficiency syndrome; transmission

INTRODUCTION

HIV (Human Immunodeficiency Virus) causes AIDS which stands for Acquired Immunodeficiency Syndrome. This virus compromises the body's immune system. The immune system contributes to the body's battle against sickness. However, if this virus is not treated, it infects and destroys CD4 cells, a class of immune cell known as T cells. Other germs and pathogens take advantage of the immune system's weakness and make things worse **[1,2].** This makes the body more vulnerable to additional infections and cancer, both of which can prove fatal. According to scientists, a certain species of chimpanzees in West Africa infected

humans with HIV. The chimpanzee variant of the immunodeficiency virus is called SIV (Simian immunodeficiency virus). It is thought that when humans hunted SIV-infected chimpanzee meat and came into touch with its blood, the virus was spread and transformed to HIV in humans. A person in Kinshasa, the Democratic Republic of the Congo, had blood tested in 1959, and it was likely this sample that revealed the first human case of HIV-1 infection. The results of the blood sample's genetic analysis indicated that the person may have acquired HIV in the late 1940s or early 1950s. Gorillas have also been reported to carry SIV strains. The SIVgor strain, which is unique from the chimpanzee strain, is the one found in gorillas. A zoonosis, or infection that affects both humans and other vertebrates, is AIDS **[3, 4].**

STRUCTURE OF HIV [1-5]

Gp120- The number "120" indicates the substance's molecular weight. It is required for virus penetration into cells since it's essential for virus allocation to precise receptors on the cell surface.
GP41- It belongs to the group of envelope proteins that are present in retroviruses like the human immunodeficiency virus. It belongs to a group of pathogens that use switch transcriptase to multiply inside of the host cell. It chases after the host cell.
P17- The viral center is constructed using protein. This appears to be a shot. HIV replication depends on the three substances integrase, protease, and turnaround the record.
P24- makes up the HIV capsid.
Protease HIV, the retrovirus that caused AIDS, requires a retroviral aspartyl protease to finish its life cycle. The protein components of the infectious HIV virion are produced when this enzyme breaks down newly formed polyproteins in the appropriate region.
Integrase- Retroviruses produce the enzyme integrase, which allows their genetic information to be incorporated into the DNA of affected cells.

CAUSES
Sexual contact between two people is the root of the problem. Among viruses, HIV is one. HIV impairs and kills the immune system of a person who thereafter becomes infected with it, rendering it incapable of fighting off illnesses **[6, 7].**

- ✓ Having shared infected needles and syringes is one of its causes.
- ✓ Oral, vaginal, or oral contact with an HIV-positive person.
- ✓ It appears that having additional STDs like syphilis, herpes, or gonorrhea increases the risk of various diseases through unprotected intercourse with an infected partner.
- ✓ Babies can acquire HIV from mothers who are HIV-positive while they are pregnant, giving birth, or nursing.

TRANSMISSION
HIV can be spread primarily through three different routes: sexual contact, blood transfusion, infected needles, or transmission from mother to infant. "Heterosexual transmission is possibly the most important method of HIV transmission in the world today,". Although homosexual interaction continues to be a significant source of HIV in the US. In developed nations, the risk of HIV transmission via infected blood products has almost been eradicated through treatment

and donor screening, but it is still present in IV drug users who exchanged needles. Contaminated blood and needles continue to be significant sources of illness in developed nations. According to estimates, 13–35% of pregnant women who test positive for HIV will pass the disease to their unborn child; the transmission can happen both before and after birth. High quantities of the virus have also been found in the breast milk of infected moms. The faecal-oral path, aerosols, insects, or casual touch like hugging or exchanging household objects do not transfer HIV. Health care personnel are mostly at risk from direct inoculation through needle sticks. Although the virus can exist in trace amounts in saliva, it cannot be transmitted through kissing **[2-5].**

SYMPTOMS

Innumerable HIV-positive individuals may not manifest or display any disease or condition. Following present day research, between 70% – 90% of individuals who have HIV exhibit some indicators or symptoms e.g. flu after one or two weeks of infection. The most typical signs include a fever, rash, and a very bad sore throat that all appear at the same time. If present in a healthy individual, these symptoms could be a sign of a recent HIV infection.

Patients with HIV may experience persistent or recurrent vaginal or oral yeast infections. Bruises around the mouth, vagina, or butt are common side effects of severe and persistent herpes infections. Herpes zoster is more likely to develop in those who have been tainted (shingles). Other lung infections, such as pneumonia, or similar conditions known as extraordinary mycobacterial illnesses may have serious consequences. Aside from other side effects including memory problems and foot shaking, the infection may impair the central and peripheral nervous system **[1-7].**

HIV-LIFE CYCLE [5-9]

Access to human cells- The only virus capable of replicating itself within human cells is HIV. When a cell carrying the CD4 protein on its surface allows the virus to enter, the process starts. For them to merge, the HIV must cling to the CD4 receptor. T-helper cells, which make up the body's immune system, are the immune cells most commonly infected by HIV. More cells become infected by HIV, weakening the immune system.

