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A Review on prevention and treatment of aids

Abstract

Human immunodeficiency virus (HIV) is a retrovirus which causes acquired immune deficiency syndrome (AIDS) a condition where CD4+ cell count falls below 200 cells/µl and immune system begins to fail in humans leading to life threatening infections. Many factors are associated with the sexual transmission of HIV causing AIDS. HIV is transmitted by three main routes sexual contact, exposure to infected body fluids or tissues and from mother to child during pregnancy, delivery or breast feeding (vertical transmission). Hence the efforts for prevention and control of HIV have to rely largely on sexually transmitted disease (STD) control measures and AIDS. In the developing countries both prevalence and incidence of AIDS are very high. The impact of AIDS on women's health adversely affected by various reasons such as more susceptibility than men, asymptomatic nature of infection etc. The management of AIDS can be controlled by antiretroviral therapy, opportunistic infections and alternative medicine. In present study is an update on origins of HIV, stages of HIV infection, transmission, diagnosis, prevention and management of AIDS.

Keywords: aids, HIV cd4+, vertical transmission, antiretroviral therapy

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Abbreviations: HIV, human immunodeficiency virus; AIDS, acquired immune deficiency syndrome; STD, sexually transmitted disease; ART, antiretroviral therapy

Introduction

AIDS is considered one of the most dangerous and a pandemic[1] disease which is present over a large demographic area of the world. It has a great impact on society such as an illness, a source of discrimination and economic condition of people. AIDS is the most serious infectious disease and actively spreading worldwide among humankind. In worldwide women and girls are vulnerable to HIV infection. Generally young women become more susceptible to HIV at early stage in some areas the prevalence of infection among women between 15-24years is more than twice that of young men. Women living in lower income countries are particularly at risk as extreme poverty and other structural factors such as gender[2] inequities, lack of education and violence reduce their ability to control health outcomes or access HIV related information and services. Human immunodeficiency virus infection/acquired immune deficiency syndrome (HIV/AIDS) is a disease of human immune system caused by infection with human immune deficiency virus. AIDS is called when a person infected with HIV has a CD4+ count of less than 200cells/µL or has an AIDS defining condition. During HIV infection the virus attacks and destroys the infection fighting CD4 cells of the body's immune system. It is difficult for immune system to fight infections due to loss CD4 cells. HIV gradually destroys the immune system by attacking and killing CD4 cells. HIV uses the machinery of the CD4 cells to multiply (make copies of it) and spread throughout the body. During the initial infection a person may feel a brief period of influenza like illness. This is followed by a prolonged period without symptoms. As the illness progresses it interferes more and more with the immune system making the person much more likely to get infections including opportunistic infections and tumors. HIV is transmitted[3] primarily via unprotected sexual intercourse (including anal and even oral sex), contaminated blood transfusions, hypodermic needles and from mother to child during pregnancy, delivery or breastfeeding. Some bodily fluids such as saliva and tears do not transmit HIV. Prevention of HIV infection primarily through safe sex and needle exchange programs is a key strategy to control the spread of disease and may lead to a near normal life expectancy. While antiretroviral treatment reduces the risk of death and complications from the disease these medications are expensive and may be associated with side effects. Due to HIV infection behavioral[4] interventions need to produce change in enough people for a sufficient time to impact transmission dynamics. Behavioral interventions targeting men who have sex with men sexually transmitted disease clinic patients, heterosexual African, Americans, sexually experienced adolescents in the United States and people living with HIV are effective in reducing self reported sexual risk behaviors.[5,6] Antiviral agents have made HIV/AIDS a more manageable disease in some industrialized nations and several vaccines are about to enter phase III clinical trials.HIV will doubtless continue to impose a terrible burden of morbidity and mortality. More importantly establishing the ground rules that underpin the evolution of HIV will lead to better vaccines[7] and antiviral agents. The present review gives idea about the origins of HIV, discovery of HIV, signs and symptoms, stages of HIV infections, transmission, diagnosis, prevention and management of AIDS.

