

Human Immunodeficiency Virus (HIV), A Serious Threat to Humans

Kinza Mushtaq, Samina Hassan, Aqsa & Muhammad Saad Bhutta *

**Institute of Molecular Biology & Biotechnology, Bahauddin Zakariya University, Multan-60880, Pakistan.*

Article Received: 12 February 2019

Article Accepted: 13 May 2019

Article Published: 26 July 2019

ABSTRACT

HIV is the type of retrovirus which attacks CD4⁺ cell and decreases their number and thus compromises the immunity of the body. The disease originated in the 1800s and spreading since then 7 million peoples get infected with this virus every year. HIV leads to cause AIDS which can kill the person. HIV spread through unprotected sexual contact, breastfeeding, and body fluid transmission and even through HIV mother to her newborn child. Various treatments and drugs are available to treat the disease. But all these remedies cannot cure the person, it just slows the virus and increases the life span of human to some extent. So precautionary measures are subscribed to avoid this disease. It includes, safe sexual contact, prescreening before getting pregnant, avoid reuse of single syringe and it can even avoid through counseling of people. It is most common in uneducated, rural area people so counseling them can great decrease the threat of a virus.

Keywords: Retrovirus, AIDS, Antiretroviral Therapy, Precautions.

INTRODUCTION

HIV or human immunodeficiency virus is a retrovirus that affects the immunity of the person (Alimonti et al. 2003). It attacks CD4⁺ T helper lymphocytes. Due to the role of helper T cell in immunity, the people with HIV have compromised immunity (Hernandez and Sherman 2011). The disease was observed in the 1900s but gets the world attention in 1980s when various homosexuals from urban areas are detected with the disease, moreover, their immune system seems to be compromised and they named the disease, acquired immunodeficiency syndrome (AIDS). After 2 years, scientists discovered the causative agent of disease i.e. HIV virus (Barré-Sinoussi et al. 2004).

HIV was introduced into humans in 1920s from non-human primates like chimpanzees and sooty mangabeys (Sharp and Hahn 2011). Thus HIV is considered a zoonotic disease that transmits from non-human to humans (Hemelaar 2012). The most commonly, it is thought to originate from Simian Immunodeficiency Virus (SIV) which was from non-human primates (de Silva et al. 2008). According to UN research, about more than 7 million people effect with the disease every year and approximately 33.3 million people are living with infection (Hernandez and Sherman 2011).

In Africa, out of 28 million people, 2 million peoples are infected with HIV within the age of 14 to 40 years. One life is lost due to HIV in every two minutes (Odhiambo 2003). The virus spread through various means like body fluid transfusion, breastfeeding, through embryo, blood transfusion, unprotected sexual contact or having various sexual partners, through multiple uses of a single syringe (Bobat and Archary 2017). Various precautionary measures and treatments are available for HIV (Boffito and Venter 2017).

Precautions are far better than its treatment because we cannot eliminate the virus completely and thus threat still remains (Boffito and Venter 2017). HIV is further divided into two types, HIV 1 and HIV 2. HIV 1 is more common and dangerous than HIV 2 (Yamazaki et al. 2016). Under all these consequences we concluded that HIV is better to be prevented than treated. It cannot always be life-threatening, only its last stage, i.e. AIDS, is life-threatening.

What is HIV?

On an individual level, HIV is well studied (Moir et al. 2011). After transmission, virus attack on mucosal tissue and in few days it spread through the lymphoid tissue (Salmi and Jalkanen 2005). Within 10 days it is detectable in the bloodstream. After a few weeks or after month, HIV antibodies are at a detectable rate and the person is mostly infectious at this stage. Sometimes the rate of HIV virus become constant and disease cannot be detectable. When the disease is detected, the immune system is mostly compromised. In some patients, this process is fast while in others it is slow proceeding procedure (Gupta et al. 2006).