Reverse transcription- Reverse transcriptase is an enzyme that aids in the process. Reverse transcriptase transforms infectious RNA into DNA as its primary job. In the cell's nucleus, the integrase enzyme inserts the DNA there once it has been carried there.

Transcription and Translation- Transcription is now happening. Messenger RNA is created when the HIV is transformed.

Assemblage, Development, and Maturation- As fresh HIV protein and enzymes are produced, copies of the virus assemble to create fresh viral particles, which bud out from the parent CD4 cell. The HIV protein's lengthy chains are divided up into manageable chunks by the enzyme protease. These newly emerging viruses can find and attack other CD4 cells.

DIAGNOSIS

Enzyme Immunoassays- For identification of HIV antibodies, the first enzyme immunoassay (EIA) was applied in year 1985 using viral lysate as the antigen. These first-generation immunoassays were applied and identified IgG antibodies to HIV type 1 (HIV-1) but were incompetent and not be able to recognize the antibody response to other HIV-1 lineages. About 6 to 8 weeks after the infection, they started to test positive. 1st generation diagnostics lack the current, commonly used tests' sensitivity and specificity.

By creating viral antigens from recombinant proteins or peptides, the second-generation assays improved specificity. Compared to first-generation assays, they may spot infection around a week sooner. Since the third-generation assays could not only disclose or expose HIV-1/2 IgM and IgG, but also could do so as soon as 3 weeks after infection, they marked a substantial advancement. Third-generation tests had replaced prior assays by 2007 and are thought to be more responsive than early generation assays.

While comparable combination assays have been used in other nations, fourth-generation assays first became accessible in the US in 2010. They concurrently identify the p24 antigen and the IgM and IgG antibodies for HIV-1/2. 4th generation assays have flourish and prosper in drastically reducing duration to detection to as soon as two weeks after infection by being able to identify p24 after the emergence of nucleic acid (around 5-7 days) **[10-13].**

HIV Confirmatory tests- Due to their superior specificity, Indirect immunofluorescence assay (IFA) or Western blot have historically been utilised as confirming tests when screening immunoassay assays are repeatedly reactive. Using a substrate to fabricate a device pattern that can be explicate as negative, positive, or inconclusive, the Western blot analysis looks for antibodies that attach to fixed HIV proteins. To test for the existence of antibodies, the IFA, a less popular alternative, combines plasma or serum samples with T cells that express HIV antigens. A fluorescent molecule-coated antihuman antibody is then used to identify the bound antibodies **[10-13].**

Rapid HIV tests- In order to distinguish HIV IgM and IgG in serum, whole blood, oral liquids, or plasma, the Food and Drug Administration (FDA) has supported rapid HIV immunizer tests since around 2002. These tests frequently use move through tapes or parallel stream devices. They benefit from having a response time of thirty minutes or fewer, which is essential for babies with poor growth and for women who are delivering birth when they arrive. The two most common tests are for HIV-1 and HIV-2. Parallel stream testing can be carried out anywhere since a lab is not necessary. According to makers, the specificities of their products vary between 99.7% and 99.9%, while the responsiveness of their products ranges from 99.3% to 100.%. Nevertheless, a few investigations have observed lower specificities and responsiveness. Comparability to third-age measures was discovered in a later interpretation of the presentation of rapid HIV tests. Productivity limits have been shown in a few studies to be applicable to both first- and second-era EIAs **[10-13].**

Preventive HIV-1 Vaccine

Neutralizing antibody induction- The creation of HIV-1 vaccine that can elicit neutralising antibodies was the primary objective of early vaccination research. Numerous studies and pieces of research were conducted in order to evaluate the effectiveness and safety of various

vaccinations, including those containing gp120, gp160, portions of gp160, and proteins from gp160. When used with HIV-1 variations taken from patients, these vaccines were able to elicit specific antibodies against the HIV-1 strain in vitro but not broadly neutralising antibodies. Two gp120-based vaccinations were evaluated on healthy volunteers in two Phase III clinical trials. Despite the fact that gp120 increased antibody production, the frequency of new infections remained constant. These results also suggest that antibodies have trouble blocking the immunobiological activities of the gp160 envelope molecule **[10-13].**

HIV-1-specific T-cell induction- Because of the challenges encountered in the formation of neutralising antibody responses, the focus of vaccine generation shifts toward the vaccinations that have the capacity to induce HIV-1-specific T cell responses. Cytotoxic T lymphocytes (CTL) are crucial for preventing the spread of HIV-1 in people and only recognise infected cells. Studies have shown that by reducing the tiny hotspots of viral infection, HIV-1-specific CTLs have the ability to prevent persistent HIV-1 infection. But even if this vaccination is unable to shield the host from infection, it can still lessen viral load following infection. The viral load four months after infection is referred to as the viral setpoint. Because patients become less contagious as viremia levels drop, a vaccine that reduces the viral setpoint by 1/2 a log has a positive therapeutic impact **[10-13].**

