

# Early Diagnosis of Oral Manifestation in HIV Infected Pediatric Patients, A Review of Current Literature

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## Abstract

Acquired Immuno Deficiency Syndrome has been remained one of the most health issue concerns till recently. HIV infection can be transmitted through unprotected sexual intercourse with an infected partner, unprotected oral sex, injection or transfusion of contaminated blood or blood products, sharing unsterilized injection equipment that was previously used by an infected person and maternal-fetal transmission during pregnancy, at birth or through breastfeeding. Transmission of HIV from an infected patient to a health-care worker has been documented after parenteral or mucous membrane exposure to blood. Oral manifestations are one of the earliest clinical indicators of HIV infection which is independent of CD4 status has a prognostic value. By the way, screening of the AIDS associated manifestations in the oral cavity is a noninvasive and feasible approach, these oral lesions should be used to help diagnose, prevent and intervene in the progression of HIV infection to AIDS. This review includes studies that investigate the impact of HIV infection on personal life and importance of oral lesion in early diagnosis of HIV infection in children. Articles were identified through searches of PubMed MEDLINE from 1970 to 2015, using the MESH based key words.

## Introduction

According to World Health Organization (WHO), until the year 2000, the acquired immunodeficiency syndrome (AIDS) has been one of the most important causes of death among the children world-wide [1]. HIV infection can be transmitted through unprotected sexual intercourse with an infected partner, unprotected oral sex [2] injection or transfusion of contaminated blood or blood products, [3] sharing unsterilized injection equipment that was previously used by an infected person [4] and maternal-fetal transmission (during pregnancy, at birth or through breastfeeding) [5,6] Occupational HIV infections of healthcare or laboratory workers may occur, but this mode of infection is not frequent [7]. Transmission of HIV from an infected patient to a health-care worker has been documented after parenteral or mucous membrane exposure to blood. However, this risk is less than 1%, is limited to exposure to blood, and can be further minimized through the availability of more effective Antiretroviral Therapy [8].

Globally estimation show that 34 million people are living with the human immunodeficiency virus (HIV), including 3.3 million children under the age of 15 [9,10]. HIV infection by maternal transmission is increasing in the world due to the increase in infected women who are not receiving appropriate antiretroviral therapy. Prognosis of Pediatric HIV infection in children is poor because the newborn is asymptomatic at birth [11] and has an immature immune system. To improve health outcomes and help monitor the progression of HIV, early diagnosis and good oral health are very important [12]. Especially early diagnosis of prenatally exposed infants and children is of paramount importance because the intervals between infection, development of AIDS and death are compressed in pediatric patients [13].

Oral manifestations are one of the earliest clinical indicators of HIV infection which is independent of CD4 status has a prognostic value [14]. Along with a thorough medical/dental history, detection of oral lesions continues to be a low cost mechanism for diagnosing and tracking HIV [15]. Furthermore, is a noninvasive and feasible approach, these oral lesions should be used to help diagnose, prevent and intervene in the progression of HIV infection to AIDS [16]. These lesions, such as oral candidiasis (OC) which is the most common oral lesion and often the first clinical manifestation in children with HIV [12], can cause discomfort, dysfunction, and disability, which should be taken into account during the oral and overall management of HIV-infected patients [17]. Dental caries, Poor socioeconomic status, reduced immunological response, painful mouth, decreased salivary function and continuous use of medicines that have been formulated as syrups or sugared solutions are other characteristics of children with AIDS [18,19].

This review provides an update of pediatric oral HIV/AIDS issues in developing countries. The objective was to review the literature on pediatric HIV with a focus on:

- Prevalence of oral lesions
- Oral Manifestations in pediatric HIV infection as a predictor
- Diagnostic criteria in pediatric
- Dental status in pediatric HIV infection: dental caries
- Quality of life
- Oral health protocol for children living with HIV
- Impact of anti-viral treatment on oral health (HAART)

## Methods and Material

This review includes studies that investigate the impact of HIV infection on personal life and importance of oral lesion in early diagnosis of HIV infection in children. Articles were identified through searches of PubMed MEDLINE from 1970 to 2015, using the following search terms HIV/AIDS-infected children,” “oral manifestations,” “pediatrics,” “HIV-infected children,” “oral health,” and “Oral lesions” .

