Prevention of Mother-To-Child Transmission of HIV (PMTCT) in Sub-Saharan Africa: Past and Present Perspectives

Elijah[1*] OB, Umukoro[1] EK, Igben[1] VO, Moke[2] EG, Ojezele[2] MO, Onitiri-Elijah[3] CB

[1] Department of Pharmacology and Therapeutics, Faculty of Basic Clinical, Delta State University, Abraka
[2] Department of Pharmacology, Faculty of Basic Medical Sciences, Delta State University, Abraka
[3]Lily Hospitals, Warri

QR CODE

Doi: https://doi.org/10.21816/ijfmi.v5i1

Corresponding author email:

kaybeeelijah@gmail.com

ABSTRACT

The foremost documentation of AIDS in the United States in 1981 primarily involved cases among individuals identifying as homosexual. However, subsequent reports have confirmed HIV infection in all nations around the globe, leading to the emergence of a global epidemic. One of the major burdens of HIV/AIDS is the mother-to-child transmission of HIV (MTCT). Pregnant women constitute a unique demographic in treatment considerations, primarily due to the potential to avert mother-to-child transmission (MTCT) by antiretroviral therapy, alongside the necessity to ensure the safety of the women and their exposed fetuses and offspring(s). The main source of pediatric HIV infection is vertical transmission from mother to child, which may occur during pregnancy, at the moment of delivery, or postnatally during breastfeeding. In 2022, the Sub-Saharan African region accounted for 84% of new pediatric infections worldwide. This essay examines the past and present preventive methods against MTCT in the region.

Materials and Methods

An online search of relevant published articles in Scopus, Research Gate, PubMed, and Embase from 1996 to 2024 was conducted; 49 of these articles were adapted for this article.

Results

The journey in the fight against vertical transmission of HIV in the Sub-Saharan African region has recorded significant successes over the years; although there are a few drawbacks to the preventive strategies currently being employed across the region. With further strengthened collaborative efforts between healthcare providers and other key stakeholders in the HIV prevention/elimination programme, mother-to-child transmission of HIV can become a thing of the past soon.

KEYWORDS: *Prevention, HIV, mother, child, transmission, Sub-Saharan Africa*

Introduction

HIV, a retrovirus with a slow growth rate, leads to progressive immunodeficiency and eventually results in AIDS. It typically infects cells that express CD4 membrane receptor molecules, including T helper cells, macrophages, dendritic cells, and microglial cells.[1]Acquired immune deficiency syndrome (AIDS) involves the compromised state of the host defense system which results in impaired immunity leading to increased susceptibility of the host to opportunistic infections or predisposition to malignancies.[2] The foremost documentation of AIDS in the United States in 1981 primarily involved cases among individuals identifying as homosexual.[3] However, subsequent reports have confirmed HIV infection in all nations around the globe, leading to the emergence of a global epidemic.[50]

Pathogenesis, Transmission and Treatment of HIV

The infection course of this virus is marked by an extended period between initial infection and the emergence of severe clinical signs.[4] The clinical manifestations of primary HIV infection include fever, tiredness, lymphadenopathy, and occasionally a macular rash. Symptoms may last for days to several weeks, whereas many individuals remain asymptomatic for a duration ranging from several months to several years after the first infection. Despite this apparent latency, there is continuous viral replication and progressive reduction in the T-helper lymphocytes over time; thereby predisposing the individual to opportunistic infections.[5] Human immunodeficiency virus (HIV) infection disarms the host immune system, primarily targeting the helper-inducer subset of lymphocytes, leading to acquired immunodeficiency syndrome (AIDS).[6]

HIV infection can be transmitted via a variety of ways, as long as there is transfer of body fluids (blood, seminal fluid, rectal fluid, breast milk and vaginal fluid) from a person living with HIV to an HIV-negative individual by whatever means.[6] This can happen during intimate sexual contact without using any protective measures such as condoms.[6] Sexual contact is the most common form of HIV transmission, responsible for approximately 85% of all HIV-1 infections;[7] However, there exists other modes of transmission of the virus. Unprotected anal intercourse presents the largest risk for HIV transmission, with the receptive partner exhibiting a greater susceptibility to infection than the insertive.[8] According to the Centre for Disease Control and Prevention (CDC) 2020 HIV surveillance report, out of the 37,968 newly diagnosed cases of HIV in 2018, 69% were due to men who have sex with men (MSM), 24% were as a result of high-risk heterosexual activity, while people who inject drugs account for 7% of the total new infections. During unprotected penetrative vaginal intercourse, while both partners are at risk of contracting the virus, a seronegative woman has the higher risk of contracting the virus from a seropositive man, than a seronegative man from a seropositive woman. This is because the virus can enter through the vaginal and cervical mucous membranes, persist and replicate within the vaginal dendritic cells.[9] HIV appears to have established a persistent presence and those who become infected must confront the long-term ramifications of living with the virus, as no cure or vaccine has been identified to safeguard against its transmission.[10]

