wjpmr, 2024, 10(7), 88-94

SJIF Impact Factor: 6.842

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Review Article

ISSN 2455-3301

WJPMR

HUMAN IMMUNODEFICIENCY VIRUS (HIV)

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Article Received on 06/05/2024 **Article Revised on 27/05/2024** **Article Accepted on 16/06/2024**

ABSTRACT

HIV virus was first identified in humans in 1959 which was transferred from chimpanzees to human during hunting. The Human Immunodeficiency Virus - HIV is responsible for causing Acquired Immunodeficiency Syndrome – AIDS. This virus also affects millions of people in the whole world, generating large global impact. It is a member of the lentivirus family of animal retrovirus and has an affinity for defense cells of the body, which the main target is the CD4 + T lymphocytes. Once connected to a component of this cell, the HIV will penetrate it and multiply, destroying them, by weakening the immune system, making it fragile and susceptible to opportunistic diseases. There are two known types of HIV, which are deeply related, named as HIV-1 and HIV-2. HIV-1 is the main cause of AIDS, HIV-2 differs in genomic structure and antigenicity, also causes the disease, but with slower progression. AIDS is the clinical manifestation generated by HIV, once the immune system is compromised. It is estimated that, in Brazil, 718 000 people living with HIV / AIDS. There is, currently, no effective vaccine or cure for AIDS, however effective antiretroviral therapies have been used. Through this literature review the paper aimed to show on the HIV virus, its general features, its immunological changes, the national level of this epidemiology, the diagnosis and treatment, warning about the importance of this infectious agent and its prevention, towards control and reduction to the AIDS epidemic. condom use one of the main prevention means1,2,5, vertical transmission is also a form of contagion, where there is transfer of the mother's virus to her child during pregnancy, childbirth or breastfeeding6.

KEYWORDS: AID, Transmission, Symptoms, Human immunodeficiency virus, Stage of infection.

INTRODUCTION

Recognition of Acquired Immune Deficiency Syndrome (AIDS) began around 1981 in the United States (US), due to the increased number of patients living in San Francisco or New York, male, gay and adult sex, which presented immune suppression of the immune system, Pneumocystis carinii pneumonia and Kaposi's sarcoma.[1,2,3] HIV is a virus that causes AIDS. Normally, our body has immune system that attack viruses and bacteria. Immune system has white blood cells which protect us from infections. White blood cells contain CD4+ cells which is also known as helper cells or T cells. A person who is infected will be able to develop. These infections take advantage of body's immune system. These infections cause several health problems and even lead to death of a person. HIV has inability to protect against diseases and count of CD4 cells also decreases in HIV. There is no cure of AIDS but there are certain medicines which are use to slow down the diseases so you stay healthier for long time. There is no medicine to get rid of diseases.[6]

H-It infects only human beings and also transmitted between humans not from animals. It is not transmitted from bites of mosquitoes, bats or any other species.

I-The body has immune system whose function is to protect our body from germs, infections etc. But a person suffering from HIV has inability to fight against diseases. However, immune system becomes deficient.

V-Virus is a small, the simplest thing which is in inactive form outside the body and becomes active when it goes inside human body.

Structure of HIV

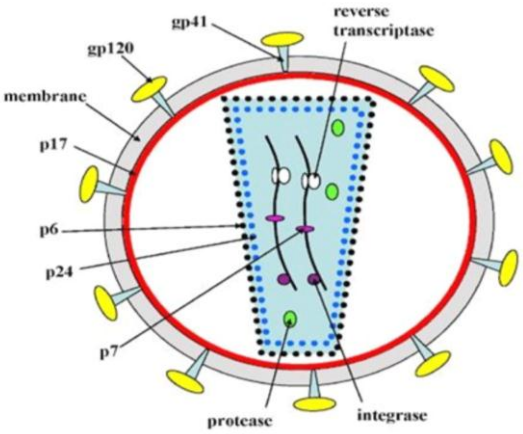

Fig. 1: Structure of HIV.

Gp120
The 120 in its name comes from its molecular weight. It is essential for virus entry into the cells as it plays vital role in attachment to specific cell surface receptors.

GP41
It is a subunit of the envelope protein complex of retroviruses including human immuno deficiencies virus. It is family of enveloped viruses that replicate in host cell through process of reverse transcriptase. It targets a host cell.

Viral envelope
It is envelope through which virus binds.

P17
Viral core is made from protein. It is bullet shaped. Three enzymes required for HIV replication are reverse transcription, integrase and protease.

P24
P24 is component of HIV capsid.

Protease
It is a retroviral aspartyl protease that is essential for life cycle of HIV, the retrovirus that caused AIDS. This enzyme cleaves newly synthesized polyproteins at appropriate place to create nature protein components of infectious HIV virion.