## Prevalence of oral lesions

The first studies involving children showed the prevalence of oral manifestations of HIV infection in children in the USA [20]. Subsequently, several studies have examined the relationship between oral manifestations and progression of HIV infection in children [16] which conclude that Orofacial lesions commonly associated with HIV infection in children include oral candidiasis, linear gingival erythema, Herpes Simplex infection, angular cheilitis, parotid enlargement and recurrent oral ulceration. In developing world, the prevalence of these lesions may vary from country to country [21] but the recent workshop on HIV and oral lesions [22] concluded that oral candidiasis is the most common lesion in children. This lesion is strongly associated with the progression of HIV disease. A high prevalence of concomitant dental disease, especially periodontal disease has been reported in HIV positive children [23].

Numerous numbers of the confounders have made comparisons among these studies impossible—for example, children in different stages of disease, variable CD4 counts, lack of calibration of examiners, no standardized criteria for diagnosis, and HAART vs. no HAART or a combination of both. It is obvious that authors need to include much more information in articles so that significant comparisons, courses, and combination of data, using standardized diagnostic criteria may be possible [24].

## Oral Manifestations in Pediatric HIV Infection as a Predictor

A number of recently published studies recruiting children [25] have reported significant correlations between the presence of oral lesions and disease progression or a suppressed immune response (CD4 cell count < 200 cells/mm<sup>3</sup>) [24].

HIV-associated orofacial lesions in children is classified into three groups based on clinical experience and clinical studies limited to the pediatric age group and on the frequency of association of these lesions with HIV infection [13].

1. Lesions commonly associated with pediatric HIV infection [12, 26] such as oral candidiasis, herpes simplex virus, linear gingival erythema (LGE), parotid enlargement, and recurrent aphthous ulcers [12,27].
2. Lesions less commonly associated with pediatric HIV infection [12,26] such as necrotizing stomatitis, necrotizing periodontal disease, human papillomavirus (HPV), xerostomia [12,27]
3. Lesions strongly associated with HIV infection but rare in children such as Kaposi sarcomas and oral hairy leukoplakia [12,26] Kaposi’s sarcoma (KS), non-Hodgkin’s lymphoma (NHL), and oral hairy leukoplakia (OHL) [12,27].

## Diagnostic Criteria in Pediatric Patients

Oral candidiasis is the most common oral lesion in children infected with HIV which occurs in up to 72% of all cases of pediatric HIV infection [28] and is the first clinically observable manifestation of the disease [13]. Furthermore, candidiasis may have prognostic value in the development of AIDS in infected children [28]. Three manifestations of oral candidiasis have been documented in HIV-infected pediatric patients: Pseudomembranous candidiasis, Erythematous candidiasis and Angular cheilitis. World rates of oral candidiasis have been described as varying from 22.5 to 83.3%. Among children in the developed and developing countries. PC infection seems to be the most prevalent form in children followed by EC, and then angular cheilitis as the third most prevalent. However, EC has been occasionally reported to be more prevalent than PC [29].

## Dental Status in Pediatric HIV Infection: Dental Caries

While there may not be a direct link between HIV and caries development, there is a symbiotic association for risk and disease development [30]. many children with HIV infection experience xerostomia [31] and intake of the high sugar content a side effect of antiretroviral therapy which exacerbates their caries risk [32] further more In HIV infection, there is a dysregulation of calcium homeostasis, which results in excessive increases of intracellular calcium induced by HIV viral proteins [33,34]. Compared with adults, the biologic mechanisms of caries development differ in young children with newly erupted teeth, continuous vertical and horizontal bacteria exposure, fragile tooth enamel, and immature immune systems. In young children with HIV, transition from infection to AIDS to death is compressed compared with adults [35]. It was concluded that children with prenatally acquired HIV, especially with advanced disease, are at greater risk for caries than their siblings. (Dental con)Untreated caries in primary dentition has been obviously associated with pain, speech impediment, and difficulty eating, and being underweight. Therefore, early detection and treatment are of particular importance to increase the quality of life [30].

## Quality of Life

Children with more severe AIDS manifestations complained of poorer status of oral symptoms, functional limitations, emotional and social well-being related to their oral health. Recognizing the factors that are associated with poorer OHR-Qu in children with AIDS may contribute to the planning of dental services for this population [36].