Vectors for recombinant viruses- Recombinant vectors can be used to induce CTLs without the issues that come with live virus. Numerous clinical investigations have evaluated the efficacy of various vectors, including adenovirus-associated virus, ALVAC canarypox viruses, adenovirus 5 (Ad5) vectors, and fowlpox vectors. Numerous clinical studies have been conducted to evaluate the effectiveness of various vaccinations.
Another novel approach uses a rhesus monkey CMV vector harbouring recombinant SIV genes. The peculiar non-canonical CD8 T cells induced by this vector, which are confined by HLA-II antigens and cannot be negatively controlled by the viral nef protein, are crucial in the generation of a long-lasting and widespread CTL response. However, it is yet unknown whether certain non-canonical CD8 T cells are existing in humans or whether it is possible to induce them through vaccination. By therapeutically immunising HIV-1-infected subjects on ART after a break in therapy, potent HIV-1 vaccinations can be created. The assessment of the vaccination's capacity to inhibit HIV-1 replication offers a crucial technique to ascertain the efficiency of the vaccine in controlling infections during treatment interruption **[13-15].**

RV 144: A Trial of a Preventive Vaccine- To far, a number of efficient cures and prevention measures have been developed to combat the intensity of the illness brought on by this lethal virus. However, none of these strategies are sufficient to stop the spread of HIV. For the time being, the HIV preventative vaccination remains a viable and optimistic option for eradicating this illness from the world. Over than 250 clinical studies (phase I and phase II) have been carried out by researchers so far in an effort to completely eradicate this pandemic. Scientists and researchers now have renewed optimism that an HIV preventive vaccine is feasible following the success of an effectiveness experiment known as RV144, which was carried out in Thailand. A prime-boost idea was used in the RV144 study, the first successful vaccine trial (4 priming and 2 booster injections), which included up to 16,000 individuals aged 18 to 30

were administered to the recipients. ALVAC-HIV (vCP1521), the primary canarypox vaccine, and AIDSVAX B/E, the secondary gp120 subunit vaccine, both stimulated immune and humoral responses.

TREATMENT

Antiretroviral drugs are adopted and utilized to treat or medicate HIV. These drugs are convenient in prolonging and advantageous for upgrading their life quality. Classification of these Antiretroviral drugs **[10, 12, 15]** is mentioned below:

Nucleoside Analogs (NRTIs)**-** NRTIs were the FDA-approved pharmaceuticals at the top of the line. The RT protein of HIV is the target of the action of nukes, also known as NRTIs. By functioning as an optional substrate, these inhibitors compete with common cell nucleosides. These nucleoside analogs' demand for hydroxyl bunches at the 3′ positions in the deoxyribose sugar prevents the originations of phosphodiester association betwixt the approaching 5′ nucleosides 3 phosphates and NRTIs. The major ramification is seen in the ending of any DNA infection chains that could otherwise arise during DNA-subordinate DNA blending or RNA-subordinate DNA. So, these analogs are regarded as drug-like since the usage of these cell kinases for phosphorylation after endocytosis to transform into active metabolites. NRTIs have long-lasting side effects such as polyneuropathy, myelotoxicity, pancreatitis, lactic acidosis, and others. There are currently eight FDA-supported medications available, including abacavir (ABC, Ziagen), zidovudine (AZT, Retrovir), stavudine (d4T, Zerit), didanosine (ddI, Videx) lamivudine (3TC, Epivir) and emtricitabine (FTC, Emtriva).

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)- HIV RT catalyst is also targeted by NNRTI, which was initially described in 1990. HIV RT protein is restrained by the origination of an aquaphobic pocket close to the dynamic site and the restriction of NNRTIs to RT. After limiting NNRTIs to the RT protein, there is a dwindling in polymerase recreation and conceptual structural substitute in the substrate-restricting region. Since they do not slow down the RT of other lentiviruses, these NNRTIs are non-serious inhibitors and are quite certain of their effectiveness.

Protease Inhibitors**-** Another major goal and objective are to target the HIV protease enzyme. Protease enzymes prompt the litigating and preparing of polyprotein (gag–pol) precursor and virion (gag) and are a major requirement for the development of viral particles. In literature, FDA approved ten protease inhibitors i.e. atazanavir (ATZ) or Reyataz, darunavir (TMC114) or Prezista, fosamprenavir or Lexiva, amprenavir (APV) or Agenerase, indinavir (IDV) or Crixivan, lopinavir (LPV), ritonavir (RTV) or Norvir), saquinavir (SQV) or Fortovase/Invirase, tipranavir (TPV) or Aptivus, and nelfinavir (NFV) or Viracept. Various studies were conducted by researchers and proved that these protease inhibitors may develop some changes or mutations because of their small size and played a prime character in HIV-1 alternation of generations. But substantial flexibility was disclosed through the protease gene (approximately > 20 substitutions along with polymorphism in 49 codons were reported) regarding its resistance. Foremost transformation or modifications were reported in most of the protease inhibitors occur adjoining with the active region of the enzyme bringing about a swap in amino acid, which has deleterious reverberations on viral replicative fitness. Besides changes in the shape of a sequence of protease genes, major changes were reported in the eight predominant bifurcation areas and also afford or give receptivity to protease inhibitors.

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