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Why HIV Failed In The Era of Treatment and Technology? - A Review

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Abstract
Human Immunodeficiency Virus, a kind of retrovirus responsible for Acquired immunodeficiency syndrome (AIDS). This virus attacks on indispensible cells like CD4+ T-helper cells resulting immunosuppression. The body becomes susceptible to get opportunistic infections and metrified to life threatening AIDS. HIV proliferates inside host cells in order to evade and elicit human immune response.The purpose behind the study is to explore more knowledge about the loop holes left in HIV infection treatment even after the world has recent technologies and treatment. The major factors responsible for failure of HIV treatment include drug toxicity, drug resistance, virological and immunological factors or effectiveness of antiretroviral drugs. The decrease in CD4 count and increase in viral load leads to progression of disease. HIV is retro-genic in nature so it is a challenge to design a vaccine for complete elimination of this virus.
Keywords: HIV, AIDS, Immune Cells, CD4+cells, Reverse Transcription, ART

Introduction

Human immunodeficiency virus has major impact on human immune system.[1] Opportunistic infections seek advantage of weak immune system and deteriorate the health.[2]This virus mainly attacks on $CD4^+$ T-helper cell, macrophages etc. threatening the $CD4^+$ cells to critical level resulting loss of cell mediated immunity. Opportunistic infections get benefit of weak immune system and disease progressed into Acquired immunodeficiency syndrome. In 1983, AIDS was clinically reported in The United States for first time. Chiefly HIV has been characterized into two subtypes as HIV-1 and HIV-2. Both subtypes trusted to be emerged from non-primates.[3] The researchers believed that HIV emerged from the evolution of Simian immunodeficiency virus affecting wild chimpanzees. In 20^{th} century, virus transmitted to humans by exposure to infected blood during hunting. HIV transmitted to body as single stranded RNA and within the host is immediately metrified to double stranded RNA genome. AIDS exerts a dreadful toll on societies, crippling their economies, decimating their labour forces.[4]Virus remains undetected for months and years before any sign of

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illness. Dysfunctioning of central nervous system is a prominent feature of AIDS. Within the CNS the primary site of active HIV-1 infection is microglia. No effective cure is currently available. But HIV infection can be managed by use of multiple antiretroviral drugs. Treatment has been successful to numerous region of world by improving immune system function. Many researchers have been working on better understanding of HIV stigma and to remove the barriers developed during treatment intervention. In this paper, reasons of treatment failure like viral resistance, virological and immunological failure, gene modification, toxicity and drug potency has been discussed.[5]

Stages of HIV infection:

The HIV infection relies upon the sign and symptoms. Few don't show any symptoms at all and remain quiescent for years. Acute primary infection or window phase isproximate phase which occurs soon after the HIV instance. The patient shows symptoms around after one to four weeks after the exposure to the virus. These symptoms alone are not reliable to make diagnosis. Symptoms in early phase are non-specific and may include pyrexiamyalgia, joint agonygastralgia, sore etc. The infected cells circulate throughout the blood and antibodies are produced in response to virus. This is called sero-conversion or window period.[6]In the asymptomatic stage i.e. after sero-conversion illness, immune system of body weakens slowly and shows almost no symptoms. This phase is also known as clinical latency.During the symptomatic stage (third stage), immune system of body is severely damaged as HIV damages primarily body fighting CD4 cells and disease is progressed into AIDS. This stage may show symptoms like loss of appetite, mal-absorption, diarrhea etc. [6]

