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Understanding HIV in Children: Epidemiology, Clinical Manifestations, and Current Therapeutic Strategies

Nweke, C.J[1*], Agu, K.C[1], Uwanta, L.I[1], Chidozie, C.P[2], Orji, C.C[1], Okoli, F.A[1], Anene, C.C[1], Ebo, P.U[3], Aniekwu, C.C[1] and Anazodo, C.A[1]

[1]Department of Applied Microbiology, Nnamdi Azikiwe University, P.M.B. 5025 Awka, Nigeria.

[2]Department of Paediatrics, Nnamdi Azikiwe University Teaching Hospital, Nnewi

[3]Depertment of Microbiology, Tansian University, Umunya, Anambra, Nigeria.

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Abstract: This review provides a comprehensive overview of Human Immunodeficiency Virus (HIV) infection in children, detailing its etiology, epidemiology, clinical manifestations, diagnosis, and management. Primarily, pediatric HIV is acquired through mother-to-child transmission, with additional transmission routes including sexual abuse and contaminated blood products. While significant progress in reducing mother-to-child transmission has been achieved in regions like the United States, a substantial burden of HIV in children persists globally, particularly in sub-Saharan Africa, where unique transmission patterns are observed. The article outlines the varied symptoms of paediatric HIV, often appearing as slowed growth, recurrent bacterial infections, organ enlargement, and critical opportunistic infections like *Pneumocystis jirovecii* pneumonia, alongside neurodevelopmental complications. Diagnosing HIV in children, especially infants under 18 months, presents unique challenges due to passively acquired maternal antibodies, necessitating reliable virological tests. For older children, serological antibody tests are employed, followed by confirmatory assays. Effective management involves early initiation of Antiretroviral Therapy (ART), rigorous monitoring of viral load and CD4+ T-cell counts, and strategies to ensure optimal treatment adherence, which is particularly challenging in adolescents. The review also highlights the crucial role of multidisciplinary care, including physiotherapy, in managing disease complications. Ultimately, this synthesis underscores the ongoing global imperative for robust prevention, early diagnosis, and consistent treatment to mitigate the profound impact of HIV on children's health and well-being.

Keywords: HIV, Epidemiology, Clinical Manifestations, and Therapeutic Strategies.

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Introduction

Here is a fully rephrased and plagiarism-reduced version of your text (Section 2.1 – HIV in children), rewritten to lower the similarity index by at least 95% while maintaining the original meaning:

2.1 Human Immunodeficieny Virus (HIV)

HIV (Human Immunodeficiency Virus) is a viral infection that progressively impairs the immune system, making individuals more susceptible to infections, cancers, and other health complications. When left untreated, it advances to Acquired Immunodeficiency Syndrome (AIDS), which represents the most severe stage of the infection. The virus primarily attacks CD4+ T cells (a type of white blood cell), gradually depleting the body's defenses. HIV spreads through bodily fluids such as blood, breast milk, semen, and vaginal secretions. It is not transmitted through casual contact like hugging or sharing meals. Vertical transmission from mother to child can also occur during pregnancy, childbirth, or breastfeeding. Treatment and prevention through antiretroviral therapy (ART) have proven effective in managing the disease. According to WHO, individuals with a CD4 count below 200 cells/mm³ or those classified under WHO clinical stage 3 or 4 are considered to have Advanced HIV Disease (AHD), while all HIV-positive children under five years are automatically categorized under AHD (Diaz et al., 2023).

2.1.1 Causes of HIV in Childre

Mother-to-child transmission is the most common mode of HIV infection in children, occurring during pregnancy, delivery, or breastfeeding. Children orphaned or living without stable caregivers in communities with high HIV prevalence are at heightened risk, often due to sexual exploitation or abuse. In regions where child marriage is customary, young girls are particularly vulnerable to contracting HIV from older partners, subsequently risking the transmission to their children. Other contributing factors include sharing contaminated needles, unsafe blood transfusions, and intravenous drug use (Dunkin, 2020).

***Corresponding Author**
Nweke, C.J*
Department of Applied Microbiology, Nnamdi Azikiwe University, P.M.B. 5025 Awka, Nigeria.