Integrase
Enzyme produce by retrovirus that enables its genetic material to be integrated into the DNA of infected cell.

RNA
All organisms including most viruses store their genetic material on long strands of DNA. Retrovirus is exception because their genes are composed of RNA.

Life cycle of HIV

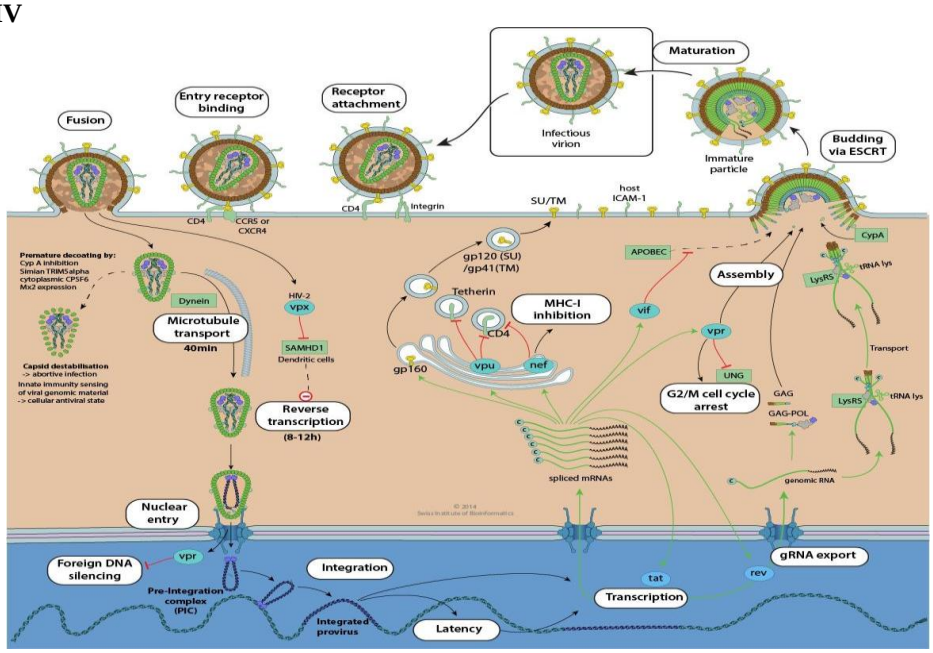

Fig. 1: Life Cycle of HIV.

Binding
During the first stage of HIV's life cycle, the virus binds to receptors on the surface of CD4 cells.

Fusion
Once HIV binds to receptors on CD4 cells, it initiates the fusion of its envelope with the membrane of the CD4 cell using a glycoprotein called GP120Trusted Source. Glycoproteins are molecules made of chains of carbohydrates and proteins. Fusing with the membrane of your CD4 cells allows the virus to enter the cell.

Reverse transcription
Reverse transcription is a process of converting genetic information in the form of RNA into DNA. RNA and DNA contain similar genetic information but are structurally different. RNA is typically made up of one long chain of genetic information, while DNA is made up of a double strand.

Integration
Once HIV has converted its RNA into DNA, it then releases another enzyme called integrase inside the nucleus of your CD4 cell. The virus uses this enzyme to combine its DNA into the DNA of your CD4 cell.

Replication
Because HIV is now integrated into your CD4 cell's DNA, it can use that cell's machinery to generate viral proteins. During this time, it can also produce more of its genetic material (RNA). These two things allow it to create more viral particles.

Assembly
In the assembly stage, new HIV proteins and RNA are sent to the edge of your CD4 cell and become immature HIV. These viruses are non-infectious in their current form.

Budding
During the budding stage, the immature viruses push out of your CD4 cell. They then release an enzyme called protease that modifies proteins in the virus and creates a mature and infectious version.

Transmission
You can get HIV only through certain activities. You cannot get HIV infection from touching an infected person, being in the same room as someone with HIV, or through contact with surfaces like toilet seats.[8]

- Certain body fluids, including semen, vaginal secretions, rectal fluids (through sexual contact with an infected person), and blood. These infected fluids have to either come in contact with mucous membranes or go directly into the bloodstream. In terms of HIV transmission, anal sex is the riskiest type of sexual activity.[9]
- Sharing needles or other equipment to inject drugs with someone who has HIV.
- Infected blood or blood products through transfusion. This is very rare in the United States but can happen in countries where blood and blood donors are not tested for HIV. Women with HIV infection can transmit the virus to their babies during pregnancy, at the time of birth, or through breastfeeding.

