ABSTRACT
Pediatric immune systems and developing organ systems are more susceptible to HIV infection and thus degrade more rapidly than adults. Oral lesions are often among the first manifestations of HIV infection due to the number of microorganisms present in the mouth which thrive during immunosuppression. In particular, the immunosuppression caused by HIV infection can lead to opportunistic fungal and bacterial infections, a propensity toward malignancy, lymphoid interstitial pneumonitis and thrombocytopenia. Half of all infected infants become symptomatic in the first year of life. Children with T-cell deficiencies tend to have more oral mucosal candidiasis, HSV and recurrent aphthous ulcerations.

Keywords: HIV infection, Children, Oral manifestations.


Source of support: Nil

Conflict of interest: None declared

INTRODUCTION
HIV infection, considered to be pandemic by World Health Organization (WHO), has killed more than 25 million people till the year 2006 and infects about 0.6% of world’s population.1 Immune defects in children have been shown to have profound effects on oral tissues. [Joint United Nations Program on HIV/AIDS (UNAIDS), 2002, 2005]. Oral manifestations of HIV are one of the earliest indicators of progression of the HIV infection and can predict the progression of the infection.2-4 Knowledge and awareness of the signs and symptoms, of oral lesions that may be indicative of the patients’ HIV status will assist in instituting the appropriate careful steps of management at an early stage for better prognosis. Due to underdeveloped immune system, disease progression in pediatric population is accelerated and severe. Most infants born with HIV infection are asymptomatic at birth, however time between birth and initial symptoms and signs varies considerably.3,5,6 The median age of pediatric patients at the time of an AIDS diagnosis is 12 months with oral manifestations often the first sign of infection in approximately half of all infected children. Majority of pediatric HIV infections are the result of mother-to-child transmission (MTCT). The increasing proportion of infected children achieving adulthood highlights the need for multidisciplinary approach to management and thus facilitates transition to adult care while maintaining strategies specific for mother to child acquired infections.7 Oral lesions commonly associated with pediatric HIV infection include oral candidiasis, herpes simplex virus infection, linear gingival erythema and recurrent aphthous ulcers. Recognition of these early oral signs during routine examinations and in surgical procedures is important for diagnosis and treatment, which allows for early intervention, clinical staging of the infection leading to better prognosis, reduced morbidity and improved quality of life in this population. The early diagnosis of these lesions will help in assessing disease progression where limited resources hamper disease specific interventions.

PATHOGENESIS
The acquired immunodeficiency syndrome (AIDS) was first observed in 1981 in young male homosexuals in the United States of America (USA); though there are evidences that sporadic cases may have been in existence before then.8,9 HIV infection in children was first described in 1983.10 HIV disease in infants and children, as in adults, is a progressive disease with a clinical spectrum ranging from asymptomatic infection to profound and eventual fatal immunosuppression. The hallmark of immunodeficiency caused by HIV infection is the depletion of cells of the immune system: CD4+ T lymphocytes, macrophages, monocytes and dendritic cells that express the CD4 receptors. The gradual decrease in the number of cells of the immune system and the functional decline of these cells lead to the breakdown of the immune system, exposing infected individuals to a wide variety of viral, bacterial, fungal and parasitic infections as well as the development of malignancies that result in full blown AIDS.11

TRANSMISSION
The epidemic in children has risen globally due to the worldwide increase in HIV prevalence in women of childbearing age. Most HIV infections in children are passed from mother to child (vertical transmission). It is estimated that without any kind of intervention risk of MTCT is 15 to 30% in non breastfeeding children and 20 to 45% in those practicing prolonged breastfeeding, while mortality is seen in 50% of HIV infected children.12,13 Other causes of pediatric HIV include blood transfusion, illicit drug use, sexual transmission, etc. Effective prevention of mother-to-child transmission involves simultaneous support for several strategies that work synergistically to reduce the odds that an infant will become infected as a result of exposure to the mother’s virus. Through the reduction in overall HIV among reproductive-age women and men, the reduction of unwanted pregnancies among HIV-positive...
women, the provision of antiretroviral drugs to reduce the chance of infection during pregnancy and delivery and appropriate treatment, care and support to mothers living with HIV (including infant feeding), programs are able to reduce the chance that infants will become infected. In ideal conditions, the provision of antiretroviral prophylaxis and replacement feeding can reduce transmission from an estimated 30 to 35% with no intervention to around 1 to 2%. Most countries have not yet reached all pregnant women with these services, let alone significantly reduced HIV prevalence among reproductive-age individuals or unwanted pregnancies among HIV-positive women.14