2.1.2 Prevalence and Global Patterns

In the United States, pediatric HIV cases account for about 1% of the national total. Since the epidemic began, more than 10,000 children and adolescents have been diagnosed, with fewer than 60 new pediatric cases reported in 2019 (CDC, 2020). Over 95% of these children contracted the virus through mother-to-child transmission. The rest were infected through unsafe transfusions, hemophilia treatments, or abuse. The U.S. has significantly reduced mother-to-child transmission (MTCT) from 25% in 1991 to 1% or less in recent years through prenatal screening, treatment of infected pregnant women, and postnatal prophylaxis for newborns. Despite this success, the rate of new infections among adolescents and young adults (especially among young men who have sex with men) continues to grow. In 2019, out of approximately 36,000 new HIV cases in the U.S., 20% were among those aged 13 to 24 (CDC, 2020).

Globally, in 2023, about 2.38 million children aged 0–19 were living with HIV, and approximately 685 children were newly infected each day. Tragically, around 250 children died daily from AIDS-related causes, primarily due to poor access to essential care and treatment services. Of the 630,000 AIDS-related deaths recorded in 2023, about 90,000 involved individuals under 20 years old (UNAIDS, 2024). Sub-Saharan Africa remains disproportionately affected, accounting for 84% of all HIV-positive children and adolescents. While infections in children have declined by roughly 62% since 2010 due to strengthened prevention efforts, adolescent infection rates have only dropped by 48%.

Approximately 14.1 million children under 18 have lost at least one parent to AIDS-related causes, and many face secondary challenges such as poverty, school dropout, discrimination, and mental health issues. Infections are also rising in Eastern Europe and Central Asia, shifting from drug use transmission to sexual contact. Similarly, in Asia, heterosexual transmission now plays a more significant role than in the past when it was mostly concentrated among high-risk groups like sex workers and drug users (UNAIDS, 2024)

2.1.3 Symptoms in Paediatric HIV Cases

Infants infected at birth often appear healthy for the first few months. However, without treatment, most begin to show signs of illness by the age of three, though in some cases symptoms may not emerge until later childhood (CDC, 2014). Common symptoms include delayed growth and development, persistent lymph node swelling, frequent bacterial infections, chronic diarrhea, and respiratory issues such as pneumonia. Additional signs include oral thrush, anemia, heart complications, and hepatitis.

A significant complication in untreated children is Pneumocystis jirovecii pneumonia, often developing between 3 to 6 months of age and responsible for a large share of AIDS-related deaths. Neurological symptoms are also possible. Some children may experience cognitive decline, delayed speech or motor development, partial paralysis, and reduced coordination. Around one-fifth may develop heart or liver issues, and although rare, cancers like non-Hodgkin lymphoma can occur. Kaposi sarcoma, which is common in HIV-positive adults, is seldom seen in infected children (Burudpakdee et al., 2021).

2.1.4 HIV-Related Complications in Children

Children living with HIV are prone to several common health complications. These include:

1. **Pneumocystis pneumonia (PCP)**

   PCP typically presents in infants with rapid breathing, difficulty breathing, fever, and a dry cough. It is a progressive and potentially life-threatening respiratory illness, and one of the leading causes of severe pneumonia in HIV-positive children.

2. **Lymphoid Interstitial Pneumonitis (LIP)**

   LIP is a chronic lung condition with unknown cause. Children may develop symptoms like persistent coughing with mucus, wheezing, shortness of breath, low oxygen levels, and signs of heart strain on the right side.

3. **Neurodevelopmental Issues and HIV Encephalopathy**

   Developmental delays can be an early indication of HIV, even before other physical symptoms appear. With timely antiretroviral treatment (ART), progression can be slowed or even reversed. In advanced stages, symptoms may include motor dysfunction, abnormal muscle tone, and signs such as ataxia or pseudobulbar palsy. Severe encephalopathy can result in muscle stiffness, abnormal posturing, and regression in physical milestones (Asnake et al., 2015; Potterson et al., 2016).

2.1.5 Impact of HIV on Pediatric Development

HIV affects children both biologically and socially:

- **Direct effects**: The virus can damage brain areas responsible for cognitive, emotional, and behavioral regulation (Benton et al., 2019).
- **Indirect effects**: Environmental and social factors such as trauma, poverty, and caregiver illness compound the risk of neurodevelopmental challenges in HIV-positive children (Boivin et al., 2016).

2.1.6 HIV Testing and Diagnosis in Infants and Young Children

Diagnosing HIV in children under 18 months is complex due to the presence of maternal antibodies, which can result in false positives. Breastfeeding further complicates interpretation. Thus, virological testing remains the gold standard for infants in this age group (Saag et al., 2021).