Challenges of HIV infection

A significant challenge of HIV/AIDS is the mother-to-child transmission of HIV (MTCT). Pregnant women represent a unique demographic in treatment considerations, primarily due to the potential to avert mother-to-child transmission (MTCT) by antiretroviral therapy, alongside the necessity to ensure the safety of the women and their exposed fetuses and offspring.[11] Maternal infections occurring during pregnancy are widely recognized to have detrimental effects on the development of the placenta and fetus, as well as on pregnancy outcomes and newborn health. HIV, specifically, induces profound immunological dysregulation defined by persistent inflammation and chronic immune activation.[12] Although some researchers argue that the effectiveness of antiretroviral therapy (ART) in limiting HIV progression is not compromised by pregnancy, individuals with HIV, particularly pregnant women, face an elevated susceptibility to opportunistic infections. This heightened risk is attributed to the depletion of cluster of differentiation 4 (CD4 cells), reduced activity of cluster of differentiation 8 (CD8) cytotoxic T cells, and decreased production of Type 1 cytokines in HIV-infected pregnant women.[13] Additionally, these women are more vulnerable to sexually transmitted infections and vertically transmissible infections such as Hepatitis B and C. Consequently, the fetus and newborn are at a significantly increased risk of acquiring these infections.[13]

Similar to other infectious diseases, the treatment of HIV has encountered challenges related to antimicrobial resistance, with Sub-Saharan Africa experiencing the most significant worldwide impact.[14] A retrospective cohort study by Zhang and colleagues analyzed drug resistance in individuals with HIV/AIDS in Shanghai, China, revealing the presence of drug resistance in this population. With varying rates of resistance occurring between different classes of antiretrovirals, non-nucleoside reverse transcriptase inhibitors (NNRTIs) were reported to have the highest rates of drug resistance.[15] This was further substantiated by a study conducted by Watera and colleagues in 2021, regarding HIV treatment resistance in people commencing antiretroviral therapy in Uganda. This cross-sectional study, which genotyped samples from 351 persons commencing ART, revealed an 18.2% prevalence of drug resistance, with the greatest rate (14.1%) observed for non-nucleoside reverse transcriptase inhibitors.[16]

Burden of HIV in Pregnancy

The primary source of pediatric HIV infection is vertical transmission of HIV from mother to child[17] with the possibility of this vertical transmission of HIV infection from mother to infant occurring during pregnancy, around the time of delivery or through breastfeeding.[18] According to the UNAIDS 2023 fact sheet,[19] out of the 39 million said to be living with HIV in 2022, 1.5 million of them were children between ages of 0 to 14years, with 130,000 of them being new infections in the year 2022.[19] Of these global statistics, Sub-Saharan Africa (Western, Eastern, Central and Southern Africa) accounted for 109,000 of the 130,000 new infections in children worldwide; a whopping 84%.[19] This illustrates that the burden of pediatric HIV infection, and by extension, mother-to-child transmission of HIV, is predominantly concentrated in the Sub-Saharan African region.

Worldwide, women represent about 52% of the total adult population living with HIV, while accounting for 46% of newly acquired infections.[20] According to a 2019 estimation, the global population consisted of over 1.22 million pregnant women who were infected with HIV.[13] Nigeria has the world's greatest burden of mother-to-child transmission (MTCT) of the human immunodeficiency virus (HIV), with a prevalence rate of roughly 1.3% of the entire population.[21] Consequently, Nigeria assumes significant importance as a focal point in ongoing global endeavors aimed at eradicating MTCT of HIV. According to the 2016 figures from the Nigerian National Agency for the Control of AIDS (NACA), it was revealed that around 180,000 HIV-positive pregnant women required assistance to prevent mother-to-child transmission (MTCT) on an annual basis in Nigeria.[22]

Effects of HIV on Pregnancy

Pregnancy is in itself an immunosuppressive state [23] therefore, there are bound to be some negative outcomes in the case of HIV (whose pathogenesis is centered around immunosuppression) in pregnancy. These effects of HIV on pregnancy could be deleterious to the mother, the placenta and even the fetus inutero. Chilaka and Konje (2021)[10] in their update on HIV in pregnancy reported that disparate rates of negative pregnancy outcomes have been associated with HIV, some of these adverse outcomes being: increased spontaneous miscarriages, stillbirths, increased perinatal mortality, intrauterine growth restriction (IUGR), low birth weight, and chorioamnionitis.[10]Physiological changes in pregnancy (such as blood volume expansion and gastro-intestinal, enzymatic, and hormonal changes) might also affect the pharmacokinetic properties of antiretroviral drugs and can lead to altered absorption, reduced protein binding and increased elimination[11] with a prospect to reducing efficacy of anti-retroviral therapy (ART) in pregnancy.