CLASSIFICATION OF ORAL MANIFESTATIONS OF HIV IN CHILDREN

EC-Clearinghouse and WHO classification of oral manifestations of pediatric human immunodeficiency virus (HIV) disease.15,16

- Group 1 lesions commonly associated with pediatric HIV infection:
  - Candidiasis
  - Erythematous
  - Pseudomembranous
  - Angular cheilitis
  - Herpes simplex virus infection
  - Linear gingival erythema
  - Parotid enlargement
  - Recurrent aphthous ulcers minor
  - Major
  - Herpetiform.
- Group 2 lesions less commonly associated with pediatric HIV infection:
  - 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.
- Group 3 lesions strongly associated with HIV infection but rare in children:
  - Neoplasms
  - Kapoši’s sarcoma
  - Non-Hodgkin’s lymphoma
  - Oral hairy leukoplakia
  - Tuberculosis-related ulcers.

ORAL MANIFESTATIONS COMMONLY ASSOCIATED WITH PEDIATRIC POPULATION

Oral Candidiasis

Most common oral lesion in HIV+ children and is associated with falling CD4+ T-lymphocytes count and rising HIV viral load.17-21 Candidiasis is often the first clinically observable manifestation of HIV infection, with up to 72% of these children developing the disease.18,22 Candidiasis has been reported as the commonest oral lesion in several studies and has been used as a clinical marker of the disease as the frequency of oral candidiasis usually correlates with a falling CD4+ T-lymphocyte count and a rising HIV viral load. Pseudomembranous candidiasis remains the commonest variant, followed by erythematous candidiasis and angular cheilitis. Pseudomembranous candidiasis manifests as non-adherent plaques covering the oral mucosa removal of which leaves an erythematous mucosal surface, which occasionally bleeds. It generally occurs on the buccal mucosa, mucobuccal folds, dorsolateral tongue and the oropharynx, but may occur throughout the oropharyngeal region.17,22,23 Erythematous candidiasis (Atrophic candidiasis) presents as diffuse to patchy redness of varying intensity present frequently on palate and dorsum of tongue. Multiple flat red patches of varying intensity occur. It sometimes presents as pinpoint to macular erythema, which mimics a bleeding diathesis or submucosal trauma. Nonadherent filmy white to creamy plaques may be seen concurrently with this lesion. When the tongue is involved, there is selective loss of filiform papillae, resulting in a red, smooth to beaded mucosal surface. Angular cheilitis is seen as linear red fissures radiating from the corner of the mouth.17,23 They are typically bilateral, and multiple red papules may be found when the adjacent perioral skin is involved. It commonly occurs in conjunction with either of the other intraoral forms.

DEFINITIVE DIAGNOSIS OF ORAL CANDIDIASIS

Definitive diagnosis of oral candidiasis is made from exfoliative cytological smears using PAS stain or potassium hydroxide or Gomori’s methenamine silver stain. Detection of fungal hyphae and/or pseudohyphae is necessary for microscopic diagnosis. Biopsy of the oral lesion can also be carried out. Fungal cultures are not usually necessary but are helpful in species identification when lesions are refractory to antifungal therapy.22,23 Candidiasis can either be treated by application of proper topical antifungal agents like nystatin or clotrimazole or systemically by ketoconazole, fluconazole and itraconazole.22,24

HERPES SIMPLEX VIRUS INFECTIONS

It is the most common mucocutaneous disease observed in children infected by HIV.25 Majority of the lesions are caused by HSV-1 presenting as diffuse mucosal erythema,
persistent ulcers. Most herpetic lesions in HIV infected children are reported to be self-limiting. Antiviral therapy is recommended in moderately to severely immunocompromised children and in cases with frequent recurrences. Oral acyclovir is most frequently used.

