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Antiretroviral Prophylaxis and Beyond: Innovations in Preventing HIV in Young Children

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Abstract

Despite substantial progress in reducing mother-to-child transmission (MTCT) of HIV, pediatric HIV infections continue to pose a significant public health challenge, particularly in low-resource settings. Antiretroviral prophylaxis administered to HIV-positive pregnant women and their infants remains the cornerstone of prevention strategies. However, limitations such as drug adherence, resistance, and access issues highlight the need for innovations beyond traditional prophylaxis to further reduce pediatric HIV incidence. Recent advances include the development of long-acting antiretroviral formulations, novel drug delivery systems, and point-of-care early infant diagnostic technologies that enable rapid detection and timely initiation of treatment. Integration of maternal health services with pediatric HIV care and the use of mobile health tools are enhancing adherence and retention in care. Additionally, community engagement and education efforts are critical to overcoming stigma and socio-cultural barriers that hinder the uptake of prevention services.

Keywords: Antiretroviral prophylaxis, Pediatric HIV prevention, Mother-to-child transmission, Early infant diagnosis, HIV treatment innovations

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Introduction

Human Immunodeficiency Virus (HIV) remains a significant global health challenge, particularly among children under five years old. Despite major advances in treatment and prevention, approximately 150,000 new pediatric HIV infections occurred worldwide in 2022, with the majority resulting from mother-to-child transmission (MTCT). Pediatric HIV is associated with high morbidity and mortality if left untreated, making prevention in early life a critical public health priority. The implementation of antiretroviral prophylaxis has been pivotal in reducing transmission rates, yet achieving elimination of pediatric HIV requires ongoing innovation and enhanced strategies [1-2].Antiretroviral prophylaxis—administered to pregnant women, during labor, and to newborns—has transformed the landscape of pediatric HIV prevention over the past two decades [3-4]. The World Health Organization's Option B+ strategy, recommending lifelong antiretroviral therapy (ART) for all pregnant and breastfeeding women living with HIV, has significantly decreased transmission rates globally [5-6]. Neonatal prophylaxis with drugs such as nevirapine or zidovudine further reduces the risk of infection during the vulnerable perinatal and postnatal periods. Despite these advances, challenges remain, including incomplete coverage, adherence issues, and the emergence of drug resistance [7].

Beyond antiretroviral prophylaxis, innovations in drug formulations and delivery methods promise to enhance the effectiveness and feasibility of pediatric HIV prevention [8-9]. Long-acting injectable ART formulations and implantable devices are currently being evaluated to reduce the burden of daily pill-taking, which can be particularly challenging for pregnant women and caregivers of infants. These innovations could improve adherence, reduce missed doses, and simplify prophylactic regimens, especially in resource-limited settings where healthcare access is constrained [10].Early infant diagnosis (EID) represents another critical pillar in preventing pediatric HIV-related morbidity and mortality. Traditional laboratory-based diagnostic tests often suffer from long turnaround times and loss to follow-up, delaying treatment initiation in infected infants. Point-of-care diagnostic technologies that allow rapid HIV detection at or near the site of care have demonstrated improvements in timely diagnosis and linkage to treatment, thus improving survival outcomes. Expanding access to these technologies remains a priority in many high-burden regions [11-12].

In addition to biomedical advances, integrating maternal health services with pediatric HIV prevention and care has gained recognition as essential for achieving sustained impact. Routine viral load monitoring, counseling on ART adherence, and management of co-morbidities during pregnancy and breastfeeding improve maternal health and reduce transmission risk. Mobile health (mHealth) interventions such as SMS reminders and digital adherence tools are increasingly used to support continuous care engagement, particularly in areas with limited healthcare infrastructure [13-14].Community engagement and social support are equally important components of effective pediatric HIV prevention [15]. Stigma, discrimination, and socio-cultural barriers often hinder women from accessing HIV testing and treatment services, leading to missed opportunities for prophylaxis and early diagnosis [16-17]. Programs that involve peer support, male partner involvement, and community education have been shown to increase uptake of prevention services and improve ART adherence among mothers and caregivers. Addressing these psychosocial factors is critical to bridging gaps in the HIV prevention cascade [18].