Women who become pregnant while living with HIV, or contract the virus during the period of pregnancy, face the possibility of worse maternal and perinatal health outcomes, particularly if the virus is not effectively managed.[10] Moreover, there exists a potentiality for vertical transmission to the fetus throughout the stages of pregnancy, labor, and postpartum via nursing.[18] Nonetheless, it is worthy of note that these patterns appear to be diminishing due to the concerted efforts being made on a worldwide scale to combat HIV/AIDS. When left untreated, HIV infection during pregnancy has significant implications for both mother and child, necessitating careful management throughout the prenatal, intrapartum, and postpartum stages. The basic objectives of management of HIV in pregnancy encompass the prevention of mother-to-child transmission of the virus, preservation of maternal well-being, and provision of a secure and conducive delivery setting for both mother and child.[10]

For pregnant women living with HIV, the placenta is a well-documented viral sanctuary site, where the virus comfortably replicates itself with minimal interference from ARV.[24] HIV is observed to sustain a low infection level in placentadespite antiretroviral therapy and can be reactivated upon cessation of treatment.[25] In the placenta, the virus is said to invade the trophoblasts, where it is less sensitive to ARV, thereby giving it room for proliferation and

reactivation.[26]In addition to the increased prevalence of chorioamnionitis, villous hypercellularity, funisitis, placental membrane inflammation, villous immaturity, allantois vasculopathy, and deciduitis associated with maternal HIV infection,[27] there is also the chance of infection with human papilloma virus (HPV), which provokes significant structural changes of the villi, potentially hampering normal interchange of gases and nutrients at the maternal-fetal interface,[28] with potential deleterious effects on the fetus.

The effects of maternal HIV infection have also been demonstrated in both the fetus in gestation and the neonate born to an infected mother. The myriads of complications or negative outcomes that could possibly arise include; increased rates of spontaneous abortion, stillbirth, perinatal and newborn death, intrauterine growth restriction, preterm birth, and low birth weight.[10]These may be due to HIV-triggered shift to significantly activated proinflammatory intrauterine immune environment, with a resultant disruption in the immunological tolerance normally present during pregnancy.[29]

PMTCT – Past Perspective

Large-scale efforts to reduce MTCT began in 1994 in developed countries following the outcome of the Pediatric AIDS Clinical Trials Group (PACTG) protocol 076, which demonstrated that The use of zidovudine (AZT) from 14 weeks of gestation and continued during the pregnancy, delivery, and to the baby reduced MTCT by 66% in non-breastfeeding populations.[30] The PACTG protocol 076 was however limited by its cost and the fact that sub-Saharan Africa which contributed the most to the burden of MTCT, were predominantly breastfeeding communities. Fast-forward to 1999 when the HIVNET 012 landmark study was released, showing that administration of single-dose nevirapine (NVP) at the commencement of labor and a single dose administered to the newborn lowered the MTCT by 47% at 6 weeks of age.[31] Despite it being cheap, simple and easy to administer, the HIVNET 012 regimen also faced some challenges especially in the developing countries; these challenges include long-term health behavior monitoring, adherence to prescribed treatments, reporting bias etc.[32,33]

Historically, one of the strategies for preventing mother-to-child transmission (PMTCT) involved the cleaning of the birth canal during labor with microbicides; this was aimed at preventing MTCT of HIV infection through reducing exposure of the infant to infective cervicovaginal secretions.[34] In 1996, Biggar and associates published an article on “Perinatal intervention trial in Africa: effect of a birth canal cleansing intervention to prevent HIV transmission”. The study compared the level of infection of infants born to 3,327 control mothers (undergoing traditional delivery methods) with that of 3,637 infants born to women who underwent intervention deliveries (intervention being manual cleansing of the birth canal using a cotton pad saturated with 0.25% chlorhexidine, performed upon admission in labor and every four hours until delivery) with the infant’s HIV status determined by polymerase chain reaction on dried blood spots collected at 6 and 12 weeks of age. The study however reported that the intervention had no significance on HIV transmission rates, hence birth canal exposure

was probably not a major contributor to perinatal infection risk.[35]

