HIV Infection in Pediatric Population

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Abstract

Human Immunodeficiency Virus (HIV) infection causes higher mortality and morbidity in children. The important route of acquisition trails to the mother. It casts a bad impact on the health of the mother–child duo. With the active support of organisations like WHO, UNICEF and, more importantly, ongoing research in the field of HIV diagnosis and treatment, there has been lot of visible changes in the field which help to reduce transmission from mother to child, better early infant diagnosis, and effective treatment of the mother and the child. All these have been directed at the possible elimination of mother-to-child transmission of HIV.

Introduction

Human Immunodeficiency Virus (HIV) infection is a deadly infection that is taking a heavy toll on the human population. In a majority of cases, infection in the pediatric age group is the result of mother-to-child transmission. As of 2014, there were 2.6 million children under the 15 years age group out of 37 million persons living with HIV, and 88 percent of the affected children were from Sub-Saharan Africa. In 2014, it as recorded that 2.2 lakh children have got new HIV infection, and approximately 600 children fail victims to new infection

every day [1]. HIV infection has been seen to be on a rise in the developing countries like India. The other routes of infection are due to blood and blood-product transfusion and, rarely, as a result of sexual abuse and adolescent sexual contacts. This article attempts to recognize the patterns of HIV disease, diagnosis, treatment and the challenges in the management of HIV in children.

Disease Manifestations in Children

Most of the patients are recognized because of their mothers' HIV infection status during antenatal period. Sometimes, the children are recognized with manifestations of HIV infection primarily, and then investigations of the mother support the diagnosis. The children present with failure to thrive, hepatosplenomegaly, persistent or recurrent pneumonia, and recurrent diarrhea. They run high risk of dental caries, recurrent aphthous ulcers, parotid enlargement, dermatophytosis, agressive and resistant bacterial and fungal infections. They also exhibit features of opportunistic infections like pneumocystis jiroveci, cytomegalovirus (CMV) infections, lymphocytic interstitial pneumonitis, and invasive candidiasis. A higher incidence of neoplasia is spotted in children with HIV infection. B-cell lymphoproliferative diseases, including non-Hodgkin lymphoma, Burkitt lymphoma, and smooth muscle tumors, have also been identified. Motor delay, hypotonia, hypertonia, and/or pyramidal tract signs may indicate opportunistic infection of the central nervous system (CNS) or progressive HIV encephalopathy. Cardiac failure, nephropathy due to virus is rare feature of pediatric HIV infection. Indian studies indicate common clinical manifestations including fever >1 month duration, weight loss, severe protein-energy malnutrition (PEM), skin manifestations, hepatomegaly and tuberculosis [2-12].

Diagnosis of HIV in Children

The disease progression is rapid among babies acquiring infection perinatally and almost 50% death occurs by 2 years. It is very vital to differentiate babies infected with HIV from HIV exposed but uninfected ones. The diagnosis of babies born to HIV positive mothers includes early virological testing (HIV-DNA-PCR) polymerase chain reaction in Integrated counseling and training centre (ICTC) at 6 weeks of age or at the earliest opportunity thereafter [10, 14]. A confirmatory test using whole blood in an ART centre is needed in positive cases, however, ART needs to be started without waiting for results [14]. In case of those who are breast fed, definitive test needs to be done after 6 weeks of stopping breast feeding. If a baby born to an HIV-positive mother presents for first time in 6-18 months of age, a rapid antibody test is done. If rapid test comes negative and the baby has not received breast milk in the last 6 weeks, then HIV-DNA-PCR testing need not be done, however, the definitive diagnosis (rapid antibody test) is to be done after 18 months. If the rapid antibody test is positive, dried blood spot needs to be done for HIV-DNA-PCR. If DNA-PCR test is negative, the guidelines to be followed are similar to earlier one. If the DNA-PCR sample is positive, then the whole blood specimen is sent for DNA -PCR. It is evident that DNA-PCR is to be done after 6 weeks of last exposure (delivery or breast feeding) for confirmation. The US Panel in 2016 has clarified that recommended virologic testing at 1–2 months of age is preferably scheduled

2-4 weeks after stopping the antiretroviral (ARV) prophylaxis. In such situations, the test would be obtained at 6 weeks (in those receiving 4 weeks ARV prophylaxis) or at 2 months (in those with 6 weeks ARV prophylaxis) [14,15]. Every case should have rapid antibody test at 18 months for definite diagnosis. The positive patients should have their CD4 count (absolute and percentage count) done at baseline and every 6 months. The children should be monitored for clinical, immunological, and virological changes periodically.

The Feb 2016 guidelines details the updates on the use of NAT (nucleic acid amplification tests) and point-of care testing for early and easy detection [16].

Prevention of Mother-to-Child Transmission

The updated recommendations support the use of ART on every pregnant mother and during lactation, irrespective of their HIV clinical stage or CD4 counts, and this should be continued lifelong [17].

The breastfed infants should receive Nevirapine once daily from birth till 6 weeks. Those babies who are on replacement feed, shall receive Nevirapine once daily (or Zidovudine once or twice daily) till 4 to 6 weeks [14].

It is recommended that either the baby receives exclusive breast feeding and ARV prophylaxis or no breast feeding at all. In breast fed infants, they can introduce complimentary foods along with breast feeding upto 12 months. The chances of HIV transmission decreases from 35% at baseline (without any intervention and breast feeding) to <5% (with ARV prophylaxis and breast feeding).