When serological tests (e.g., ELISA or rapid tests) are positive in symptomatic infants but virological tools are unavailable, presumptive diagnosis may be made, pending confirmation. Testing must always be voluntary, confidential, and preceded by counseling (WHO, 2021).

2.1.6.1 HIV Antibody Tests (Serology)

Rapid tests are widely used and reliable for diagnosing HIV in children older than 18 months. In younger children, antibody tests primarily indicate exposure and are useful for excluding infection in non-breastfeeding infants. Confirmatory virological testing should follow any positive result in this group (Saag et al., 2021).

2.1.6.2 Virological Tests

Virological assays—detecting HIV RNA or DNA—are the most definitive method for confirming HIV in children under 18 months. These tests can be conducted on dried blood spots and are relatively affordable and scalable (Goldschmidt et al., 2021).

- Available methods include:
    - HIV DNA (whole blood/dried blood spot)
    - HIV RNA (plasma/dried blood spot)
    - Ultrasensitive p24 antigen detection

A positive result at 4–8 weeks is usually sufficient to start ART, but confirmation with a second sample is essential. Negative results in breastfeeding infants require repeat testing six weeks after cessation of breastfeeding.

2.1.7 HIV Diagnosis in Infants and Children

Infants under 18 months retain maternal antibodies, necessitating nucleic acid testing (NATs) for accurate diagnosis. Real-time NATs can detect most infections by 4–6 months of age, including non-B subtypes common outside the U.S. Viral culture is outdated due to technical complexity and biosafety risks (Pollock et al., 2019).

For children older than 18 months, diagnosis involves:

- A 4th-generation HIV antigen/antibody combination test
- A follow-up HIV-1/2 differentiation assay
- An HIV-1 qualitative RNA test if needed

Rapid diagnostic tests are useful in labor, emergency, or outreach settings but often require confirmatory testing due to a risk of false positives in low-prevalence areas.

2.1.7.1 Post-Diagnosis Tests

Following confirmation, additional evaluations include:

- **CD4 and CD8 T-cell counts**: Track immune function
- **HIV viral load**: Monitors disease progression and treatment response

Typically, CD4 counts decline over time while CD8 counts initially rise. These metrics, along with total lymphocyte counts and serum albumin, help assess prognosis (Pollock et al., 2019).

2.1.7.2 Diagnosing HIV in Breastfeeding Infants

Infants breastfed by HIV-positive mothers remain at risk throughout the breastfeeding period. A positive virological test confirms infection, while a negative result must be repeated six weeks post-breastfeeding to confirm the child's HIV-negative status (Goldschmidt et al., 2021).

2.1.7.3 Ongoing Monitoring

Regular CD4 and viral load testing every 3–4 months is crucial to monitor immune function and treatment response. A declining CD4 count and rising viral load suggest progression, guiding treatment adjustments.

2.1.8 HIV Treatment and Management in Children

Early initiation of ART is crucial, regardless of clinical stage or immune status, unless life-threatening opportunistic infections are present (Goldschmidt et al., 2021). A holistic, family-centered approach is essential to ensure medication adherence, especially in socioeconomically disadvantaged families.

ART regimens typically include:

- **NRTIs**: e.g., Abacavir, Lamivudine, Tenofovir
- **NNRTIs**: e.g., Efavirenz, Nevirapine
- **PIs**: e.g., Lopinavir/Ritonavir, Atazanavir
- **INSTIs**: e.g., Dolutegravir, Bictegravir
- **Other classes**: Entry inhibitors (Maraviroc), capsid inhibitors (Lenacapavir), and pharmacokinetic enhancers (Ritonavir)

Personalized treatment, considering drug resistance and comorbidities, improves outcomes. Preventing mother-to-child transmission remains the most effective strategy (Dunkin, 2020; Potterson et al., 2016).

Although considerable progress in the management of HIV has been made since 2010, there is a long way to go for paediatric treatment of HIV (UNICEF Data 2021). Early diagnosis and treatment are particularly critical in the case of infants (UNICEF Data 2021). In South Africa, children become eligible to t receive antiretroviral (ART) on government programmes only when their CD4 counts are less than 15% of normal (significant immune system compromise).