Aside from disinfection of the birth canal, another strategy to prevent mother-to-child transmission of HIV entailed administering post-exposure prophylaxis to infants delivered by HIV-infected mothers.[34] Taha and associates reported a study in Malawi that sought to assess the effectiveness of short post-exposure prophylaxis in newborn babies to reduce mother-to-child transmission of HIV-1; a randomized clinical trial (NVAZ trial). The study involved 1119 babies of Malawian women with HIV-1 who presented late (within 2 hours of expected delivery) and they were randomized to receive either nevirapine alone, or both nevirapine and zidovudine immediately after delivery, with infant diagnosis of HIV determined at birth and at 6-8weeks post-partum. The study revealed a lesser transmission rate among infants who received both medications at birth (15.3%) in comparison with infants who received nevirapine only at birth (20.9%).[36]

The importance of the administration of post-exposure prophylaxis to infants was further corroborated by a study published by Lallemant and associates in 2004.[37] The study on "Single-Dose Perinatal Nevirapine plus Standard Zidovudine to Prevent Mother-to-Child Transmission of HIV-1 in Thailand"; a clinical trial named the "PHPT2 trial" evaluated the efficacy of a single dose of nevirapine added to a standard short-course zidovudine regimen in a non-breastfeeding population. It was a randomized double-blind trial of three treatment regimens; where in one group, mothers and infants received a single dose of nevirapine (nevirapine–nevirapine regimen); in another, mothers and infants received nevirapine and placebo, respectively (nevirapine–placebo regimen); and in the last, mothers and infants received placebo (placebo–placebo regimen). The study concluded that there was a lower transmission rate (1.9%) in the arm where both mother and baby received nevirapine as well as the zidovudine prophylaxis, in comparison with the arm where only the mother received nevirapine (2.8%).[34,37] Different studies, trials and postulations came up thereafter, all of which ultimately culminated in the WHO ART protocols for the implementation of PMTCT in resource-constrained environments.[38]

A team of technical experts' meeting at Geneva in 2000 birthed the recommendation of using ART for the prevention of mother-to-child transmission of HIV (PMTCT). The following year, at the United Nations General Assembly, 189 countries met to endorse a declaration of commitment and set the goal to reduce the MTCT of HIV by 20% in 2005 and by 50% before the end of 2010.[38] The successful implementation and expansion of early PMTCT programs, however, faced obstacles such as poor participation in antenatal care services and insufficient awareness of HIV status among pregnant women, particularly in resource-limited environments. The WHO therefore recommended a four-prong approach, all in a bid to achieve meaningful reduction of MTCT. This approach involved; primary prevention of HIV among women (prong 1); prevention of unintended pregnancies among HIV-infected women (prong 2); support for PMTCT through practical measures to reduce MTCT including antiretroviral prophylaxis, infant-feeding counseling and support, and maternal care including safe delivery practices, post-natal care and early childhood care (prong 3); and provision of care and

support to HIV-infected women, their infants, and their families (prong 4).[39]

PMTCT – Present Perspective

The administration of antiretroviral therapy (ART) to HIV-positive pregnant women constitutes one of the interventions (prong 3) within the continuum of care for the prevention of mother-to-child transmission of HIV (PMTCT); consequently, ART coverage during pregnancy at the national level has been recognized as a key process indicator by the World Health Organization.[40] This approach to preventing mother-to-child HIV transmission has undergone three iterations, with the implementation of a specific indicator being contingent upon the resources available in a given country. "Option A" specifies antiretroviral prophylaxis for HIV-infected pregnant women with a cluster of differentiation 4 (CD4) cell counts > 350 cells/mm^3 from 14 weeks of gestation alongside infant nevirapine (NVP) prophylaxis throughout breastfeeding or lifelong triple ART for HIV infected pregnant women with CD4 cell counts ≤ 350 cells/mm^3 or WHO stage 3–4 disease with six weeks of infant NVP prophylaxis. "Option B" specifies triple ARV drug regimens for the mother throughout pregnancy and breastfeeding, with cessation after weaning.[41] Option B+ describes triple ARV drug regimens for expectant mothers that are consistent throughout their lives, including breastfeeding and subsequent pregnancies, and are administered regardless of maternal CD4 cell counts.[42,43] This present UNAIDS/WHO recommendations which state that all HIV-infected pregnant and breastfeeding women should initiate triple ART and continue treatment for life (Option B+), stemmed from the 2016 IMPAACT (International Maternal Pediatric Adolescent AIDS Clinical Trials) perinatal HIV prevention clinical trial and PROMISE (Promoting Maternal and Infant Survival Everywhere) trial, which demonstrated that triple ART consisting of tenofovir (TDF), Lamivudine (3TC), and lopinavir/ritonavir (LPVr) during pregnancy was superior (1% vs. 0.6%) to prophylaxis with Zidovudine (AZT) and Lamivudine (3TC) in reducing vertical transmission.[42] Since then, various guidelines and recommendations have been implemented to increase the coverage of antiretroviral therapy (ART) among pregnant women living with HIV (PWLHIV) with a view to drastically reducing the burden of MTCT of HIV and by proxy decrease the incidence of pediatric infections.[51,52]

