**UNDERSTANDING HIV: A REVIEW OF PATHOGENESIS AND THERAPEUTICS**

**ABSTRACT:**

HIV (Human Immunodeficiency Virus) is a significant global health challenge that has led to the ongoing AIDS (Acquired Immunodeficiency Syndrome) epidemic. HIV primarily targets and weakens the immune system by infecting CD4 cells, T cells, and macrophages, thereby reducing the body's ability to fight off infections and diseases. The virus is transmitted through the transfer of blood, breast milk, semen, and vaginal secretions. HIV infection progresses through various stages, starting with acute infection, followed by clinical latency, and eventually leading to AIDS if untreated. While there is no cure for HIV, antiretroviral therapy (ART) has proven effective in managing the virus, prolonging the lives of those infected, and reducing the risk of transmission. Preventative measures, such as condom use and safe blood transfusion practices, play a crucial role in mitigating the spread of HIV. Despite extensive research, no vaccine is currently available to prevent HIV infection. Continued efforts in education, prevention, and treatment are essential to combatting this pervasive virus and improving the quality of life for those affected.

***Keywords:*** *HIV; health; AIDS; virus; immune system*

**INTRODUCTION:**

HIV leads to “Human Immunodeficiency Virus”. It is usually a sexually transmitted infection that usually occurs during intimation, blood transfusion, transfer of semen and vaginal fluids. HIV is the virus that is responsible for AIDS in human. The immune system of the human body is designed in such a way that it can protect from various bacterial as well as viral infections. White blood cells of the immune system contains CD4+ cells which are also known as helper T cells. During HIV infection the count of CD4+ cells decreases(Kapila A et.al.,2016). The diagnosis as well as testing of HIV is very crucial as the diagnostic strategies need to be continuously revised according to any new discoveries on replication as well as pathogenic mechanism of the infection. There are mainly two types of HIV virus grouped so far, namely- HIV -1 and HIV – 2, out of which the main agent of AIDS is HIV (Emanuele et.al.,2010). HIV belongs to the *Retroviridae* family. Although the basic structure of HIV-1 & HIV-2 is same but they differ in the organization of their genome (Emanuele et.al.,2010). This virus usually omit the central nervous system. Although disease of the central nervous system is more frequent in HIV-2, both the viruses potentially cause AIDS (Lucus et.al.,1993). HIV-2 is less virulent as compared to HIV-1 and takes longer time to progress to AIDS (Whittle H et.al., 1994). A person infected with HIV virus show several health problems and may even lead to the death of a person. HIV was first reported in United states 37 years ago and from then more then 77 million people have infected with virus implies resulting of over 35 million deaths (Tara A et.al.,2019). According to Joint United Nations Programme, 36.9 million people are living with this virus and 1.8 million people are newly getting infected and nearly 1 million people are facing death annually (Tara A et.al.,2019). There is cure of AIDS , but there are medicines that slows down the pathogenesis. Antiretroviral therapy is the most impressive research in the treatment of this disease. If a person gets infected with this virus in their early 20s and he is treated with Antiretroviral drugs , then there is a possibility of him living for more than 50 years with suppression of the viral replication that can also lead to a healthy life (Samji H et.al.,2013).

**STRUCTURE AND COMPOSITION OF HIV VIRUS:**

* Envelope: It is a spherical, enveloped virus which is around 90-120 nm in size. The nucleocapsid has an outer icosahedral shell and an inner cone-shaped core which encloses the ribonucleoprotein. (Ananthanarayan, 2006)
* Genome: The genome is composed of two identical single stranded, positive-sense RNA copies, with the reverse transcriptase enzyme. During infection, the viral RNA is converted into first single-stranded and then into double-stranded DNA (provirus) through transcription and then integrated into the host cell chromosome. This provirus influences the function of host cell by remaining latent for a long period. (Ananthanarayan, 2006)
* Lipoprotein envelope: During viral replication, the buds out virus acquires a lipoprotein envelope. The virus coding envelope proteins are knob-like spikes that remains on the surface which in turn anchors the transmembrane pedicles. The spikes binds to the CD4 receptors on host cells. Cell fusion is caused by the transmembrane pedicles. (Ananthanarayan, 2006)

**TRANSMISSION OF HIV VIRUS:**

The transmission of HIV virus occurs mainly by three possible ways: by sexual contact, by blood transfusion and from mother to her child. Another means by which HIV can be transmitted is by sharing the same needle between two persons [17-20]. Spread of HIV through contaminated blood products remains the most important means of infection in developing countries (Kapila A et.al.,2016). Transmission of HIV from infected mother to child occurs during breastfeeding, and the milk is found to contain high levels of the virus. The virus can also be transmitted before the birth of the child (Kapila A et.al.,2016). Health care workers are at high risk of getting infected by needle stick injury.

HIV can be transmitted from infected person to healthy ones by:

* Sexual contact without protection.
* Contaminated blood products i.e., by blood transfusion, sharing of same needle among drug users and also by some health care products.
* Mother to baby (both before and during birth) (Kapila A et.al.,2016)
* Through body fluids such as Semen, blood, vaginal secretions, breast milk, pre ejaculatory fluid.

The concentration of HIV is high in fluids like – semen, blood components, vaginal secretions, breast milk, pre ejaculatory fluids whereas fluids like pus, saliva, tears, urine, feces, vomiting and nasal mucosa contains low concentration of HIV (Kapila A et.al.,2016).

