

Susceptibility to HIV and Strategies to Prevent AIDS

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Abstract: HIV (Human Immunodeficiency Virus) is an infectious disease that can progress to AIDS (Acquired Immunodeficiency Syndrome), causing deaths. Despite all the advances in understanding the molecular mechanism of virus entry, replication, propagation and transmission, there is not a complete cure for this disease. Although the disease can be controlled by antiretroviral therapy, the treatment is not available for many people, causing a disparity in the care of the population who are infected. Furthermore, as HIV is mainly transmitted by contact with infected body fluid, such as during sexual intercourse and sharing contaminated needles, some vulnerable groups in the population are more susceptible to becoming infected. This article provides an overview of HIV and AIDS by reviewing the current references from an epidemiological perspective, in addition to discussing treatments available. Moreover, susceptible groups who are vulnerable to HIV, such as people living in Sub-Saharan Africa, sexual workers, and drug abusers are discussed, and some solutions are suggested. Finally, a connection between the COVID-19 pandemic and lessons which can be learned for the HIV diagnosis and treatments is established. In conclusion, HIV and AIDS still remain a threat to global health, and measures should be taken to not only to study the disease better, but also to find permanent treatments such as vaccines, despite challenges.


1 INTRODUCTION

HIV (Human Immunodeficiency Virus) is an infectious disease caused by retroviruses, which can develop into AIDS (Acquired Immunodeficiency Syndrome) if it remains untreated. HIV can be transmitted through sexual contact, using contaminated and shared needles, passed from mother to child during pregnancy and childbirth, and via contaminated blood transfusion (Cdc.gov. 2021). Many infected patients do not show any symptoms during the first few months of infection, and therefore, can transmit the virus. Some people may have flu-like symptoms, including fever, headache, and sore throat during the early phases of the infection, when the viral load is at its highest (aidsmap.com. 2021). As the disease develops, the immune system succumbs, and symptoms become more pronounced, including swollen lymph nodes, diarrhea, fever and rapid weight loss (HIV.gov. 2021). HIV weakens the body's ability to fight other infections, and people who do not receive treatment are more susceptible to other diseases, such as

cholera, bacterial infections, cryptococcal meningitis and some cancers (Who.int. 2021). In the battle against AIDS, the best tactic for the treatment of HIV is antiretroviral therapy (ART). Approximately 25 unique antiretroviral drugs are already used for the treatment of adults. But there has not been a definitive cure for HIV yet. The treatment objectives are to minimize and sustain the viral load, to obtain immune function reconstruction and maintain immune function, to improve the quality of life, and to reduce morbidity and mortality associated with HIV.

2 EPIDEMIOLOGY OF HIV

After initial uncertainties in the early 1980s surrounding the emergence of a new disease, it soon became apparent that an epidemic and then a pandemic was underway. Since then, 38 million people have acquired HIV, including 36.2 million adults and 1.8 million children under 15 years old. It is estimated that the number of people living with HIV has increased by 1.9 million recently, but the

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incidence rate is still 23% lower than in 2010. Approximately 81% of people are tested for HIV each year, so the figures are an underestimation, and the actual number of infections is much higher than the number recorded. Among people who are now known to have been infected with HIV, by the end of the 2019, 36.2 million people living with HIV (67%) had access to antiretroviral drugs, and nearly 12.6 million people are still waiting for treatment (HIV.gov. 2021), demonstrating a huge gap between diagnosis and treatment.