The Role of Antiretroviral Prophylaxis in Pediatric HIV Prevention

Antiretroviral prophylaxis remains the cornerstone of preventing HIV transmission from mother to child, significantly reducing the incidence of pediatric HIV infections worldwide. The primary mechanism involves suppressing

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maternal viral load during pregnancy, labor, and breastfeeding, thereby minimizing the likelihood of viral transmission to the infant. For HIV-exposed infants, prophylactic antiretroviral drugs provide a protective barrier during the high-risk perinatal and early postnatal periods when exposure to the virus is most likely [19-20].The implementation of the World Health Organization's Option B+ strategy, which recommends lifelong antiretroviral therapy (ART) for all pregnant and breastfeeding women living with HIV regardless of CD4 count or clinical stage, has been a game-changer in reducing vertical transmission. This approach not only improves maternal health outcomes but also dramatically decreases the risk of HIV transmission to the infant during pregnancy and breastfeeding. Studies have shown that consistent maternal ART adherence can reduce the risk of transmission to less than 2%, highlighting the critical importance of early and sustained therapy [21-22].

For infants born to HIV-positive mothers, neonatal prophylaxis typically involves administering drugs such as nevirapine or zidovudine starting immediately after birth and continuing for several weeks. This regimen serves as a safeguard during the infant's initial exposure to HIV through birth or breast milk. Recent research supports the use of extended prophylaxis, particularly in high-risk infants born to mothers with unsuppressed viral loads or inadequate ART adherence. While antiretroviral prophylaxis has been effective, challenges including drug toxicity, adherence difficulties, and the emergence of resistant viral strains necessitate continuous monitoring and development of new prophylactic strategies [23].

Innovations in Prophylactic Regimens and Drug Delivery

While traditional antiretroviral prophylaxis has substantially reduced mother-to-child transmission of HIV, ongoing challenges such as adherence difficulties, drug resistance, and limited healthcare access have driven the development of innovative prophylactic regimens and drug delivery systems. These innovations aim to simplify treatment, improve effectiveness, and extend protection to infants and mothers, particularly in resource-limited settings [24].One of the most promising advances is the development of long-acting antiretroviral formulations. Injectable drugs like cabotegravir and rilpivirine, currently approved for adult HIV treatment and pre-exposure prophylaxis (PrEP), are under investigation for potential use in pregnant women and infants. These formulations offer the advantage of sustained drug release over weeks or months, reducing the burden of daily pill adherence and minimizing missed doses. Long-acting injectables could transform prophylaxis by providing consistent therapeutic drug levels during critical transmission windows, improving maternal viral suppression and infant protection [25-26].

In addition to injectables, novel drug delivery platforms such as implantable devices, microarray patches, and nanosuspensions are being explored to facilitate controlled, sustained release of antiretrovirals. Implantable devices, for instance, can provide months-long protection with a single procedure, which is particularly advantageous in areas with poor healthcare infrastructure or where frequent clinic visits are impractical. Microarray patches, a minimally invasive technology, offer the potential for self-administration without needles, improving acceptability and access [27].Combination drug regimens are also evolving to maximize efficacy and reduce resistance risks. New fixed-dose combinations tailored for pregnant women and infants aim to simplify dosing schedules and improve pharmacokinetics. For example, integrating integrase inhibitors with nucleoside reverse transcriptase inhibitors has shown promising results in achieving rapid viral suppression. Furthermore, prophylactic regimens that extend beyond the neonatal period, especially in high-risk infants, are being evaluated to provide prolonged protection during breastfeeding—a critical transmission phase [28-29].

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Early Infant Diagnosis and Point-of-Care Technologies

Early infant diagnosis (EID) of HIV is a critical component of pediatric HIV prevention, enabling timely identification of infected infants and prompt initiation of lifesaving antiretroviral therapy. Infants infected with HIV have a rapid disease progression compared to adults, and without early treatment, mortality rates are high within the first two years of life. Therefore, accurate and early detection of HIV in exposed infants is essential to reduce morbidity and mortality [12].Traditional EID relies on nucleic acid-based tests, such as polymerase chain reaction (PCR), to detect HIV DNA or RNA in infants. However, these tests require sophisticated laboratory infrastructure, skilled personnel, and often involve prolonged turnaround times due to sample transport and result processing delays. Such delays can result in loss to follow-up, missed treatment opportunities, and poorer clinical outcomes. In many resource-limited settings where the burden of pediatric HIV is highest, these systemic challenges significantly hinder the effectiveness of EID programs [12].

