A REVIEW ARTICLE ON HIV/AIDS

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Abstract: The article provides overall information about Human immunodeficiency virus (HIV) and Acquired immune deficiency (AIDS), the immunology and biology of the virus from its genetic biodiversity to the life cycle of the virus, the different phases of HIV disease and its progression, sub-group of HIV, modes of HIV transmission, their symptoms, the different test method present currently for determining the presence of HIV in humans, immune response to the infection and the current treatment available and given to treat HIV with the therapeutic strategies. As well as the preventive measure to be taken to prevent spreading of HIV virus.

Index Terms: HIV/AIDS, lifecycle and disease progression, immune response, treatment.

1. Introduction

Human immunodeficiency virus (HIV) is a virus that targets and attacks the immune system of the human being, thus it alters the immune system and increases the risk of infections and disease. Without proper treatment the infection may increase and proceed to advance stage of disease called as AIDS.

What is HIV?

Human immunodeficiency virus (HIV) is a virus that attacks immune cells of the human body which are called CD4 cells, which are a type of T cell. These are white blood cells that move around the body, whose function is to detecting faults and abnormalities in cells as well as infections. When HIV targets these CD4 cells and infiltrates these cells, it reduces the body's ability to fight against the infection and other diseases. This increases the risk of getting infections and cancers. However, a person may carry HIV without experiencing symptoms for a long time. HIV is a lifelong infection. However, receiving the treatment and managing the disease effectively can prevent HIV from reaching a severe level which reduces the risk of a person passing the virus to another person.

HIV stands for:

H- This virus infects only the human beings and it’s also been transmitted between the humans and not from the animals. This virus is not been transmitted through the bites of mosquitoes, bats or any other species.
I – immune system of the human body has the function to fight against the germs, virus or any other foreign particle that enter the body and protect the body from disease, but the person affected with HIV is unable to perform the protection function against the diseases as the immune system becomes deficient.
V- Virus is the small as well as simple form which is inactive when its outside the body and becomes active as soon as it enters the body.

What is AIDS?

Advance stage of HIV infection is AIDS. When the HIV infection develops into the AIDS, the risk of getting infection and cancer increases. If HIV infection remains without treatment it leads to the development of AIDS as the immune system gets weak. The advances in Anti retro viral therapy (ART) means than the ever-decreasing numbers of people progress at this stage.

AIDS stands for:

A-It’s not inherited means it cannot be transmitted from one generation to different generation. It’s transmitted to healthy person by infected person.
I-It weakens the immune system.
D-Creates a deficiency of CD4+ cells within the immune system.
S-It’s the collection of diseases.
Advance stage of HIV infection is AIDS. In the normal human being, the healthy immune system attacks the virus, bacteria and the foreign substance that enters the body. The healthy immune system of the human body has the presence of white blood...
cells which contains CD4+ also called as helper cells or T cells whose function is to protect the body from infection and disease. The person who gets infected by HIV develops various health problems as the HIV virus attacks the immune cells of the humans and makes immune cells dysfunction and thus makes it incapable to protect body against disease and the count of the CD4 cells also decreases in HIV infected person. [1]

**HIV SUBGROUPS –**
Prevalence of 0.06% which identified in the pregnant women in France. [4]

**HIV-2**

HIV-2 is the mostly reported with West Africa, with Senegal and Guineas-Bissau having the high number of incidence. HIV-2 exists in 8 different types, which are labeled from HIV-A to HIV-H. Where the Group A is been detected all over in the sub-Saharan region [5]. Group B is found in the Ivory Coast’s [6]. Group C to H are

**HIV-1**

HIV-1is the most common type of HIV which is been seen all over the world. According to Avert (HIV awareness charity) around 95% of people having HIV is detected with HIV-1.

HIV-1 has the four different lineage coming under it are M, N, O, P. The mostly been reported HIV -1 virus all over world is group M [2]. Group N is less prevalent which is reported only from Cameroon [2]. Whereas Group O is 1% of total HIV-1 cases which is found mainly in Gabon and Cameroon [3], and Group P is found very rarely with categorized as dead- ends transmissions that produce no infection due to the sporadic nature. [7]

Thus HIV-1 and HIV-2 both of them are retro viruses which have similar effect on human’s immune system they are genetically distinct. The study in 2008 showed that both the viruses (HIV-1 &HIV-2) had only 55% sequence identity. This clearly means that not all the test and treatments works for both HIV.[2]

<table>
<thead>
<tr>
<th>Table Difference between HIV-1 and HIV-2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HIV-1</strong></td>
</tr>
<tr>
<td>This strain is found in all over world and is very common</td>
</tr>
<tr>
<td>Its most likely to get more worse infections progress and which get many of those infected humans remain the lifelong non progression.</td>
</tr>
<tr>
<td>The immune system activation is higher at the average level</td>
</tr>
<tr>
<td>HIV -1 has lower level of CD4 count than HIV-2 during progression</td>
</tr>
<tr>
<td>Viral load in plasma is higher</td>
</tr>
</tbody>
</table>

**Structure of HIV virus:**

![Structure of HIV virus](image)
Gp120 – it’s the essential part of the virus that helps it to get enter into the cell and also plays a vital role in the attachment to the specific cell receptor on surface. The Gp 120 in which 120 represents the molecular weight.