HIV is the member of genus Lentivirus of family Retroviridae. Its shape is icosahedral with two single-stranded RNA. These RNA changes into double-stranded DNA and then RNA is degraded (Levy 2011). This dsDNA are then integrated into the human genome and produce viral mRNA and other proteins, like viral capsid and glycoprotein, etc. The viron of HIV consists of 9749 nucleotides (Usmani et al. 2013).

The virus enters into a human in about 1920 to 1940. It seems that the virus enters into a human from non-human primates like chimpanzees and sooty mangabeys from Africa. The history of HIV is linked to Africa and these primates are also found in Africa (Faria et al. 2015). A large number of HIV/AIDS cases has been observed across Africa and a large number of death causalities also observed in the same (Odhiambo 2003).

Types of HIV

HIV is divided into two main types:

- Human immunodeficiency virus type 1 (HIV-1)
- Human immunodeficiency virus type 2 (HIV-2)

HIV-1 is more common and dangerous as compared to HIV-2. Even the speed or time taken by the virus to transmit, in HIV-2, is 5 to 10 times lower than HIV-1 (Burgess 2019)

Human immunodeficiency virus type 1 (HIV-1)

Human immunodeficiency virus type 1 or HIV-1 is the most common cause of AIDS. Moreover, HIV-1 is the most commonly found type of HIV which leads to AIDS (Vallari et al. 2010). So the origin of this virus is as old as that of HIV/AIDS (Deposition et al. 1984).

HIV-1 is further divided into three subtypes, i.e. M (main) group, O (outlier) group, N (novel or not M nor O) group. Among these, group M is the most common and problematic (Kiwanuka et al. 2008). The effect and occurrence of these subtypes and geographically dependent (Hemelaar et al. 2006). The subtype M is further divided into nine classes i.e. A, B, C, D, F, G, H, J, and K. These all strains of HIV accumulate about 95% of HIV virus causing across the worldwide (Lau and Wong 2013).

In transmission HIV-1, the mode or path of transmission doesn't depend much. The most important thing is from where the virus is coming and also on the host which is being infected by the virus (Galvin and Cohen 2004). More

generally, the cause or mode of transmission of HIV-1 is similar to that of causative agents of AIDS, i.e. body fluid transmission, from mother to child through breastfeeding, etc.

HIV-1 can be treated through antiretroviral therapy. It seems that the patient treated with ART, have fewer chances of spreading HIV-1 through sexual contact as it is the major course of transmission of the virus (Odiambo 2003). Another modification of ART is Highly Active Antiretroviral Therapy (HAART), seemed to be effective for treating HIV-1. In spite of these, some additional procedure is done to treat the disease as the patient is unaware of disease and didn't treat himself with HAART (Lange et al. 2008)

Human immunodeficiency virus type 2 (HIV-2)

HIV-1 is the most commonly known HIV virus. The usual HIV virus is HIV-1 virus but in some cases, another type of HIV virus cause disease which is called human immunodeficiency virus type 2 or simple HIV-2 (Campbell-Yesufu and Gandhi 2011). The origin of HIV-2 virus is western African countries (Gottlieb et al. 2008), but now the number of HIV-2 begins to decline in these countries as compared to HIV-1 (C. et al. 2010)

Both viruses replicate in the T cells of infected patients but only HIV-2 replicates efficiently in dendritic cells. Dendritic cells play a major role in the induction of immune responses. DCc only differs in their ability to induce an innate immune response against HIV-1 and HIV-2. These cells do not efficiently activate and infected by HIV-1, whereas they are naturally activated and infected by HIV-2. The reason of inactivity of DCs by HIV-1 is due to restriction factor SAMHD1 (Lahaye et al. 2013).

Symptoms of HIV-2 is not so quickly expressed as it progressed very slowly as compared to HIV-1 (MacNeil et al. 2007). In some cases, it is observed that HIV-2 infected patient show symptoms similar to HIV-1, but it progresses at relatively slow speed (van der Loeff et al. 2010). It is also suggested that encephalitis is more commonly occurs in HIV-2 patient as compared to HIV-1 because the former is more neurotropic as compared to later (Moulignier et al. 2006).