The origins of HIV

The origin of HIV was the discovery[8] that closely related viruses the simian immunodeficiency viruses (SIVs) were present in a wide variety of African primates.[9] Collectively HIV and SIV comprise the primate lent viruses and SIVs have been isolated in more than 20 African primate species. There is no case (other than laboratory associated infections of Asian macaque monkeys) has been reported that the SIVs cause disease in their hosts. The evolutionary history of HIV-1 and HIV-2 was discovered that the two human viruses are related to different SIVs and therefore have different evolutionary origins. HIV-1 is most closely related to SIVcpz which is found in some subspecies of chimpanzee (Pantroglodytes and Pantroglodytes schweinfurthii) that inhabit parts of equatorial Western and Central Africa respectively.[10,11] SIV cpz from Pan troglodytes has closest relationship with the abundant HIV-1 M group. The geographical

range of P. t. troglodytes belongs to the region in Africa that has the greatest genetic diversity of HIV-1 containing groups M, N and O such a distribution is expected if this was where HIV-1 first emerged. By contrast HIV-2 is most closely related to SIVsm[12] which is found at high prevalence in sooty mangabeys are most frequent in the regions of West Africa where HIV-2 is likely to have emerged. Molecular phylogenies show that there have been many cross species transmissions to humans because there is a mixing of a HIV and SIV lineages.

HIV types

There are two types of HIV that cause AIDS such as HIV type1 (HIV-1) and HIV-2.[13] The modes of transmission of both types are similar and are associated with the same opportunistic infections, but HIV-2 appears to progress slowly. Most HIV-2 cases are found in Western Africa and in countries related to western Africa in some way such as Portugal, Angola, Mozambique, Brazil and India. Various subtypes of HIV-1 have been found in specific geographic areas and in specific high risk groups. The following are HIV-1 subtypes and their geographic distributions such as

i. Subtype A: Central Africa, sub-Saharan Africa
ii. Subtype B: South America, Brazil, United States, Thailand, Europe, Caribbean, India, and Japan.
iii. Subtype C: Brazil, India, and South Africa.
iv. Subtype D: Central Africa, and sub-Saharan Africa.
v. Subtype E: Central African Republic, Thailand, and Southeast Asia.
vi. Subtype F: Brazil, Romania, and Democratic Republic of Congo (Zaire).
vii. Subtype G: Democratic Republic of Congo (Zaire), Gabon, Thailand, Russia, and Central Africa.
viii. Subtype H: Democratic Republic of Congo (Zaire), Gabon, Thailand, Russia, and Central Africa.
ix. Subtype I: Cyprus.
x. Subtype O: Cameroon, and Gabon.

Subtypes are unevenly distributed throughout the world. Subtype C currently accounts for more than half of all new HIV infections worldwide. Africa has most subtypes although subtype B is less prevalent.

Discovery of HIV

AIDS was first recognized in the United States in June 5, 1981. There were rare opportunistic infections observed unusual clusters of Pneumocystis pneumonia (PCP) caused by a form of Pneumocystis carinii (now recognized as a distinct species Pneumocystis jirovecii) in five homosexual men in Los Angeles. PCP clusters were found among healthy men in cities throughout the country along with other opportunistic diseases such as Kaposi's sarcoma and persistent generalized lymphadenopathy. It was reported among gay men in Southern California in 1982 that a sexually transmitted infectious agent might be the etiological agent. The syndrome was initially termed as GRID or gay related immune deficiency. It was identified by health authorities that some people with the syndrome were not homosexual men. The same opportunistic infections were found among hemophiliacs heterosexual intravenous drug users. The disease was named by CDC as AIDS by august 1982. A new retrovirus[14] from lymphoid ganglions was isolated by doctor's from Dr. Luc Montagnier's team at the Pasteur Institute in France in May 1983. It was suspected that the virus was the cause of AIDS. The virus was later named lymphadenopathy associated virus (LAV). Robert Gallo et al.[15] of United States confirmed the discovery of the virus, but they called it as human T-lymphotropic virus type III (HTLV-III) in May 1984. The International Committee on Taxonomy of Viruses named the virus as HIV (Human Immunodeficiency Virus) in May 1986. Francoise Barre Sinoussi and Montagnier were awarded Nobel Prize in Physiology or Medicine for their discovery of human immunodeficiency virus in 2008.

Signs and symptoms

These symptoms usually disappear within a week to a month and are often mistaken for another viral infection such as flu. However during this period people are highly infectious because HIV is present in large quantities in genital fluids and blood. Some people infected with HIV may have more severe symptoms at first or symptoms that last a long time while others may have no symptoms for 12years.

Acute infection

The initial period following the contraction of HIV is called acute HIV, primary HIV or acute retroviral syndrome. Many patients feel an influenza like illness or a mononucleosis like illness 2-4weeks post exposure while others have no significant symptoms. Symptoms[16] occur in 40-90% of cases and most commonly include fever, large tender lymph nodes, throat inflammation, a rash, headache, sores of the mouth and genitals etc. There is presence of rash on the trunk and is maculopapular classically among 20-50% of patients. Some patients develop opportunistic infections at these stage gastrointestinal symptoms such as nausea, vomiting or diarrhea may occur as may neurological symptoms of peripheral neuropathy or guilain barre syndrome.