3 DISCUSSION MECHANISMS

3.1 Virus Structure

Studying the susceptibility to HIV and strategies to prevent AIDS, such as developing antiretroviral drugs and vaccines, requires an understanding of the HIV structure, which is discussed below. HIV

particles are spherical and 90-130 nanometers in diameter (Wikipedia. 2021). The core of the virus is hollow conical and consists of two identical single-stranded RNA chains, reverse transcriptases and proteins (Figure1). Outside the core is the viral shell, which is three-dimensional symmetry of 20 polyhedromes and contains nuclear shell proteins. The outermost layer is the envelope, where glycoproteins have puncture-like structures, and these are the main binding site of HIV and host cell receptors. HIV is a retrovirus, with RNA containing the gag, env and pol genes, as well as six regulatory genes (tat, vif, vpr, vpx (vpu), nef, rev) (Online Biology Notes. 2021). The core protein of the gag gene encodes the virus; the enzymes (retroviruses, integrated enzymes and proteases), which are required for replication of the pol gene to encode virus envelope protein, which is the main antigen for HIV immunological diagnosis (Wikipedia. 2021). Regulatory genes encode aid proteins and regulate viral protein synthesis and replication.

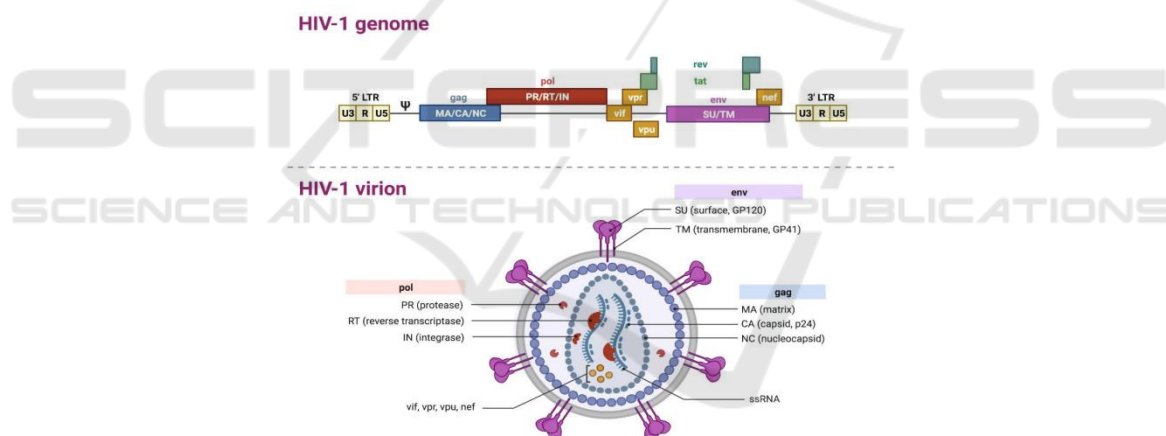


Figure 1. An overview of HIV-1 virus genome (top) and its structure (bottom). The figure was generated using Biorender.

There are two main types of HIV present: HIV-1 and HIV-2. Both are transmitted through the same routes, but HIV-2 has a lower chance of transmission than HIV-1 because the immune system responds better to HIV-2 and responds (Nyamweya, Hegedus, Jaye, Rowland-Jones, Flanagan, Macallan 2013). While there are still many essential differences between HIV-1 and HIV-2, an extended comparison is beyond the scope of this paper, and an overall comparison of HIV-1 and HIV-2 is shown in table 1.

Table 1. A comparison of HIV-1 and HIV-2, including their prevalence, origin, transmission and disease course.

	HIV-1	HIV-2
Prevalence	Global	West Africa, Mozambique and Angola
Origin	Chimpanzees	Sooty mangabeys
MTCT	Relatively common	Relatively rare
Heterosexual spread	Higher	Lower

Genetic Diversity	More	Less
Time to AIDS	Less than 10 years	More than 20 years

3.2 HIV Transmission

Studying the transmission of HIV is essential for tackling susceptibility and preventing disease progression. HIV can be transmitted through body fluids during sexual relations with people living with HIV (anal or vaginal sex), through the sharing of infected needles, syringes or other drug injection equipment, and from mother to fetus during pregnancy and birth.