Various methods are available to detect HIV-2, including ELISA, Multispot HIV-1/HIV-2 Rapid Test, and other antibody assay test. The difference between HIV-1 an HIV-2 virus can be detected by immunoblot technique. So HIV-1 and HIV-2 can be differentiated despite their close similarity (Campbell-Yesufu and Gandhi 2011).

HIV-2 is mostly present before seroconversion and thus it is difficult to detect and treat. But once it is detected, it can be treated with antiretroviral treatment or therapy. It is tested that HIV-2 patients can be treated, if treated at the right time, with ART (Lebouché et al. 2013)

Not always life-threatening

HIV doesn't mean that a person must have AIDS. AIDS is the last stage of HIV and difficult to treat. This virus can also infect infants. HIV exposed infants are observed to have abnormal and deficient growth. HIV transmitted to infant through multiple ways (Becquet et al. 2012; Sankar et al. 2015). HIV in the initial stages can be treatable and various techniques and methodologies are present to do this task (Winslow and Kerdel 2016). The most common technique is Antiretroviral therapy, and it has been using worldwide to cure HIV (Kumarasamy et al. 2016).

Many deaths that are causing due to HIV are not directly linked to HIV. Those deaths are causing due to immunodeficiency which is then linked to HIV. So that death is indirectly related to HIV (Article 2010).

Detection of HIV

HIV can be detected by a number of ways as the science is progressing. One of them is through enzyme-linked immunosorbent assay (ELISA). ELISA is the common detection method of any disease and even allergens (Kucharska and Wróblewska 2017). Similarly, it is used to detect HIV. With the advancement in science, the ELISA technique has also been modified according to need. Through modification in ELISA technique, we can detect HIV even when it is in very small quantity as 1×10^{-18} g/ml (Malou and Raoult 2011; De La Rica and Stevens 2012). If ELISA results are positive for HIV, a confirmatory test is done through southern blotting. In southern blotting, one can detect the small quantity of the desired product as the product is labeled with any dye. The dye can be fluorescently or radioactively labeled for detection of desired product or protein (Brown 2001). Thus after detection through ELISA, Southern blotting is used to confirm the presence of the virus.

We can detect HIV through tears of the infected patient. It has been observed that tear glands of HIV infected persons contain a virus, so precautionary measures should be taken by a medical person while doing eye examination (Yang Hana, M, Ning Wua, M, Weijun Zhub et al. 2011).

Due to a high number of infants affected by the virus, the detection of HIV is crucial in infants. Normal techniques cannot detect the virus until the age of 18 months of the child. A technique, called Recombinase polymerase amplification (RPA), helps to detect the virus at early stages of life (Boyle et al. 2013)

Possible Causes

The four most common modes of transmission of HIV are through unsafe sex, breastfeeding, through needles and through infected mother to child (Deeks and Phillips 2009).

Primarily the HIV is caused by unprotected sexual contact or having more than one sexual partners. People already having HIV, are some more reluctant towards separating it to others. They deliberately take risks of separating HIV. But there found some cases in which people didn't do so and use special care for this so they don't harm (Attanasio 2006). There are some organizations that counsel such patients for their treatments as such patients, who have HIV are reluctant to go to health care societies due to negative social behavior of people towards them (Deeks and Phillips 2009)

HIV also transmits through needles or syringes. It can be through known or unknown means. E.g. deliberately using already used syringes and also by mistakenly infected oneself during handling or disposing of used syringes. Some adults, addicted to drugs, use the single syringe in a group of addicts can spread HIV easily (Maimaiti et al. 2014). Moreover, it is observed that syringes used by diabetic patients and by HCV or HBV patients, spread HIV largely. Thus such syringes or lancets should be handled and discard properly (Ishtiaq et al. 2012).