SYMPTOMS

According to centres for disease control, classification of clinical manifestation of HIV infection is divided into 4 groups [7]. Group 1 is acute infection- it is obscure that how many HIV infected individuals will have symptoms of an acute viral infection. Individual may develop following symptoms after HIV exposure like pyrexia, nausea, rashes, aphthous ulcers, lymphadenopathy, cephalgia etc.[6]. Group 2 is asymptomatic infection- person can remain asymptomatic or in dormant phase for decades as after 1-2 weeks acute illness resolves spontaneously. But it may leads to weakening of immune system due to deficiency of CD4+ cells and elevated level of CD8 lymphocytes.Group 3 is persistent generalized lymphadenopathy- few individuals may show symptoms of larger lymph node and persistent for longer period at different sites. Apart from this, it may also include tuberculosis, syphilis, toxoplasmosis and lymphoma.Group 4 includes other diseases- Because of immunosuppression other opportunistic infections and malignancies are associated with HIV like diarrhoea, pulmonary infections, neurological problems, secondary cancers etc.[7]
But recent evidences show 70% - 90% HIV infected individuals show flu like symptoms after HIV exposure. Kaposi's sarcoma is specific marker but Herpes infection is also common which causes mouth, and genital sores. Other symptoms may include enlarged glands, skin rashes, growth retardation, shortness of breath, mental confusion, vision loss etc.[8, 9]

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HIV STRAINS AND TYPES

HIV-1 is the frequent and predominate distribution over worldwide than HIV-2. [10]Like other viruses, it has ability to mutate and change with respect to time. HIV-2 is least pathogenic disease mainly concentrated in West Africa. This classification is mainly based on genetic and antigen characteristics.[11]

HIV-1

In genomic structure of HIV-1, DNA is fringed at terminal ends. The 5' long terminal repeat sequences codes the promoter. The gag and pol reading frame codes for specific enzymes like reverse transcriptase, RNase, integrase etc. Regulatory proteins like Vpu, Vpr and gp120, gp41 glycoproteins are also involved.[12] HIV type 1 has mainly four strains i.e. M, N, O, P and out of which M stain is major one. This virus mutates comprehensively and show high genetic diversity resulting significant complications and challenges for effective disease control. [13]

HIV-2

The HIV-2 has mainly two groups i.e. A1 and A2. This type is least pathogenic but it can also be progressed into AIDS by lowering the immunity.[14] Instead of Vpu gene, HIV-2 consist Vpx gene. HIV-1 enters immune system by interacting CD4+ receptor and is more likely to progress and worsen whereas type 2 strain is least i.e. Progression is slower. [15]

HIV Structure and Function

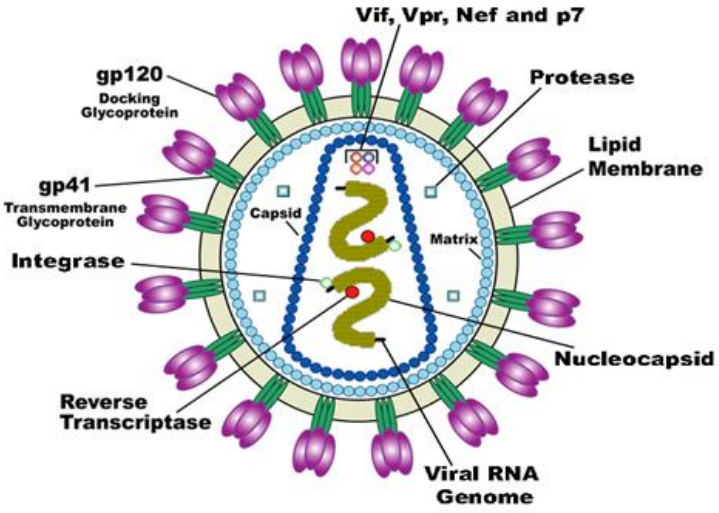

Fig:1- Structure of HIV virus

The HIV virus consist RNA as genetic material in its genome and other enzymes like reverse transcriptase, protease and integrase are associated with protein core. Over the

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enveloped surface gp120 antigen is located which helps in binding. Its genome also consist gag, pol and env genes.[16, 17]

Mechanism of Infection

HIV infects mainly those cells that are having CD4 receptor on their surface for virus entry [17]. The cells devoid of CD4 receptors have Fc or complement receptor site which are used for HIV entry. [18] In human body, the monocytes, tissue macrophages, T lymphocytes, hematopoietic stem cells, endothelial cell and gastrointestinal epithelial cells are the main targets of HIV infection. [19] Like all viruses, HIV replicates using the host machinery.[20] HIV inserts its genetic material into host genome and with enzyme reverse transcriptase starts genomic replication. The newly synthesized viral proteins assemble to produce new virus. Followed by assembling, virus exits the infected cell via budding. [21]