**LINEAR GINGIVAL ERYTHEMA**

Linear gingival erythema (LGE) is the most common form of oral manifestations found in the pediatric population is a persistent ulcers. Primary herpetic gingivostomatitis is a systemic viral infection which presents with sudden onset of fever, swollen and tender cervical lymph nodes, irritability and malaise. Classically, there is widespread mucosal erythema, vesicles and painful coalescing ulcers. The gingiva, palate, dorsum of tongue, lip and the perioral skin are the commonest sites. Excessive drooling of saliva and pharyngitis often accompanies this infection. Resolution usually occurs within 14 days but the disease may linger for several more weeks in immunocompromised children. Recurrent herpes simplex virus infection occurs when the herpes simplex virus is reactivated within the trigeminal ganglion by factors such as excessive exposure to sunlight, physical injury, febrile systemic illness, immunosuppression, emotional stress and hormonal alterations. It is characterized by sudden onset of focal erythema, clustered vesicles and painful coalescing ulcers. The ulcers usually involve the vermilion border of the lip, perioral skin, and nasal mucosa and may form crusts extraorally. Intraorally, the gingivae and palatal mucosa are usually involved. Lesions typically heal within 7 to 10 days. In immune suppressed children, lesions may be multifocal in distribution and occur on nonkeratinized mucosa. The infection may run a chronic course, lasting 4 to 6 weeks and producing large crater form lesions with irregular serpentine to scalloped margins. Extraoral vesicular to crusted lesions that bleed on manipulation are characteristic. Deep persistent lesions may result in significant scarring. Cytomegalovirus coinfection has been observed in these persistent ulcers. Most herpetic lesions in HIV infected children are reported to be self-limiting. Antiviral therapy is recommended in moderately to severely immunocompromised children and in cases with frequent recurrences. Oral acyclovir is most frequently used.

**MAJOR SALIVARY GLAND ENLARGEMENT**

Children affected by HIV may show xerostomia or major salivary gland enlargement due to lymphocyte mediated salivary gland disease. Parotid and submandibular glands are generally affected. It is also called diffuse infiltrative lymphocytosis syndrome or Sjogren syndrome-like disease. Major salivary gland enlargement is more common in children than in adults with HIV infection and the prevalence in HIV infected children varies widely in different studies with up to 58% of them being affected. The etiology of major salivary gland enlargement is unknown but infection with EBV or HIV or the interaction between these two viruses is suspected to be responsible. As the condition is benign it is generally left untreated. But in case of secondary infection antibiotics like clindamycin can be prescribed.

**RECURRENT APHTHOUS ULCERS**

The prevalence of recurrent aphthous ulcer (RAU) in HIV infected children ranges from 0 to 7% similar to HIV infected adults. In general RAU tend to recur more frequently in the HIV infected child; and with immunosuppression, major aphthous ulcers are also more likely to develop. It occurs as major, minor and herpetiform RAU. Minor RAU are shallow, round ulcers, 5 mm in diameter which are self-limiting and heal without scarring. While major RAU are larger (1-2 cm), fewer and heal with scar formation. They are painful and may interfere with mastication and swallowing. They tend to occur on the soft palate, buccal mucosa, tonsillar area, and tongue. They have well delineated to irregular borders and depressed bases and are often covered by a thick, tenacious, fibrinous exudate. The herpetiform RAU occur in crops; each ulcer measuring 1 to 2 mm diameter. They tend to occur in the soft palate, buccal mucosa, tonsillar area and tongue. Diagnosis is usually clinical, based on the size, site, appearance and duration of the ulcers. A definitive criterion for all three types of RAU is the response to treatment with steroid agents. Tissue cultures for viral, fungal and mycobacterial organisms and incisional biopsy are necessary for persistent lesions to rule out other causes of ulcers. All three respond to steroid therapy; topical route being the first line of treatment. Steroids administered are fluocinonide, clobetasol propionate and dexamethasone elixir.