At present, 4 measures have been designed to address the oral health-related quality of life in children [37]: The Child Perception Questionnaire 11-14, the Michigan Oral Health-Related Quality of Life Scale, the child version of the Oral Impacts on Daily Performance Index (i.e., the Child Oral Impacts on Daily Performance Index), and the Child Oral Impact Profile. Among HIV+ adults, only 3 studies [38] reported on patients who presented with oral lesions, all of which cited adverse/negative oral health-related quality-of-life impacts in HIV+ cohorts. Unfortunately, no studies have investigated the impact of oral lesions associated with HIV infection on oral health-related quality of life in children. However, the existence of child-specific quality-of-life measures presents an opportunity for researchers to apply these indices to pediatric HIV+ cohorts so that current management protocols can be adjusted to take into account patients' subjective needs [24].

Studies have found that relationships between biological/clinical variables and health related quality of life are not direct but mediated by a variety of personal, social, and environmental variables as well as by the child's development, which influence comprehension about the relationship among health, illness, and quality of life [24].

## Oral Health Protocol for Children Living with HIV

While a comprehensive care program for both caregiver and child is optimal, offering such a program relies upon access to care. An oral health protocol starting at infancy should be organized for HIV-infected children like an infant oral care visit (IOCV) which is a simple and effective protocol that do not need to be conducted in a dental clinic nor by a dentist for use with HIV-infected children, this includes 6 simple steps: a caries risk assessment, proper positioning of the child in a knee-to-knee posture to actively engage the child's caregiver, a toothbrush prophylaxis, a clinical dental exam, fluoride varnish application, and the establishment of self-management behavior goals utilizing motivational interviewing techniques [38].

Positioning of the child is vital to ensuring that a child is comfortable and cooperative as well as to visualizing the child's oral cavity to the examiner. Generally, infants and toddlers ages 6 months to 3 years, or up to age 5 for children with special needs, should be placed in a knee-to-knee position. The child's head lies in the examiner's lap with the child's legs wrapped around the caregiver's waist. Then the caregiver can hold the child's hands and stabilize the child's legs and body with her arms. Children older than 3 years can sit forward on their caregiver's lap or sit alone in a chair. In this position, the examiner can now retract the child's lips and cheek to do a tooth brush prophylaxis while demonstrating the proper tooth-brushing technique to the caregiver. The spongy handle of an age-appropriate sized toothbrush can be used to prop open the child's mouth. This "Tell-Show-Do" encounter provides an opportunity to encourage the caregiver to brush her own and her child's teeth at least twice a day, especially before bed time, with fluoridated toothpaste. Children under the age of 2 should only use a smear of fluoridated toothpaste, while children over 2 should use a small, pea-sized dab.

During the clinical examination, the examiner counts the child's teeth aloud, using the toothbrush handle as a mouth prop if necessary with the following information documented: visible plaque and location; chalky white spots; brown spots that indicate decay; tooth defects; deep pits/fissures; tooth anomalies; oral and other tooth abnormalities; missing and decayed teeth; existing restorations; untreated caries, and/or defective restorations; presence and location of gingivitis; presence and location of soft tissue abnormalities; occlusal status; malocclusion or developmental pathology; and, indications of trauma.

While the IOCV emphasizes screening children for caries, it also affords health care providers an opportunity to address oral hygiene practices and techniques, dietary counseling, and oral health behaviors with the child's caregiver. These simple practices are important for the oral health of children with HIV and can prevent their otherwise increased risk for caries and other oral health disease [30].

## Impact of Anti-Viral Treatment on Oral Health (HAART)

The introduction of highly active antiretroviral therapy (HAART) in the mid-1990s was an important landmark with therapeutic effects and surprising changes in the clinical aspects of HIV infection [40]. Overall, this type of treatment is effective in reducing the occurrence of oral candidiasis, presumably in part by the inhibition of *Candida proteases*. The impact of HAART on decreasing the prevalence of hairy leukoplakia has not been proved but increasing evidence of an increase in prevalence of oral warts in patient being treated by protease inhibitors are accessible [41].

## Conclusion

Oral manifestations are common in HIV infection children which may have prognostic value in HIV disease progression [13]. While HIV-infected children are at higher risk for developing oral health diseases so they need careful dental examination of all soft and hard tissues. In the absence of more conclusive, consistent data as to the increased risk for oral disease in HIV-patients, and in consideration of the disproportionate burden of disease on underserved populations, an oral health protocol that is based on HIV status with assumptions of increased disease risk should be used starting in infancy [42].

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