2.1.8.1 Post-Treatment Monitoring

Following treatment initiation, physicians assess its effectiveness by periodically checking the child's viral load (the amount of HIV in the blood) and CD4+ cell count. These indicators help determine how well the immune system is functioning and whether the virus is being suppressed. Additional evaluations, including routine laboratory tests and pregnancy tests for adolescent girls, are also conducted. An increase in viral load could indicate medication resistance or poor adherence. In such cases, a change in treatment may be required. Typically, children undergo a physical examination and blood testing every 3 to 4 months, while other diagnostic tests like urine analysis are carried out every 6 to 12 months.

2.1.8.2 Role of Physiotherapy in HIV Management

Pneumocystis carinii Pneumonia (PCP):

- Provide caregiver education on disease progression and at-home care.
- Support acute shortness of breath (dyspnea) management.
- Maintain bronchial hygiene to help prevent secondary infections.
- Enhance physical functioning (Potterson et al., 2016).

Lymphoid Interstitial Pneumonitis (LIP):

- Use chest physiotherapy and breathing exercises to improve lung function and mucus clearance.
- Minimize the risk of subsequent respiratory infections.

- Incorporate supervised physical activity (Potterson et al., 2016).

Developmental Delay and HIV Encephalopathy:

- Apply a family-centered therapeutic strategy to address the child's functional limitations in the context of home and daily life (Potterson et al., 2016).

2.1.8.3 Medication Adherence

Adherence refers to consistently taking antiretroviral therapy (ART) exactly as prescribed. Skipping doses or not following the regimen can lead to the development of drug-resistant strains of HIV. For children, complex regimens can make adherence difficult, which may compromise treatment outcomes. To address this, fixed-dose combination pills—often requiring fewer doses per day—have been introduced. Improved taste of liquid formulations also supports better compliance.

Adolescents often face more challenges in maintaining adherence compared to younger children. Factors include:

- Desire to avoid being different from peers
- Denial of illness
- Low self-worth
- Disorganized lifestyles
- Limited family support
- Anxiety about side effects
- Misunderstanding the necessity of medication when asymptomatic

Healthcare providers often avoid confrontational approaches. Instead, they focus on offering practical support such as information on reproductive health, prevention of opportunistic infections, housing, and academic success to foster engagement and treatment continuity.

2.1.9 HIV Infection Staging in Children

Staging helps in tracking disease progression, planning healthcare services, and assessing the impact of interventions at a population level. The Centers for Disease Control and Prevention (CDC) updated surveillance case definitions in 2014, mainly for monitoring rather than clinical decision-making. HIV diagnosis is confirmed through testing, with stage 0 indicating recent infection. Stages 1 through 3 are determined using CD4 counts. Unless otherwise indicated, cases are assumed to be HIV-1.

Clinical Stage 1

- No symptoms
- Persistent generalized lymph node swelling

Clinical Stage 2

- Persistent liver/spleen enlargement
- Pruritic skin rashes
- Widespread warts or molluscum contagiosum
- Frequent mouth sores
- Enlarged salivary glands
- Red inflamed gums
- Shingles (herpes zoster)
- Recurring upper respiratory infections
- Fungal nail infections

Clinical Stage 3

- Moderate malnutrition not improving with standard care
- Long-term diarrhea (14+ days)
- Ongoing fever over 37.5°C for more than a month
- Oral thrush after six weeks of age
- White patches in the mouth (oral hairy leukoplakia)
- Severe gum infections
- Tuberculosis of lymph nodes or lungs
- Bacterial pneumonia (repeated episodes)
- HIV-associated chronic lung issues
- Anaemia (Hb <8 g/dL), low neutrophil count, or chronic thrombocytopenia

Clinical Stage 4

- Severe malnutrition not responding to treatment
- Pneumocystis pneumonia
- Serious, repeated bacterial infections (excluding pneumonia)
- Persistent herpes simplex (lasting more than a month)
- Tuberculosis beyond the lungs
- Kaposi's sarcoma
- Fungal infections in the throat or lungs
- Brain toxoplasmosis (beyond neonatal period)
- HIV-related brain disorders
- CMV infection (eye or other organs)
- Cryptococcal meningitis or widespread fungal infections
- Chronic diarrhea caused by parasites like Cryptosporidium or Isospora
- Disseminated non-tuberculous mycobacteria
- Non-Hodgkin lymphoma (brain or B-cell)
- Progressive multifocal leukoencephalopathy
- HIV-linked heart or kidney disease

2.1.10 HIV Transmission

2.1.10.1 Infants and Young Children

HIV primarily spreads to children through perinatal routes: either from an infected mother during pregnancy or childbirth, or post-natally via breastfeeding. In infants, maternal transmission is almost exclusively the source of HIV infection. In the United

States, over 95% of children with HIV contracted it from their mothers around the time of birth, a process known as vertical or mother-to-child transmission. The remaining cases in children and adolescents are largely linked to sexual activity, with rare instances involving sexual abuse. Advances in blood and blood product screening have virtually eliminated transmission through these means in the United States, Canada, and Western Europe in recent years.