Point-of-care (POC) diagnostic technologies have emerged as transformative tools to overcome these barriers. POC tests for HIV nucleic acids enable rapid, on-site diagnosis within hours, allowing healthcare providers to initiate ART immediately if needed. Several POC platforms have received regulatory approval and are being deployed in high-burden countries with encouraging results. Studies show that POC EID reduces the time to diagnosis and treatment initiation, improves retention in care, and ultimately enhances survival outcomes in HIV-infected infants [30].In addition to nucleic acid-based POC tests, innovative technologies like microfluidic chips, isothermal amplification assays, and portable biosensors are under development to further simplify and reduce the cost of infant HIV testing. These technologies aim to be user-friendly, robust, and compatible with low-resource environments, expanding access to early diagnosis even in remote or underserved communities [31].Integrating POC EID with routine immunization and maternal-child health visits maximizes coverage and streamlines care pathways. Additionally, digital health tools such as electronic health records and mobile phone alerts support follow-up and linkage to care. Together, these advancements in early diagnosis and rapid testing technologies are critical to closing the gap in pediatric HIV prevention, ensuring that infected infants receive timely treatment and uninfected infants remain protected [30-31].

Beyond Prophylaxis: Integrating Maternal Health and Community Support

Preventing pediatric HIV transmission extends beyond the administration of antiretroviral prophylaxis to infants; it requires a holistic approach that integrates maternal health services with community engagement and support systems. Maternal health plays a pivotal role in the success of prevention efforts, as the mother's viral suppression, adherence to antiretroviral therapy, and overall wellbeing directly influence transmission risk. Comprehensive care models that support mothers throughout pregnancy, delivery, and breastfeeding are essential to sustaining low rates of vertical transmission [32-33].Routine monitoring of maternal viral load is a cornerstone of integrated maternal care, allowing healthcare providers to identify women with suboptimal viral suppression and intervene promptly. In addition to viral load testing, management of co-morbidities such as tuberculosis, sexually transmitted infections, and malnutrition improves maternal health outcomes and reduces the likelihood of HIV transmission. Counseling on ART adherence, infant feeding options, and family planning further empower women to make informed decisions that support both their health and that of their children [34].

Community engagement and social support structures are equally crucial in enhancing the effectiveness of maternal and pediatric HIV prevention programs. Stigma, discrimination, and gender inequality remain significant barriers to accessing HIV services, leading to missed testing, delayed treatment initiation, and poor adherence.

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Programs that involve male partner participation, peer support groups, and community health workers have shown success in fostering supportive environments, reducing stigma, and improving retention in care [35].Mobile health (mHealth) technologies also play an increasingly important role in supporting maternal and infant health. SMS reminders, digital adherence monitoring, and telehealth consultations facilitate continuous engagement with healthcare providers and provide psychosocial support, especially in hard-to-reach populations. These tools can bridge gaps in healthcare delivery, ensuring timely appointments, medication refills, and follow-up testing [36].Moreover, integrating HIV prevention efforts with broader maternal and child health services—such as antenatal care, immunizations, and nutrition programs—can streamline service delivery, reduce fragmentation, and increase uptake. This "one-stop-shop" approach minimizes the burden on mothers and caregivers, making it easier to maintain continuity of care [37-38].

Conclusion

Antiretroviral prophylaxis has dramatically transformed the prevention of pediatric HIV, significantly reducing mother-to-child transmission rates worldwide. However, persistent challenges such as adherence barriers, drug resistance, and limited healthcare access necessitate the development and integration of innovative strategies. Advances in long-acting drug formulations, novel delivery platforms, and point-of-care diagnostic technologies are reshaping the landscape of HIV prevention for infants and young children, offering new hope for more effective and accessible interventions. Beyond pharmacological innovations, the integration of comprehensive maternal health services and robust community support systems is vital for sustained success. Addressing social determinants, reducing stigma, and leveraging digital health tools enhance adherence and retention in care, ensuring that both mothers and infants receive timely and continuous support. A multidisciplinary approach that combines biomedical advances with socio-behavioral interventions strengthens the prevention continuum and bridges gaps in service delivery.

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