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REVIEW ON HIV AND AIDS DISEASE

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ABSTRACT

This review covers key aspects of HIV and AIDS, including genetic diversity, viral structure, life cycle, transmission, infection mechanisms, clinical symptoms, diagnostic methods, and the central role of Antiretroviral Therapy (ART). Emphasis is placed on ART as the standard treatment, detailing commonly used drugs and highlighting the significance of treatment adherence. The review also addresses preventive strategies, providing a concise yet comprehensive overview for healthcare professionals, researchers, and policymakers involved in the fight against HIV/AIDS.

❖ The Main Objective Are

1) To comprehensively explore and analyze the genetic diversity of HIV, elucidating the various strains and their implications on transmission and treatment.
2) Investigate the structural intricacies of HIV, examining how its unique features contribute to the virus's resilience and adaptability.
3) Examine the life cycle of HIV, from initial transmission to replication within host cells, providing a thorough understanding of the key stages in the virus's progression.
4) Explore the mechanisms of HIV transmission, shedding light on the various routes by which the virus spreads and identifying critical points for intervention.
5) Investigate the intricate processes involved in HIV infection, delving into the ways the virus interacts with the host's immune system and initiates disease progression.
6) Analyze the diverse symptoms associated with HIV infection, highlighting the variability in manifestations and their implications for diagnosis and management.
7) Evaluate the efficacy of antigen/antibody testing in diagnosing HIV, exploring its role in early detection and monitoring of the infection.

8) Assess the principles and practices of antiretroviral therapy (ART) for managing HIV infection, emphasizing its role as the standard treatment and its impact on patient outcomes.
9) Examine commonly used antiretroviral drugs in clinical practice, detailing their mechanisms of action, side effects, and overall significance in HIV treatment.
10) Investigate the critical importance of treatment adherence in managing HIV infection, exploring the impact of consistent therapy on viral suppression and long-term outcomes.
11) Explore preventive strategies for HIV and AIDS, encompassing both behavioral interventions and biomedical approaches, to provide a comprehensive overview of the multifaceted efforts in curbing the spread of the virus.

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 week. 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]

Human immunodeficiency virus (HIV), causes Acquired Immune deficiency Syndrome (AIDS). It is one of the mortal diseases known to the humankind. The estimated number of people living with HIV is 37.7 Milionis worldwide and about 25.5 Million estimated in Sub Sahara alone (SSA). Among them, 34.9 are adults and 17.8 from this population are women and 1.8 Millions are children under 15 years old. During 2015, it is estimated that 2.1 Million people are newly infected. From the 2.1 million newly infected, 1.4 million are in Africa alone. Among the global HIV/AIDS related deaths which were 1.1 million during 2015,

800,000 of them are from Africa. When looking at the prevalence of HIV among adults aged 15 to 49 globally the percentage is 0.8%, while Africa holds 4.4% of prevalence in the same population. It is evident that Sub-Sahara Africa carries the heaviest burden of the HIV. Two genetically distinct species of HIV exist- HIV-1 and HIV-2, which tough are differ in the epidemiology, they are similar in terms of pathogenicity and both can lead to AIDS. The importance of the distinction when it comes to the SSA context is the fact that HIV-2 is relatively endemic to West Africa alone, with other specific and limited geographical regions outside of the continent. HIV-1 on the other hand is considered more of pandemic, thus receives more attention from the scientific community than the HIV-2. HIV-1 is further subdivided in to strains, which are each representing different pathogenesis speeds and risk factors. Pathogenicity of HIV has been observed with infections such as Tuberculosis (TB), Hepatitis B and C, and parasitic like Malaria and Leishmania, some of which are spread through out the SSA. Moreover, co-infection with more than one strain of HIV is possible too. The new combination of the different strains can lead to viral recombination which than new recombinant form and be passed on to another individual. This phenomenon was reported in several geographical areas in different continents alongside with reports about coinfection with two distinct main groups of HIV (i.e. group M and group O).[2]

Numerous studies on the biology, pathophysiology or therapy of HIV-associated malignancies are single-center experiences with few randomized controlled trials. Hence, multi institutional collaboration is mandatory. AIDS Malignancy Consortium (AMC) is a clinical trials group supported by the National Cancer Institute, specifically focused on performing clinical and laboratory studies in HIV/AIDS patients with cancer. Concern for HIV infected patients extend beyond medical and psychiatric complications. Many caregivers develop symptoms of depression and anxiety leading them to burnout and also there was high level of depression in HIV patients. Hence every HIV patients attending the clinic should also be assessed thoroughly for depression. When there is no effective HIV vaccines, behavior change is the key to prevention efforts. Social Health Insurance consultancy program delivered by nurse's support to increase HIV patients' willingness to obtain it.