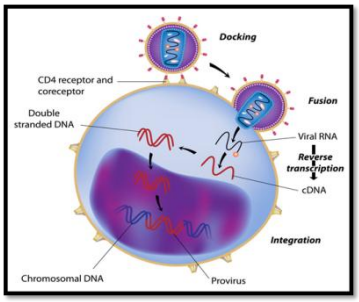

Fig:2 - Mechanism of HIV replication inside host cell

HIV treatment failure: A matter of concern

Treatment failure is said to be when antiretroviral drugs are unable to eliminate or reduce the HIV viral activity resulting weak immune system.[22] It is classified as virologic, *immunologic* or both. The main causes responsible for treatment failure are: suboptimal drug adherence, poor drug absorption, low CD4 count, poor adherence to food restrictions. Virologic Failure: If detectable viraemia is >400/mL during treatment, then it is considered as virologic failure. Thus immediate possible switch to new antiretroviral agents is necessary. [23] Similarly, if viral load is less than 200 is not to be taken good response by antiretroviral drugs but it is still a matter of concern. [24]Inadequate drug adherence and drug resistance are main causes of virologic failure. Though, even if the virologic failure is established, it is necessary to correct any adherence issues before proceeding to new therapy. [25]Immunologic Failure: Even after viral suppression if CD4 level fails to increase in required amount then it is known as immunological failure.[26] Some scientists suggest that changing therapy is helpful, although there is no evidence. Several immunity based therapies are being investigated, tested and established but currently none are recommended beyond the context of a clinical trial.[27]

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Obstacles in fighting and eradicating HIV:

Few individuals are even aware of their infection, largely due to misconception and fear that prevent them from finding out there status. Symptoms appear later so early diagnosis is not possible. [28] Patients who are HIV positive do not receiving continuous treatment. Eradicating HIV is challenging due to several factors, including economic and financial issues, health care literacy and the feeling of stigmatization.[29]Adverse Drug Reactions (ADR) is noxious drug response and occurs at doses is one of the major challenge. A serious consequence of leaving treatment in between is the emergence of antibiotic resistance.[30] The adverse effects of drugs are nausea, diarrhoea, vomiting, constipation, dyspepsia, abdominal pain, headache, numbness/tingling, peripheral neuropathy, memory problems, impairment of sense organs, haematological, psychological, and dermatological likeskin rash, facial discoloration. [31]

Socioeconomic status: The probable risk in women is higher than others who are at social position. [32] Poverty-induced stress is another cause of non-adherence. Illiterate patients show treatment failure because of irregular medication therapy. [33] Social stigma: Internalized stigma and patients with HIV/AIDS feel uncomfortable to adjust in society induces stress and ART non-adherence. [34]

Vaccines for HIV:

There is no cure for AIDS but some medicines are used to decrease its growth rate to enhance the affected individual life span. [35] Currently, the first HIV vaccine experimental study is underway in South Africa. The results of the studies are expected to be in favour of human population to eradicate HIV completely and results will be out hopefully in 2021. [36] Diagnosis HIV screening and diagnosis are important aspect for patient's health and survival. [37] Normally it can be diagnosed on saliva, blood and other body fluids for detection of antibodies to the virus. [38] Classification of laboratory diagnosis of HIV into following groups is [38-42] Group-1 includes ELISA i.e. enzyme linked immune sorbent assay and rapid tests like Dot blot assays, particle agglutination, coomb tests, fluorimetric analysis. [39] Group-2 includes confirmatory tests like immunofluorescent assay, western blot, and radio immuno precipitation assay. Group-3 are p24 antigen test, culturing, PCR, viral load etc. In group-4 alternative tests like oral fluid and urine analysis are included. Drug resistance test used to check whether the strain of HIV is resistant or sensitive to particular antiviral drug therapy. [43]