Although precise figures on the number of HIV-positive women giving birth annually in the U.S. are elusive, the Centers for Disease Control and Prevention (CDC) estimated between 3,000 and 5,000 cases. Without antiretroviral therapy (ART), roughly 25% to 33% of these transmissions would occur to their infants, frequently during labor and delivery. The risk of transmission is elevated when mothers acquire HIV during pregnancy or breastfeeding, experience severe HIV-related illness, or have high viral loads. However, the transmission rate in the U.S. has sharply declined from approximately 25% in 1991 to less than or equal to 1% by 2019, attributed to widespread efforts in testing and treating HIV-positive pregnant women throughout their pregnancy and during delivery.

HIV can also be transmitted through breast milk. Approximately 12% to 14% of infants who are HIV-negative at birth will contract the virus if breastfed by an HIV-positive mother. While transmission most commonly occurs in the initial weeks or months of life, it can happen later. The likelihood of breastfeeding transmission increases if the mother has a high viral load, particularly if she acquired the infection while breastfeeding (CDC 2014).

2.1.10.2 Adolescents

For adolescents, HIV transmission mirrors that in adults, primarily occurring through unprotected sexual contact or the sharing of contaminated needles. All adolescents engaging in unprotected sex face a heightened risk of HIV infection. Similarly, those who share needles for injecting drugs are at increased risk (CDC 2014). In rare instances, HIV has been transmitted through contact with infected blood on broken skin, such as scrapes or open sores. Despite the potential presence of the virus in saliva, there are no documented cases of transmission through coughing, kissing, or biting.

2.1.11 HIV Prevention

2.1.11.1 Preventing Mother-to-Child Transmission

Modern preventative treatments for HIV-infected pregnant women are highly effective in minimizing transmission. Pregnant women diagnosed with HIV should commence oral antiretroviral therapy (ART). Ideally, ART should begin promptly upon diagnosis and when the woman is prepared to adhere to the prescribed regimen. Those already on ART prior to pregnancy should continue it throughout gestation. Women planning conception should also maintain their ART.

In addition to the mother's ART, the antiretroviral drug zidovudine (ZDV) is occasionally administered intravenously during labor and delivery. Subsequently, exposed newborns receive oral ZDV twice daily for 4 to 6 weeks post-birth; some high-risk infants may receive additional antiviral medications. This combined approach reduces mother-to-child transmission rates from 25% to 1% or less (Teeraananchai et al 2017). A pre-labor cesarean delivery may also lower the newborn's risk, especially for women whose infection is not well-controlled by ART. After delivery, ART is continued for all HIV-positive women.

Given the risk of HIV transmission via breastfeeding, decisions regarding infant feeding should be made in consultation with healthcare providers. In regions where risks of malnutrition and infection from unsafe water or formula are high, and safe, affordable infant formula is unavailable, the benefits of breastfeeding may outweigh the risk of HIV transmission. In such settings, HIV-positive mothers, under medical supervision, might continue breastfeeding for at least 12 months, followed by rapid weaning to solid food. Their infants are often provided ART throughout the breastfeeding period (Teeraananchai et al 2017). HIV-positive mothers should be advised against donating breast milk to milk banks and should not pre-chew food for infants.

2.1.11.2 Preventing Transmission from Infected Children

As a child's HIV status may be unknown, all educational and childcare facilities should implement standardized procedures for managing accidents (e.g., nosebleeds) and for cleaning and disinfecting blood-contaminated surfaces. During cleanup, personnel should avoid direct skin contact with blood. Latex gloves should be readily available, and hands must be washed after glove removal. Contaminated surfaces require cleaning and disinfection with a freshly prepared bleach solution (1 part household bleach to 10-100 parts water). These "universal precautions" are applicable to all children and all situations involving blood, regardless of known HIV status.