Clinical latency

The initial symptoms are followed by a stage called clinically latency, asymptomatic HIV or chronic HIV. If there is no treatment this second stage of the natural history of HIV infection can last from about threeyears to over 20years(on average about 8years). Initially patient experiences no symptoms but at the end of the stage patient feels fever, weight loss, gastrointestinal problems and muscle pains. There is persistent generalized lymhadenopathy characterized by unexplained, on painful enlargement of more than one group of lymph nodes(other than in the groin) for over three to sixmonths among 50 to 70% of patients. Most HIV-1 infected patients have a detectable viral load and in the absence of treatment will eventually progress to AIDS, a small proportion(about 5%) retain high levels of CD4+T cells (T helper cells) without antiretroviral therapy for than 5years.

Acquired immunodeficiency syndrome

Acquired Immunodeficiency Syndrome (AIDS) is defined in terms of either a CD4+T cell count below 200 cells per μL or the occurrence of specific diseases in association with an HIV infection. The most common initial conditions of AIDS are pneumocystis pneumonia (40%), cachexia in the form of HIV wasting syndrome (20%) and esophageal Candidiasis. Other common signs include recurring respiratory tract infections. Opportunistic infections may be caused by bacteria, viruses, fungi and parasites. These infections affect nearly

every organ system e.g. brain, eye, liver, genitals, skin etc. Patients with AIDS have an increased risk of developing various viral induced cancers including Kaposi's sarcoma,[17] Burkitt's lymphoma, primary central nervous system lymphoma and cervical cancer. Additionally patients have systemic symptoms such as prolonged fevers, sweats (particularly at night), swollen lymph nodes, chills, weakness and weight loss. Diarrhea is another common symptom present about 90% of patient with AIDS.

HIV

The human immunodeficiency virus (HIV) is a retrovirus belonging to the family of lenti viruses. Retroviruses use their RNA and host DNA to make viral DNA and are known for their long incubation periods. The HIV infects the body has a long incubation period(clinical latency) and ultimately causes the signs and symptoms of disease AIDS.HIV consists of a cylindrical center surrounded by a sphere shaped lipid bilayer envelope. There are two major viral glycoprotein's in this lipid bilayer gp120 and gp41.[18] The major function of these proteins is to mediate recognition of CD4+ cells and chemokine receptors thereby enabling the virus to attach to and invade CD4+ cells. The inner sphere contains two single stranded copies of the genomic material RNA as well as multiple proteins and enzymes necessary for HIV replication and maturation p24, p17 reverse transcriptase integrase and protease. HIV uses nine genes to code for the necessary proteins and enzymes. The three principal genes are gag, pol and env. The gag gene encodes core proteins. The pol gene encodes the enzymes reverse transcriptase, protease and integrase. The env gene encodes the HIV structural components known as glycoproteins. The rest of the genes rev, nef, vif, vpu, vpr and tat are important for viral replication[19] and enhancing HIV's infectivity rate. Host cells infected with HIV have a shortened life span as a result of the virus's using them as factories to produce multiple copies of new HIV. Thus HIV continuously uses new host cells to replicate itself. As many as 10million to 10billion virions (individual viruses) are produced daily. In the first 24h after exposure HIV attacks or is captured by dendritic cells in the mucous membranes and skin. Within 5days after exposure these infected cells make their way to the lymph nodes and eventually to the peripheral blood where viral replication becomes rapid. CD4+lymphocytes that are recruited to respond to viral antigen migrate to the lymph nodes. These become activated and then proliferate via complex interaction of cytokines released in the microenvironment of the lymph nodes. This sequence of events makes the CD4+ cells more susceptible to HIV interaction and it explains the generalized lymphadenopathy characteristic of the acute retroviral syndrome seen in adults and adolescents. In contrast HIV infected monocytes allow viral replication but resist killing. Thus monocytes act as reservoirs of HIV and as effectors of tissue damage in organs such as the brain.

Stages of HIV infections

There are two main clinical staging systems used to classify HIV and HIV related disease for surveillance such as the WHO disease staging system for HIV infection and disease and the CDC classification system for HIV infection. The CDC's classification system is more frequently adopted in developed countries.