**TARGET CELLS OF HIV:**

HIV primarily targets T lymphocytes, macrophages, monocytes, and dendritic cells (DCs). This specificity is mainly due to the cell surface receptors needed for the virus's entry. The primary receptor for HIV is CD4, which is mainly found on T-helper cells but is also present on monocytes, macrophages, and DCs. In addition to CD4, a co-receptor is necessary for HIV to fuse with the target cells. (De Goede et al., 2014b)

**SIGNS AND SYMPTOMS OF HIV INFECTION/AIDS:**

People with HIV infection are usually seen to show flu-like symptoms like fever, sore throat and fatigue. Yeast infections are also seen in HIV infected people. Herpes zoster is also seen to occur in infected people. The virus also attack the nervous system and produces symptoms like tingling in feet and trouble in walking to memory loss (Downs et.al.,1996).

Symptoms usually include:

* Frequent fevers
* Swollen glands
* Growth becomes slow in children
* Cough and shortness in breath
* Nausea
* Cramps
* Diarrhea
* Vomiting
* Weightloss.

**LIFE CYCLE:**

The life cycle of HIV AIDS occurs in four steps- Entry to human cells, reverse transcription, transcription and translation, assembly budding and maturation (Kapila A et.al.,2016).

HIV virus makes copies of itself when it enters into the human cells. This virus contain CD4 cells on its surface which is protein in nature. HIV virus remains stick to the surface of CD4 cells and allows them to fuse. This virus mainly attacks the immune cells thereby weakening the immune system. After their entry into the cells there occurs reverse transcription which is done by an enzyme called reverse transcriptase. This enzyme converts viral RNA into DNA. This DNA gets transported to the nucleus of cell and the insertion of DNA is done by an enzyme integrase. After transcription HIV virus converts itself into messenger RNA (Kapila A et.al.,2016).

The viral particle is formed by the gathering of copies of HIV with the newly made HIV protein and enzyme and the viral particle gets separated from the original CD4 cell through a process called budding. The HIV protein is broken down into smaller particles by the enzyme protease and this newly formed virus becomes able to target and infect CD4 cells (Amborzia J and Lavy J A et.al.,1998).

**LABORATORY DIAGNOSIS OF HIV/AIDS:**

The most common method of diagnosis of HIV is by testing the blood and saliva sample of a person as the antibody to that virus remains present there. But the procedure takes quite longer time as the body takes around 12 weeks to produce these antibodies.

Tests that are performed for the detection of HIV/AIDS:

Home Test:

This test is known as Food and Drug Administration – approved test. For the test swab sample is taken from the upper and lower gums. If the test becomes positive then further diagnosis is performed and if the test becomes negative then the process is repeated after three months for the confirmation of the results (Kapila A et.al.,2016).

Diagnosis of HIV/AIDS is performed by the following tests:

* CD4 Count: CD4 cells are targeted and destroyed by HIV virus during infection.
* Viral load: This test is performed to measure the presence of amount of virus in patient's blood.
* Drug resistance: This test is performed to observe the resistance to drugs by the body that is provided during HIV infection (Pope M et.al.,2003).
* HIV Immunoassay: In this technique, detection of HIV is done by targeting anti-HIV antibodies. HIV immunoassays are also called as “Generations” of test and with each generation, improvement in performance is observed (Eloise Williams et.al.,2023). There has been a recent development of highly sensitive HIV immunoassay which has the capability of discriminating HIV-1 antibody, HIV-2 antibody and HIV-1 p24 antigen reactivity (Salmona M et.al.,2014). This test has been made available internationally since 2015(Eloise Williams et.al.,2023).
* Nucleic acid tests: Nucleic acid amplification test (NAAT) is also used for the detection of HIV. In this test, Reverse transcription polymerase chain reaction (RT-PCR) and transcription mediated amplification (TMA) is used to detect HIV RNA OR HIV DNA. HIV viral load is also observed by NAATs. Blood banks have been using NAATs for HIV treatment since 1990 and it is also used for screening donors before organ donation (Seed CR et.al.,2005).

Treatment of HIV/AIDS:

The very first drug that was used for the treatment of HIV virus was Nucleoside Analogue Reverse Transcriptase inhibitors (NARTIs). It was first used in the year 1987. Non nucleoside reverse transcriptase inhibitors was also approved in 1997 (Tripathi K.D. et.al.,).

HIV are treated with antiretroviral drugs. The classification of antiretroviral drugs are as follows:

* Nucleoside reverse transcriptase inhibitors:

Zidovudine, Didanosine, Lamivudine, Tenofovir.

* Nonnucleoside reverse transcriptase inhibitors:

Nevirapine, Delavirdine, Efavirenz.

* Protease inhibitors:

Indinavir, Nelfinavir, Amprenavir, Lopinavir, Atazanavir (Kapila A et.al.,2016).

Another active antiretroviral therapy is HAART. This drug is also used for the treatment of HIV infection (Kapila A et.al.,2016).

There is no effective vaccine released yet for HIV infection. Although a vaccine composed of poxvirus have been made trial with but that provided only 30% protection.

**HEALTH IMPACT POST-HIV DIAGNOSIS:**

People infected with the HIV virus experience various adverse effects on their bodies after treatment. Individuals treated with antiretroviral therapy may face mild adverse effects, such as bloating, nausea, and diarrhea, which can persist throughout the therapy (Carr A et al., 2000). In addition to these, other possible adverse effects include hepatotoxicity, hyperglycemia, fat maldistribution, dyslipidemia, etc.

**CONCLUSION:**

HIV is a virus that primarily leads to AIDS. AIDS weakens the immune system. As it is a sexually transmitted infection, care and precautions should be taken during intimation by the couple. It has been reported that use of condoms reduces the chance of infection by less than 1%. Various screening test and drugs are used during the treatment of HIV infection. People are made aware for this infection through ICTC. There is no vaccine made available yet for the prevention of HIV. Proper protection and awareness can prevent the spread of HIV among people.

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