3.2.1 Sexual Contact

People can contract HIV from their sexual partners during sexual intercourse without using protection measures, such as condoms or other medicines that can prevent or control HIV. Anal sex is the greatest risk factor for transmitting HIV, especially in men who have sex with other men, due to the thin lining of the rectum, which facilitates the HIV virus entry into the body (Cdc.gov. 2021). Most women contract HIV from vaginal sex because HIV can enter the body through the mucous membranes that line on the vaginal and cervix (Cdc.gov. 2021). Men also can get HIV from this process because of contact with contaminated vaginal secretion and blood that carry the HIV, which enters the body through the opening penis, which is not circumcised (Cdc.gov. 2021). Oral sex can also cause transmission if both sexual partners have small cuts in the mouth and one of them has HIV. However, HIV transmitted from female to female is rare (Cdc.gov. 2021).

3.2.2 Transmission Via Blood

The risk of HIV infection from blood transfusions is very rare worldwide (Avert. 2021). Nowadays, all blood products (organs and tissues) are tested for the presence of infections such as HIV. Blood transfusing is the direct route of transmission (Avert. 2021). Other factors that may cause direct contact in the blood are tattoos or body piercings. However, sharing needles, syringes, or other injection equipment also puts people at risk for getting HIV. HIV particles can survive on the syringes for nearly 42 days, depending on storage temperature and other surrounding factors (Abdala, Reyes, Carney, Heimer 2000), causing infection through blood exchange. The use of contaminated needles in hospitals is extremely rare,

and used needles are treated safely in hospitals (Avert. 2021). HIV infection via contaminated needles is a direct route among drug users (Cdc.gov. 2021). Therefore, the Government should increase drug control, especially intravenous drugs, while vigorously screening drug users within its jurisdiction and testing them for HIV. Many of these addicts are pregnant women, and the vast majority of their infants become drug addicted to drug and are born with HIV from birth.

3.2.3 MTCT (Mother to Child Transmission)

MTCT, as a vertical propagation way of transmission, is the most common way that children get HIV, which occurs during pregnancy or breastfeeding. Without any intervention, transmission rates range from 15% to 45% (<https://www.who.int/hiv/topics/mtct/about/en>. 2021). MTCT is relatively rare with HIV-2. During pregnancy, the HIV hidden in blood can enter into the baby's body through the placenta and umbilical cord. In addition, it is worth noting that infection can lead to damage to other organs (cardiovascular, nervous, bone and other tissues) in adults (Hazra, Siberry, & Mofenson 2010).

3.3 Immune Response to HIV

At the beginning of HIV infection, the virus first attacks the mucous membrane tissue of the cell and then spreads to the lymphatic system (eclipse phase) (Avert. 2021). About three weeks later, the genetic material for HIV can be detected, and the virus begins to proliferate and reach its peak (Avert. 2021). At this acute phase, the spread of the virus can also be partially controlled by the action of the adaptive immune response. Patients show some flu-like symptoms during the acute phase, which can last about nine weeks, after which viral load reach the set point, a stable level (Avert. 2021). Damage to CD4 T cells caused by HIV viruses can lead to immunodeficiency and chronic inflammation. After up to nine years from the onset of infection, HIV develops into AIDS, a period known as the latent infection (Figure3). CD4 T cells in a normal adult body are typically between 500 cells and 1500 cells per μl (aidsmap.com. 2021); however, the number frequency of CD4 T cells decreases after HIV infection as the CD4+ T cell number declines to <350 cells per μl , opportunistic infections and cancers can develop (Figure2).

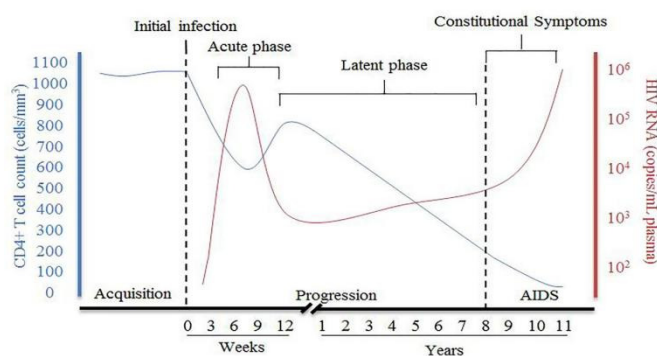


Figure 2. A graph demonstrating changes in the CD4+ T cell count and HIV viral load during the disease progression from HIV to AIDS. The figure is adopted from (An, Ping, and Cheryl A Winkler. 2010).