The WHO system uses the following categories[20]

Primary HIV infection or acute retroviral syndrome

Primary infection refers to the time when HIV first enters the body. There are many viruses present in the blood of patients at the time of primary infection of HIV. The signs and symptoms of acute retroviral syndrome are fever, myalgia (muscle pain), headache, nausea, vomiting, diarrhea, night sweats, weight loss and rash. It occurs 2-4weeks after infection, subside after a fewdays and often are misdiagnosed as influenza or infectious mononucleosis. The CD4+ count in the blood falls remarkably but rarely drops to less than 200cells/μL during primary infection. The number of copies of virus per milliliter of plasma or blood can exceed 1million. The HIV attacks CD4+ cells in the lymph nodes and the thymus during this time. The patient is more vulnerable to opportunistic infection.

Stage I

Clinical latency/Asymptomatic disease (Clinical stage 1): HIV infection is asymptomatic with a CD4+T cell count greater than 500 per microlitre (μl or cubic mm) of blood. It includes generalized lymph node enlargement. During clinical stage 1 immune system generates antibodies in an attempt to protect itself from HIV. The viral set point is established during this time. Patients with higher viral load set points tend to exhibit more rapid disease progression than those with lower viral load set points. During latency HIV-infected patients experiences persistent lymphadenopathy is common. In HIV infected adults, this phase may last 8-10years.

Stage II

Mild Signs and Symptoms of HIV (Clinical stage 2): In clinical stage 2 patients suffers from mucocutaneous manifestations and recurrent upper respiratory tract infections. HIV-infected patient feels to be healthy foryears, but then minor signs and symptoms of HIV infection begins to appear. Patients suffer from candidiasis, lymphadenopathy, molluscan contagiosum, persistent hepatosplenomegaly, popular pruritic eruptions, herpes zoster, peripheral neuropathy etc. The viral load increases and the CD4+ count falls is between 350-499/μl in children older than 5years.

Stage III: Advanced signs and symptoms of HIV (clinical stage 3)

In clinical stage 3 patients suffers from severe bacterial infections including tuberculosis of the lung. During this period CD4+ cell count falls to 350/μl. The patients with weakened immune systems develop life threatening infections. The common symptoms are development of cryptosporidiosis, pulmonary and lymph node tuberculosis, wasting, persistent fever (longer than one month), persistent Candidiasis, recurrent bacterial pneumoniaor other opportunistic infections etc. Patients loss their weight significantly. Their viral increases and the CD4+ count falls to less than 200-349cells/μl in children older than 5years.

Stage IV or AIDS

During this period CD4+ cell count falls to 200/μl. In this stage patient observes severe symptoms such as toxoplasmosis of the brain, candidiasis of the esophagus, trachea, bronchi or lungs and kaposi's sarcoma. Patients also develop new opportunistic infections such as pneumocystis jirovecii pneumonia (formerly Pneumocystis carinii pneumonia) cytomegalo virus infection, mycobacterium avium complex, cryptococcal meningitis, progressive multifocal leukoencephalopathy and other infections. At this point in the disease course death can be imminent.

The CDC system uses the following categories:[21] The United States

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Center for Disease Control and Prevention classifies HIV infections based on CD4 count and clinical symptoms updated it in2008. The stages are

Stage 1: CD4 count ≥500 cells/µl and no AIDS defining conditions

Stage 2: CD4 count 200 to 500 cells/µl and no AIDS defining conditions

Stage 3: CD4 count ≤200 cells/µl and AIDS defining conditions

Transmission

HIV is transmitted by sexual contact, exposure to infected body fluids or tissues and from mother to child during pregnancy, delivery or breastfeeding (vertical transmission). There is no risk of acquiring HIV if exposed to feces, nasal secretions, saliva, sputum, sweat, tears, urine or vomit unless these are contaminated with blood. It is possible to be co infected by more than one strain of HIV a condition known as HIV superinfection.HIV can be isolated from virtually all body fluids of HIV infected persons including blood, sweat, tears, saliva, semen, vaginal fluids and breast milk. The virus has been found in abundance in infected blood and semen. So far only blood, semen, vaginal fluids and breast milk have been implicated in transmission.

Sexual transmission

In worldwide the most frequent mode of transmission of HIV through sexual[22] contact with an infected person. The majority of all transmissions worldwide occur through heterosexual contacts, with regard to unprotected homosexual contacts, estimates of the risk of HIV transmission per sexual act appear to be 4 to 10times higher in low in countries than in high income countries. The risk of transmission from anal intercourse is especially high, estimated as 1.4-1.7% per act in both heterosexual[23] and homosexual[24] contacts. The risk of transmission from oral sex is relatively low, but it is still present. The risk of transmission from oral sex is estimated at 0-0.04% for receptive oral intercourse. There is low risk of transmission of other sexually transmitted infections such as gonorrhea, chlamydia, trichomoniasis, bacterial vaginosis etc. Commercial sex workers have high risk of transmission of HIV. Rough sex also increases the transmission of HIV.