In a study conducted by Muyunda and associates and published in 2020, the "Effectiveness of Lifelong ART (Option B+) in the Prevention of Mother-to-Child Transmission of HIV Programme in Zambia" was ascertained. The study which was a retrospective cohort study, sought to estimate the rate of mother-to-child transmission of HIV among pregnant women who were on lifelong ART (OPTION B+) and comparing this with pregnant women who were on other mother to child transmission prevention interventions. The study demonstrated that Option B+ was more effective in preventing mother-to-child transmission of HIV, as evidenced by the lower rate of transmission among women who received it.[44]

In 2022, Astawesegn and associates reported a country-level longitudinal ecological study on the trends and effects of antiretroviral therapy coverage during pregnancy on mother-to-child transmission of HIV in Sub-Saharan Africa. This study which was conducted between the period of 2010–2019,

involved forty-one (41) Sub-Saharan African countries and it was reported that ART coverage in pregnant women increased from 32.98% in 2010 to 69.46% in 2019, resulting in a 36.48% increase in ART coverage during pregnancy within the study period. Over the same period, the rate of HIV transmission from mother to child reduced from 27.18% in 2010 to 16.90% in 2019; a 10.28% decrease.[45] The study's conclusion established an inversely proportional relationship between ART coverage in pregnancy and the rate of MTCT of HIV in the Sub-Saharan Africa region, further strengthening the claims laid to the effectiveness of the Option B+ strategy in reducing/eliminating MTCT.

Maingi and associates did a systematic review of "the impact of Option B+ on mother-to-child transmission of HIV in Africa", which was published in 2022.[46] Relevant studies which were conducted in 11 African countries (Cameroon, Ethiopia, Lesotho, Malawi, Rwanda, South Africa, Swaziland, Tanzania, Uganda, Zambia and Zimbabwe) and published between 2015 when the World Health Organisation (WHO) released the guideline and initiated Option B+ as a strategy for PMTCT, and 2021 were reviewed. Although the ultimate conclusion of the study was that standardized protocols for impact evaluation must be established to provide evidenced-based data on the efficacy of Option B+ in Africa, a majority of the studies reported transmission rates between <2% to 5%; which was close to the WHO targets.[46]

In a cross-sectional study conducted between January and April 2014 and published in 2016 by Anigilaje and associates on barriers to uptake of prevention of mother-to-child transmission of HIV services among mothers of vertically infected HIV-seropositive infants in Makurdi, Nigeria, it was reported that the most prevalent reason for pregnant women living with HIV to neglect antenatal care visits was financial constraints. The study also revealed that the most prevalent reason for the non-administration of prophylactic nevirapine to infants born to mothers living with HIV was that the mothers delivered the infants at home or outside of the hospital where they had registered for antenatal care.[47]

Finally, in a systematic review and meta-analysis of "Adherence to option B + antiretroviral therapy and associated factors in pregnant and breastfeeding women in Sub-Saharan Africa" carried out by Fassinou and associates, and published recently (2024), the adherence to this strategy for prevention of mother-to-child transmission of HIV by pregnant and breastfeeding women in the region was assessed. The meta-analysis which included 42 studies across 15 different countries in the region, concluded that despite the implementation of this strategy, the level of adherence among these sub-groups fell short of meeting the critical thresholds for viral load suppression as outlined in the 95-95-95 objectives set for 2025.[48] There is therefore the need for the development of tailored approaches and strategies based on individual and structural factors, to achieve country-level elimination of MTCT and new pediatric HIV infections which is defined by the World Health Organization (WHO) as the MTCT rate of <2% in non-breastfeeding population or <5% in breastfeeding population, and the reduction of new pediatric HIV infections due to MTCT to less than 50 cases per 100,000 live births.[48,49]

Conclusion

The journey in the fight against vertical transmission of HIV in the Sub-SaharanAfrican region has recorded significant successes over the years, although there are a few drawbacks to the preventive strategies currently being employed across the region. While we are not where we should be, especially as it regards meeting the set targets by UNAIDS, we are not where we used to be a decade ago. With further strengthened collaborative efforts between healthcare providers and other key stakeholders in the HIV prevention/elimination programme, mother-to-child transmission of HIV can become a thing of the past soon.

REFERENCES

1) Klatt, E.C., 2017. Pathology of HIV/AIDS. *The Mercer University of Medicine Savannah*, pp.6-50.
2) Arora, S.K. and Mehta, G., 2018. HIV-AIDS: An unconquered immunewar. *Infectious Diseases and Your Health*, pp.337-348.
3) De Cock, K.M., Jaffe, H.W. and Curran, J.W., 2012. The evolving epidemiology of HIV/AIDS. *Aids*, *26*(10), pp.1205-1213.
4) Peruski, A.H., Wu, B., Linley, L., Delaney, K.P., DiNenno, E.A. and Johnson, A.S., 2021. Time from HIV infection to diagnosis in the US, 2014–2018. *American journal of preventive medicine*, *61*(5), pp.636-643.
5) Kervevan, J. and Chakrabarti, L.A., 2021. Role of CD4+ T cells in the control of viral infections: recent advances and open questions. *International Journal of Molecular Sciences*, *22*(2), p.523.
6) Tahir, N.B., Shah, M.M. and Uddin, Q.T., 2015. Assessment of different modes of transmission of HIV in Patients with HIV/AIDS. *Gomal Journal of Medical Sciences*, *13*(3).
7) Simon, V., Ho, D.D. and Karim, Q.A., 2006. HIV/AIDS epidemiology, pathogenesis, prevention, and treatment. *The Lancet*, *368*(9534), pp. 489-504.
8) Nambiar, P. and Short, W.R., 2019. Mechanisms of HIV Transmission *Fundamentals of HIV Medicine 2019*, p.20.
9) Pena-Cruz, V., Agosto, L.M., Akiyama, H., Olson, A., Moreau, Y., Larrieux, J.R., Henderson, A., Gummuluru, S. and Sagar, M., 2018. HIV-1 replicates and persists in vaginal epithelial dendritic cells. *The Journal of clinical investigation*, *128*(8), pp.3439-3444.
10) Chilaka, V.N. and Konje, J.C., 2021. HIV in pregnancy–An update. European Journal of Obstetrics & Gynecology and Reproductive Biology, 256, pp.484-491.
11) Bailey, H., Zash, R., Rasi, V. and Thorne, C., 2018. HIV treatment in pregnancy. *The lancet HIV*, *5*(8), pp.e457-e467.
12) Ikumi, N.M., Matjila, M., Gray, C.M., Anumba, D. and Pillay, K., 2021. Placental pathology in women with HIV. *Placenta*, *115*, pp.27-36.
13) Shiadeh, M.N., Esfandyari, S., Ashrafmansouri, M., Mirzapour, A., Taghipour, A., Spotin, A., Arefkhah, N., Gamble, R., Safa, A. and Rostami, A., 2020. The prevalence of latent and acute toxoplasmosis in HIV-infected pregnant women: A systematic review and meta-analysis. *Microbial Pathogenesis*, *149*, p.104549.
14) Elijah, O.B., Umukoro, E.K., Moke, E.G., Igben, V.J.O., Arighwrode, O., Onakpoya, E.E., Dennis-Eboh, U. and Ekuerhare, B.E., 2024. Challenges of antimicrobial resistance in Sub-Saharan Africa: The past, present, and future perspectives. *Orapuh Journal*, *5*(2), pp.e1120-e1120.
15) Zhang, F., Liu, L., Sun, M., Sun, J. and Lu, H., 2017. An analysis of drug resistance among people living with HIV/AIDS in Shanghai, China. *PLoS One*, *12*(2), p.e0165110.
16) Watera, C., Ssemwanga, D., Namayanja, G., Asio, J., Lutalo, T., Namale, A., Sanyu, G., Ssewanyana, I., Gonzalez-Salazar, J.F., Nazziwa, J. and Nanyonjo, M., 2021. HIV drug resistance among adults initiating antiretroviral therapy in Uganda. *Journal of Antimicrobial Chemotherapy*, *76*(9), pp.2407-2414.

17) Musoke, P., Namukwaya, Z. and Mosha, L.B., 2018. Prevention and treatment of pediatric HIV infection. *Current Tropical Medicine Reports*, *5*, pp.24-30.
18) Thorne, C. and Newell, M.L., 2003. Mother-to-child transmission of HIV infection and its prevention. *Current HIV research*, *1*(4), pp.447-462.
19) UNAIDS 2023 fact sheet https://www.unaids.org/en/resources/fact-sheet Accessed December 2023
20) Harris, K. and Yudin, M.H., 2020. HIV infection in pregnant women: a 2020 update. *Prenatal Diagnosis*, *40*(13), pp. 1715- 1721.
21) Nigerian National Agency for the control of AIDS (NACA) 2023 statistics https://www.naca.gov.ng/wp-content/uploads/2022/03/National-HIV-and-AIDS-Strategic-Framework-2021-2023-Final.pdf(Accessed in December 2023).
22) Nigerian National Agency for the control of AIDS (NACA) 2016 statistics https://naca.gov.ng/wp-content/uploads/2016/11/NACA-Annual-Report-20141_0.pdf (Accessed in December 2023)
23) Luppi, P., 2003. How immune mechanisms are affected by pregnancy. *Vaccine*, *21*(24), pp. 3352-3357.
24) Dahl, V., Josefsson, L. and Palmer, S., 2010. HIV reservoirs, latency, and reactivation: prospects for eradication. Antiviral research, 85(1), pp.286-294.
25) Tang, Y., Woodward, B.O., Pastor, L., George, A.M., Petrechko, O., Nouvet, F.J., Haas, D.W., Jiang, G. and Hildreth, J.E., 2020. Endogenous retroviral envelope syncytin induces HIV-1 spreading and establishes HIV reservoirs in placenta. *Cell reports*, *30*(13), pp.4528-4539.
26) Al-Husaini, A.M., 2009. Role of placenta in the vertical transmission of human immunodeficiency virus. *Journal of Perinatology*, *29*(5), pp.331-336.
27) Schwartz, D.A., Sungkarat, S., Shaffer, N., Laosakkitiboran, J., Supapol, W., Charoenpanich, P., Chuangsuwanich, T. and Mastro, T.D., 2000. Placental abnormalities associated with human immunodeficiency virus type 1 infection and perinatal transmission in Bangkok, Thailand. *The Journal of infectious diseases*, *182*(6), pp.1652-1657.
28) Chandrasekar, V., Singh, A.V., Maharjan, R.S., Dakua, S.P., Balakrishnan, S., Dash, S., Laux, P., Luch, A., Singh, S. and Pradhan, M., 2022. Perspectives on the Technological Aspects and Biomedical Applications of Virus-Like Particles/Nanoparticles in Reproductive Biology: Insights on the Medicinal and Toxicological Outlook. *Advanced NanoBiomed Research*, *2*(8), p.2200010.
29) Altfeld, M. and Bunders, M.J., 2016, November. Impact of HIV-1 infection on the feto-maternal crosstalk and consequences for pregnancy outcome and infant health. In *Seminars in immunopathology* (Vol. 38, pp. 727-738). Springer Berlin Heidelberg.
30) Connor, E.M., Sperling, R.S., Gelber, R., Kiselev, P., Scott, G., O'sullivan, M.J., VanDyke, R., Bey, M., Shearer, W., Jacobson, R.L. and Jimenez, E., 1994. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. *New England Journal of Medicine*, *331*(18), pp.1173-1180.
31) Guay, L.A., Musoke, P., Fleming, T., Bagenda, D., Allen, M., Nakabiito, C., Sherman, J., Bakaki, P., Ducar, C., Deseyve, M. and Emel, L., 1999. Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: HIVNET 012 randomised trial. *The Lancet*, *354*(9181), pp.795-802.
32) Paintsil, E. and Andiman, W.A., 2009. Update on successes and challenges regarding mother-to-child transmission of HIV. *Current opinion in pediatrics*, *21*(1), p.94.
33) Chi, B.H., Adler, M.R., Bolu, O., Mbori-Ngacha, D., Ekouevi, D.K., Gieselman, A., Chipato, T., Luo, C., Phelps, B.R., McClure, C. and Mofenson, L.M., 2012. Progress, challenges, and new opportunities for the prevention of mother-to-child transmission of HIV under the US President's Emergency Plan for AIDS Relief. *Journal of acquired immune deficiency syndromes (1999)*, *60*(Suppl 3), p.S78.