3.4 Diagnosis and Clinical Behaviors

Early HIV testing is significant, and if a patient is HIV-positive, treatment options should be discussed with the doctor as soon as possible, as well as decreasing high-risk behaviors to decrease the virus spread. The most important approach is to prevent transmission to others during this period and prioritizing the treatment. Many medical facilities also offer anonymous and free counseling, including asking patients about symptoms, psychological state, medical history, and allergens. There are four main HIV tests including, ELISA test, home test, saliva test and viral load test (Parker, Botchan, and Berger 2021).

ELISA (enzyme-linked immunosorbent assay). This test can be used to detect HIV infection. If an ELISA test is positive, the Western blot test (blood test) is usually administered to confirm the diagnosis. ELISA is very sensitive to chronic HIV infection, but because antibodies do not produce immediately after infection, and the infected person may test negative within weeks to months of infection. Even if the person's test results turn negative in this window, the infected person may have a high level of the virus and is at risk of spreading the infection.

Home test: AIDS test paper is a new generation of test reagents developed using colloidal gold immunotomography technology to detect HIV-1/2 endemic antibodies in whole blood, serum or plasma specimens. Test time is six weeks (42 days), and with short operating time (generally 15-20 minutes to observe the results), and without the need for additional equipment, as well as a high accuracy rate of 97% to 99%, this method is very fast, and efficient. However, additional testing confirmation tests may be required (Bhiva.org. 2021).

Saliva test, a piece of cotton in the test box is used to collect saliva, which is sent to the laboratory to test,

and test results are usually available within three days. Further blood tests are required if tested positive. This test is only checking for antibodies, not the actual disease (HowStuffWorks, Health, Medicine and Treatment 2021).

Viral Load test measures the number of HIV viruses detected in the body. Three techniques for detecting HIV viral load: reverse transcription and polymerase chain reaction (RT PCR), branched DNA (bdna), and nucleic acid sequence based amplification analysis (Nasba) (Tests 2021).

As mentioned previously, there are three stages between the development of HIV and AIDS. Within the acute infection phase, most infected people have flu-like symptoms such as cough, fever, red rash, muscle soreness and sore throat. Some people have no symptoms during the early stage of HIV. If an individual feels infected with HIV or recently exposed to HIV, they need to do the HIV test immediately. In the latent phase, viruses continue to increase or mutate. Infected people may not feel uncomfortable or have any symptoms at this stage. Insisting on treatment at this stage can be effective in suppressing the disease, but if not treated, it will develop into the next stage of AIDS in about a decade (Hivinfo.nih.gov. 2021). When the disease develops into AIDS, the immune system is already very weak. Symptoms can also be more severe than before. For example, rapid weight loss, pneumonia, memory loss, depression and other neurologic disorders (Bhiva.org. 2021). At this stage, it is likely that a small cold will threaten the patient's life. So, HIV should be detected early and early treatment should initiate to avoid AIDS.

4 TREATMENT & PREVENTION

As mentioned previously, a latent period occurs

before the development of HIV into AIDS, and such progression be hindered by drug treatments. To this day, there is no complete cure for HIV; however, six families of antiretroviral drugs are used for treatments: Non-nucleoside reverse transcriptase inhibitors, nucleoside reverse transcriptase inhibitors, protease inhibitors, fusion inhibitors, CCR5 receptor antagonists and integrase inhibitors (Table 2 shows below and Figure 3) (HIV.gov. 2021). Antiretroviral drugs are often used in combination to prevent drug resistance and multiple viruses from mutating in the

body in a timely manner (Hivinfo.nih.gov. 2021). These drugs have many side effects, so many patients cannot adhere long-term to their treatment, which is also an important factor for the high prevalence of HIV disease progression to AIDS. Only patients who respond positively to the condition will cooperate with their doctors. Maintaining a positive attitude is also one of the important treatments for diseases. Drugs are also very expensive, which is an important reason for patients' non-compliance.