Parenteral transmission

The frequent mode of HIV transmission is via blood and blood products. Blood borne transmission[25] occurs by needle sharing during intravenous drug use, needle stick injury, transfusion of contaminated blood or blood product or medical injections with unsterilized equipment. There is risk of HIV transmission from recipients of body organs/semen/other body tissues from an HIV infected donor.[26] There is chance of infection from giving or receiving tattoos, piercings and scarification. It is not possible for mosquitoes or other insects to transmit HIV.

Vertical transmission

The transmission of HIV occurs from mother to child during pregnancy, during delivery or through breast milk.[27] Without treatment the risk of transmission before or during birth is around 20% and in those who also breast feed 35%. With treatment the risk of mother to child infection reduces up to about 1%. Preventive treatment involves the mother taking anti retroviral during pregnancy and delivery an elective caesarean section, avoiding breast feeding and administering antiretroviral drugs to the new born.[28]

Diagnosis

HIV infected patient develops specific antibodies (i.e. seroconvert) within 3 to 12weeks of initial infection. Diagnosis of primary HIV before seroconversion is done by measuring HIV-RNA or p24 antigen. Antibody tests in children younger than 18months are inaccurate because of the presence of maternal antibodies. Hence HIV infection can only be diagnosed by PCR testing for HIV, RNA or DNA or via testing for the p24 antigen. There are many tests available for the diagnosis of AIDS such as ELISA test, saliva test, viral load test etc.[29,30]

ELISA test/enzyme linked immune sorbent assay

The blood sample of patient is taken and it is gone for ELISA test. If the test is positive the western blot test is usually administered to confirm the diagnosis. If the test is negative it should be tested again in one to threemonths. ELISA test is very sensitive to HIV infection, but antibodies are not produced immediately upon infection. Hence the test may show negative during a window of a fewweeks to a fewmonths after being infected. But it may have a high level of the virus and be at risk of transmitting infection.

Saliva tests

A cotton pad is placed to obtain saliva from the inside of the cheek. The pad is kept in a vial and submitted to a laboratory for testing. Results are available in 3days. Positive results should be confirmed with a blood test.

Viral load test

This test determines the amount of HIV in patient's blood. It is used to control treatment progress or detect early HIV infection. The technologies measure HIV viral load in the blood are reverse transcription polymerase chain reaction (RT-PCR), branched DNA (BDNA) and nucleic acid sequence based amplification assay (NASBA).HIV is detected using DNA sequences that bind specifically to those in the virus.

Prevention of AIDS

Sexual contact

Male and female condoms[31] are effective at preventing sexual transmission of HIV. Regular condom use reduces the risk of HIV transmission by approximately 80% over the long term. By consistent use of condoms by a couple in which one person is infected the rate of HIV infection is less than 1% per year. Female condoms[32] provide an equivalent level of protection to partners. It is observed that by application of a vaginal gel containing tenofovir[33] immediately before sex seems to reduce infection rates by approximately 40% among African women. Male circumcision is a method of preventing female to male HIV transmission in 2007 recommended by WHO and UNAIDS.[34] Comprehensive sexual education should be provided at school to decrease high risk behavior.

Pre exposure prophylaxis

By treating with antiretroviral protects 96% of their partners from infection whose CD4 count ≥350cells/µL in blood. There is about a 10 to 20 fold reduction in transmission risk among patients. Pre exposure prophylaxis (PrEP) with daily dose of the medications tenofovir with or without emtricitabine is effective in a number of groups including men who have sex with men couples where one

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is HIV positive and young heterosexuals in Africa. It is effective to decrease the risk of HIV by taking universal precautions within the health care environment.[35,36] The needle exchange programmes and opoid substitution therapy may effective in decreasing the HIV transmission for intravenous drug users.

Post exposure prophylaxis

It is known as post exposure prophylaxis (PEP) when a course of antiretroviral is administered within 48 to 72hours after exposure to HIV positive blood or genital secretions.[37] Zidovudine reduces the risk of a HIV infection fivefold following a needle stick injury.[38] The prevention regimen recommended in the United States consists of three medications such as tenofovir, emtricitabine and raltegravir. The duration of treatment is usually fourweeks and frequently associated with adverse effects.