Even in developed countries, there is a large proportion of spreading HIV through breastfeeding from mother to infant. Mother's feed is the only nutritious and beneficial diet for the infant. So breastfeeding is crucial for the

development of an infant (Sankar et al. 2015). It is also that stage when the infant's immune system gets compromised and gets HIV. So special care should be taken to avoid this (Prendergast et al. 2019). The cause of infection depends on various factors like duration of feeding, maternal immunodeficiency and also on maternal immune response (Bulterys et al 2004). Memory cells are more active in breastmilk cells than in lymphoid cells so they are more sensitive to the virus (Viljoen et al. 2015).

The virus also spreads from mother to child; it is also called, in the vertical direction, directly from mother to child (Deeks and Phillips 2009). This transmission of HIV from mother to child is more dangerous as compared to through breastfeeding. The mortality rate is more in later. So mother to child transmission is caused before the birth of the baby so the mortality chance of child decreased drastically and a child born with suppressed immunity (Becquet et al. 2012)

Treatment

Prerequisites also decrease the effect of the disease. Blood screening greatly eliminates the transmission of HIV. Moreover, various treatments are present that decrease the effect of HIV and help in increasing the life of the patient. This includes Antiretroviral therapy, reverse transcriptase inhibitors, and protease inhibitors (Deeks and Phillips 2009).

(A) Antiretroviral therapy

HIV is the retrovirus so Antiretroviral therapy (ART) is used to treat HIV. In ART, the combination of drugs is used which helps to increase the CD4+ cell count in the patient (Martin et al. 2011). In HIV patient, CD4+ cell count decrease to a very low value and this causes the suppression of the immune system of the patient. Various experiments have been conducted and the CD4+ cell count seems to reach the threshold value. Moreover, it is estimated that, if antiretroviral therapy is started in the early stage of HIV (6 months after infections), it is more useful and have much positive effect on the patient. (Lundgren et al. 2015). After treatment with ART, the HIV content in patient genital excretion decreased. Genitals are focused because HIV virus is present in genital excretions in large quantity and most commonly transmitted from their (during sexual contact) (Cohen and Cynthia L. Gay 2014).

Drawback:

Antiretroviral therapy helps to treat the disease, but this treatment cannot restore health. It is observed that HIV treated persons with antiretroviral therapy have a high risk of different diseases like cardiovascular disease, liver failure, kidney failure, cancer and other neuron linked diseases. These diseases are more common in HIV patient than in non-HIV patients (Deeks and Phillips 2009). It also observed that people who are treated with Antiretroviral therapy are more likely to have premature aging and gets old quicker as compared to non-HIV patients (Deeks and Phillips 2009).

Moreover, ART-treated persons are observed to causing more HIV. This is because such a person thought that they got the treatment and thus they started unprotected sexual contacts and the use of syringes again. It should be

educated that ART cannot remove the virus completely, it just increases the life span of the patient by decreasing number of viruses and by increasing the CD4+ cells (Cohen and Gay 2010).

(B) Reverse transcriptase inhibitors (RTI)

Various drugs have been introduced to treat HIV, but, an naturally present drug is most beneficial (Mehellou and De Clercq 2010). Retroviruses have an RNA genome. The RNA first reverse transcribe through reverse transcriptase and thus convert into double-stranded DNA. That DNA then takes host machinery and cause infections (York 2018). dsDNA molecule then inserted into the host chromosome through another enzyme called integrase (Das and Arnold 2013).

One mechanism is that the activity of reverse transcriptase is inhibited by binding it with some molecule and thus when reverse transcriptase didn't perform its task, viral RNA didn't convert into dsDNA and virus didn't grow and expands. And another method is that an enzyme produced, which binds to integrase and restrict the integration of dsDNA in the host chromosome. In this way, when DNA didn't take the host machinery, it cannot produce viral protein and in this way, the virus cannot spread and also not produced (Hare et al. 2010). And so when virus didn't produce, virus population remained minimized and thus CD4+ contents can remain high and host can survive easily.