Huge proportions of students were involved in multiple sexual partners and unprotected sex. Several factors such as income deficit, Pre-college residence, pornographic film viewing and believe in sexual abstinence for HIV prevention were found to be significant predictors of initiating premarital sex. Younger generations could be advised to maintain the virginity as

cultural norm and use of condom during sex before marriage is to be suggested. Incorporation of sociostructural elements and geospatial techniques in analytical approaches would lead to better understanding of local dynamics and develop mediations that increase our facility of targeted HIV prevention services. Assumed disgrace seems to play a large role in HIV revelation decision making and that mediation to reduce internalized HIV stigma may support in efforts to increase HIV disclosure and thus reduce secondary transmission of HIV.[3]

Oral health can offer clues to various systemic disorders affecting the individuals, one such disease being HIV/AIDS. Oral lesions are not only indicators but can also be predictors of the progression of this disease, as well as its response to treatment. No oral lesion is unique to HIV. However, certain lesions are strongly associated with this disease. Seven cardinal lesions associated with HIV are oral candidiasis, necrotizing ulcerative gingivitis, necrotizing ulcerative periodontitis, linear gingival erythema, hairy leukoplakia, Kaposi's sarcoma (KS), and non-Hodgkin lymphoma.7 Even though various treatment modalities have been instituted, till date no medication has been able to eradicate this infection in totality. However, there is a deceleration in the death rate due to education and emergence of ARTs. Since the advent of highly active antiretroviral therapy (HAART) there has been a drastic reduction in the incidence of most HIV/AIDS-related oral lesions and an increase in life expectancy. Highly active antiretroviral therapy suppresses the viral multiplication and increases the CD4 cell count. If instituted in the early stage of the disease, HAART can also improve the quality of life of an individual. The therapy includes a combination of nucleoside reverse transcriptase inhibitors (NRTIs), non-NNRTIs, protease inhibitors, fusion inhibitors, entry inhibitors, and HIV integrase inhibitors.8 Studies pertaining to the oral manifestations of HIV/ AIDS patients on HAART therapy are sparse. Hence, the present study was undertaken with the aim of evaluating the oral manifestations in HIV/AIDS patients on HAART.[4]

❖ Genetic Diversity of HIV

Two genetically distinct viral types of HIV have been identified. HIV-1 is the type associated with disease in the United States, Europe, central Africa, and most other parts of the world. HIV-2 has been found mainly in infected individuals in western Africa and is very similar to HIV-1 in that it has the same tropism for cells of the immune system and causes illness that results from immune deficiency. All HIV types and subtypes are thought to be derived from zoonotic introductions from nonhuman primates. HIV-1 variants are classified into three

major groups: group M (main), group O (outlier), and group N (non-M/non-O). Group M, which is responsible for the majority of infections in the worldwide HIV-1 epidemic, can be further subdivided into 10 subtypes, or clades (A to K). Sub-subtypes and circulating recombinant forms (CRFs) have emerged over the past few decades. Genetic variation for HIV-1 is especially high, with rapid turnover of HIV-1 virions. Over 20 different CRFs have been defined within group M alone. The HIV-1 subtypes C and A account for the majority of HIV cases in the pandemic, but the other viral forms circulate globally. HIV-1 subtype B is predominant in North America, Western Europe, and Australia. Information garnered from the study of the biophysical, biochemical, and in vitro studies of the HIV-1 subtype B was used to develop the antiretroviral drugs we currently have available. However, subtype B only accounts for only a small portion of the virus subtypes comprising the HIV pandemic. The proliferation of these various viral forms has serious implications for the feasibility of vaccine development and will have a major impact on diagnostic testing, monitoring, and treatment.[5]

- **HIV SUBGROPUS**

Prevalence of 0.06% which identified in the pregnant women in France.

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-Sahara region. Group B is found in the Ivory Coast's.

HIV-1

HIV-1 is 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. Group N is less prevalent which is reported only from Cameroon. Whereas Group O is 1% of total HIV-1 cases which is found mainly in Gabon and Cameroon. and Group P is found very rarely with categorized as dead- ends transmissions that produce no infection due to the sporadic nature. 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.[1]

- **Table Difference between HIV-1 and HIV-2 (Table No 1.)**

HIV-1	HIV-2
This strain is found in all over world and is very common.	This strain is found in West Africa.
Its most likely to get progress and which get more worse infections	This strain is less likely to get progress and many of those infected humans remain the lifelong non progression.
The immune system activation is higher at the average level	The immune system activation is lower at the average level
HIV -1 has lower level of CD4 count than HIV-2 during progression	CD4 counts are higher than HIV1 during progression
Viral load in plasma is higher	Viral load in plasma is lowe

❖ **Structure of HIV virus**

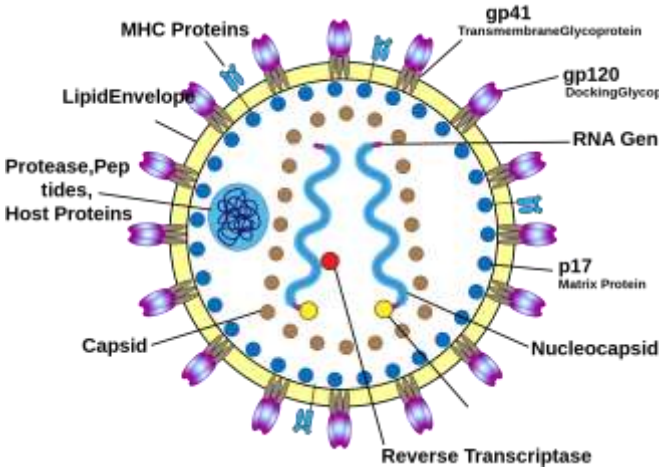

Fig. 1: Structure of HIV Virus.

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.

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.