TREATMENT

Antiretroviral drugs or therapy (ART) are very effective against HIV. These drugs are very useful in prolonged and improving quality of life. Approximate 20 various antiretroviral drugs have been designed which are effective. [44] These drugs are mainly categorised into six classes i.e. a) nucleotide reverse transcriptase inhibitors (NRTI), b) non-nucleoside reverse transcriptase inhibitors (NNRTI), c) protease inhibitors, d) fusion inhibitors, e) CCR5 antagonist, f) integrase inhibitors. NRTI act like false building blocks and compete with nucleoside and nucleotide preventing DNA synthesis. NNRTI mainly targets reverse transcriptase. Examples are zidovudine, combivir, tenofovir and didanosine. Protease Inhibitorsdrugseffectively block the function of protease enzyme resulting release of non-infectious viral particles like indinavir, ritonavir, amprenavir etc. Chemokine Receptor 5 Antagonistblocks the chemokine Receptor (CCR5) on CD4 cells**.** Integrase Inhibitors inhibit host and viral genome integration.[45]

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HAART

Highly active antiretroviral therapy i.e. HAART is currently used and consist multiple drugs of antiretroviral agents. [45] Regular diagnosis and treatment assessment reduce the excess mortality rate. This therapy controls the viral proliferation and increases CD4 cells. Thus it decreases the disease progression and reduces transmission risk. [46]

Interpretation and conclusion:

The research for successful and effective vaccine over the last two decades has been dawning of a more sober optimism. [47] HIV is more concerned topic for improvement and accelerating scientific research process for betterment of human health. [48] It is not only affecting health, but also affecting the socio-economic development of countries. [49].It is very challengeable to design a vaccine or to deliver a drug on target because it is retrogenic. [44] HIV is improving with the development of antiretroviral drugs (HAART THERAPY) that reduces undetectable viral load. Currently the research is in dormant period as no effective trials because researchers are failed to understand that what kind of vaccine might best gives a truly effective response against HIV. [51]

CONFLICT OF INTEREST

No conflict of interest.

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References

[1] G. K. Ravindra, G. John, P. Neil, H. S. Hiwot, T. Amilcar, A. F. Liliana, K. Pontiano et al, "HIV-1 drug resistance before initiation or re-initiation of first-line antiretroviral therapy in low-income and middle-income countries: a systematic review and meta-regression analysis." The Lancet infectious diseases, vol.3, pp.346-355, 2018.

[2] D. Vancampfort, J. Mugisha, D. M. Hert, M. Probst, J. Firth, P. Gorczynski, B. Stubbs,"Global physical activity levels among people living with HIV: a systematic review and meta-analysis."Disability and Rehabilitation, vol.4, pp.388-9, Feb 2018.

[3] Mikkelsen, J. A. C. Hunterz , M. P. M. Jenson, T. Bärnighausen, K. Hauck, K. Johansson, et al,"Evidence for scaling up HIV treatment in sub-Saharan Africa: a call for incorporating health system constraints."PLoS Med, vol.14, 2017.

[4] J. Riddell, K. R. Amico, K. H. Mayer,"HIV preexposure prophylaxis: a review." Jama, vol.12, pp.1261-1268, Mar 2018.

[5] Giri, Juan, J. R. Horacio, M. Alejandra, and P. Norma, "Case report of a novel amino acid deletion in codon 67 and T69G substitution in the reverse transcriptase of HIV-1." Antiviral therapy, vol.3, pp.227-228, 2000.

[6] Chadwick, G. Ellen, V. C. Edmund, Y. Ram, A. P. Jorge, R. Brian, H. R. John, C. Jie et al, "Pharmacokinetics, safety and efficacy of lopinavir/ritonavir in infants less than 6 months of age: 24 week results." Aids, vol.2, pp.249-255, 2008.

[7] Miedzinski, J. Lil, "Early clinical signs and symptoms of HIV infection: delaying progression to AIDS." Canadian Family Physician, p.1401, 1992.