(C) Protease inhibitors

Protease inhibitors (pi) are the drugs, which inhibits the viral replication by binding itself to the protease enzyme. Protease enzyme is necessary for proteolytic cleavage of protein precursor. Thus Pi restricts the cleavage, which is necessary for the production of infectious viral protein. Thus viral protein didn't produce and CD4+ cell count remains high and the patient didn't get the infection.

Precautions

General precautions for HIV are according to their causes. It includes, not having more than one sexual partner and avoiding unprotected sex. In a group of sexually linked people, if a single person gets HIV, the whole group has a chance to get HIV (Odhiambo 2003).

To avoid the mother to child transmission, the mother should do proper screening before getting pregnant. She should also take proper measures in breastfeeding her child. Proper screening should be necessary to avoid mother to child transmission of HIV (Sankar et al. 2015; Prendergast et al. 2019)

The reuse of syringes should be prohibited. Used syringes should be discarded properly by the hospital facility and disposed of or dump them properly to eliminate the transmission of the virus. On a personal level, never reuse the syringe. Discard the syringe properly after every use so no one can use it again (Ishtiaq et al. 2012).

HIV patients are more sensitive towards society as they continuously face different hate comments and criticism. This could lead them to hurting someone else or they can also infect others for their revenge. So such patients are treated well and within a friendly environment, so they could also express their feelings towards society and can be the part of society happily (Stutterheim et al. 2014)

Health care personals should also take precautions while treating or dealing with HIV patients. These precautions include the use of double gloves, face masks, to cover body and try not to expose the skin to the virus (Dhaliwal et al. 2011)

CONCLUSION

HIV is not always life-threatening and a person having HIV doesn't mean that he must have AIDS. AIDS is the last stage of HIV and is life-threatening and difficult to treat. The virus can be treated and also be avoided. Various treatments are available but antiretroviral therapy is most commonly used. Numerous drugs have been designed for this purpose. Moreover, precautionary measures should be taken to avoid transmission of HIV virus. A common mode of transmission of the virus is through sexual contact, body fluid transmission and also through mother to child transfer. These all can be avoided by taking special precautions.

HIV patients are relatively more sensitive as they are not accepted by society. So such patients need special attention and care so they don't harm others and also for their own wellbeing. This can be done by various psychological therapies and also by interacting with such patients.

HIV is most common in 3rd world countries and even in rural areas of developed countries. The main cause is the lack of education and proper guidance. There should be some programs and seminars should be held which aware people about HIV, its harms and how to avoid it. By proper counseling of peoples and by proper guidance, we can decrease the death toll caused by HIV-AIDS and also decreased the people affecting by this virus.

REFERENCES

- Alimonti JB, Ball TB, Fowke KR (2003) Mechanisms of CD4+ T lymphocyte cell death in human immunodeficiency virus infection and AIDS. *J Gen Virol* 84:1649–1661. doi: 10.1099/vir.0.19110-0.
- Article M (2010) Causes of Death in HIV-1–Infected Patients Treated with Antiretroviral Therapy, 1996–2006: Collaborative Analysis of 13 HIV Cohort Studies. *Clin Infect Dis* 50:1387–1396. doi: 10.1086/652283
- Attanasio O (2006) Intertemporal consumption choices, transaction costs and limited participation to financial markets: reconciling data and theory. *J Appl Econom* 343:322–343. doi: 10.1002/jae
- Barré-Sinoussi F, Chermann JC, Rey F, et al (2004) Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). *Rev Investig Clin* 56:126–129
- Becquet R, Marston M, Dabis F, et al (2012) Children Who Acquire HIV Infection Perinatally Are at Higher Risk of Early Death than Those Acquiring Infection through Breastmilk: A Meta-Analysis. *PLoS One* 7:e28510. doi: 10.1371/journal.pone.0028510
- Bobat R, Archary M (2017) HIV Infection. In: *Viral Infections in Children, Volume I*. Springer International Publishing, Cham, pp 69–100
- Boffito M, Venter F (2017) The triumph of HIV treatment: another new antiretroviral. *Lancet* 390:2019–2021. doi: 10.1016/s0140-6736(17)32297-3