RNA Gen

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

P17

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

Nucleocapsid

The HIV -1 nucleocapsid protein (NC) is a nucleic acid chaperone, which remodels nucleic acid structures so that the most thermodynamically stable conformations are formed. This activity is essential for virus replication and has a critical role in mediating highly specific and efficient reverse transcription.[6]

Reverse Transcriptase

Reverse transcription and integration are the defining features of the Retroviridae; the common name "retrovirus" derives from the fact that these viruses use a virally encoded enzyme, reverse transcriptase (RT), to convert their RNA genomes into DNA. Reverse transcription is an essential step in retroviral replication.[7]

Capsid

Assembled HIV-1 capsids are highly asymmetric cone-shaped structures, with sizes ranging from 100 to 200 nm long and 45 to 50 nm wide, that are made of pentamers and hexamers following Eberhard's theorem. The location of the pentamers induces high curvature and permits the closure of the capsid. Indeed, in the HIV-1 capsid seven pentamers are located at the base and five pentamers at the tip.[8]

Protease Peptides Host Protiens

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.

Lipid envelope

It is envelope through which virus binds.

MHC Protiens

Major Histocompatibility Complex (MHC) proteins play a crucial role in the immune system by presenting antigens to T cells, which are essential for recognizing and eliminating pathogens, including viruses like HIV. However, it's important to note that the HIV virus itself does not possess MHC proteins. Instead, MHC proteins are found on the surface of host cells that have been infected by the virus.[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. 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.[1]

Life cycle

The HIV virus gets attach to the CD4+ receptor and their co-receptors of the host cell (human cell). 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. 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. The activation of CD8+ T cell correlated +ve with the progression risk of AIDS. If the CD4+ cells are not activated it's possible that the virus continues to exist in latent stage for several years. 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.

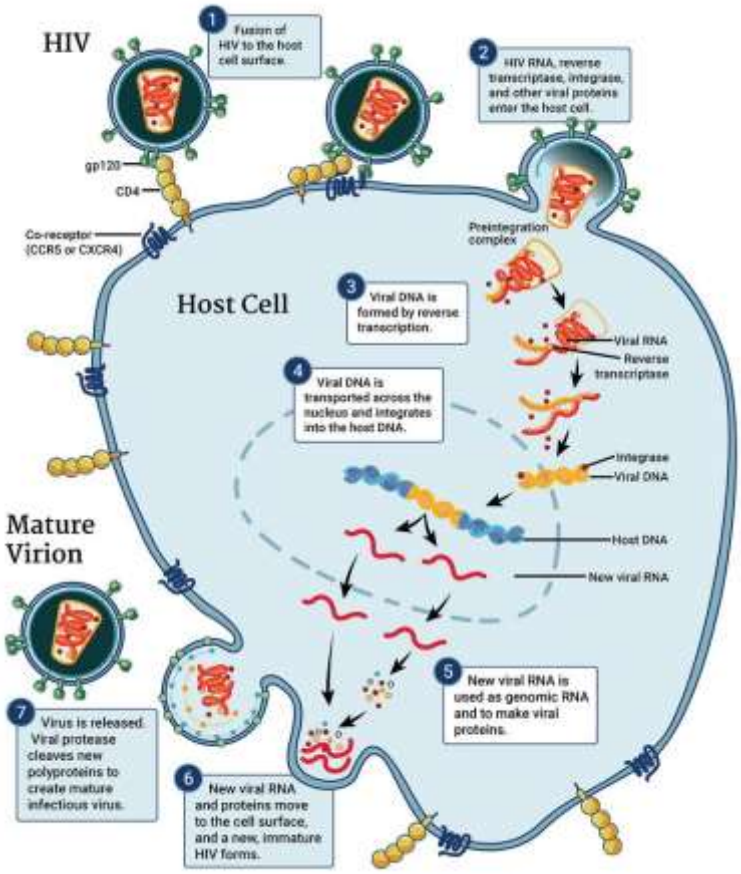

Figure No. 2: Life cycle of HIV.

The activated cell then later makes the viral protein by coping the DNA to RNA by process of transcription. The virus RNA transcripted 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 .The single cell can make 1000 of infectious particle of HIV.[1]

❖ **HIV transmission**

Human immunodeficiency virus (HIV) is transmitted when infected blood, semen, vaginal fluids, or breast milk enter another person's body. Once the virus enters the body, it can spread through target cells as a free viral particle or in cell-associated form. Cell-free virus, is the plasma virus, whereas cell-associated virus, is the intracellular progeny virion that has been produced but not yet budded off the manufacturing T-cell. In cell-associated viral spread, the processes of budding, attachment and entry, proceed quickly at the sites of cell-to-cell contact. This partially protects the virus from the hostile extracellular environment and also concentrates the viral particles at the sites of infection. In cell-free viral spread, the replicated viruses bud off from the producer cell, the virus has to diffuse and find a CD4 receptor on the $CD4^+$ T cell, attach to the cell and finally enter the cell. Infected blood, semen, vaginal secretions, and breast milk contain both cell-free and cell-associated virus.[10]

➢ Since the 1980s,

The routes of HIV transmission have been delineated

• Materno-fetal–child (MTC)

◦ In utero.

◦ Around the time of delivery.

◦ Via breast milk.

• Ano-rectal in men who have sex with men (MSM).

• Heterosexual in both directions (vaginal and penile infection).

• Injection in intravenous drug users (IVDU).

• Transfusion of HIV-infected blood products.

• Accidental inoculation, eg to health care workers.

• Organ transplantation.

Globally, most infections are heterosexual, but MSM transmission is rising in high-income countries, bringing with it unusual distal gut infections (see Gut infections, below). The clinical pathologies are different in the various HIV transmission groups, relating to co-infections and age at infection, eg the infrequency of Kaposi's sarcoma (KS) in IVDU and MTC patients, compared with MSM, provided a clue that it is a virus infection-related tumour.