[8] A. Kapila, S. Chaudhary, R. B. Sharma, H. Vashist, S. S. Sisodia, and A. Gupta. "A REVIEW ON: HIV AIDS." Indian Journal of Pharmaceutical and Biological Research, vol. 3, pp. 69-73, 2016.

[9] Vancampfort, Davy, M. James, R. Justin, D. H. Marc, P. Michel, and S. Brendon, "Physical activity correlates in people living with HIV/AIDS: a systematic review of 45 studies." Disability and rehabilitation, vol. 14, pp.1618-1629, 2018.

[10] Welles, S. L., J. B. Jackson, B. Yen-Lieberman, L. Demeter, A. J. Japour, L. M. Smeaton, V. A. Johnson et al, "Prognostic Value of Plasma Human Immunodeficiency Virus Type 1 (HIV-l) RNA Levels in Patients with Advanced HIV-l Disease and with Little or No Prior Zidovudine Therapy." Journal of Infectious Diseases, vol.4, pp. 696-703, 1996.

ISSN:0971-1260
Vol-22-Issue-16-August-2019

[11] Garey, Lorra, B. Jafar, S. Carla, N. Clayton, J. Z. Michael, and G. Adam, "Anxiety, depression, and HIV symptoms among persons living with HIV/AIDS: the role of hazardous drinking." AIDS care, vol.1, pp. 80-85, 2015.

[12] Piketty, Christophe, R. Esther, C. Philippe, B. Laurent, P. Gilles, S. M. Ali, G. C. Gustavo, W. Laurence, C. François, and D. K. Michel, "Efficacy of a five-drug combination including ritonavir, saquinavir and efavirenz in patients who failed on a conventional triple-drug regimen: phenotypic resistance to protease inhibitors predicts outcome of therapy." Aids, vol.11, pp. F71-F77, 1999.

[13] Alaeus, Annette, "Significance of HIV-1 genetic subtypes." Scandinavian journal of infectious diseases, vol. 5, pp. 455-463, 2000.

[14] Blattner, William, C. G. Robert, and H. M. Temin, "HIV causes aids." Science, vol.4865, pp. 515-516, 1988.

[15] Duesberg, H. Peter, "HIV is not the cause of AIDS." Science, vol. 4865, pp. 514-517, 1988.

[16] Downs, M. Angela, and D. V. Isabelle, "Probability of heterosexual transmission of HIV: relationship to the number of unprotected sexual contacts." JAIDS Journal of Acquired Immune Deficiency Syndromes, vol. 4, pp. 388-395, 1996.

[17] Levy, A. Jay, "HIV pathogenesis: 25 years of progress and persistent challenges." Aids, vol. 2, pp. 147-160, 2009.

[18] Sauter, Daniel, U. Daniel, V. Michael, M. U. Shariq, H. Anke, F. K. Silvia, H. Elisabeth et al, "Human tetherin exerts strong selection pressure on the HIV-1 group N Vpu protein." PLoS pathogens, e1003093, vol. 12, 2012.

[19] Vicenzi, E., and G. Poli, "Novel factors interfering with human immunodeficiency virus-type 1 replication in vivo and in vitro." Tissue Antigens, vol. 2, pp. 61-71, Feb, 2013.

[20] Kuiken, Carla, et al, “HIV sequence compendium 2010.” No. LA-UR-10-03684. Los Alamos National Lab.(LANL), Los Alamos, NM (United States), Dec. 2010.

[21] Peeters, Martine, and M. Paul, "Genetic diversity of HIV-1: the moving target." Aids, vol. 3, pp. S129-S140, 2000.

[22] Simon, François, M. Philippe, R. Pierre, L. A. Ibtissam, C. Michaela, T. Müller, S. Sentob, C. G. C. Marie, B. C Françoise, and B. V. Françoise, "Identification of a new human immunodeficiency virus type 1 distinct from group M and group O." Nature medicine, vol. 9, p.1032, 1998.