- Boyle DS, Lehman DA, Lillis L (2013) Rapid Detection of HIV-1 Proviral DNA for Early Infant Diagnosis Using Rapid Detection of HIV-1 Proviral DNA for Early Infant Diagnosis. *MBio* 4:e00135-13. doi: 10.1128/mBio.00135-13. Editor Brown (2001) *Im1006a.Pdf*. 1–13
- Bulterys et al (2004) Late Postnatal Transmission of HIV-1 in Breast-Fed Children: An Individual Patient Data Meta-Analysis. *J Infect Dis* 189:2154–2166. doi: 10.1086/420834
- Burgess L (2019) Differences between HIV-1 and HIV-2. 2–7
- C. VT, M.S. VDL, S.M.A. Z, et al (2010) Two distinct epidemics: The rise of HIV-1 and decline of HIV-2 infection between 1990 and 2007 in rural guinea-bissau. *J Acquir Immune Defic Syndr* 53:640–647
- Campbell-Yesufu OT, Gandhi RT (2011) Update on human immunodeficiency virus (HIV)-2 infection. *Clin Infect Dis* 52:780–787. doi: 10.1093/cid/ciq248
- Cohen MS, Cynthia L. Gay (2014) Treatment to prevent transmission of HIV-1. *Clin Infect Dis* 50:1–15. doi: 10.1086/651478. Treatment
- Cohen MS, Gay CL (2010) Treatment to Prevent Transmission of HIV-1. *Clin Infect Dis* 50:S85–S95. doi: 10.1086/651478
- Das K, Arnold E (2013) HIV-1 reverse transcriptase and antiviral drug resistance. Part 1. *Curr Opin Virol* 3:111–118. doi: 10.1016/j.coviro.2013.03.012
- De La Rica R, Stevens MM (2012) Plasmonic ELISA for the ultrasensitive detection of disease biomarkers with the naked eye. *Nat Nanotechnol* 7:821–824. doi: 10.1038/nnano.2012.186
- De Silva TI, Cotten M, Rowland-Jones SL (2008) HIV-2: the forgotten AIDS virus. *Trends Microbiol* 16:588–595. doi: 10.1016/j.tim.2008.09.003
- Deeks SG, Phillips AN (2009) HIV infection, antiretroviral treatment, ageing, and non-AIDS related morbidity. *BMJ* 338:288–292. doi: 10.1136/bmj.a3172
- Deposition A, Blasing J, Division ES (1984) Detection, Isolation, and Continuous Production of Cytopathic Retroviruses (HTLV-111) from Patients with AIDS and Pre-AIDS. 2–5
- Dhaliwal B, Saha PK, Goel P, et al (2011) Universal Precautions against HIV and other Blood- Borne Pathogens - Knowledge, Attitude and Compliance among health professionals in Obstetrics and Gynecology. 6:13–16
- Faria NR, Rambaut A, Suchard MA, et al (2015) Continuation of targeted therapy after disease progression. *Nowotwory* 65:424–427. doi: 10.1126/science.1256739. The
- Galvin SR, Cohen MS (2004) The role of sexually transmitted diseases in HIV transmission. *Nat Rev Microbiol* 2:33–42. doi: 10.1038/nrmicro794
- Gottlieb GS, Eholié S-P, Nkengasong JN, et al (2008) A call for randomized controlled trials of antiretroviral therapy for HIV-2 infection in West Africa. *Aids* 22:2069–2072. doi: 10.1097/qad.0b013e32830edd44