The critical factor in the likelihood of HIV transmission is the HIV blood viral load in the infected partner, with a direct logarithmic relationship.[2] Viral load is highest early after infection, when persons are asymptomatic and even still antibody-negative, or at the time of seroconversion. Hence, multiple sexual contacts at this time are a significant contributor to spread of infection. Nearly all infections are with HIV type 1 (HIV-1, which has several clades, or subtypes, with varied virulences); HIV-2 derives from West Africa, is less common, and overall is less virule.[11]

❖ HIV infection Mechanism

HIV begins its infection by voluntary to the CD4 receptor on the host cell. CD4 is present on the surface of several lymphocytes, which are a serious part of the body's immune system. It is now known that a co-receptor is needed for HIV to enter the cell. Following combination of the virus with the host cell, HIV enters the cell. The genetic material of the virus, which is RNA, is free and undergo reverse transcription into DNA. An enzyme in HIV called reverse transcriptase is necessary to catalyze this change of viral RNA into DNA. Once the genetic material of HIV has been altered into DNA, this viral DNA enters the host cell nucleus where it can be combined into the genetic material of the cell. The enzyme integrase catalyzes this process. Once the viral DNA is incorporated into the genetic material of the host, it is promising that HIV may persist in certain latently infected cells is the chief barrier to eradication or cure of HIV.[12]

➢ Infectious HIV At Sexual Sites

It is now well established that infectious HIV can be found in semen, as well as in cervical and vaginal secretions. The potential for HIV transmission from these sites to oral mucosa has not been well studied, although inhibitory substances in saliva (see below) suggest that such transmission is not facile. More recently, information has emerged about the presence of infectious HIV in pre-ejaculatory fluid. Pudney and colleagues reported the presence of HIV-1-positive cells in three sperm-free samples from four donors. They also noted a variable number of positive pre-ejaculate specimens from persons who were symptom-free (five out of six), symptomatic (one out of three), on zidovudine (two out of five), and not on therapy (four out of four). The presence of virus in these situations highlights the possibility of penile–oral transmission of HIV even in the absence of ejaculation. Similar possibilities would exist from the transfer of vaginal/cervical secretions, and would similarly be

dependent on a variety of as yet incompletely explored factors that affect the degree of shedding and the receptivity of the oral cavity to infection.[13]

➢ **Virus In Saliva**

As noted above, the first report of virus in saliva was followed quickly by a more extensive evaluation that found virus in only one out of 83 specimens. Subsequently, investigators have reported a frequency of detection from 0 to 83%, depending on the type of specimen and the type of laboratory method (Table 3), but most of this work occurred before current staging methods were available. Culture attempts have generally placed the isolation proportion at under 5%, with the exception of a 21% positivity for low levels of virus found by Yeung et al. Results with PCR testing. have been more variable. For example, in an extensive study, 218 simultaneous blood and saliva specimens from 75 HIV-positive persons were tested for viral p24 antigen and infectious virus; 38% of blood specimens and 1% of saliva specimens were positive for cell-free infectious virus.

Goto et al. used PCR testing to study 20 patients for long terminal repeat (LTR), gag, and env proviral sequences. With LTR probes, 10 out of 20 specimens were positive, but only 25% were positive with probes for gag and env. Repeated testing confirmed the higher positivity for LTR. With PCR testing, Quereshi and colleagues detected virus in 83% of specimens. In an extensive review of the mechanisms of infectivity for salivary secretions, Shine et al. concluded that the precise balance between infectious secretions and inhibitory effects in vivo remains to be elucidated. They stated that, ‘it is important to establish the correlations among the amount of HIV, its infectivity in salivary secretions, and the level of anti-HIV factors present in these secretions.[13]

❖ **Stages 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.

➢ **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)

➢ **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/mm.

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.

❖ **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 nodes.

These symptoms are very similar to flu and are usually compared with it. The symptoms appears after 2-6 weeks after infection and vanishes after a week. If they are left untreated, the disease progresses to second stage.

➢ **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.

These symptoms are treated and medication is given to increase the life span of the patient.

❖ **Antigen/Antibody Testing**

Antigen can show positive test within few days of infection but immune system requires time to produce antibodies to infection and hence my require time (2-6 weeks) to be positive. Hence a combination of Antigen/Antibody test may take 2- 6 weeks to show positive results after exposure to virus.

➢ **ELISA Test**

ELISA (enzyme-linked immunosorbent assay) is used to detect the presence of HIV infection. After getting positive result of ELISA test, usually western blot test is administered to confirm the infection. Though ELISA test may show negative result, but if patient thinks that there may be HIV infection present, he/she should again get tested after one or three months. ELISA is a very sensitive to HIV infection, but antibodies are not produced

immediately after infection so one may test negative within few weeks after being infected. Although, you may get negative test results, the level of virus present is high and you will be at risk of transmitting infection.

➢ **Home Tests**

The home access expert test is approved by US FDA and is sold in pharmacies. It is the only approved home test kit.

➢ **Saliva Tests**

By using a cotton pad, saliva is obtained from the inside of patient's cheek. It is placed in vial and submitted for testing. Results are usually available within 3 days and positive results are confirmed with blood tests.