ISSN:0971-1260
Vol-22-Issue-16-August-2019

[23] Tadesse, T. Wondmagegn, B. M. Alemayehu, H. T. Wubshet, and T. T. Yidnekachew, "Self-reported adverse drug reactions and their influence on highly active antiretroviral therapy in HIV infected patients: a cross sectional study." BMC pharmacology and Toxicology, vol.1, p.32, 2014.

[24] K. Ingersoll, "The impact of psychiatric symptoms, drug use, and medication regimen on non-adherence to HIV treatment." AIDS care, vol.2, pp.199-211, 2004.

[25] Azar, Pouya, W. Evan, N. Paul, L. Maxo, M. Julio, K. Thomas, and M. J. Milloy, "Drug use patterns associated with risk of non-adherence to antiretroviral therapy among HIV-positive illicit drug users in a Canadian setting: a longitudinal analysis." BMC infectious diseases, vol.1, p.193, 2015.

[26] Dlamini, S. Priscilla, W. Dean, N. M. Lucy, C. Maureen, W. K. Thecla, G. Minrie, N. Joanne, M. Joseph, R. U. Leana, and L. H. William, "HIV stigma and missed medications in HIV-positive people in five African countries." AIDS patient care and STDs, vol.5, pp.377-387, 2009.

[27] Saag, S. Michael, A. B. Constance, T. G. Rajesh, F. H. Jennifer, J. L. Raphael, J. M. Michael, E. S. Paul et al, "Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2018 recommendations of the International Antiviral Society–USA Panel." Jama, vol.4, pp.379-396, 2018.

[28] Klimas, Nancy, O. K. Anne, and A. F. Mary, "Overview of HIV." Psychosomatic medicine, vol.5, pp.523-530, 2008.

[29] Chang, Linda, E. Thomas, S. Oliver, P. Hetal, D. Menaka, L. Maria, and N. M. Eric, "Perfusion MRI and computerized cognitive test abnormalities in abstinent methamphetamine users." Psychiatry Research: Neuroimaging, vol.2, pp. 65-79, 2002.

[30] Willie, C. Tiara, M. Nicole, Overstreet, P. S. Tami, J. S. Kathleen, and B. H. Nathan, "Barriers to HIV medication adherence: examining distinct anxiety and depression symptoms among women living with HIV who experienced childhood sexual abuse." Behavioral Medicine, vol. 2, pp.120-127, 2016.

[31] Nutbeam, Don, "Health promotion glossary." Health promotion international, vol. 4, pp. 349-364, 1998.

[32] V. Waldrop, Drenna, L. J. Deborah, W. Stephen, K. Mahendra, and M. Lisa, "The effects of low literacy and cognitive impairment on medication adherence in HIV-positive injecting drug users." AIDS care, vol.10, pp. 1202-1210, 2008.

ISSN:0971-1260
Vol-22-Issue-16-August-2019

[33] Samet, H. Jeffrey, L. Howard, A. S. Kathleen, K. D. Rajeev, C. John, H. S. Abby, D. D. Rebecca, L. Suzette, K. Donald, and E. C. Donald, "Compliance with zidovudine therapy in patients infected with human immunodeficiency virus, type 1: a cross-sectional study in a municipal hospital clinic." The American journal of medicine, vol.5, pp. 495-502, 1992.

[34] Nagpal, Manish, T. Vandana, K. Suresh, and G. Usha, "Adverse drug reactions to antiretroviral therapy in AIDS patients at a tertiary care hospital in India: A prospective observational study." Indian Journal of Medical Sciences, vol.6, June 2010.

[35] Baveja, U. K, "HIV Antibody Testing with special reference to HIV-1." HIV Testing Manual, Laboratory diagnosis, Biosafety and Quality Control, pp.45-67, 1999.

[36] N. Kumarasamy, V. Snigdha, P. F. Timothy, H. M. Kenneth, and S. Suniti, "Clinical profile of HIV in India." Indian J Med Res, vol. 4, pp. 377-94, 2005.