Mother to child

There is reduction of vertical transmission of HIV by using a combination of antiretroviral medications during pregnancy and after birth in the infant and potentially includes bottle feeding rather than breastfeeding.[39] If replacement feeding is acceptable, feasible, affordable, sustainable and safe mothers should avoid breastfeeding to their infants. If exclusive breastfeeding is carried out the provision of extended antiretroviral prophylaxis to the infant decrease the risk of transmission.

Effective options for preventing mother to child transmission[40]

A) Prevention of acquisition of infection in women of child bearing age

   i. Behavioral changes, immediate and permanent

B) Prevention of transmission from HIV infected women to their infants

   i. Voluntary counseling and testing services

   ii. Identification of uninfected women

   iii. Does it reduce child mortality?

C) Reducing maternal peripheral viral load

   i. Antiretroviral therapy during pregnancy, delivery or post partum

   ii. Monotherapy or combination therapy

D) Avoidance of exposure to contaminated maternal secretions

   i. Delivery by elective caesarean section

   ii. Cleansing of birth canal

   iii. Modification of infant feeding practices

E) Boosting host defence

   i. Micronutrient supplementation

   ii. Immune therapy (passive or active)

Vaccination

With most vaccine preventable diseases, naturally occurring (or vaccine induced) immune responses correlate with protection against infection or disease. In contrast, even though most people infected with HIV develop a broad range of immune responses against the virus, these responses neither eliminate the infection nor prevent progression to AIDS. Ongoing HIV vaccine[41] development strategies are targeted at the two major types of immune responses, humoral and cells mediated immunity, and include strategies to induce both of them. A single trial of vaccine RV 144 published in 2009 found a partial reduction in the risk of transmission of roughly 30% stimulating some hope in the research community of developing a truly effective vaccine.[42]

Management

There is currently no cure or effective HIV vaccine. Treatment consists of antiretroviral therapy (ART), opportunistic infections and alternative medicine.

Antiviral therapy

These are various classes of drugs which are usually used in combination to treat HIV infection. The combination use of drugs can be termed anti retroviral therapy (ART), combination anti retroviral therapy (CART), or highly active anti retroviral therapy (HAART). Anti retroviral drugs are broadly classified by the phase of the retrovirus life cycle. The types of antiretroviral therapies are non-nucleoside reverse transcriptase inhibitors, nucleoside reverse transcriptase inhibitors, protease inhibitors, integrase inhibitors, fusion inhibitors and combination therapy.[43–45]

Non-nucleoside reverse transcriptase inhibitors (NNRTIs)

It inhibits reverse transcriptase by binding to an allosteric site of the enzyme. It acts as non competitive inhibitor of reverse transcriptase. It affects the handling of substrate (nucleotide) by reverse transcriptase by binding near the active site. It can be classified into 1st generation NNRTIs and 2nd generation NNRTIs. 1st generation NNRTIs include nevirapine and etravirine. 2nd generation NNRTIs are etravirine and rilpivirine. NNRTIs are shown in Table 1.

Nucleoside reverse transcriptase inhibitors (NRTIs)

It inhibits reverse transcription. NRTIs are chain terminators such that once incorporated work by preventing other nucleosides from also being incorporated into the DNA chain because of the absence of a 3' OH group. NRTI's are represented in Table 2.

Protease inhibitors (PIs)

It blocks the viral protease enzyme necessary to produce mature virions upon budding from the host membrane. It prevents the cleavage of gag and gag/pol precursor proteins. PIs are represented in Table 3.

Integrase inhibitors(IIs)

It is known as integrase nuclear strand transfer inhibitor. It inhibits the viral enzyme integrase which is responsible for integration of viral DNA into the DNA of infected cell. IIs are shown in Table 4.

Fusion inhibitors (Entry inhibitors)

It interferes with binding, fusion and entry of HIV-1 to the host cell by blocking one of several targets. Fusion inhibitors are represented in Table 5.