➢ **Viral Load Test**

The amount of HIV in blood is measured using viral load test. This test is generally used to monitor treatment progress and also is helpful in detecting early HIV infections. The three technologies which measure HIV viral load with same basic principle are

1. Branched DNA (bDNA).
2. NA(nucleic acid) sequence based amplification assay.
3. Reverse transcription PCR.

DNA sequences that bind specifically to HIV virus are detected, although results may vary between tests.

➢ **Western Blot**

The most sensitive test used to confirm ELISA test results is western blot test.[14]

❖ **Antiretroviral therapy and management of HIV infection**

Antiretroviral therapy of HIV infection has changed a uniformly fatal into a potentially chronic disease. There are now 17 drugs in common use for HIV treatment. Patients who can access and adhere to combination therapy should be able to achieve durable, potentially lifelong suppression of HIV replication. Despite the unquestioned success of antiretroviral therapy, limitations persist. Treatment success needs strict lifelong drug adherence. Although the widely used drugs are generally well tolerated, most have some short-term toxic effects and all have the potential for both known and unknown long-term toxic effects. Drug and administration costs limit treatment in resource-poor regions, and are a growing concern even

in resource rich settings. Finally, complete or near complete control of viral replication does not fully restore health. Long-term treated patients who are on an otherwise effective regimen often show persistent immune dysfunction and have higher than expected risk for various non-AIDS-related complications, including heart, bone, liver, kidney, and neurocognitive diseases.[15]

Antiretroviral therapy (ART) is a critical component in the management of HIV (human immunodeficiency virus) infection. ART involves the use of a combination of antiretroviral drugs to suppress the virus and slow the progression of HIV disease. The goal of ART is to reduce the viral load in the body, maintain or improve immune function, and prevent the development of opportunistic infections and other HIV-related complications.

- **Initiation of Antiretroviral Therapy**

The decision to start ART is based on various factors, including CD4 cell count, viral load, clinical symptoms, and the patient's readiness to adhere to the treatment.

The World Health Organization (WHO) provides guidelines for the initiation of ART, taking into account different populations and settings.[16]

- **Antiretroviral Drug Classes**

ART typically consists of a combination of drugs from different classes, including nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse.

Transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), integrase strand transfer inhibitors (INSTIs), and entry inhibitors.[17]

- **Monitoring and Adherence**

Regular monitoring of viral load, CD4 cell count, and clinical symptoms is crucial to assess the effectiveness of ART.

Adherence to the prescribed medication regimen is essential for the success of ART and the prevention of drug resistance.[18]

➢ **Prevention of Opportunistic Infections**

In addition to ART, prophylaxis for opportunistic infections, such as Pneumocystis jirovecii pneumonia (PJP) and Mycobacterium avium complex (MAC), may be recommended based on CD4 cell count and other factors.[19]

➢ **Pregnancy and HIV**

ART is crucial for preventing mother-to-child transmission of HIV during pregnancy, childbirth, and breastfeeding.[20]

❖ **ART as the standard treatment**

Antiretroviral therapy (ART) has emerged as the standard and cornerstone treatment for individuals infected with the human immunodeficiency virus (HIV). ART involves the use of a combination of antiretroviral drugs that target variouss stages of the HIV life cycle, effectively suppressing viral replication and mitigating the progression of the disease. The adoption of ART represents a transformative milestone in HIV care, significantly improving the quality of life and life expectancy of individuals living with HIV.

➢ **Viral suppression and immune restoration**

ART aims to achieve and maintain undetectable levels of HIV in the bloodstream, known as viral suppression. This not only benefits the individual's health but also plays a crucial role in preventing the transmission of the virus to others.

By suppressing viral replication, ART allows for the restoration and preservation of immune function, as reflected in the elevation of CD4 T-cell counts.[21]

➢ **Treatment Initiation Criteria**

International guidelines, such as those provided by the World Health Organization (WHO), offer clear criteria for initiating ART. These criteria consider factors such as CD4 cell count, viral load, clinical symptoms, and readiness for treatment.[22]

➢ **Drug Classes and Combination Therapy**

ART involves the use of various classes of antiretroviral drugs, including nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), and integrase strand transfer inhibitors (INSTIs).

Combination therapy, utilizing drugs from different classes, is fundamental to achieving optimal viral suppression and reducing the risk of drug resistance.[23]

➢ **Monitoring and Adherence**

Regular monitoring of viral load, CD4 cell count, and clinical status is essential to assess treatment effectiveness.

Adherence to the prescribed medication regimen is critical for achieving and maintaining viral suppression, preventing resistance, and optimizing long-term outcomes.[24]

➢ **Preventing Transmission and Mother-to-Child Transmission**

Effective ART not only benefits the individual but also plays a pivotal role in preventing the transmission of HIV to sexual partners.