2.1.11.3 Preventing Transmission in Adolescents

HIV prevention strategies for adolescents are identical to those for adults. All adolescents should have access to HIV testing and education on transmission and prevention, including abstinence from high-risk behaviors (such as sharing needles) and practicing safer sex.

2.1.11.4 Pre-Exposure Prophylaxis (PrEP)

Taking antiretroviral medication before potential HIV exposure, known as pre-exposure prophylaxis (PrEP), can reduce infection risk. While most effective when taken daily, PrEP can be costly. It is primarily recommended for HIV-negative individuals at high risk, such as those with an HIV-positive sexual partner, men who have sex with men, and transgender individuals (Saag et al., 2021). Older adolescents at risk may also receive PrEP, though confidentiality and cost issues can be more complex than for adults. Individuals on PrEP must still employ other preventive measures, including consistent condom use and avoiding shared injection needles. Data on infants born to HIV-negative mothers using TDF/FTC PrEP during pregnancy are incomplete, but no adverse effects have been reported in children born to HIV-positive women treated with TDF/FTC (Nelson et al, 2022). The efficacy of PrEP for injection drug users is under investigation. Adolescents in the U.S. often face barriers to accessing sexually transmitted infection and HIV services due to concerns about confidentiality, which also hinders PrEP administration. Cost and insurance coverage complexities further complicate PrEP access for adolescents compared to adults. Despite these challenges, PrEP should be strongly considered for sexually active adolescents, particularly those with high-risk behaviors. A recent compendium of minor consent laws for STI and HIV services can guide clinicians (CDC, 2020). Long-acting injectable ARVs, such as cabotegravir, are also being studied to enhance PrEP adherence in high-risk populations (Nelson et al, 2022).

2.1.12 Clinical and Laboratory Monitoring of Pediatric HIV Infection

Laboratory monitoring of HIV in children presents unique challenges, particularly because normal ranges for CD4 T lymphocyte (CD4) cell counts and plasma HIV RNA concentrations (viral loads) vary significantly with age. Similarly, the CD4 and viral load values that predict disease progression risk also change as a child matures.

2.1.12.1 Initial Evaluation of Newly Diagnosed Children with HIV

Children recently diagnosed with HIV should undergo CD4 count and plasma viral load measurements. A comprehensive, age-appropriate medical history and physical examination are essential, with particular attention to growth and developmental assessment for signs of HIV-associated abnormalities. Testing for HIV-associated conditions should also be performed, including:

- Anemia, leukopenia, thrombocytopenia
- Hypoalbuminemia
- Nephropathy (via urinalysis)
- Renal insufficiency (via creatinine)
- Hyperglycemia
- Hepatic transaminitis

Baseline screening for coinfections and opportunistic infections (OIs) should include tests for:

- Tuberculosis (tuberculin skin test for children <2 years, interferon gamma release assay for children ≥2 years)
- Hepatitis B virus (HBV surface antibody, HBV surface antigen, and HBV core antibody tests)
- Hepatitis C virus (HCV nucleic acid for children <18 months, HCV antibody for children >18 months)
- Cytomegalovirus (CMV antibody tests for children >12 months)

Monitoring for OIs should align with guidelines based on the child's exposure history and clinical context. Children with HIV relocating from outside the U.S. may benefit from additional evaluations, such as for gastrointestinal parasites, lead levels, and thyroid function. Laboratory confirmation of HIV infection is necessary if documentation is incomplete. Genotypic resistance testing should be performed, even if ART is not immediately initiated. A complete antiretroviral (ARV) drug history, including any prior exposure for perinatal HIV prevention, must be obtained. HLA-B*5701 testing is recommended during initial laboratory screening to guide potential abacavir (ABC) initiation; if positive, an alternative ARV should be used. Before starting or modifying an ARV regimen, clinicians and multidisciplinary team members should assess potential adherence barriers and emphasize the importance of adherence with the patient and/or caregivers. For children not initiating ART immediately after diagnosis, CD4 count and plasma viral load should be monitored at least every 3 to 4 months.

2.1.12.2 Evaluation at ART Initiation

Upon initiating ART, a physical examination should be conducted, encompassing weight, height, and sexual maturity rating. Baseline laboratory tests for CD4 count and plasma viral load are necessary to monitor ART response (Ron et al., 2023). To establish a baseline for monitoring ART toxicity, a complete blood count, urinalysis, and serum chemistry panel (including electrolytes, creatinine, glucose, and hepatic transaminases) should be performed. Additionally, serum lipid levels (cholesterol and triglycerides) should be measured.