Table 2. A summary of some of current antiretroviral drugs used for the treatment of HIV. The information in this table was derived mainly from (Hivinfo.nih.gov. 2021), (Drugs 2021).

Inhibitors	Mechanism of action	Drug name	Side effect	
Non-nucleoside reverse transcriptase inhibitors	Directly inhibit the HIV-1 reverse transcriptase by binding in a reversible and non-competitive manner to the enzyme	Efavirenz	Associated with rashes including Stevens-Johnson syndrome	pPasma cholesterol concentrations
		Nevirapine		Occasionally with fatal hepatitis
Protease inhibitors	These inhibit HIV enzyme required to produce mature infectious viral particles by cleaving structural proteins and enzymes from their precursors.	Atazanavir	Cough, insomnia, depression, numbness of hands and feet, etc.	
		Darunavir	Fatigue, anorexia, nausea, jaundice, darker urine color	
		Indinavir	Multi-dream, urine pain, blood urine, crystalline urine	
Fusion inhibitors	Inhibits HIV from fusing to the host cell	Enfuvirtide	Insomnia, anxiety, peripheral neuropathy, fatigue	
CCR5 receptor antagonists	Block the CCR5 receptor on the outside of CD4 cells.	Maraviroc	Cough, stomach pain, or tiredness may occur. Lightheadedness or dizziness	
Integrase inhibitors	Integrase inhibitor and is indicated in combination with other antiretroviral drugs for HIV infection resistant to first-line ART.	Raltegravir	Trouble sleeping insomnia, headache, dizziness, nausea, tiredness	
Nucleoside reverse transcriptase inhibitors	These inhibit the RNA-dependent DNA polymerase (reverse transcriptase) which HIV uses to convert viral RNA into DNA before its incorporation into the cell genome.	Zidovudine	As the disease progresses, adverse reactions increase	
		Abacavir	increased cardiovascular risk	
		Didanosine	Hair loss, allergic reactions, weakness, pain, chills and fever	
		Stavudine	Anemia, white blood cell deficiency	

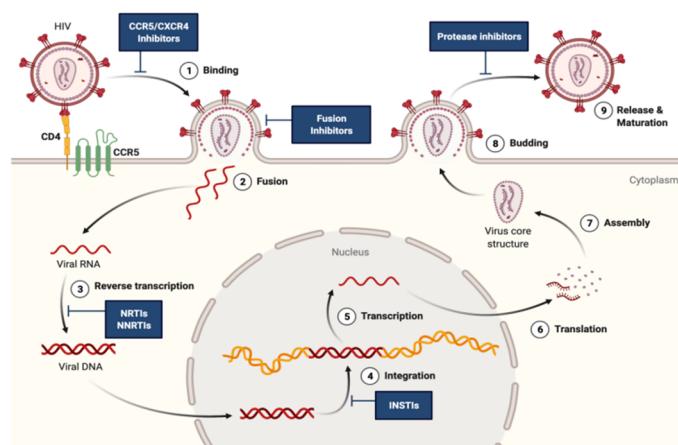


Figure 3. An overview of antiretroviral therapy approaches used to tackle entry and propagation of HIV. The figure was generated using Biorender.

Avoiding early HIV infection is the most effective way to reduce the incidence of AIDS. The early stages of avoiding infection require a holistic approach from society and the government. The following are some suggestions for preventive measures for both individuals and government.

Personal:

1. Drug use should be strictly prohibited and syringes are not shared with others.
2. Blood transfusion should be prohibited without authorization, should be used under the guidance of a doctor.
3. Personal items such as toothbrushes, razors, shavers, etc. should not be shared.
4. Condom use as one of the most effective preventive measures in sexual life for the prevention of diseases and AIDS should be encouraged.
5. Direct contact with the blood, semen and milk of AIDS patients be avoided.