ART is a cornerstone in preventing mother-to-child transmission during pregnancy, childbirth, and breastfeeding.[25]

❖ **Antiretroviral drugs generally used in clinical practice**

Table No 2:- Antiretroviral drugs generally used in clinical practice.[26]

	Drugs	Comments
Nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs)	Tenofovir, abacavir, zidovudine,* stavudine,* lamivudine, emtricitabine	Tenofovir is associated with renal and perhaps bone dysfunction. Abacavir is associated with hypersensitivity reactions in at risk individuals (HLA B5701) and is associated in some studies with an increased risk of cardiovascular disease. Abacavir might be less potent than tenofovir in patients with high viral loads. Zidovudine and stavudine are associated with profound fat redistribution (lipoatrophy). All NRTIs are associated with potential to cause risk of severe lactic acidosis. The combination of tenofovir and emtricitabine is the preferred fi rst-line regimen in most regions
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)	Efavirenz, nevirapine,* etravirine	Efavirenz can cause CNS toxicity (which is usually time limited). Efavirenz has teratogenic potential and should be used with caution in woman who might become pregnant. Nevirapine can cause severe hepatoxicity when used in patients with higher CD4 cell counts (more than 250 cells per µL for women and more than 400 cells per µL for men). Etravine is given twice daily and has generally been used as second-line regimen.
Integrase inhibitors	Raltegravir	Raltegravir has no short-term and no known long-term toxic eff ects, although data are scarce

Protease inhibitors	Fosamprenavir, atazanavir, darunavir, lopinavir, saquinavir (ritonavir)	Most protease inhibitors are extensively metabolised by the P450 CYP3A system; ritonavir is generally given at low doses (100–200 mg per day) to inhibit P450 and boost the co-administered protease inhibitors. Most protease inhibitors are associated with hyperlipidaemia and other metabolic abnormalities such as insulin resistance. Long-term protease inhibitor exposure has been associated with increased risk of cardiovascular disease
CCR5 inhibitors	Maraviroc	Maraviroc is only active in patients who do not have virions that use CXCR4 for cell entry. A specialised assay is therefore needed to screen for coreceptor tropism. By contrast with other antiretroviral drugs, maraviroc binds to a host rather than a viral target. Maraviroc has an immunomodulatory eff ect that is independent of its eff ect on HIV replication; the clinical signifi cance of this activity is unknown.
Fusion inhibitors	Enfuvirtide	Enfuvirtide must be given subcutaneously twice daily and is very expensive. The drug is generally used only in patients with no other therapeutic options

❖ Significance Of Treatment Adherence

The significance of treatment adherence in antiretroviral therapy (ART) for individuals living with HIV cannot be overstated. Adherence to prescribed medication regimens is a critical factor in the success of HIV treatment, as it directly influences viral suppression, immune reconstitution, and overall health outcomes.

➢ Viral Suppression and Prevention of Resistance

Consistent adherence to ART is essential for achieving and maintaining viral suppression. Missing doses or inconsistent adherence can lead to increased viral replication, compromising the effectiveness of the treatment.

Poor adherence is a major contributor to the development of drug resistance, which limits future treatment options and jeopardizes the long-term success of HIV management.[27]

➢ Optimizing Immune Reconstitution

Adherence to ART is crucial for the restoration and preservation of immune function, as reflected in the rise of CD4 T-cell counts. Inconsistent adherence may result in suboptimal immune reconstitution, leaving individuals vulnerable to opportunistic infections and other HIV-related complications.[28]

➢ **Preventing Transmission**

Adherence to ART is not only crucial for individual health but also plays a key role in preventing the transmission of HIV to sexual partners. Viral suppression achieved through consistent adherence significantly reduces the risk of transmitting the virus to others.[29]

➢ **Quality of Life and Long-Term Outcomes**

Adherence to ART contributes to improved overall quality of life for individuals living with HIV. Properly managed HIV with sustained viral suppression allows individuals to lead healthier lives, reducing the impact of HIV-related illnesses and complications.[30]

➢ **Challenges and Support Strategies**

Adherence can be challenging due to various factors, including medication side effects, complex dosing schedules, and psychosocial issues. Recognizing and addressing these challenges are crucial for promoting adherence.

Support strategies, such as patient education, counseling, and the use of adherence aids, play a significant role in enhancing treatment adherence.[31]

❖ **Preventions From Hiv And Aids**

Preventing HIV infection involves a combination of behavioral, biomedical, and structural interventions.

➢ **Condom Use and Safe Sex Practices**

Consistent and correct use of condoms is an effective barrier method to prevent the sexual transmission of HIV.[32]

➢ **Pre-Exposure Prophylaxis (PrEP)**

PrEP involves taking antiretroviral drugs before potential exposure to HIV to reduce the risk of infection.[33]

➢ **Treatment as Prevention (Undetectable = Untransmittable, U=U)**

Effective HIV treatment that achieves and maintains an undetectable viral load makes the transmission of HIV through sexual contact virtually impossible.[34]

- **Needle and Syringe Programs (NSPs)**

NSPs provide sterile injecting equipment to people who inject drugs, reducing the risk of HIV transmission through sharing of contaminated needles.[35]

- **Voluntary Medical Male Circumcision (VMMC)**

Male circumcision has been shown to reduce the risk of heterosexual transmission of HIV.[36]

- **Comprehensive Sexuality Education:**

Providing education on safe sex practices, STI prevention, and HIV awareness can contribute to reducing the risk of HIV transmission.[37]

- **HIV Testing and Counseling**

Routine HIV testing and counseling promote early detection and linkage to care, reducing the risk of onward transmission.[38]

❖ CONCLUSION

The study of HIV encompasses a vast array of interconnected factors, each playing a crucial role in our understanding and management of this complex virus. From its intricate genetic diversity to the structural components that define its existence, the life cycle of HIV presents multiple points of intervention for therapeutic development.

HIV transmission, primarily occurring through specific bodily fluids, underscores the importance of awareness and preventive measures. A deep understanding of the virus's infection mechanism, particularly its affinity for CD4+ T cells, highlights the need for early diagnosis and timely intervention to mitigate immune system compromise.

