HIV/AIDS: A Brief Overview

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INTRODUCTION

AIDS (acquired immunodeficiency syndrome) is a disease caused by a virus called HIV (human immunodeficiency virus) [1]. It kills or damages the body's immune system cells. It is the most advanced stage of infection with HIV. AIDS was first reported in the US (United States) in 1981 and since then it became a major worldwide epidemic [2-6]. By killing or destroying cells of the body's immune system, HIV progressively destroys the body's ability to fight infections and certain type of cancers [7-10]. People diagnosed with AIDS may get life-threatening diseases called opportunistic infections. These infections are caused by microbes (such as viruses/bacteria) that usually do not make healthy people sick. HIV attacks the immune system by destroying CD4 positive (CD4+) T cells, a type of white blood cell that is essential for fighting off infections [3,11,12]. The destruction of these cells leave people infected with HIV vulnerable to other infections, diseases and other complications. A person infected with HIV is diagnosed with AIDS when he/she has one or more opportunistic infections, such as pneumonia or tuberculosis, and has a dangerously low number of CD4+ T cells (less than 200 cells per cubic millimeter of blood) [3,4,13]. Nearly 35 million people all over the world are infected with human immunodeficiency virus (HIV). Around 2 million people get infected with the virus each year and the pandemic continues to devastate despite three decades of our understanding of the pathogenesis [14,15]. The AIDS epidemic, in spite of considerable efforts continues to spread at formidable rate worldwide with an estimated 34 million people being infected with HIV at the end of 2010 [5]. The key step in the disease progression is viral binding to the host T lymphocytes and the entry [16]. Due to the constant mutation tendencies of the HIV virion it has become a big challenge to target this virus and eradication of the virus infection all together [12]. However, not everyone who has HIV progresses to AIDS.

EPIDEMIOLOGY of HIV/AIDS

HIV/AIDS is a global threat. All of the countries are affected by HIV/AIDS but the count varies from region to region [17-20]. Sub-Saharan Africa is the region that is most affected. In 2010, an estimated 68% of all HIV cases and 66% of all deaths occurred in this region. This implies that about 5% of the adult population in this area is infected. South Africa has the highest count of HIV infected individuals in the world. In South and South-East Asia HIV prevalence rate is less than 0.35 percent. The AIDS image in South Asia is dominated by the epidemic in Indian subcontinent. There is a rapidly growing epidemic of HIV in European Union, the rate of HIV infections began to grow rapidly from the mid-1990s [21-24].

HOW HIV is TRANSMITTED
Scientists believe that a virus similar to HIV first occurred in some populations of monkeys in Africa, where they were hunted for food. Contact with an infected monkey's blood during butchering or cooking may have allowed the virus to cross into humans and become HIV.

Person can be infected with HIV through contact with bodily fluids. HIV is found in the blood, semen, or vaginal fluid of someone who is infected with the virus. HIV cannot be transmitted through hugging, kissing, dancing or shaking hands with someone who has HIV or AIDS. This is due to the fact that HIV cannot survive for very long outside of the body [25].

There are some of the common ways of HIV transmission [26-28]

Having unprotected sex: A person can become infected if he/she have vaginal, anal or oral sex with an infected partner whose blood, semen or vaginal secretions enter the body. The virus can enter your body through mouth sores or small tears that sometimes develop in the rectum or vagina during sexual activity. Also, engaging in activities like anal, vaginal, or oral sex with men who have sex with men, multiple partners, or anonymous partners without using a condom can lead to HIV transmission. Even though use of protective measures (mainly condoms), also don’t guarantee 100% protection from HIV transmission [29-32].

Blood transfusions: Virus may be transmitted through blood transfusions. A study shows that individuals who received blood or clotting factor in United States from 1978 to 1985 have a greater risk of infection from HIV. Since then, American hospitals and blood banks now screen the blood supply for HIV antibodies. The rate of HIV transmission through blood transfusion is 100% [5,33].