[37] J. Palella, J. Frank, M. D. Kathleen, C. M. Anne, O. L. Mark, F. Jack, A. S. Glen, J. A.. Diane, D. H. Scott, and HIV Outpatient Study Investigators."Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection." New England Journal of Medicine, vol. 13, pp.853-860, 1998.

[38] Olem, David, M. S. Kelly, M. T. Jonelle, and O. J. Mallory, "Overcoming barriers to HIV treatment adherence: A brief cognitive behavioral intervention for HIV-positive adults on antiretroviral treatment." Cognitive and behavioral practice, vol.2, pp.206-223, 2014.

[39] World Health Organization, “International drug monitoring: the role of national centres, report of a WHO meeting” [held in Geneva from 20 to 25 September 1971]. World Health Organization,1972.

[40] Rintamaki, S. Lance, C. D. Terry, S. Silvia, L. B. Charles, and S. W. Michael, "Social stigma concerns and HIV medication adherence." AIDS Patient Care & STDs, vol. 5, pp.359-368, 2006.

[41] Bartlett, J. G, "Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents." The Department of Health and Human Services Panel on Antiretroviral Guidelines for Adult and Adolescents, pp.42-43, 2008.

ISSN:0971-1260
Vol-22-Issue-16-August-2019

[42] Medley, Amy, K. Caitlin, O. R. Kevin, and S. Michael, "Effectiveness of peer education interventions for HIV prevention in developing countries: a systematic review and meta-analysis." AIDS Education and Prevention, vol.3, pp.181-206, 2009.

[43] Johnson, C. Cheryl, K. Caitlin, F. Virginia, S. Nandi, F. Carmen, D. Shona, S. Anita, and B. Rachel, "Examining the effects of HIV self-testing compared to standard HIV testing services: a systematic review and meta-analysis." Journal of the International AIDS Society, vol.1, p.21594, 2017.

[44] Knoll, Bettina, L. Britta, and T. Zelalem, "Current status of HIV infection: a review for non-HIV-treating physicians." International journal of dermatology, vol.12, pp.1219-1228, 2007.

[45] Ford, Nathan, B. Andrew, B. Rachel, V. Marco, L. B. Daniel, P. Martina, V. Lara et al, "The WHO public health approach to HIV treatment and care: looking back and looking ahead." The Lancet Infectious Diseases, vol.3, pp.e76-e86, 2018.

[46] Simbayi, C. Leickness, S. Kalichman, S. Anna, C. Allanise, H. Nomvo, and M. Ayanda, "Internalized stigma, discrimination, and depression among men and women living with HIV/AIDS in Cape Town, South Africa." Social science & medicine, vol.9, pp.1823-1831, 2007.

[47] Kalichman, C. Seth, and G. Tamar, "Stress and poverty predictors of treatment adherence among people with low-literacy living with HIV/AIDS." Psychosomatic medicine, vol.8, p.810, 2010.

[48] Traeger, W. Michael, E. S. Sophia, J. W. Edwina, E. H. Margaret, J. C. Vincent, Joseph S. Doyle, and A. S. Mark, "Effects of pre-exposure prophylaxis for the prevention of HIV infection on sexual risk behavior in men who have sex with men: a systematic review and meta-analysis." Clinical Infectious Diseases, Mar. 2018.

[49] Stevens, R. Danielle, J. V. Caroline, E. D. Raviv, and E. K. Jeffrey, "A global review of HIV self-testing: themes and implications." AIDS and Behavior, vol.2, pp.497-512, 2018.

[50] Lekkerkerker, N. Annemarie, V. K. Yvette, and B. H. G. Teunis, "Viral piracy: HIV-1 targets dendritic cells for transmission." Current HIV research, vol.2, pp.169-176, 2006.

ISSN:0971-1260
Vol-22-Issue-16-August-2019

[51] Earnshaw, A. Valerie, and R. C. Stephenie, "From conceptualizing to measuring HIV stigma: a review of HIV stigma mechanism measures." AIDS and Behavior, vol.6, p.1160, 2009.