Symptoms of HIV infection, ranging from subtle signs to more severe manifestations, emphasize the importance of prompt medical attention and the necessity of widespread testing. Antigen/antibody testing stands as a pivotal tool in identifying infections and initiating treatment strategies at the earliest stage possible.

The advent of Antiretroviral Therapy (ART) marks a transformative milestone in the management of HIV. As ART becomes the standard treatment, its success relies heavily on the adherence of individuals to prescribed regimens. Ensuring consistent access to antiretroviral drugs and maintaining treatment adherence are critical factors in achieving sustained viral suppression and preventing the emergence of drug-resistant strains.

An array of antiretroviral drugs, each targeting different stages of the virus's life cycle, underscores the complexity and precision required in HIV treatment. The significance of treatment adherence cannot be overstated, as it directly influences the long-term efficacy of therapy and overall health outcomes.

In the realm of prevention, a multi-faceted approach is essential. Safe sex practices, needle exchange programs, pre-exposure prophylaxis (PrEP), and community education efforts all contribute to reducing the spread of HIV and eliminating the stigma associated with the virus.

In conclusion, the comprehensive understanding of HIV, from its genetic makeup to its transmission, treatment, and prevention strategies, forms the foundation of our global response to the epidemic. Ongoing research, education, and international collaboration remain imperative in addressing the ever-evolving challenges posed by HIV and AIDS. Through continued efforts, we strive not only to manage the impact of the virus but ultimately to eliminate its devastating consequences on a global scale.

❖ SUMMARY

HIV (Human Immunodeficiency Virus) is a retrovirus that attacks the immune system, specifically CD4+ T cells, weakening the body's ability to fight off infections and diseases. HIV can lead to Acquired Immunodeficiency Syndrome (AIDS), the advanced stage of the infection. The virus is transmitted through specific body fluids, such as blood, semen, vaginal fluids, and breast milk.

The genetic diversity of HIV poses challenges for treatment and vaccine development. The virus's structure includes an envelope, glycoproteins, and key enzymes crucial to its life cycle. Understanding the stages of the HIV life cycle, from attachment to host cells to replication and release, is essential for developing effective interventions.

Early symptoms of HIV may include fever, fatigue, and weight loss. Antigen/antibody testing is crucial for diagnosis, enabling timely initiation of treatment. Antiretroviral Therapy (ART) has become the standard treatment, suppressing viral replication and preserving immune function. Adherence to ART is vital for its success, preventing the emergence of drug-resistant strains.

Preventive measures against HIV include safe sex practices, needle exchange programs, pre-exposure prophylaxis (PrEP), and community education to reduce stigma. While ART has

transformed HIV into a manageable chronic condition, ongoing efforts in research, education, and prevention are crucial for addressing the global impact of HIV and AIDS and working towards an HIV-free future.

❖ REFRENCES

1. Shilpa P. Chaudhari And Nikita M. Handge, A Review Article On HIV/AIDS, International Journal of Creative Research Thoughts (IJCRT), 2020; 8(4): 2399-2405.
2. Einav L*, Psychosocial Aspects of HIV/ AIDS, A SciTechnol journal, 2018; 1(1): 1-4.
3. Kishmu Lingan*, A Review on Various Aspects of HIV Infection, An open access journal, 2018; 3(1): 1-6.
4. 1 Ceena E Denny, 2 John Ramapuram, 3 TS Bastian, 4 Ravikiran Ongole, 5 Almas Binnal, 6 Srikant Natarajan and 7 Junaid Ahmed, Oral Lesions in HIV/AIDS Patients on a highly Active Antiretroviral Therapy, World Journal of Dentistry, 2016; 7(2): 95-99.
5. Nancy Klimas, Md, Anne o'brien Koneru, Msn, Arnp, And Mary Ann Fletcher, Phd, Overview of HIV, the American Psychosomatic Society, 2008; 70: 523–530.
6. Judith G Levin, Mithun Mitre, Anjali Mascarenhas and Karin Musier-Forsvth, Role of HIV-1 nucleocapsid protein in HIV- 1 reverse, Publish on RNA Biology, 2010; 7(6): 754-774.
7. Wei-Shau Hu and Stenhen H. Hughes, HIV-1 Reverse Transcription, Cold Spring Harb Perspect Med, 2012; 2(10).
8. Juan R. Perilla & Klaus Schulten, Physical properties of the HIV-1 capsid from all-atom molecular dynamics simulations, nature communications, Article number, 2017; 15959.
9. Janeway's Immunobiology Authors: Kenneth Murphy, Paul Travers, Mark Walport, Garland Science, 2011.
10. Sarudzai P Showa, Farai Nyabadza And Senelani D Hove. Musekva, On the efficiency of HIV transmission: Insights through discrete time HIV models, Publish on PLos One, 2019; 14(9).
11. Sebastian Lucas1 and Ann Marie Nelson2, HIV and the spectrum of human disease, Journal of Pathology, 2015; 235: 229–241.
12. Ansari Vikhar Danish Ahmad1, Nikhil S. Sakle1, Swaroop R. Lahoti2, Sarfaraz Khan3 And Syed Ayaz Ali*, A review on treatment of Human Immunodeficiency Virus (HIV) by Naturopathy, Journal of Innovations in Applied Pharmaceutical Science, 2018; 3(4): 01-06.