HIV infection is not transmitted through saliva.[10]

Stage of infection
There are 3 stages of infections and severity increases as the stage of disease increases.
Stage 1:- (Acute HIV infection)
Stage 2 :- (Chronic infection)
Stage 3:- (Acquired immunodeficiency syndrome)

Stage 1
Acute HIV Infection The earliest stage of infection is called as acute HIV, and generally develops within 2 to 4 weeks after the patient is infected with HIV virus. In this very first stage of infection, the virus multiplies and spreads rapidly throughout the body. The HIV starts to attack and destroy the infection-fighting CD4 cells. This gradually collapses the immune system. The risk of HIV transmission is increased in the acute stage because of high levels of HIV in blood.[11]

Stage 2
Chronic HIV Infection This is the second stage of HIV infection also named as asymptomatic HIV or clinical latency. In this second stage of infection, the virus is in state of continuous multiplication but at very low levels. If the ART is not given to patient is this stage, the stage may advance to AIDS in about 10 years (may be more or less depending on immune system of patient).[12]

Stage 3
AIDS The third stage is actually called AIDS and is the most severe stage of HIV infection. In this stage, the HIV has severely damaged the immune system and the body is unable to fight to the opportunistic infections. People with HIV are diagnosed with AIDS when their CD4 count is less than 200 cells/mm3. Once the person is diagnosed with AIDS, they have a high viral load and can transmit disease to others very easily. Without treatment a person with AIDS typically survives for up to 3 years.[13]

Symptoms of disease
Symptoms of the disease vary according to the stage of infection. Symptoms according to the stage of disease are mentioned below

Symptoms of Stage 1
1. Headache
2. Fatigue
3. A red rash that doesn't itch
4. Sore throat

5. Swollen lymph

Symptoms of Stage 2
After the person advances to the second stage of HIV infection, seroconversion process takes place and patient often feel better. In the second stage, patient may not show any other symptoms nearly for 10 years or even more (depending upon the health background of patient) But, the virus will still be active and continue to infect new cells of body. The virus also continues to replicate itself and risk of transmission is present during this stage. If ART is not given to patient overtime, HIV will continue to severely damage the immune system

Symptoms of Stage 3
1. Being tired all the time
2. Fever that lasts for merely about 10 days
3. Night sweats
4. Weight loss with no obvious reasons
5. Shortness of breath
6. Severe long-lasting diarrhea
7. Purplish spots on your skin
8. Swollen lymph nodes in your neck and groin region
9. Yeast infections in your mouth, throat, vagina.[34]

Diagnosis
The diagnosis of HIV-1 infection is based on the detection of specific antibodies, antigens, or both, and many commercial kits are available. Serological tests are generally used for screening. A major advance has been the availability of rapid HIV-1 antibody tests. These assays are easy to do and provide results in as little as 20 minutes,[14] enabling specimen collection and proper diagnosis at the same visit. Rapid tests are important tools for surveillance, screening, and diagnosis, and can be reliably done on plasma, serum, whole blood, or saliva by health-care providers with little laboratory expertise. The two limitations of these serological tests are detection of infection during primary infection when antibodies are absent, and in infants younger than 18 months who might bear maternal HIV-1 antibodies. In these instances direct virus detection is the only option (eg, quantification of viral RNA [standard] or p24 antigen in heat denatured serum [less expensive]).

(i) A historical perspective on the evolution of HIV diagnostics (serologic and molecular) and their interplay with WHO normative guidelines.

(ii) A description of the role of conventional and POC testing within the tiered laboratory diagnostic network.

(iii) Information on the evaluations and selection of appropriate diagnostics.

(iv) A description of the quality management systems needed to ensure reliability of testing.

(v) Strategies to increase access while reducing the time to return results to patients. Maintaining the central role of HIV diagnostics in programs requires periodic monitoring and optimization with quality assurance in order to inform adjustments or alignment to achieve epidemic control.[15]

Standard methods for quantifying viral load and CD4+ cell counts need advanced laboratory infrastructures, and assays require a specimen to be tested within a short time of collection. These requirements pose challenges for resource-constrained settings. The use of dried blood spot specimen has resolved some of the difficulties associated with transportation of samples needed for virological assessments.[16] Measurement of reverse transcriptase activity in plasma samples, simplification of gene amplification methods (eg, Taqman technology), and paper-strip quantification (dipstick assays) might provide cost-effective alternatives for the future.[17-18] Similarly microcapilliary flow-based systems, CD4+ chips, or total white counts (panleucocyte gating) provide alternatives for establishment of the level of immunodeficiency in resource-limited settings.[19-20]

Treatment
In November 1996, Brazil became the first country to make available free of charge through the Unified Health System (SUS), all drugs necessary for the treatment of patients living with HIV / AIDS[35]

Are currently used in Brazil, four classes of antiretrovirals, which are considered more potent and less toxic, divided as Nucleoside Reverse Transcriptase Inhibitors (NRTIs) Nucleoside Inhibitors No Reverse Transcriptase (INN-TR), inhibitors protease (IP), and Integrase Inhibitors.[36]

Antiretroviral Therapy
Antiretroviral treatment is the best option for longlasting viral suppression and, subsequently, for reduction of morbidity and mortality. However, current drugs do not eradicate HIV-1 infection and lifelong treatment might be needed.