- Gupta P, White RM, Mellors JW, et al (2006) Prognosis in HIV-1 Infection Predicted by the Quantity of Virus in Plasma. *Science* (80-) 272:1167–1170. doi: 10.1126/science.272.5265.1167
- Hare S, Vos AM, Clayton RF, et al (2010) Molecular mechanisms of retroviral integrase inhibition and the evolution of viral resistance. *Proc Natl Acad Sci* 107:20057–20062. doi: 10.1073/pnas.1010246107
- Hemelaar J (2012) The origin and diversity of the HIV-1 pandemic. *Trends Mol Med* 18:182–192. doi: 10.1016/j.molmed.2011.12.001
- Hemelaar J, Gouws E, Ghys PD, Osmanov S (2006) Global and regional distribution of HIV-1 genetic subtypes and recombinants in 2004. *Aids* 20:13–23. doi: 10.1097/01.aids.0000247564.73009.bc
- Hernandez M, Sherman K (2011) HIV/HCV coinfection natural history and disease progression, a review of the most recent literature. *Curr Opin HIV AIDS* 6:478–482. doi: 10.1097/COH.0b013e32834bd365.HIV/HCV
- Ishtiaq O, Qadri AM, Mehar S, et al (2012) Disposal of syringes, needles, and lancets used by diabetic patients in Pakistan. *J Infect Public Health* 5:182–188. doi: 10.1016/j.jiph.2012.02.002
- Kiwanuka N, Laeyendecker O, Robb M, et al (2008) Effect of Human Immunodeficiency Virus Type 1 (HIV-1) Subtype on Disease Progression in Persons from Rakai, Uganda, with Incident HIV-1 Infection. *J Infect Dis* 197:707–713. doi: 10.1086/527416
- Kucharska E, Wróblewska B (2017) Food allergens. *Toxins Other Harmful Compd Foods* 1592:337–368. doi: 10.1201/9781315368535
- Kumarasamy N, Hakim JG, Kumwenda J, et al (2016) Antiretroviral Therapy for the Prevention of HIV-1 Transmission. doi: 10.1056/NEJMoa1600693
- Lahaye X, Satoh T, Gentili M, et al (2013) The Capsids of HIV-1 and HIV-2 Determine Immune Detection of the Viral cDNA by the Innate Sensor cGAS in Dendritic Cells. *Immunity* 39:1132–1142. doi: 10.1016/j.immuni.2013.11.002
- Lange J, Levy JA, Cohen MS, et al (2008) The spread, treatment, and prevention of HIV-1: evolution of a global pandemic. *J Clin Invest* 118:1244–1254. doi: 10.1172/jci34706
- Lau KA, Wong JKL (2013) Current trends of HIV recombination worldwide. *Infect Dis Rep* 5:4. doi: 10.4081/idr.2013.s1.e4
- Lebouché B, Engler K, Lévy JJ, et al (2013) French HIV Experts on Early Antiretroviral Treatment for Prevention. *J Int Assoc Provid AIDS Care* 13:160–169. doi: 10.1177/2325957413488196
- Levy JA (2011) Virus-Host Interactions in HIV Pathogenesis. *Adv Dent Res* 23:13–18. doi: 10.1177/0022034511398874
- Lundgren JD, Babiker AG, Gordin F, et al (2015) Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection. *N Engl J Med* 373:795–807. doi: 10.1056/NEJMoa1506816