National and international recommendations are as follows:

Awareness of HIV among the public should be raised by organizing regular community events, national awareness campaigns, TV and social media advertisements, etc.

HIV education should be incorporated into school and national education curriculum.

Discrimination and stigma against HIV should be removed by raising awareness.

HIV drug prices should be subsidized and if possible, free and anonymous HIV testing should be available.

New needles should be supplied to drug abusers.

Condoms and other preventative measures should become available in public places such as colleges, universities, leisure areas, etc.

More funding should be invested on HIV research.

4.1 Vaccines in the Future

Vaccines have traditionally been the most effective means of preventing or even eradicating infectious diseases. Vaccines are safe and cost-effective in preventing various diseases, disabilities and death. Similar to smallpox and polio vaccines, preventive HIV vaccines can help save millions of lives. Vaccines are synthesized using inactivated and detoxified microorganisms, injecting treated bacteria, viruses and toxins into the body to induce an immune response to help the body fight infection more effectively (HIV.gov. 2021). But so far, there has been no vaccine that can completely cure HIV. The biggest obstacle to the development of HIV vaccines is the variety of genetic material of the virus. HIV not only replicates quickly, but also tends to have a high error rate, during which mutations can form a new type of HIV virus; new HIV strains will also be re-integrated in human-to-human transmission (Verywell Health. 2021). As conventional vaccines can only prevent a limited number of strains, developing a single vaccine that eradicates more than 60 dominant strains and multiple recombinant strains worldwide becomes even more challenging (Verywell Health. 2021). Developing a safe, efficient, and affordable vaccine to prevent HIV infection in uninfected people and end the global spread of HIV is the highest priority of HIV researchers. Recent research has shown that use cytomegalovirus (CMV) as a vaccine vector can protect against multiple infectious diseases including simian immunodeficiency virus in rhesus macaques

(Barry, Peter A et al. 2020). This technology is expected to be used in HIV in humans.

4.2 Susceptible People to HIV Infection Groups

4.2.1 People Living in Sub-Saharan Africa

Large generalized epidemics of HIV-1 is a potential cause of mass mortality and morbidity in sub-Saharan Africa (UNAIDS 2017). The World Health Organization reported that almost 70% of the population in sub-Saharan Africa live with HIV (Gleason 2012). In addition, approximately 92% of women and 90% of children living with HIV in the sub-Saharan area (Ilo.org. 2021). As the availability of antiretroviral therapy and male medical circumcision has increased, the rate of new infections has been reduced (Grabowski, et al. 2017). Despite such progress, HIV still remains a major problem in the sub-Saharan Africa region. Some natives still keep eating uncooked meat, like chimpanzees (most prevalent strains HIV-1 Group M originated from these), causing exposure to primate blood (Avert. 2021). Chaotic sexual behavior is also one of the main ways of transmission. A person with HIV may have many sexual partners, and in the chronic phase, the carrier of HIV may not notice, causing the virus to spread. But in practice, far more people actually have HIV than are recorded because many people may fear discrimination or isolation, so they would deliberately hide their illness or refuse to take HIV tests. Some people even do not know about HIV and how it spreads. Racial discrimination still exists in many Sub-Saharan areas, and many black people fear that white hospitals misdiagnose them, and many white doctors do not want to visit and treat a black man. This can lead to a crisis of confidence in the local health care system, which reduces medical efficiency. The class disparity is also one of the reasons why the health care system of some African countries is struggling under pressure. Many poor people with HIV do not receive formal treatment, and more and better medical resources are in the hands of those with money and power. Poor people deserve good housing and equal access to education, factors that directly or indirectly increase the risk of HIV infection. The best way to reduce the incidence of HIV is to spread HIV knowledge across the board so that everyone knows and understands the disease. The second is to implement compulsory education and formulate policies to make education compulsory are free for all school-age children, similar to the

strategy adopted in China. Furthermore, the availability of scholarships and bursaries as financial incentives for school children can prompt their parents to allow children to attend school. Finally, there is the fight against the industry, which will be mentioned in the next section.