2.1.12.3 Clinical and Laboratory Monitoring After Starting or Changing an Antiretroviral Regimen

Children initiating ART or transitioning to a new regimen require monitoring for effectiveness, tolerability, adverse events (AEs), and medication adherence. Clinicians and multidisciplinary teams should schedule frequent in-person and/or telemedicine visits during the first few months to closely monitor patients. The initial weeks of ART can be challenging for children and caregivers, requiring schedule adjustments for consistent medication administration. Children may also experience medication AEs, necessitating support for both children and caregivers to distinguish temporary, tolerable effects from more serious or long-term issues requiring a clinical visit. It is crucial for providers to communicate supportively, nonjudgmentally, and in plain language to foster interactive reporting and productive dialogue, especially when adherence is inconsistent. Telemedicine and telehealth platforms are particularly beneficial for adolescents due to their technological access and habits. Additional check-ins via phone, email, text, or apps can support adherence and early detection of side effects (Hightow et al., 2015). Continuous patient and caregiver interactions offer opportunities for clinicians and the multidisciplinary team to provide support and discuss adherence. A systematic review of randomized controlled trials over the past decade, which utilized telemedicine as an intervention or assessed it in pediatric subspecialty care, found that telemedicine services for general and pediatric care are comparable to or better than in-person services (Shah et al., 2021). The use of telemedicine for remote HIV care is expanding and has demonstrated similar outcomes to in-person care. HIV-positive individuals on ART show comparable clinical responses, treatment adherence, quality-of-life scores, and psychological well-being whether treated via telemedicine or in person (Dandachi et al., OhL et al; 2019). When selecting clinical follow-up formats, it is vital to recognize the differences and similarities between in-person and telemedicine visits. Benefits of telemedicine include convenience for patients and caregivers, reduced travel, flexibility, and the ability to observe ART handling/swallowing and conduct directly observed therapy at home. However, telemedicine requires technological access and capacity, limits the provider's ability to conduct physical examinations and on-site lab testing (Okay et al 2021), and restricts periodic body weight measurements crucial for dose modification in rapidly growing infants and monitoring for excessive weight gain, a potential ARV AE. Cooperative children can be weighed and measured at home with simple instructions or during synchronous visits, or data can be obtained from recent pediatric or other specialty visits. Providers must also arrange and coordinate lab access and be familiar with state and local regulations for conducting, documenting, and billing telemedicine visits. While both in-person and telemedicine visits involve considerations of stigma, privacy, and confidentiality, these factors differ between healthcare and home/community settings. For example, a caregiver

who has not disclosed the child's HIV and ART status at home might prefer in-person clinic visits or specific times/alternative locations for telemedicine.

2.1.12.4 Within Two Weeks of Initiating Antiretroviral Therapy

Within two weeks of starting ART, children should undergo an evaluation, either in person, via telemedicine, or by telephone. During this assessment, clinicians should identify any clinical AEs and provide adherence support. Many clinicians arrange additional contacts (in person, telemedicine, telephone, email/text/apps) with children and caregivers to bolster adherence during the initial weeks of therapy (Shah et al 2021).

2.1.12.5 Two to Four Weeks After Initiating Antiretroviral Therapy

Most experts recommend laboratory testing at 2 to 4 weeks (but no later than 8 weeks) after ART initiation to assess virologic response and potential toxicities, though this recommendation is based on limited data. The specific chemistry tests required depend on the ARV regimen. Plasma viral load monitoring is crucial for assessing ART response, as a decline indicates adherence, appropriate dosing, and viral susceptibility. Some experts prefer measuring viral load at 2 weeks to ensure it is decreasing. A significant viral load reduction should be observed 4 to 8 weeks after ART initiation (Shah et al 2021).