Sharing needles: HIV can be transmitted through needles and syringes contaminated with infected blood. Local street sellers of syringes may repack used syringes and sell them as sterile syringes. For this reason, people who continue to inject drugs should get syringes from reliable sources, such as pharmacies or hospitals. It is important to know that sharing a needle or syringe for any use, including skin popping and injecting steroids, hormones, or silicone, can put you at risk for HIV infections. Tattooing or body piercing present a potential risk of HIV transmission. But, there is no significant evidence to prove the statement [34].

From mother to fetus: Infected mothers can infect their babies. According to Kourtis et al [35] approximately 4,00,000 children are infected with HIV in 2008. Mother-to-child transmission of HIV can occur during pregnancy, labour, delivery, or through breastfeeding. Breastfeeding is responsible for one third to one half of HIV infections in infants but, majority of infants are infected during delivery [36]. Various drugs have been developed to reduce the mother to child transmission (MTCT) of HIV. These drugs significantly reduce the risk of transmission of infection but do not completely eradicate it. Despite continuous researches the origin of HIV in the breast milk is not completely understood. One of the best approach to prevent HIV infection in infants, including transmission through breast milk, is to prevent HIV infection in young girls and women that have attained puberty. Also, educating them about safer sex, condoms, and diagnosis and treatment of sexually transmitted infections may reduce the risk of MTCT. Replacement feeding i.e. modifying feeding options of infants for HIV infected women may also reduce the risk of transmission. Commercial infant formula can be used for feeding infants with partial breast feeding [37-42].

**COMMON MISCONCEPTIONS ABOUT HIV [43]**

HIV cannot be transmitted through:

- Breathing the same air as someone who is HIV-positive
- Hugging, kissing, or shaking hands with someone who is HIV-positive (HIV may be found in saliva, but it is in too small amount to infect anyone)
- Sharing utensils with an HIV-positive person
- Using exercise equipment at a gym
- Mosquito bites

Antiretroviral therapy can decrease the amount of HIV in the body. But, it can still be transmitted to others.

**FROM HIV INFECTION to AIDS**
HIV is an enveloped RNA virus and is roughly spherical having a diameter of about 120 nm [5]. The viral core/capsid is usually bullet-shaped and is made from the protein p24 [44]. Inside of the core there are three enzymes which are required for HIV replication [34, 45, 46]:

- reverse transcriptase
- integrase
- protease [47-51].

HIV's genetic material is enclosed within the core and it consists of two identical strands of RNA [52, 53].

HIV can only replicate inside human cells. The process typically begins when a virus bumps into cells that have surface protein called CD4. The spikes on the surface of the HIV particle stick to the CD4 and allow them to fuse [54-58]. This results in releasing of the contents of HIV into the cell. HIV mainly infects helper T cells that are very important for the body's immune system. As HIV infects more cells, the immune system becomes weaker and thus results in AIDS. Once inside the cell reverse transcriptase converts the viral RNA into DNA. This is then transported to nucleus of human cell where it is inserted into the human DNA by the HIV enzyme integrase. At this stage the HIV DNA is known as provirus and the cell begins to die thereby, weakening the immune system.

Now, these proviruses remain dormant for a long time. But, after activation HIV genes works as human gene and secretes HIV proteins and enzymes which help in synthesizing new viral particles. After some time they are released from the cells by the process called budding. The enzyme protease then chops up the long strands of protein into smaller pieces, which are used to construct mature viral cores of new HIV particles. These newly formed HIV particles now infect new cells and same process repeats. In this way the virus quickly spreads through the body.

As a result of the above process the helper T cells die thus, weakening the immune system. At this stage, due to weak immune system various opportunistic infections attack the body and causes AIDS [59-62].

Common opportunistic infections that dominate in HIV infections are [63, 64]:

- Tuberculosis
- Salmonellosis
- Candidiasis
- Meningitis
- Pneumonia [65]
- Lymphomas etc.