20 of the 21 antiretroviral drugs currently approved by the US Food and Drug Administration target the viral reverse transcriptase or protease (table 1). Eight nucleoside/nucleotide analogues and three non-nucleoside reverse transcriptase inhibitors inhibit viral replication after cell entry but before integration. Fixed-dose combination tablets simplify treatment regimens by reducing the daily pill burden, and drugs with long half-lives allow once or twice daily dosing. Eight protease inhibitors prevent the maturation of virions resulting in production of non-infectious particles. The recently approved darunavir (June, 2006) is the first of its class that retains activity against viruses with reduced susceptibility to protease inhibitors. Enfuvirtide targets a gp41 region of the viral envelope and stops the fusion process before the cell is infected. This drug needs to be injected twice daily and its use is reserved for treatment of heavily drug-experienced patients since it can help

overcome existing drug resistance.[21-22] Development of new antiretrovirals focuses on molecules that target entry, reverse transcription, integration, or maturation. Compounds that have been designed to inhibit resistant viruses are urgently needed since many patients treated during the past decades harbour viral strains with reduced susceptibilities to many if not all available drugs.

Table 1
Antiretroviral drugs currently approved by US food and drugs administration

	Entry	Reverse transcriptase			Protease
		Nucleoside	Nucleotide	Non-nucleoside	
Single compound tablets	Enfuvirtide	Abacavir	Tenofovir	Delaviridine	(Fos)-Ampren
		Didanosine		Efavirenz	Atazanavir
		Emtricitabine		Nevirapine	Darunavir
		Lamivudine			Indinavir
		Stavudine			Nelfinavir
		Zalcitabine			Ritonavir
		Zidovudine			Saquinavir
					Tripanavir
Fixed-dose combination tablets		Abacavir/lamivudine (Epzicom)			Lopinavir/ritor
		Zidovudine/lamivudine (Combivir)			
		Tenofovir/emtricitabine (Truvada)			
		Abacavir/lamivudine/zidovudine (Trizavir)			
		Tenofovir/emtricitabine/efavirenz (Atripla)			

Drugs Used In Art
Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs)
HIV virus is forced to use faulty versions of building blocks by NRTIs so that more HIV are not made by infected cells.

- Abacavir or Ziagen*
- Zidovudine or Retrovir*
- Stavudine or Zerit*
- Didanosine or Videx*
- Emtricitabine or Emtriva*
- Lamivudine or Epivir*
- Tenofovir alafenamide or Vemlidy*
- Tenofovir disoproxil fumarate or Viread*

Prevention
Mother to child transmission

Prevention of mother-to-child transmission has seen advances in both industrialised and resource-constrained settings.[24-26] Intrapartum transmission has been reduced by increasing access to interventions such as one dose of nevirapine to mother and newborn baby.[27] Concerns about drug-resistant viral strains have led to several trials with combination treatments to reduce transmission during the intrapartum period.[23-25-28] In some settings, elective delivery by caesarean section can further reduce HIV-1 transmission during the intrapartum period, but the benefits of the intervention could be countered by post-partum sepsis and increasing maternal mortality.[29]

Sexual transmission
Reduction of heterosexual transmission is crucial for control of the epidemic in many parts of the world[30-37] Prevention is achieved through reduction in the number of discordant sexual acts or reduction of the probability

of HIV-1 transmission in discordant sexual acts. The first can be achieved through abstinence and sex between concordantly seronegative individuals. Abstinence and lifelong monogamous relationships might not be adequate solutions for many people and therefore several interventions aimed at lowering the risk of transmission per discordant sexual act are in the process of clinical testing. Male and female condoms provide a proven and affordable prevention option.[32-33] In combination, these options are also more commonly referred to as the ABC (abstinence, be faithful, condom use) approach.

CONCLUSION

An important gateway to both prevention and care is knowledge of HIV-1 status.[38] Fear of knowledge of status, including stigma and discrimination, has discouraged many from seeking voluntary counselling and testing services.[39] As access to antiretroviral interventions (prevention of mother-to-child transmission, antiretroviral treatment) increases, the opportunities for HIV-1 testing will grow and create opportunities for a prevention-care continuum, with the voluntary counselling and testing services as a point of entry. These changes will result in a shift in prevention efforts from a focus on individuals not infected with HIV-1 to a more effective continuum of prevention that includes uninfected, recently infected, infected, and asymptomatic people, as well as those with advancing HIV disease and on antiretroviral therapy.

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