

Acquired immunodeficiency syndrome – A pedodontist's perspective

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ABSTRACT

AIDS was believed to be associated with a certain group of people, later the belief changed when the disease start encroaching other set of people. As science evolved, the knowledge about transmission of the virus grew and the evidences for the maternal transmission of the virus were found. Among children, most cases of infection by HIV are transmitted vertically, i.e., from mother to child. As they have an immature immune system, which may cause the rapid and severe progression. Children who are vertically infected present considerable weight loss, delayed development, delayed dental eruption, fewer permanent teeth, prolonged retention of primary teeth and various number of dental anomalies.

The most important comeback by the science was by the establishment of antiretroviral protocols which has reduced the occurrence of oral changes. There been a decline in the rate of HIV-related oral manifestations following the introduction of HAART. Many studies evaluating the efficacy of HAART demonstrated positive results and better lifestyle of the infected children. It is clearly known fact that there are considerable regional variations in the oral manifestations of HIV infection, depending both on the populations studied and on the clinical expertise available, among other factors. This review article explains the manifestations, dental implications and the various treatment regimens to be followed in pediatric patients.

Key word: AIDS, pediatric dentistry, HIV, HAART, oral manifestations, dental caries

Introduction

Before 1983, it was believed that AIDS (acquired immunodeficiency syndrome) was restricted to a specific group of people. In the following year, the first cases were reported of the syndromes affecting children. [1] Among children, most cases of infection by HIV are transmitted vertically, i.e., from mother to child. The immune system of newborn children is immature and hence the progression of the disease is rapid and severe. [2]

Children who are vertically infected present considerable weight loss and delayed development. [3-7] They may also present the following changes: delayed

dental eruption, fewer permanent teeth, prolonged retention of primary teeth and a slightly larger number of dental anomalies. [8] The establishment of antiretroviral protocols has reduced the occurrence of oral changes. [9, 10] However, some authors have reported delayed development even with the use of antiretroviral drugs. [11]

The introduction of highly active antiretroviral therapy (HAART) in the mid-1990s was an important landmark with therapeutic effects and dramatic changes in the clinical prospects of HIV infection. The rate of HIV-related oral manifestations has declined following the introduction of

HAART. [12] A study was done in Ugandan HIV-infected children who were on various medications including HAART, results reported a prevalence of 68.6% dental caries, 40% gingivitis and 8.6% pseudomembranous candidiasis in them. [13] It is clearly known fact that there are considerable regional variations in the oral manifestations of HIV infection, which depends on the population sample studied and the clinical judgment and expertise available in that area.

This review article explains the Manifestations, Dental implications and the various treatment regimens to be followed.

Mode of Action

HIV is transmitted either across mucosal membranes by sexual contact, through haematogenous exposure to virally contaminated blood or blood products and from mother to fetus or neonate. [14]

After gaining entry to the host, virus infection involves binding the virion to the surface of a target cell, mediated by binding of the envelope gp120 to the CD4 surface protein found on most helper T cells. [15]

After binding to the cell surface the virus becomes internalized into the host cell where it, becomes uncoated. The viral RNA is then reverse transcribed into linear double-stranded viral DNA by the viral DNA polymerase and then transported to the nucleus, where it is first 'circularized' and then integrated into the host cell. [16]

The integrated viral DNA is transcribed into full-length RNA by the host cell RNA polymerase II. These RNA transcripts can either be packaged within virus particles, to serve as the genome of progeny virus, or they can serve as mRNA for the synthesis of viral gene products. [16]

The main process of clinical disease progression is the functional abnormalities and quantitative depletion of CD4 T lymphocytes which causes the profound immunosuppression characteristic of advanced HIV infection. [17]

Diagnosis of HIV

Clinical symptoms vary widely between infants, children and adolescents; most of which are asymptomatic at birth and do not have any abnormal findings. [18] Presumptive Diagnosis of Severe HIV diseases in infants by WHO is given in table 1.

Conventional screening tests like rapid test, ELISA will only detect the presence of maternal antibodies and hence the diagnosis of HIV infection in the infants who are exposed is difficult. Therefore such tests are useful in children > 18 months of age; and for children < 18 months it is necessary to do DNA-PCR testing which, uses dried blood spots (DBS) to detect viral DNA. [20]

In infants and children who are undergoing virological testing, the following assays (and respective specimen types) are recommended for use:

- HIV DNA on whole blood specimen or dried blood spots (DBS)
- HIV RNA on plasma or DBS
- Ultrasensitive p24 antigen (Up24 Ag) on plasma or DBS

All diagnostic testing done for HIV should be kept confidential and done only after getting the informed consent of the parent or guardian.

Oral Manifestations of HIV in children

One of the first classification of the oral manifestations associated with HIV-infection was based on etiological aspects

and the classification distinguishes between lesions caused by fungi, bacteria, viruses, neoplastic lesions, and other alterations by Pindborg in 1989. Another classification by

EC-Clearinghouse and WHO for oral manifestations of pediatric HIV disease is given in table 2.