**Symptoms of HIV infection**

In the primary stages of HIV infection, most of the people have very few or no symptoms. But, after one or two months of infection, individuals may experience flu like symptoms which includes [66]:

- Fever
- Headache
- Tiredness
- Enlarged lymph nodes in the neck and groin area

These symptoms disappear within two weeks. People infected from HIV may have no symptoms for 12 yrs. or more.

During later stages of HIV infection individuals may have following symptoms:

- Rapid weight loss
- Recurring fever
- Profuse night sweats
- Extreme tiredness
- Prolonged swelling of the lymph glands
- Diarrhea
- Sores of the mouth, anus, or genitals
- Pneumonia
- Red, brown, pink, or purplish blotches on or under the skin or inside the mouth, nose, or eyelids
- Memory loss, depression, and other neurologic disorders [67]
- Kidney disease [68-70]

**DIAGNOSIS and TREATMENT**

HIV is commonly diagnosed by testing blood or saliva for antibodies to virus. However, these antibody tests may not detect HIV antibodies in someone who has been recently infected with HIV (i.e. up to 12 weeks). There are two methods by which HIV can be tested are ELISA (enzyme linked immunosorbent assay) and western blot [71-76].

Newer test that detects HIV antigen (a protein produced by the virus immediately after infection) confirms the diagnosis within the days of infection. This earlier diagnosis aids in taking extra precautions to prevent transmission of the virus to others and early treatment which may increase the patient’s life time [77,78].

Various classes of drugs are used in the treatment of HIV these are [4,21,22,79-84):

1. **Entry Inhibitors**: It interferes with the virus’s ability to bind to receptors on the outer surface of the cell. When receptor binding fails, HIV cannot infect the cell. E.g. Fosfonet, Enfuvirtide etc.
2. **Fusion Inhibitors**: It interferes with the virus’s ability to fuse with a cellular membrane, preventing HIV from entering a cell. E.g. Maraviroc, Enfuvirtide, Fostemsavir etc.
3. **Reverse Transcriptase Inhibitors**: It prevents the HIV enzyme reverse transcriptase from converting single-stranded HIV RNA into double-stranded HIV DNA.
4. **Nucleoside/nucleotide RT inhibitors (NRTIs)**: They are faulty DNA building blocks. When one of these faulty building blocks is added to a growing HIV DNA chain, no further correct DNA building blocks can be added on thereby halting HIV DNA synthesis. E.g. zidovudine, lamivudine, emtricitabine, abacavir etc. [85-90]
5. **Non-nucleoside RT inhibitors (NNRTIs)**: It binds to reverse transcriptase, interfering with its ability to convert HIV RNA into HIV DNA. E.g. tenofovir, etravirine, efavirenz, nevirapine etc. [91,92]
6. **Integrase Inhibitors**: It blocks the HIV enzyme integrase, which the virus uses to integrate its genetic material into the DNA of the cell it has infected. E.g. raltegravir, dolutegravir etc.
7. **Protease Inhibitors**: It interferes with the HIV enzyme called protease, which normally cuts long chains of HIV proteins into smaller individual proteins. When protease does not work properly, new virus particles cannot be made. E.g. saquinavir, ritonavir etc.

**CONCLUSION**

Since its first clinical discovery in 1981, AIDS emerges as the global epidemic which has taken many lives of the people and continues to do so in the coming years [93]. It was believed that HIV was originated from primates in Africa, where they were hunted for food. Since then it continues to spread all over the world. The epidemiological distribution is not same for all the continents, yet it is one of the most dangerous and life threatening disease. Treatment options are available which can prolong the life of the patient but cannot cure the disease [94,95]. This is due to the complex structure of the HIV and rapid resistance to the drugs [96-99]. Now-a-days combination therapy [100] is given to combat resistance thereby, prolonging the life but, still cannot cure the disease [101,102]. In the end there is only one option left to be safe from HIV infection i.e. self-awareness and sex education. These also do not guarantee 100% safety but can limit the infection from spreading. As very well said that prevention is better than cure and so in the case of HIV same rule follows.

**REFERENCES**
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