Gp41 – it’s the subunit of the protein complex of retro viruses including the HIV virus. It’s from the family of enveloped viruses that replicated in the host cell through the reverse transcriptase process.

Viral Envelope – It’s the envelope through which the virus binds.

P17 – it’s the core made of protein with the bullet shape. Three enzymes which are required for the replication of HIV are transcription, integrate and protease.

P24 – it’s the component of HIV capsid

Protease – it’s the retroviral aspartyl protease which is an essential component for the life cycle of HIV that causes AIDS. This enzyme cleaves the new synthesized polyproteins at the appropriate place that creates the nature protein component of the infectious HIV virion.

Integrase – it’s the enzyme that is produced by the retro virus that activates its genetic material to enter into the DNA of the infected cell.

RNA – all the viruses store their genetic material on the long strand of DNA even the retro virus stores their DNA on long strand as their gene contains of RNA [9]

Life Cycle of HIV virus –
HIV virus belongs to the group of retro virus and subgroup of retrovirus called as Lentiviruses or slow viruses[11]. In the course of HIV infection virus are characterized by long interval between the initial infections to the serious symptoms. HIV virus gets replicated only inside the cell.
The ribo nucleic acid (RNA) is present in the retro virus gene where the human genes are made of dioxyribo nucleic acid (DNA). However once the retro virus enters into human cell, they use reverse transcriptase enzyme to convert RNA to DNA, which easily gets incorporate into human gene[12].

Life cycle –
The HIV virus gets attach to the CD4+ receptor and their co-receptors of the host cell (human cell) [10]. The virus then fuses with the host cell and HIV virion enters the cell. After binding to one of several co-receptors which is necessary for the further process of fusion & viral particle to disgorge its content (2 copy of viral RNA). Inside the cytoplasm of the host cell the HIV reverse transcriptase enzyme converts the virus RNA to DNA and further the full-length DNA copy is made and this further gets converted into small functional pieces [12, 13].
The DNA of HIV further moves to the cell’s nucleus where HIV integrase helps to join HIV viral DNA to the host cell’s DNA. After the viral DNA gets linked with the host cell’s DNA then the activated cell produces viral proteins. Current model of HIV pathogenesis demonstrates that the activation of abnormal immune is considered as the major factor in the disease progression by making a pool of the activated CD4+ T cells that may be targeted by HIV, which causes immune exhaustion [14]. The activation of CD8+ T cell correlated +ve with the progression risk of AIDS [15]. If the CD4+ cells are not activated it’s possible that the virus continues to exist in latent stage for several years [14]. Thus, the virus present in the latently infect cell has greatly complicate attempts to get rid of out completely of HIV. Due to this reason the HIV +ve patient must remain in Antiviral drug therapy [16].
The activated cell then later makes the viral protein by coping the DNA to RNA by process of transcription. The virus RNA transcribed by the DNA is called mRNA, which is transported from nucleoside to the cytoplasm of cell. Once the mRNA enters cytoplasm the cell starts to produce the protein of HIV virus using mRNA as template by process known as Translation. Later the sequence of mRNA is translated to RNA & protein which comprises of envelop and core of virus. The translated gene product is large in size than to those of final virus which is needed to connect the small functional units. These large size genes are reduced to small size with the help of viral protease. This HIV protease is very highly specific for the HIV and also the target of Anti HIV drugs. After spliced, the enveloped protein of virus comes in contact with the host’s cell membranes with the help of RNA, core protein, and enzyme that are present inside the membrane. The virus then gets pinched off in the cell and buds \cite{12,13}. The single cell can make 1000 of infectious particle of HIV.