Treatment of Pediatric HIV Infection

Initiation of ART

Based on data from the multi-national START and PENPACT1 trials, the Panel now recommends antiretroviral treatment (ART) for all HIV-infected children (includes adolescents), irrespective of clinical symptoms, CD4 T lymphocyte count or viral load [14, 18, 19]. Experts recommend Accelerated ART to reduce the time between diagnosis and initiation of ART. In cases of combined HIV and TB disease, TB treatment should be started first, followed by ART as early as possible within the first 8 weeks of treatment. HIV-positive TB patients with profound immunosuppression (e.g. CD4 counts less than 50 cells/mm3) should be started on ART within the first 2 weeks of TB treatment [13, 14].

What to start?

It is prudent to have good supportive care in the form of balanced nutrition, adequate micronutrients (vitamin A, D, and Zinc), vaccination and growth monitoring [20]. The recommended ART options are as follows:

The first line ART includes Abacavir (ABC) or Zidovudine (AZT) with Lamuvudine (3TC) and Lopinavir/ritonavir (LPV/r) for children less than 3 years of age. Older children should receive Abacavir with Lamuvidine and Efavirenz. The recent updates recommend the use of tenofovir disoproxil fumarate(TDF) for adolescents with Efavirenz (EFV) and Lamuvidine or Emticitabine (FTC). The alternative regimens included Nevirapine instead of Lopinavir or Efavirenz.

What ART to switch to?

Table 1. The following are recommendations for switching of ART drugs[13].

First Line Regimen	Second Line Regimen	Third Line Regimen
2 NRTIs with LPV/r	Less than 3 years: 2 NRTIs with RAL	DTG with 2 NRTIs DRV/r with 2 NRTIs DRV/r with DTG+1–2 NRTIs
	More than 3 years: 2 NRTIs with EFV or RAL	
2 NRTIs with EFV	2 NRTIs with ATV/ror LPV/r	

NRTIs: Nucleoside reverse transcriptase inhibitors, DRV/r =darunavir/ritonavir, RAL=raltegravir, ATV/r=atazanavir/ritonavir.

Prophylaxis and Management of Opportunistic Infections [13]

1) Co-trimoxazole prophylaxis is recommended for HIV-exposed infants between 4 and 6 weeks of age and should be continued until HIV infection has been excluded by an age-appropriate HIV test to establish final diagnosis after complete cessation of breastfeeding.
2) Co-trimoxazole prophylaxis is recommended for infants, children and adolescents with HIV, regardless of the clinical and immunological conditions.
3) In settings where malaria and/or severe bacterial infections are highly prevalent, co-trimoxazole prophylaxis should be continued until adulthood whether or not ART is being taken. In settings of low prevalence for both malaria and bacterial infections, co-trimoxazole prophylaxis may be discontinued for children of 5 years of age and older who are clinically stable and/or virologically suppressed on ART for at least 6 months and CD4 >350 cells/mm3.

ART toxicity

The toxic effects of drugs used in ART are depicted in the Table 2.

Table 2. Side effects of ART Drugs in Pediatric Population

Drugs	Side Effects
Zidovudine	Headache, asthenia, nausea, anemia, neutropenia, lactic acidosis, lipodystrophy. If Hb<8gm%, shift to Abacavir.
Abacavir	Safe, but occasional hypersensitivity reaction (HSR)
Lamuvidine	Low side effects
Lopinavir	Nausea, vomiting, hypertriglyceridemia, diarrhea
Tenofovir	
Emtricitabine	Low side effects
Dolutegravir	Insomnia, headache, hepatotoxicity
Nevirapine	Elevated transaminases, hepatotoxicity, Steven-Johnson syndrome (SJS)

Efavirenz	CNS(Insomnia, dizziness, vivid dreams), headaches, elevated transaminases, hepatotoxicity, SJS
Darunavir	Skin rash, nausea, diarrhea, SJS
Raltegravir	Headache, diarrhea, fever, elevated CPK.
Atazanavir	Indirect hyperbilirubinemia, 1st degree AV block, nephrolithiasis, dyslipidemia
Ritonavir	GI intolerance, taste perversion, dyslipidemia, hepatotoxicity, SJS. Coadministration even at low doses with antihistamines, antihypertensives, ergot, hypnotics result in severe adverse effects.

A study from Wadia hospital, Mumbai, reported 43 HIV positive children from the age group of 5 months to 14 years who were started on antiretroviral therapy (ART). 30% reported adverse effects related to the ART. 16% had hepatotoxicity, 12% had raised serum amylase without symptomatic pancreatitis, 12% had zidovudine (AZT) induced anemia, 9% had Nevirapine (NVP) induced rash [21]. The children on ART need frequent monitoring of LFT (liver function tests), complete hemogram to avert the serious side effects and maintaining compliance [19].

Conclusion

It may be observed that it is super critical in maintaining ART compliance, administering appropriate formulation, decrease dose burden, monitoring by recall, maintaining easy accessibility to drugs, counseling regarding testing, giving and interpretation of test results, psychological counseling of patients, parents/caregivers, and maintaining good level of nutrition, healthy lifestyle, exercise, vaccination appropriately to attain good level of acceptance and coverage. But it is possible now to eliminate mother-to-child transmission with drugs and appropriate practices.

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- *To promote research on human sexuality*
- *To impart training on 'Sexology' and strengthen the discipline of 'Sexual Medicine'*
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