Table 1: Presumptive Diagnosis of Severe HIV diseases in infants by WHO^[19]

<p>Clinical criteria for presumptive diagnosis of severe HIV disease in infants and children less than 18 months of age requiring ART in situations where virological testing is not available</p> <p>A presumptive diagnosis of severe HIV disease should be made if:</p> <ul style="list-style-type: none">• The infant is confirmed HIV antibody positive; and• Diagnosis of any AIDS-indicator condition(s) can be made; or• The infant is symptomatic with two or more of the following:<ul style="list-style-type: none">*Oral thrush*Severe pneumonia*Severe sepsis• Other factors that support the diagnosis of severe HIV disease in an HIV seropositive infant include:<ul style="list-style-type: none">*Recent HIV-related maternal death; or advanced HIV disease in the mother;*CD4+ < 20% <p>Confirmation of the diagnosis of HIV infection should be sought as soon as possible.</p>

Dental disease in HIV infection

HIV-infected children are more prone to dental caries, which affects both the deciduous and the permanent dentition, than healthy children. However, while the frequency of caries may be higher than in healthy controls, the DMFT and DMFT of children who are HIV-infected, is not always higher than that of children of same age group and geographic area. In some instances it probably reflects the differences in fluoride levels in local water supplies.^[5, 13, 22-24] In addition the caries experience of HIV-infected children appears to be largely similar to that of other chronic sick children of comparable age.^[13]

It has been however presumed that HIV-infected children may display slightly different pattern of caries progression to that of healthy children, which possibly is

related to HIV-associated conditions like xerostomia.^[25] A greater frequency of carious lesions in HIV-infected children might be attributed to an increased level of carbohydrate and sugar intake required to provide sufficient calories in these children who fail to thrive, and to the ingestion of sucrose-based medications, particularly the set of antibiotics and antifungals, but also antiretrovirals, which includes zidovudine.^[24, 26]

Moreover, poor social economic status and low use of fluoride might also contribute to an increased risk of dental caries in children with HIV disease.^[26] In Romania, HIV infected children showed delayed and accelerated eruption of permanent teeth and over-retention of primary teeth (affecting 25% of patients).^[22] The accelerated eruption pattern of

teeth may be related to previous dental and periodontal disease. [22] The etiology of delayed eruption of teeth is unknown, although the important co-factor could be,

poor general health status of some children, particularly when there is malnutrition. [22, 27]

Table 2: EC-Clearinghouse and WHO classification of oral manifestations of pediatric HIV disease [21]

Group 1 lesions commonly associated with pediatric HIV infection.	Group 2 lesions less commonly associated with pediatric HIV infection	Group 3 lesions strongly associated with HIV infection but rare in children
Candidosis Erythematous Pseudomembranous Angular cheilitis Herpes simplex virus infection Linear gingival erythema Parotid enlargement Recurrent aphthous ulcers Minor Major Herpetiform	Seborrheic dermatitis Bacterial infections of oral tissues Necrotizing (ulcerative) stomatitis Periodontal diseases Necrotizing (ulcerative) gingivitis Necrotizing (ulcerative) periodontitis Viral infections Cytomegalovirus Human papilloma virus Molluscum contagiosum Varicella-zoster virus Herpes zoster Varicella Xerostomia	Neoplasms Kaposi’s sarcoma Non-Hodgkin’s lymphoma Oral hairy leukoplakia Tuberculosis-related ulcers

Treatment

The use of multiple medications specially three ARV medications is the standard treatment for HIV infection in order to achieve the best possible suppression of viral load, increase CD4 count and improve clinical staging. [28] The preferred regime

when choosing a first-line drugs for infants and children is two nucleoside reverse transcriptase inhibitors (NRTIs) plus one non-nucleoside reverse transcriptase inhibitor (NNRTI). [19] Table:3 depicts the summary of preferred first line ARV regimen for infants and children.

Table 3: Summary of preferred first line ARV regimens for infants and children^[29]

Patient group	Standard first-line Regimen
Infants Infant or child <24 months not exposed to ARVs Infant or child <24 months exposed to NNRTI Infant or child <24 months with unknown ARV exposure	NVP + 2 NRTI LPV/r + 2 NRTI NVP + 2 NRTI
Children Children 24 months to 3 years Children >3 years	NVP + 2 NRTI NVP or EFV + 2 NRTI

NVP=Nevirapine, LPV=Lopinavir, NRTI=Nucleoside Reverse Transcriptase inhibitor, EFV=Efavirenz

For children more than 3 years of age with tuberculosis (TB), the preferred regimen is EFV + 2 NRTIs. For infants and children less than 3 years of age with TB, the preferred regimens are NVP + 2 NRTIs or a triple nucleoside regimen. For a child or adolescent with severe anemia (<7.5 g/dl) or severe neutropenia (<500 cells/mm³), the preferred regimen is NVP + 2 NRTIs (avoid AZT). For adolescents more than 12 years of age with hepatitis B, the preferred regimen is tenofovir (TDF) + emtricitabine (FTC) + NNRTI.^[29]

Clinical and laboratory monitoring

CD4 should be measured at the initial time of diagnosis of HIV infection, and every 6 months thereafter. VL determination is desirable, but not essential, prior to initiating ART. VL should be assessed to confirm clinical or immunological failure where possible, prior to switching a treatment regimen.^[29] Routine clinical and laboratory monitoring Baseline hemoglobin level (and white cell count, if available) should be determined at initiation of ART and then at week 8 after initiation of AZT-

containing regimens, or more frequently if symptoms indicate.^[29]

Conclusion

More than 2.1 million children have been living with AIDS who are below the age of 15. 1000 children are newly infected every day. The most important thing is the prevention strategies to be applied. Diagnosis is the next important point and what comes next in line is the treatment, which involves HAART and treating specific causes. With the new advances in HAART, the symptoms can be reduced a lot.

The majority of the HIV/AIDS-infected children have more than one or more oral lesions. Except for dental caries, the oral lesions were more frequently seen in children who were not on HAART. Some of the lesions were associated with discomfort during regular normal oral functions.^[30, 31] The complete medical management of children with HIV should include oral health care to ensure routine screening for oral lesions and timely intervention of the symptoms. The oral management should be given importance in children with HIV.

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