13. Richard B. Rothenberg, Margaret Scarlett, Carlos del Rio, David Reznik and Christine O'Daniels, Oral transmission of HIV, Lippincott Williams & Wilkins Journals, 1998; 12(12): 2095–2105.
14. Revati Wable, A Review Article On Hiv And Aids, World Journal of Pharmaceutical And Life Science, 2020; 6(9): 146-149.
15. Paul A Volberding, Steven G Deeks, Antiretroviral therapy and management of HIV infection**,** Lancet, 2010; 376: 49–62.
16. World Health Organization. (2016). Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Retrieved from WHO website.
17. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Retrieved from Department of Health and Human Services website, 2021.
18. Nachega, J. B., & Marconi, V. C., Van Zyl, G. U., e Barriers to Adherence to Antiretroviral Guidelines: A 16-Year Prospective Study. PLoS ONE, 2017; 12(1).
19. Kaplan, J. E., Benson, C., Holmes, K. H., Brooks, J. T., Pau, A., Masur, H., & Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH), HIV Medicine Association of the Infectious Diseases Society of America, 2009.
20. World Health Organization. Use of Antiretroviral Drugs for Treating Pregnant Women and Preventing HIV Infection in Infants. Retrieved from WHO website, 2013.
21. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Retrieved from Department of Health and Human Services website, 2021.
22. World Health Organization, 2016.
23. Saag, M. S., & Gandhi, R. T., Antiretroviral Agents in the Treatment of HIV Infection. In Goodman & Gilman's The Pharmacological Basis of Therapeutics (12th ed.).
24. Nachega, J. B., & Marconi, V. C. Van Zyl, G. U., et al. Barriers to Adherence to Antiretroviral Guidelines: A 16-Year Prospecti. PLoS ONE, 12(1): e0172183.
25. Cohen, M. S., Chen, Y. Q., McCauley, M., Gamble, T., Hosseinipour, M. C., Kumarasamy, N & Hakim, J. G, Antiretroviral therapy for the prevention of HIV-1 transmission. New England Journal of Medicine, 2016; 375(9): 830-839.
26. Paul A Volberding, Steven G Deeks, Antiretroviral therapy and management of HIV infection**,** Lancet, 2010; 376: 49–62.

27. Bangsberg, D. R., Perry, S., Charlebois, E. D., Clark, R. A., Roberston, M., Zolopa, A. R., & Moss, A. Non-adherence to highly active antiretroviral therapy predicts progression to AIDS. AIDS, 2001; 15(9): 1181–1183.
28. Parienti, J. J., Massari, V., Descamps, D., Vabret, A., Bouvet, E., Larouzé, B., & Verdon, R. Predictors of virologic failure and resistance in HIV-infected patients treated with nevirapine- or efavirenz-based antiretroviral therapy. Clinical Infectious Diseases, 2004; 38(9): 1311–1316.
29. Cohen, M. S., Chen, Y. Q., McCauley, M., Gamble, T., Hosseinipour, M. C., Kumarasamy, N., ... & Hakim, J. G., Antiretroviral therapy for the prevention of HIV-1 transmission. New England Journal of Medicine, 2016; 375(9): 830-839.
30. Paterson, D. L., Swindells, S., Mohr, J., Brester, M., Vergis, E. N., Squier, C., ... & Singh, N., Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. Annals of Internal Medicine, 2000; 133(1): 21-30.
31. Simoni, J. M., Pearson, C. R., Pantalone, D. W., Marks, G., & Crepaz, N., Efficacy of interventions in improving highly active antiretroviral therapy adherence and HIV-1 RNA viral load: a meta-analytic review of randomized controlled trials. Journal of Acquired Immune Deficiency Syndromes, 2006; 43(1): 23-35.
32. Holmes, K. K., Levine, R., & Weaver, M., Effectiveness of condoms in preventing sexually transmitted infections. Bulletin of the World Health Organization, 2004; 82(6): 454-461.
33. Grant, R. M., Lama, J. R., Anderson, P. L., McMahan, V., Liu, A. Y., Vargas, L., ... & Glidden, D. V., Preexposure chemoprophylaxis for HIV prevention in men who have sex with men, New England Journal of Medicine, 2010; 363(27): 2587-2599.
34. Rodger, A. J., Cambiano, V., Bruun, T., Vernazza, P., Collins, S., Degen, O., ... & Collins, S., Sexual Activity Without Condoms and Risk of HIV Transmission in Serodifferent Couples When the HIV-Positive Partner Is Using Suppressive Antiretroviral Therapy. JAMA, 2016; 316(2): 171-181.
35. Aspinall, E. J., Nambiar, D., Goldberg, D. J., Hickman, M., Weir, A., Van Velzen, E., ... & Hutchinson, S. J., Are needle and syringe programmes associated with a reduction in HIV transmission among people who inject drugs: a systematic review and meta-analysis. International Journal of Epidemiology, 2014; 43(1): 235-248.
36. Auvert, B., Taljaard, D., Lagarde, E., Sobngwi-Tambekou, J., Sitta, R., & Puren, A., Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: the ANRS 1265 Trial. PLoS Medicine, 2005; 2(11).

37. Kirby, D, The impact of schools and school programs upon adolescent sexual behavior. The Journal of Sex Research, 2002; 39(1): 27-33.
38. Weinhardt, L. S., Carey, M. P., Johnson, B. T., & Bickham, N. L, Effects of HIV counseling and testing on sexual risk behavior: a meta-analytic review of published research, 1985–1997. American Journal of Public Health, 1999; 89(9): 1397-1405.