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Table 1 FDA approved medications for Non-nucleoside reverse transcriptase inhibitors (NNRTIs)

Generic name	Adult dose (mg)/day	Half life(hr)	Brand name	Manufacturer	FDA approval date
Delavirdine	400(3)	5.8	Rescriptor	ViiV Healthcare	April4,1997
Efavirenz	600(1)	48	Sustiva	Bristol-Myers Squibb	Sept.17,1998
Etravirine	200(2)	41	Intelence	Tibotec	Jan18,2008
Nevirapine	200(1)first 14days then 2times daily	25	Viramune	Boehringer Ingelheim	June21,1996
Rilpivirine	25-150(3)	50	Edurant	Janssen Pharmaceuticals, Inc	May 20,2011

Table 2 FDA approved medications for nucleoside reverse transcriptase inhibitors (NRTIs)

Generic name	Adult dose(mg)/ day	Half life(hr)	Brand name	Manufacturer	FDA approval date
Zidovudine	200(3)	1.1	Retrovir	GlaxoSmithKline	March19,1987
Abacavir	300(2)	1.5	Ziagen	ViiV Healthcare	Dec.17,1998
Lamivudine	150(2)	5	Epivir	GlaxoSmithKline	Nov.17,1995
Stavudine	30-40(2)	1.4	Zerit	Bristol Meyers Squibb	June 24,1994
Zalcitabine	0.75(3)	2	Hivid	Hoffmann La Roche	Mar.19,1992
Didanosine	200(2)	1.4	Videx Videx EC	Bristol Meyers Squibb	Oct.9,1991
Tenofovir disoproxil fumarate	300(1)	17	Viread	Gilead Sciences	Oct.26,2001
Emtricitabine	200(1)	10	Emtriva	Gilead Sciences	July 2,2003

Table 3 FDA approved medications for protease inhibitors (PIs)

Generic name	Adult dose(mg)/day	Half life(hr)	Brand name	Manufacturer	FDA approval date
Atazanavir	300(1)	8.6	Reyataz	Bristol Meyers Squibb	June20,2003
Indinavir	800(3)	1.5	Crixivan	Merck	March13,1996
Darunavir	600(2)	15	Prezista	Janssen Cilag Pty Ltd.	June 23,2006
Fosamprenavir	1400(2)	7.7	Lexiva	ViiV Healthcare	Oct.20,2003
Nelfinavir	1250(2)	2.6	Viracept	ViiV Healthcare	March14,1997
Ritonavir	600(2)	5-Mar	Novir	Abbot Laboratories	March1,1996
Tipranavir	500(2)	5.5-6	Aptivus	Boehringer Ingelheim	June 20,2005
Saquinavir	1200(3)	3	Invirase	Hoffmann La Roche	Dec.6,1995

Table 4 FDA approved medications for integrase inhibitors (IIs)

Generic name	Adult dose(mg)/day	Half life(hr)	Brand name	Manufacturer	FDA approval date
Raltegravir	400(2)	9	Isentress	Merck	Oct.12,2007

Table 5 FDA approved medications for fusion inhibitors (Entry inhibitors)

Generic name	Adult dose(mg)/day	Half life(hr)	Brand name	Manufacturer	FDA approval date
Enfuvirtide	90(2) Subcutaneously	3.8	Fuzeon	Hoffmann La Roche	March 13,2003
Maraviroc	400(2)	16	Selzentry	Pfizer	Aug.6,2007

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Combination therapy / fixed dose combinations(FDCs)

Fixed dose combinations are multiple anti retrovirals drugs combined into a single pill. Antiretroviral combination therapy defends against resistance by suppressing HIV replication as much as possible, thus reducing the potential pool of spontaneous resistance mutations. Combinations of antiretroviral create multiple obstacles to HIV replication to keep the number of offspring low and reduce the possibility of a superior mutation. If a mutation that conveys resistance to one of the drugs being taken arises, the other drugs continue to suppress reproduction of that mutation. FDCs are represented in Table 6.

Table 6 FDA approved medications for fixed dose combinations

Generic name	Brand name	Manufacturer	FDA approval date
Zidovudine+Lamivudine	Combivir	GlaxoSmithKline	Sept.26,1997
Abacavir+Lamivudine	Epzicom(USA), Kivexa (Europe)	GlaxoSmithKline	Aug.2,2004
Abacavir+Zidovudine =+Lamivudine	Trizivir	GlaxoSmithKline	Nov.15,2000
Lopinavir+ritonavir	Kaletra	Abbot Laboratories	Sept.15,2000
Tenofovir+Emtricitabine	Truvada	Gilead Sciences	August 2,2004
Efavirenz+Tenofovir +Emtricitabine	Atripla	Gilead Sciences and Bristol Meyers Squibb	12-Jul-06
Rilpivirine+Tenofovir +Emtricitabine	Complera	Gilead Sciences and Tibotec	August 10,2011
Elvitegravir+Cobicistat =+Tenofovir/Emtricitabine	Stribild	Gilead Sciences	August 27.2012
Dolutegravir+Abacavir/ Lamivudine	Triumeq	ViiV Healthcare	August 22,2014