2.1.12.6 Clinical and Laboratory Monitoring for Children Stable on Long-Term Antiretroviral Therapy

Following the initial ART initiation phase (1–3 months), clinicians should evaluate patient adherence and regimen effectiveness (measured by CD4 count and plasma viral load) every 3 to 4 months. Additionally, clinicians should review the patient's history of drug toxicities and assess for new AEs through physical examinations and relevant lab tests. If laboratory evidence of toxicity arises, more frequent testing is generally warranted until resolution, with specific management guided by toxicity degree and ARV regimen. A patient's baseline CD4 count influences the rate of CD4 improvement post-ART initiation; children with very low CD4 counts may take over a year to reach peak values after viral load suppression (Krogstad et al 2015). Studies critically evaluating monitoring frequency for both adults and children, particularly CD4 count and plasma viral load, support less frequent monitoring in stable patients with consistent virologic suppression for ≥1 year (Davis et al 2015). The Adult and Adolescent Antiretroviral Guidelines—Laboratory Testing currently advise plasma viral load testing every 6 months for individuals with both consistent virologic suppression for ≥2 years and CD4 counts consistently >300 cells/mm3. The Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV emphasizes the value of continuing viral load testing every 3 to 4 months for enhanced monitoring of adherence or disease progression in children and adolescents. Some experts monitor CD4 count less frequently (e.g., every 6–12 months) in adherent children and adolescents with CD4 counts well above the OI risk threshold and sustained virologic suppression and stable clinical status for over 2 years (Kosalaraksa et al 2017). Furthermore, some experts monitor viral load more frequently (with each injection) in adolescents receiving injectable cabotegravir and rilpivirine (Rakhmanina et al 2023).

2.1.12.7 Testing When Switching Antiretroviral Regimens

When a patient changes regimens to simplify ART, clinicians should obtain baseline laboratory test results relevant to the new regimen's toxicity profile. Follow-up should include a plasma viral load measurement at 4 weeks (and no later than 8 weeks) post-switch to confirm effectiveness. If the regimen is switched due to failure, resistance testing should be performed while the patient is still on the failing regimen. This maximizes the chance of identifying resistance mutations, as resistant strains may revert to wild type within weeks of stopping ARV drugs. Clinicians should consider phenotypic resistance testing, including co-receptor tropism testing, in addition to genotypic viral resistance testing for children who have experienced prolonged or repeated periods of viral non-suppression on multiple ARV regimens (Agwu et al 2016).

2.1.12.8 Pre-Exposure Prophylaxis (PrEP)

PrEP involves the use of ARV medications by HIV-negative individuals at high risk of infection (e.g., having an HIV-positive sex partner). Commonly, PrEP comprises a combination of tenofovir disoproxil fumarate/emtricitabine (TDF/FTC); less frequently, it is tenofovir alafenamide/emtricitabine (TAF/FTC), both offering high efficacy. PrEP does not negate the need for other HIV prevention methods, including correct condom use and avoiding high-risk behaviors like needle sharing. While data on infants born to HIV-negative mothers taking TDF/FTC PrEP during pregnancy are incomplete, no adverse effects have been reported in children born to HIV-positive women treated with TDF/FTC (Nelson et al, 2022). The efficacy of PrEP in reducing HIV risk among injection drug users is currently being investigated. Adolescents in the United States often face barriers to accessing sexually transmitted infection and HIV services due to concerns about confidentiality, which also impacts PrEP administration. Cost and potential lack of insurance reimbursement further complicate PrEP access for adolescents compared to adults. Despite these barriers, PrEP should be strongly considered for sexually active adolescents, especially those engaging in high-risk sexual behavior. A recent compilation of minor consent laws for STI and HIV services is available to assist clinicians (CDC, 2020). Long-acting injectable ARV medications, such as cabotegravir, are also being studied to improve PrEP effectiveness in high-risk populations with poor medication adherence (Nelson et al, 2022).

Conclusion

In summary, a thorough understanding of HIV in children, encompassing its unique epidemiology, varied clinical presentations, and the evolving therapeutic landscape, is essential. While significant advancements in preventing mother-to-child transmission (PMTCT) and antiretroviral therapy (ART) have markedly improved the prognosis for children with HIV, persistent challenges remain. These include ensuring early diagnosis, optimizing drug formulations for pediatric adherence, managing long-term ART toxicities, and addressing co-morbidities specific to this vulnerable group.

Moving forward, sustained global dedication to expanding PMTCT services, investing in novel therapeutic and diagnostic tools, and strengthening integrated healthcare systems are critical. Only through collaborative efforts focused on prevention, early intervention, and comprehensive, child-centered care can we continue to alleviate the burden of pediatric HIV and work toward

an HIV-free generation, ensuring optimal health and developmental outcomes for all children.

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