- MacNeil A, Sarr AD, Sankale J-L, et al (2007) Direct Evidence of Lower Viral Replication Rates In Vivo in Human Immunodeficiency Virus Type 2 (HIV-2) Infection than in HIV-1 Infection. *J Virol* 81:5325–5330. doi: 10.1128/jvi.02625-06
- Maimaiti N, Shamsuddin K, & Nurungul Tohti AA, Maimaiti R (2014) Knowledge, Attitude and Practice regarding HIV/AIDS among University students in Xinjiang. *Glob J Health Sci* 2:. doi: 10.5539/gjhs.v2n2p51
- Malou N, Raoult D (2011) Immuno-PCR: A promising ultrasensitive diagnostic method to detect antigens and antibodies. *Trends Microbiol* 19:295–302. doi: 10.1016/j.tim.2011.03.004
- Martin M, Press M, Ph D, et al (2011) new england journal. *New Engl J Med* Vol 365:1273–1283
- Mehellou Y, De Clercq E (2010) Twenty-six years of anti-HIV drug discovery: Where do we stand and where do we go? *J. Med. Chem.* 53:521–538
- Moir S, Chun T-W, Fauci AS (2011) Pathogenic Mechanisms of HIV Disease. *Annu Rev Pathol Mech Dis* 6:223–248. doi: 10.1146/annurev-pathol-011110-130254
- Moulinier A, Lascoux C, Bourgarit A (2006) HIV Type 2 Demyelinating Encephalomyelitis. *Clin Infect Dis* 42:e89–e91. doi: 10.1086/503909
- Odhiambo W (2003) HIV/AIDS and debt crises: threat to human survival in sub-Saharan Africa. *Med Confl Surviv* 19:142–147. doi: 10.1080/13623690308409681
- Prendergast AJ, Goga AE, Waitt C, et al (2019) Transmission of CMV, HTLV-1, and HIV through breastmilk. *Lancet Child Adolesc Heal* 3:264–273. doi: 10.1016/S2352-4642(19)30024-0
- Salmi M, Jalkanen S (2005) Cell-surface enzymes in control of leukocyte trafficking. *Nat Rev Immunol* 5:760–771. doi: 10.1038/nri1705
- Sankar MJ, Sinha B, Chowdhury R, et al (2015) Optimal breastfeeding practices and infant and child mortality: A systematic review and meta-analysis. *Acta Paediatr Int J Paediatr* 104:3–13. doi: 10.1111/apa.13147
- Sharp PM, Hahn BH (2011) Origins of HIV and the AIDS pandemic. *Cold Spring Harb Perspect Med* 1:1–22. doi: 10.1101/cshperspect.a006841
- Stutterheim SE, Sicking L, Brands R, et al (2014) Patient and Provider Perspectives on HIV and HIV-Related Stigma in Dutch Health Care Settings 1. 28:23–27. doi: 10.1089/apc.2014.0226
- Usmani SM, Bibollet-Ruche F, Peeters M, et al (2013) Human Tetherin Exerts Strong Selection Pressure on the HIV-1 Group N Vpu Protein. *PLoS Pathog* 8:e1003093. doi: 10.1371/journal.ppat.1003093
- Vallari A, Holzmayer V, Harris B, et al (2010) Confirmation of Putative HIV-1 Group P in Cameroon. *J Virol* 85:1403–1407. doi: 10.1128/jvi.02005-10
- van der Loeff MFS, Larke N, Kaye S, et al (2010) Undetectable plasma viral load predicts normal survival in HIV-2-infected people in a West African village. *Retrovirology* 7:2–11. doi: 10.1186/1742-4690-7-46

Viljoen J, Tuailon E, Nagot N, et al (2015) Cytomegalovirus, and possibly Epstein-Barr virus, shedding in breast milk is associated with HIV-1 transmission by breastfeeding. *Aids* 29:145–153. doi: 10.1097/QAD.0000000000000527

Winslow CY, Kerdel FA (2016) Human immunodeficiency virus. In: *Dermatological Manifestations of Kidney Disease*. pp 45–56

Yamazaki S, Kondo M, Sudo K, et al (2016) Qualitative Real-Time PCR Assay for HIV-1 and HIV-2 RNA. *Jpn J Infect Dis* 69:367–372. doi: 10.7883/yoken.JJID.2015.309

Yang Hana, M, Ning Wua, M, Weijun Zhub YL, Lingyan Zuo, Junjie Yec, Zhifeng Qiu JX and, Lia T (2011) *Research Letters*. 1925–1929

York A (2018) An aquatic origin of retroviruses. *Nat Rev Microbiol* 16:455–455. doi: 10.1038/s41579-018-0052-x