Opportunistic infections of AIDS

Without effective antiretroviral treatment over time HIV destroys[46] immune system of patient and makes much more vulnerable to opportunistic infections. As a result of which significant morbidity in both developed countries and developing countries. The common symptoms of opportunistic infections[47] with AIDS are coma, coughing, shortness of breath, painful swallowing, confusion, nausea, abdominal cramps, fever, weight loss, and diarrhea etc. Treatment with antiretroviral reduces the risk of developing additional opportunistic infections. It is advised to take vaccine against hepatitis A and hepatitis B before or after to the patient. It is recommended to take trimethoprim/sulfamethoxazole prophylaxis between 4 to 6weeks of rage and ceasing breast feeding in infants born to HIV positive mothers.

Alternative Medicine for AIDS

By taking good diet and micronutrient supplements patient has improved health condition. There is some advantages of vitamin A supplementation in children that reduces mortality and improves growth. There is improvement of health condition to lactating mothers when a multivitamin supplement[48] is given. Evidence for supplementation with selenium is mixed with some tentative evidence of benefit. Dietary intake of micronutrients at RDA levels by HIV-infected adults is recommended by the World Health Organization. The WHO further states that several studies indicate that supplementation of vitamin A, zinc, and iron can produce adverse effects in HIV positive adults. There is insufficient evidence to recommend or support the use of medical cannabis to try to increase appetite or weight gain. Herbal compounds are used for treatment of HIV/AIDS which are given below.[49] Some plant species which are used for AIDS are represented in Table 7.

Table 7 Plant species used to treat and manage AIDS

Species name	Family	Growth habit	Part(S) used	Pharmacological activity
Allium sativum L.	Amaryllidaceae	Herb	Bulb	HIV-1 revese transcriptase
Mangifera indica L.	Anacardiaceae	Tree	Bark/leaves	Inhibits HSV-1 and 2 replication
Artemisia annua L.	Asteraceae	Shrub	Leaves	Anti-HIV activity
Raphanus sativus L.	Brassicaceae	Herb	Leaves	Anti viral activity
Carica papaya L.	Caricaceae	Tree	Leaves/roots/seeds	Anti HIV-1 activity
Cleome gynandra L.	Cleomaceae	Herb	Leaves	Anti HIV activity

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Table Continued..

Species name	Family	Growth habit	Part(S) used	Pharmacological activity
Cucurbita maxima L.	Cucurbitaceae	Climber	Leaves	Anti HIV activity
Euphorbia tirucalli L.	Euphorbiaceae	Shrub	Leaves	Anti HIV activity
Dichrostachys cinerea L.	Fabaceae	Shrub	Leaves	Inhibits HIV-1 reverse transcriptase
Ocimum basilicum L.	Lamiaceae	Herb	Leaves	Inhibits HIV-1 reverse transcriptase
Azadirachta indica A.	Meliaceae	Tree	Leaves	Inhibits HIV-1 replication and protease
Moringa oleifera Lam.	Moringaceae	Shrub	Leaves/seeds	Anti HIV activity
Eucalyptus globules Labil.	Myrtaceae	Tree	Leaves	Anti HSV-1 and 2 activity
Ximenia Americana L.	Oleaceae	Shrub	Bark/root	Inhibits HIV-1 replication
Passiflora edulis Sims	Passifloraceae	Climber	Leaves	Anti HSV-1 activity
Citrus lemon L.	Rutaceae	Tree	Leaves/roots/fruits	Anti HIV-1 activity
Solanum americanum L.	Solanaceae	Shrub	Leaves	Anti viral activity
Aloe vera L.	Xanthorrhoeaceae	Herb	Leaf sap/leaves	Anti HSV-2 activity
Bulbine alooides L.Wild	Xanthorrhoeaceae	Herb	Leaves/roots	Anti HIV activity
Zingiber officinalis L.	Zingiberaceae	Herb	Bulb	Anti HIV-1 activity

Conclusion

Sexually transmitted infections including HIV/AIDS are a major source of morbidity and mortality in the world. HIV/AIDS is one of the biggest problems that has puzzled the medical world, this is because AIDS is life threatening and as of present there is no cure for disease but it can be controlled. AIDS is the most advanced stage of HIV infection. Antiretroviral therapy (ART) recommended treatment for HIV. ART involves taking a combination of three or more anti-HIV medications from at least two different drug classes every day to control the virus. It is better to control AIDS by taking preventive measure, awareness among people regarding AIDS.

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Conflict of interest

Author declares that there is no conflict of interest.

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