**Transmission of HIV –**

HIV is the sexual transmitted disease. During sexual contact, the virus crosses the mucosal barrier of penis, rectum, vagina, and vulva by coming in contact with the immune dendritic cells that carries the HIV virus across the mucosa.\cite{17} The dendritic cell then picks the virus from external and crosses into the interior of cell and then release the infectious virus into the lymphatic node or lymphatic tissue. Then virus binds to the CD4 cell, then travels to the lymphatic tissue, and begins their first cycle of infection. The risk of infection during the sexual intercourse increases \cite{18}. Women’s are highly prone to acquire the HIV infection during the hetero sexual intercourse, because of the physiological characteristic of female, such as presence of high amount of mucosal surface are that gets exposed to the seminal fluid\cite{19}. HIV also gets spreads by the contact with the blood of HIV infected person, by practicing of re-use of needle or sharing the same syringes with drugs\cite{20}. It can also be transmitted by the using the infected blood product by the healthier patient. There is also the risk of transmitting the HIV virus from the pregnant mother (HIV infected) to the fetus or new born baby during the pregnancy, during the delivery or during breast feeding.\cite{21}

**Activities that allow the HIV transmission **\cite{2}

- Unprotected sexual contact
- Direct blood contact, including re-use of injection drug needles, blood transfusion with HIV infected person
- HIV infected mother to baby (before, during the birth or during breast feeding)

**The risk of HIV transmission depends on-**

- The concentration of HIV virus in the infected fluid
- The quantity of fluid(containing HIV virus ) introduced in the body
- The access of the HIV virus in infected fluid to the T4 cells

**Fluids that contain high concentration of HIV –**

- Semen
- Blood and blood component
- Menstrual flow
- Vaginal secretion
- Pre ejaculatory fluid
- Beast milk

**Fluids that contain Low concentration of HIV –**

- Pus
- Saliva
- Tears
- Urine
- Nasal mucosa

**Symptoms –**

Many times the people that gets infected with HIV show no signs and symptoms, where 70 to 90 % people infected with HIV infection shows symptoms like [22]

- Flu short-term and memory loss
- Rash
- Saviour sour throat
- Yeast infection by vaginal or oral route
- Weight loss.
- sweats skin rashes, flaky skin that does not go away
- slow growth & frequent illness in children,
- cough and shortness of breath,
- Seizures, lack of coordination,
- difficult or painful swallowing.
- Forgetfulness and confusion, nausea, cramps, vomiting or diarrhoea that do not go away,
- vision loss,

**Test used to determine the presence-**

There are three main test used to diagnosis the presence of HIV are falling-

1. Anti-body screening test
2. Antigen/ antibody test
3. Nucleic acid test / RNA test

1. **Anti-body screening test** - This test is used to determine the protein that is made by the human body within 2to8 weeks of an HIV infection. They are also called as ELISA test or immunoassay test. This test is generally very accurate. They use oral fluid or blood sample for then test which shows result in 30minutes or less.

2. **Antigen/ antibody test** – The CDC have recommended this blood test. They detect the HIV earlier than above test. They determine for presence of HIV antigen, a protein called as p24 which is a part of virus and shows it in 2-4 weeks after infection. They also check the presence of HIV antibodies. This test gives result in 20 minutes.

3. **Nucleic acid test / RNA test** - This test determines for the virus itself and can determine HIV after the 10 days of infection. This test is expensive thus not preferred as a first choice. But if the infection risk is high and also having flu like symptoms then this test may be proffered by physician.
Treatment of HIV:

Antiretroviral Therapies (ART)
Currently 20 of the retro viral drugs are been approved for the used in the treatment of HIV \cite{23}. Six classes of ART are available that are used to treat HIV. Each of these ART class drugs are used to treat HIV virus at different stage in its life cycle.

### Table- ART classification of drug

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Class of the ART drug</th>
<th>Example of drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Nucleoside/Nucleotide reverse transcriptase inhibitor (NRTIs)</td>
<td>Zidovudine, Abacavir</td>
</tr>
<tr>
<td>2</td>
<td>Non-Nucleoside reverse transcriptase inhibitor (NNRTIs)</td>
<td>Efavirenz, Nevirapine</td>
</tr>
<tr>
<td>3</td>
<td>Protease inhibitor (PI)</td>
<td>Lopinavir, Ritonavir</td>
</tr>
<tr>
<td>4</td>
<td>Integrase Inhibitor</td>
<td>Raltegavir</td>
</tr>
<tr>
<td>5</td>
<td>CCR5 Antagonist</td>
<td>Maraviroc</td>
</tr>
<tr>
<td>6</td>
<td>Fusion Inhibitor</td>
<td>Enfuvirtide</td>
</tr>
</tbody>
</table>

Highly active antiretroviral therapy (HAART)
The current treatment consists of highly active antiretroviral therapy (HAART) therapy, that least contains three drugs belonging to two classes of antiretroviral agents \cite{23}.

Conclusion –
The HIV viral life cycle and the host response to viral (infection) is comprehensive which results that the virus specific intervention have developed which is highly active that may contain viral replication. The damaged immune system (infected by the HIV virus) can be at least partially immune reconstituted and those individuals with the last stage of infection can have expectation for long survival if they are properly treated with Anti retro viral drugs.
References: