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Vertical Transmission of HIV in Children: Epidemiology, Prevention, and Progress Toward Elimination

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Abstract

The vast majority of new HIV infections in children (more than 90%) are due to mother-to-child (vertical) transmission, primarily affecting sub-Saharan Africa. Although much progress has been made in recent decades, it has stagnated in recent years, and there are still regions and countries where vertical transmission of HIV is a significant problem. The risk of transmission without antiretroviral therapy (ART) is high (between 15% and 45%), and the most determining factor is the mother's viral load. Transmission can occur during pregnancy, childbirth, or breastfeeding. The most important prevention strategy is the use of ART for both mother and infant, with regimens widely recommended worldwide. In addition, other measures—such as early diagnosis in pregnant women, medical follow-up, breastfeeding and feeding counseling, and sound family planning—are essential. It is extremely important that health services and HIV and pregnancy-care programs be integrated and prepared to care for these patients.

Keywords

HIV; Vertical transmission; Breastfeeding; Antiretroviral therapy.

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Abbreviations

HIV: Human Immunodeficiency Virus; AIDS: Acquired Immunodeficiency Syndrome; ART: Antiretroviral Therapy; MTCT: Mother-to-Child Transmission; EMTCT: Elimination of Mother-to-Child Transmission; PrEP: Pre-Exposure Prophylaxis; WHO: World Health Organization; UNAIDS: Joint United Nations Programme on HIV/AIDS; CMV: Cytomegalovirus; NNRTI: Non-Nucleoside Reverse-Transcriptase Inhibitor; NAT: Nucleic Acid Amplification Test; DTG: Dolutegravir; ZDV/AZT: Zidovudine; NVP: Nevirapine; TDF: Tenofovir Disoproxil Fumarate; 3TC: Lamivudine; FTC: Emtricitabine; HAART: Highly Active Antiretroviral Therapy.

Key Points

- More than 90% of new pediatric HIV infections are due to vertical transmission, with the greatest burden of disease in sub-Saharan Africa.
- Without antiretroviral therapy (ART), the risk of vertical transmission ranges between 15% and 45%, with maternal viral load being the most important risk factor.
- Vertical transmission can occur during pregnancy, during childbirth, or in the postnatal period (through breastfeeding).
- The most important strategy to prevent transmission is the use of ART by both the mother and the infant. In pregnant women, dolutegravir-based regimens are the treatment of choice; in infants, zidovudine and/or nevirapine are used as prophylaxis depending on the risk of infection.
- Programs must also include other strategies, such as early HIV diagnosis in pregnant women; monitoring, support, and follow-up during pregnancy and the postnatal period; counseling on breastfeeding (recommended) and alternative feeding options; and efficient family-planning and reproductive-health programs.

Introduction

The vast majority of pediatric infections with the human immunodeficiency virus (HIV) result from vertical transmission, which can occur during pregnancy (in utero), during childbirth (perinatal), and after childbirth (postnatal) through breastfeeding. Although vertical transmission of HIV is uncommon in high-income countries, it still occurs in resource-limited regions. However, increased access to antiretroviral therapy (ART) and to quality health services for pregnancy and HIV care has led to a marked decline in vertical transmission of HIV in low-resource countries [1].

It is estimated that programs to prevent HIV transmission during pregnancy, childbirth, and breastfeeding have prevented an estimated 4 million (2.9–5.8 million) infections in children (0 to 14 years) since the year 2000 [1]. According to a study conducted in Mexico, a reduction in the HIV mortality rate in children was observed from 2003 onward, except in the 10-to-14-year age group. In the population with Social Security coverage, mortality rates decreased in all age groups; however, in the group without Social Security coverage or under Seguro Popular (a subsidized system), mortality rates decreased significantly only in children under 5 years of age [2].

This review describes the epidemiology and risk factors for vertical transmission of HIV, the strategies to prevent transmission, and the current progress toward elimination of vertical transmission as well as the pending challenges.

Epidemiology

Burden of disease

Surveillance data from the Joint United Nations Programme on HIV/AIDS (UNAIDS) over the past two decades demonstrate the major impact that HIV infection has on mothers and infants, especially in resource-limited regions [3]. More than 90% of all new pediatric HIV cases result from vertical transmission; in 2024, an estimated 120,000 (82,000–170,000) new infections occurred in children, 83% of them in sub-Saharan Africa [1]. Over the past decade, access to specialized HIV-care services—and, above all, to prevention of vertical transmission—has increased. In 2024, an estimated 84% of pregnant women with HIV were receiving ART [1]. However, this figure has remained constant over the years, and most new pediatric infections still arise from pregnant or breastfeeding women who were not receiving ART (49%), who had received ART but discontinued it (18%), who were receiving ART but did not achieve viral suppression (8%), or who had unknown HIV infection or were newly diagnosed during pregnancy (24%) [1,2].

The World Health Organization estimated that, in 2010, 21,000 pregnant women were HIV-positive in Latin America, and only 10,600 (50.5%) were receiving ART; that year, 3,400 children under 15 years of age were diagnosed with HIV. In 2017, there were again 21,000 HIV-positive women, of whom 15,300 (72.9%) were receiving ART, and the number of new pediatric HIV diagnoses decreased to 2,400 (a 29% reduction), mainly owing to the implementation of vertical-transmission prevention measures [4].

Risk of vertical transmission

Without any intervention, the risk of vertical transmission of HIV ranges between 15% and 45%, depending on maternal risk factors and breastfeeding [5]. The most important risk factor is the absence of viral suppression—in other words, the plasma viral load. In addition, infections acquired during pregnancy or breastfeeding are also associated with a higher risk of transmission.

- **Maternal viral load:** multiple studies have shown a direct positive correlation between maternal plasma viral load and the risk of transmission to the infant, with the risk clearly greater at high viral loads (>10,000 copies/mL), especially near delivery (12.7% without ART and 5% with ART) [6-11].
- **New infection detected during pregnancy:** acute HIV infection acquired during pregnancy is associated with a higher risk of vertical transmission, most likely related to the high viral loads observed in acute infection. In a meta-analysis of 37 studies, an incidence of 3.6 HIV infections per 100 person-years of follow-up was observed [12].
- **Other described maternal risk factors:** these include a low CD4 count, more advanced clinical disease, anemia, and the presence of other sexually transmitted infections; however, many of these factors tend to be correlated with an elevated plasma viral load [10,13].

- **Other described infant risk factors:** these include preterm birth, concurrent neonatal infection with cytomegalovirus (CMV), and mixed feeding; however, many of these factors were identified before the global availability of ART [10].
- **Breastfeeding:** HIV transmission through breastfeeding can account for an important proportion of pediatric HIV cases, especially in low-resource settings [14]. Evidence includes studies detecting HIV in breast milk, studies in which breastfed children had a higher transmission rate than non-breastfed children, and cases of women who acquired HIV after pregnancy and transmitted it to their children through breastfeeding [15,16]. The risk of transmission through breastfeeding is greatest in the first months of the infant's life [17,18]; the most important risk factors for this route are the maternal blood viral load, the mother's immune status, the presence of drug-resistant HIV in the mother (independent of viral-load level), the presence of mastitis, and certain mixed-feeding patterns [19-22]. Although viral load is the most important predictor, a recent study suggests that viral suppression would not eliminate 100% of the chance of transmission through breastfeeding [11].

Finally, regarding when transmission occurs, in the absence of any intervention most vertical-transmission events take place in the third trimester of pregnancy or during childbirth. Studies evaluating the timing of transmission observed that, in non-breastfeeding scenarios before the availability of ART, in utero infections represented one-third of infant infections, while the remaining two-thirds were estimated to occur at the time of delivery (assessed according to the timing of viral-load positivity in the infant) [23]. In breastfeeding scenarios before the availability of ART, an estimated 25% to 40% of infections were acquired in utero, 50% during delivery, and the remaining 10% to 20% during breastfeeding [24].

With respect to intrauterine transmission, the conclusion that most events occur in the third trimester is based on the low viral load detected in fetal tissue from abortions occurring in the first and second trimesters [25], on stochastic models [26], and on data from studies using zidovudine as prophylaxis, in which the transmission rate was significantly lower when prophylaxis was started at 28 weeks of gestation versus 36 weeks (1.6% vs. 5.1%) [27].

Finally, a study conducted in Mexico observed that the factors associated with greater vertical transmission included the absence of ART during pregnancy, vaginal or forceps-assisted delivery, breastfeeding, and mixed feeding [28].

Mechanisms of transmission

- **In utero:** described mechanisms include disruption of placental integrity, leading to microtransfusions of viremic maternal blood across the placenta to the fetus, an effect that is enhanced by local inflammation (especially in the context of chorioamnionitis) [29,30].
- **Intrapartum:** transmission is thought to occur through contact of the infant's mucous membranes with viremic maternal blood and secretions during birth, including a greater effect produced by uterine contractions; in this setting, rupture of membranes for more than 4 hours (in the absence of ART) is associated with a higher risk of transmission [29,31].

- **During breastfeeding:** studies have shown that HIV-infected cells in breast milk are responsible for transmission, and that other factors—such as intestinal integrity in the infant and lymphocytes located in the tonsils—also play a role [32,33].

Prevention of Transmission

ART is the cornerstone of strategies to prevent vertical transmission of HIV. However, multiple services and stages within the health system are essential to prevent transmission, including the following.

High-risk pregnant patients without known HIV

- HIV testing at the first visits to detect patients with HIV in the early stages of pregnancy.
- In serodiscordant couples with a negative HIV test and in women at high risk of acquiring infection, discussing and recommending the initiation of pre-exposure prophylaxis (PrEP) is fundamental. It is important to remember that infections acquired during pregnancy or breastfeeding account for approximately 24% of all new pediatric HIV infections [1]; in this regard, long-acting injectable agents such as cabotegravir or lenacapavir have proven highly effective and safe in women, including pregnant women [34,35].
- Repeat HIV testing in the third trimester or during labor (in those with a previous negative test).

Prenatal and perinatal care for pregnant patients with HIV and their infants

- Rapid initiation of ART at the time of HIV diagnosis.
- CD4 count and clinical assessment.
- Scheduling frequent visits during pregnancy to assess ART adherence and adverse effects, in addition to routine pregnancy evaluation.
- Delivery/cesarean section at a health facility with obstetric services.
- Rapid initiation of ART as postnatal prophylaxis in the infant.

Postpartum care for patients with HIV and their infants

- Continued lifelong ART management, especially during the breastfeeding period.
- Family-planning and reproductive-health consultations.
- Discussion and counseling on infant feeding, promoting exclusive breastfeeding during the first 6 months of life.
- Early HIV testing of the newborn and follow-up (using nucleic acid amplification tests).
- Ensuring access and adherence to health services to allow long-term follow-up.
- In HIV-infected infants, prompt referral for HIV treatment and follow-up with specialists, with rapid initiation of ART.

Maternal antiretroviral therapy

ART is recommended for all pregnant patients with HIV, regardless of CD4 count or disease stage, because it reduces the risk of transmission (in addition to improving the patient's clinical status). The goal of ART is to reduce plasma viral-load levels until they are undetectable [36].

Type of ART regimen:

- **Patients already receiving ART before pregnancy, with undetectable viral load:** the recommendation is to continue the same regimen during pregnancy. In most resource-limited countries, most patients would be receiving ART with drugs recommended by the World Health Organization (WHO) that have satisfactory safety profiles for pregnancy (dolutegravir, protease inhibitors, lamivudine, tenofovir). If a patient is receiving ART with an agent for which there are few safety data in pregnancy, the decision to change or continue should be individualized. Evidence shows that patients with an undetectable viral load during pregnancy and delivery have minimal or no risk of transmitting HIV to their infants [11].
- **Patients already receiving ART before pregnancy, without viral suppression (detectable load):** every effort should be made to achieve viral suppression as quickly as possible, including efforts to increase ART adherence and counseling. If an undetectable viral load cannot be achieved by 8 weeks, a change to ART with next-level drugs is recommended (according to local/national guidelines), together with more frequent viral-load monitoring.
- **Patients not receiving ART before pregnancy:** ART should be started immediately upon HIV diagnosis. The WHO recommends dolutegravir, tenofovir fumarate, and lamivudine (or emtricitabine) as the first-line regimen [36]. The choice of second- and third-line drugs is the same as for non-pregnant patients and is beyond the scope of this review. Multiple studies show that sustained viral suppression is the most important factor in protecting the infant [11,37-40]. Dolutegravir-based regimens are preferred as first-line therapy, based on data from multinational clinical trials [41,42]. Although preliminary data from a study in Botswana suggested an association between dolutegravir and neural-tube defects in infants [43], the final analysis showed that the increase in absolute risk was very low (0.2%) [44]. Although surveillance of neural-tube defects with this regimen continues, the WHO continues to recommend dolutegravir as a first-line drug.
- **Drug resistance:** At the population level, increased levels of resistance to non-nucleoside and nucleoside reverse-transcriptase inhibitors (NNRTIs) are being observed in patients with newly diagnosed HIV. In addition, multidrug resistance in both mother and infant is possible if there is poor maternal ART adherence; therefore, evaluation, follow-up, and counseling are fundamental to completing treatment, preventing transmission, and preventing the emergence of resistance [45]. HIV resistance testing at diagnosis is recommended in high-resource countries but not in low-resource countries. The WHO recommends using dolutegravir-based regimens, not using NNRTIs in countries with resistance greater than 10%, and not waiting for resistance-test results to start treatment [36]. Studies in pregnant women evaluating resistance show resistance mutations in 10% of cases [21,46], and studies conducted after the introduction of dolutegravir as first-line therapy are beginning to show some cases of resistance to this drug, although this remains uncommon [47].

Infant postnatal prophylaxis

In addition to maternal ART, the WHO recommends that all exposed newborns receive postnatal prophylaxis for 4 to 6 weeks to reduce the risk of vertical transmission. Prophylaxis should be started as soon as possible after birth, preferably within the first 6 to 12 hours of life [36].

- **High-risk infants:** those born to mothers with HIV who have a high viral load (>1,000 copies/mL) measured in the last 4 weeks before birth, who are not taking ART or started it less than 4 weeks earlier, or whose mother acquired HIV during pregnancy or was newly diagnosed. In these cases, zidovudine plus nevirapine is recommended for the first 6 weeks of life; then, if breastfeeding is initiated, the same regimen or nevirapine alone is continued for another 6 weeks. If the mother does not tolerate or discontinues ART, the neonate should continue this regimen throughout the entire duration of breastfeeding [36]. In clinical trials this regimen has been shown to considerably reduce transmission in resource-limited countries, whereas in high-resource countries the combined regimen of zidovudine + lamivudine + nelfinavir is used, although this regimen has not shown lower transmission rates in high-risk infants and was associated with greater hematologic toxicity [48].
- **Low-risk infants:** those born to mothers with HIV on ART with a low (<1,000 copies/mL) or undetectable viral load, or who have been taking ART for more than 4 weeks. In these cases, nevirapine or zidovudine is recommended for 4 weeks, and then for 2 additional weeks in breastfed infants.
- **Adverse effects / safety:** in general, the ART recommended as prophylaxis is considered safe in infants. Expected adverse effects are transient anemia and neutropenia that usually resolve by 12 weeks (zidovudine). No cases of rash or hepatotoxicity from nevirapine have been reported in infants receiving the postnatal prophylaxis regimen.
- **Drug resistance:** infants may acquire drug-resistant HIV either pre-/perinatally or through breastfeeding. Studies show that the main risk factors are ART interruptions or loss to follow-up. If resistant HIV is confirmed, the patient should be managed by a specialist [47].

Vaginal delivery or cesarean section?

The presence of HIV and the mother's infection status do not affect the decision to perform vaginal delivery or cesarean section. In high-resource countries, cesarean section is recommended in patients who have not achieved viral suppression (viral load >1,000 copies/mL) at the time of delivery [49,50]. In resource-limited countries, however, this practice is not currently recommended.

Postnatal prevention and breastfeeding

ART is fundamental for reducing transmission rates during breastfeeding. The WHO recommends that, for mothers with HIV, the focus should be on promoting breastfeeding with lifelong ART use or, in cases where ART cannot be received, avoiding breastfeeding and promoting alternative feeding options [36]. Promoting ART together with breastfeeding is the most appropriate strategy; multiple studies have shown that the absence of breastfeeding was associated with higher mortality in HIV-exposed (but uninfected) infants and with an overall increase in infant mortality [51,52]. Infants in whom HIV exposure is documented after delivery should receive prophylaxis as high-risk infants and should also undergo diagnostic testing (based on polymerase chain reaction) to assess infection.

Final Reflections and Future Research

Progress toward elimination

Enormous progress has been made in identifying and treating pregnant women with HIV in resource-limited countries. In 2023, an estimated 84% of pregnant women with HIV worldwide were receiving ART, and vertical-transmission rates had halved since 2010 [1,3]. Success has been particularly marked in sub-Saharan Africa, where South Africa reports a transmission rate of 2% and Uganda a rate of 3%. Moreover, greater access to ART means that more people with HIV attend their first obstetric visit already receiving ART (estimated at more than 60% in 2020). In addition, greater access to viral-load monitoring and to newer, more effective and simpler ART regimens is increasingly available [1].

Despite these advances, an estimated 150,000 new pediatric HIV infections occurred in 2023 [53]. According to UNAIDS data, the factors contributing most to this were new infections in very young patients, maternal ART adherence, limited postpartum follow-up, and the persistence of structural deficiencies in health systems that prevented the full implementation of vertical-transmission prevention strategies [53].

Current challenges

Barriers to the prevention of vertical transmission. Many real-world challenges still hinder the implementation of all prevention strategies in the antenatal, pregnancy, and postnatal periods. Some of these include:

- Scarce or absent prenatal care.
- Scarce or absent access to ART and HIV-care services.
- Deliveries occurring at home, without specialized care.
- High rates of loss to follow-up.
- Lack of diagnostic tests, ART, and routine laboratories.
- Lack of specialized human resources.
- Stigma associated with care (HIV-specific clinics).
- External factors that disrupt health systems and care cascades.

- **HIV testing during pregnancy.** Diagnosing HIV in pregnant women is fundamental to controlling vertical transmission, and routine testing at the first prenatal visit is widely implemented worldwide. The strategy of informing pregnant patients that they will be tested for HIV (unless they specifically decline) has consistently led to rapid, same-day testing in more than 95% of cases across multiple settings [54]. Repeat testing of patients who tested negative—whether in the third trimester, the immediate postpartum period, or during breastfeeding—is another very important intervention. This strategy is widely used in high-resource countries, whereas in resource-limited settings it has been difficult to establish consistently [55].
- **ART coverage in pregnant women.** Large-scale implementation of effective ART to prevent vertical transmission has faced multiple difficulties in many low-resource countries. However, with the new dolutegravir-based regimens and the “test and treat all” approach, enormous progress has been made in reducing vertical transmission. According to UNAIDS data, ART coverage of pregnant women increased from 36% in 2009 to 85% in 2020 (across the 21 UNAIDS

priority countries) [14].

- **Poor ART adherence and limited follow-up.** Inadequate ART adherence and lack of follow-up in the postpartum period are two major obstacles that vertical-transmission prevention programs must confront [56-58]. Some strategies that have improved retention in health programs include integrating HIV care into routine pregnancy and pediatric care services, financial incentives, and counseling in the general population [59-61]. According to multiple studies, patients with unplanned pregnancies are at high risk of ART non-adherence in the postpartum period [62].

Conclusion

Although much progress has been made in preventing vertical transmission of HIV, many challenges remain, especially in resource-limited regions and countries. Having robust, universal, and well-funded prevention programs that allow universal access to early testing, ART for mother and child, and specialists and institutions responsible for pregnancy and infant care integrated with HIV care will be fundamental to achieving the WHO elimination goals and preventing all pediatric HIV infections.

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Conflict of interest

The author declares that he has no conflict of interest.

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