34) Newell, M.L., 2006. Current issues in the prevention of mother-to-child transmission of HIV-1 infection. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, *100*(1), pp.1-5.
35) Biggar, R.J., Goedert, J.J., Miotti, P.G., Taha, T.E., Mtimavalye, L., Justesen, A., Chiphangwi, J.D., Broadhead, R., Yellin, F., Liomba, G. and Miley, W., 1996. Perinatal intervention trial in Africa: effect of a birth canal cleansing intervention to prevent HIV transmission. *The Lancet*, *347*(9016), pp.1647-1650.
36) Taha, T.E., Kumwenda, N.I., Gibbons, A., Broadhead, R.L., Fiscus, S., Lema, V., Liomba, G., Nkhoma, C., Miotti, P.G. and Hoover, D.R., 2003. Short postexposure prophylaxis in newborn babies to reduce mother-to-child transmission of HIV-1: NVAZ randomised clinical trial. *The Lancet*, *362*(9391), pp.1171-1177.
37) Lallemant, M., Jourdain, G., Le Coeur, S., Mary, J.Y., Ngo-Giang-Huong, N., Koetsawang, S., Kanshana, S., McIntosh, K. and Thaineua, V., 2004. Single-dose perinatal nevirapine plus standard zidovudine to prevent mother-to-child transmission of HIV-1 in Thailand. *New England Journal of Medicine*, *351*(3), pp.217-228.
38) United Nations. Declaration of commitment on HIV/AIDS. United Nations General Assembly Special Session on HIV/AIDS; 25–27 Jun 2001; Geneva.
39) WHO, UNFPA, IPPF. Sexual and reproductive health & HIV/AIDS: a framework for priority linkages Geneva 2005. Available on https://www.who.int/reproductivehealth/publications/linkages/HIV_05_5/en/index.html. Accessed 20 June 2024
40) World Health Organization. Global guidance on criteria and processes for validation: Elimination of mother-to-child transmission of HIV and Syphilis, Second edition Geneva, Switzerland WHO; 2017. Available on https://apps.who.int/iris/bitstream/handle/10665/259517/9789241513272-eng.pdf?sequence=1. Accessed 20 June 2024.
41) World Health Organization. Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants Recommendations for a public health approach 2010 version Geneva, Switzerland: WHO; 2010. Available on https://apps.who.int/iris/bitstream/handle/10665/75236/9789241599818_eng.pdf?sequence=1. Accessed 20 June 2024
42) Fowler, Mary Glenn, Hoosen Coovadia, Casey M. Herron, Yvonne Maldonado, Tsungai Chipato, Dhayendre Moodley, Philippa Musoke *et al*. "Efficacy and safety of an extended nevirapine regimen in infants of breastfeeding mothers with HIV-1 infection for prevention of HIV-1 transmission (HPTN 046): 18-month results of a randomized, double-blind, placebo-controlled trial." *JAIDS Journal of Acquired Immune Deficiency Syndromes* 65, no. 3 (2014): 366-374.
43) World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection Recommendations for a public health approach - Second edition Geneva, Switzerland WHO; 2016 [Available from: https://www.who.int/hiv/pub/arv/arv-2016/en/. Accessed 20 June 2024.
44) Muyunda, B., Musonda, P., Mee, P., Todd, J. and Michelo, C., 2020. Effectiveness of lifelong ART (Option B+) in the prevention of mother-to-child transmission of HIV programme in Zambia: observations based on routinely collected health data. *Frontiers in public health*, *7*, p.470826.
45) Astawesegn, F.H., Stulz, V., Conroy, E. and Mannan, H., 2022. Trends and effects of antiretroviral therapy coverage during pregnancy on mother-to-child transmission of HIV in Sub-Saharan Africa. Evidence from panel data analysis. *BMC Infectious Diseases*, *22*(1), p.134.
46) Maingi, M., Stark, A.H. and Iron-Segev, S., 2022. The impact of Option B+ on mother-to-child transmission of HIV in Africa: A systematic review. *Tropical Medicine & International Health*, *27*(6), pp.553-563.

47) Anigilaje, E.A., Ageda, B.R. and Nweke, N.O., 2016. Barriers to uptake of prevention of mother-to-child transmission of HIV services among mothers of vertically infected HIV-seropositive infants in Makurdi, Nigeria. *Patient preference and adherence*, pp.57-72.
48) Fassinou, L.C., SongwaNkeunang, D., Delvaux, T., Nagot, N. and Kirakoya-Samadoulougou, F., 2024. Adherence to option B+ antiretroviral therapy and associated factors in pregnant and breastfeeding women in Sub-Saharan Africa: a systematic review and meta-analysis. *BMC public health*, *24*(1), p.94.
49) World Health Organization (WHO). Validation of eliminating of mother-to-child transmission of HIV, syphilis and hepatitis B. 2023. Available on:https://www.who.int/initiatives/triple-elimination-initiative-of-mother-to-child-transmission-of-hiv-syphilis-and-hepatitis-b/validationAccessed 20 June 2024.
50) Quinn, T.C., 1996. Global burden of the HIV pandemic. *The lancet*, *348*(9020), pp.99-106.
51) Liu, Z., Chen, Z., Cui, F., Ding, Y., Gao, Y., Han, G., Jia, J., Li, J., Li, Z., Liu, Y. and Mao, Q., 2022. Management algorithm for prevention of mother-to-child transmission of hepatitis B virus (2022). *Journal of Clinical and Translational Hepatology*, *10*(5), p.1004.
52) World Health Organization, 2021. Global guidance on criteria and processes for validation: elimination of mother-to-child transmission of HIV, syphilis and hepatitis B virus.