4.2.2 Sex Workers

Sex workers are more likely than other groups to be infected with HIV because of various reasons, such as agreeing to high-risk sexual behaviors because of financial incentives (Cdc.gov. 2021). While HIV prevention programs are feasible for most people, there are many barriers and discrimination for sex workers, making them more than thirteen times more likely to be infected with HIV than the general population (Avert. 2021). Many sex workers are discriminated and marginalized, often receive unfair treatment, such as lack of access to HIV testing or treatment, which can delay their treatments if they are infected with HIV (Cdc.gov. 2021). They also have to have sexual intercourse with various people, but in some cases, they cannot convince their clients to use preventative measures, which can make them prone to infection. Furthermore, sex workers can be young and lack sufficient knowledge about HIV; for example, a study in Ukraine found that 20% of female sex workers were aged between 10 and 19 (Silverman 2011).

5 CORRELATION WITH OTHER DISEASE

The COVID-19 pandemic has affected almost everyone's lives since its spread in 2019. The negative consequences of COVID-19 have been more on some people compared to others. COVID-19 has caused a huge challenge for people living with HIV as well. Restrictions on travel and cargo transfer have caused it more difficult to obtain drugs and treatments available (BMC Public Health. 2021). Therefore, while there have been some positive effects of the COVID-19 pandemic on HIV due to a decrease in the number of HIV cases due to restrictions on people meeting each other and observing social distancing, the availability of drugs has become a challenge too. However, while there has been a global decrease in HIV cases, some groups in populations still remain prone to the disease, poverty, sexual exploitation, food insecurity and drug abuse.

Beyond the disparity in catching the disease, people with HIV are more susceptible to being

infected with COVID-19 and facing severe consequences due to a compromised immune system (Cdc.gov. 2021). But at the same time, governments, organizations and healthcare systems can learn many lessons from the COVID-19 pandemic to fight HIV. In this global fight against the epidemic, various governments quickly responded to the public health crisis and imposed strict measures to prevent the spread of the disease. Additionally, public health campaigns increased the public's awareness about COVID-19, helping to reduce disease transmission. Furthermore, a global effort resulted in the production of effective vaccines against SARS-CoV-2 in an unprecedented time. The rapid development of vaccines in this fight is also one of the most important reasons for controlling the disease, and government funding and researchers' efforts have allowed the COVID-19 vaccine to be quickly designed, synthesized, manufactured and be approved by regulatory agencies. Additionally, the development and availability of user-friendly COVID-19 diagnosis kits have enabled rapid and effective diagnosis to identify infected patients and prevent further transmission of the disease. While HIV is a complex disease, many lessons can be learned from an infectious disease such as COVID-19 to improve our public health strategies. For example, a global effort supported by increased funding and attention is required to find possible vaccines. Moreover, the development of user-friendly and accessible diagnosis kits can identify infected patients to prevent HIV transmission. Finally, effective public health campaigns can remove the stigma of HIV and raise awareness of the disease.

6 CONCLUSIONS

HIV is a major public health concern, which can cause the development of AIDS and finally death if it remains untreated. In comparison, the incident rate has decreased in developed countries over the past three decades, many developing countries, especially those in the Sub-Sahara region struggle with the disease. Even in developed countries, certain groups within the population, such as those with lower socioeconomic status, sexual workers, and drug abusers are more prone to HIV than others. This demonstrates a social disparity resulting in public health inequality. Despite all advances in the understanding of HIV over the past few decades, more research is required to find better treatment with fewer side effects in addition to global efforts to

develop vaccines against HIV. The COVID-19 pandemic can provide a fresh perspective in public health strategies for combatting HIV and AIDS, and many lessons can be learned at personal, national and international levels.

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