**CONCLUSION**

Oral lesions are frequent and profuse in HIV infected children. Hence, a thorough understanding about the various oral manifestations found in the pediatric population is a necessary prerequisite for a responsible pedodontist. Primary
oral healthcare regimen for an infected child should include
an extensive oral examination time and again to ensure early
detection and intervention of the lesions found in the oral
cavity. Even though these steps are not a cure for HIV
infection; it can definitely provide a better quality of life to
the child.

REFERENCES

1. Ponnam SR, Srivastava G, Theruru K. Oral manifestations of
human immunodeficiency virus in children: an institutional study
at highly active antiretroviral centre in India. Journal of Oral
2. Elderidge K, Gallagher JE. Dental caries prevalence and dental
4. Sullivan. Prevention of mother to child transmission of HIV:
5. Magalhaes MG, Bueno DF, Serra E, Gonclaves R. Oral
2001;25(2):103-106.
Greenspan JS. Oral manifestations and dental status in paediatric
7. Giaquinto C, Penazzato M, Rosso R, Bernardi S, Rampon O,
infection working group. Italian consensus statement on 
8. Scully C. The HIV global pandemic: the development and
10. Agbelusi GA, Wright AA. Oral lesions as Indicators of HIV
infection among routin patients in Lagos, Nigeria. Oral
11. De Cock KM, Fowler MG, Mercier E, de Vincenzi I, Saba J,
Hoff E, et al. Prevention of mother-to-child HIV transmission
in resource-poor countries: translating research into policy and
12. Newell ML, Coovadia H, Cortina Borja M, Rollins N,
Gaillard P, Dabis F. Mortality of infected and uninfected infants
born to HIV-infected mothers in Africa: a pooled analysis.
13. Ketchen L, Berkowitz RJ, McIlveen L, Forrester D, Rakusan T.
Oral findings in HIV-seropositive children. Pediatr Dent
Dorenbaum A. Collaborative workgroup on oral manifestations
of paediatric HIV infection. Oral Aids Centre, University of
California, San Francisco. Classification, diagnostic criteria, and
treatment recommendations for orofacial manifestations in HIV
15. Oral manifestations in human immunodeficiency virus infected
children in highly active antiretroviral therapy era. Raquel dos
Pinheiro S, Franc TT, Ribeiro CMB, Leao JC, de Souza IPR,
16. Patton LL, Phelan JA, Ramos-Gomez FJ, Nittayananta W,
Shiboski CH, Mbuguye TL. Prevalence and classification of
98-109.
17. Barasch A, Salford MM, Catalantto FA, Fine DH, Katz RV.
Oral soft tissue manifestations in HIV-positive vs HIV-negative
children from an inner city population; a two-year observational
18. Fonseca R, Cardoso AS, Pomarico I. Frequency of oral
manifestation in children infected with human immunodeficiency
19. Kline MW. Oral manifestations of pediatric human immuno-
deficiency virus infection: a review of the literature. Pediatr
20. Flaitz CM, Hicks MJ. Oral candidiasis in children with immune
suppression: clinical appearance and therapeutic considerations.
21. Flaitz CM, Hicks MJ. Oral manifestations in paediatric HIV
infection. In: Shearer WT, Hanson IC, editors. Medical
Management of AIDS in Children. USA: Elsevier Science
2003;248-269.
22. Abrams EJ. Opportunistic infections and other clinical
classification system for human immunodeficiency virus
infection in children less than 13 years of age. MMWR 1994;43:
1-10.
24. William DM. In: EC-clearing house on oral problems related to
HIV infection of the immunodeficiency virus: classification and
diagnostic criteria for oral lesions in HIV infection. J Oral Pathol
25. Flaitz C, Nichols CM, Hicks MJ. Herpes viridea-associated
persistent mucocutaneous ulcers in acquired immunodeficiency
AIDS-related linear gingival erythema: a form erythematous of
27. Pinto A, De Rossi SS. Salivary gland disease in pediatric HIV

ABOUT THE AUTHORS

Priya Nagar (Corresponding Author)
Reader, Department of Pedodontics and Preventive Dentistry
Krishnadevaraya College of Dental Sciences and Hospital
Bengaluru, Karnataka, India, Phone: 0804164213, e-mail:
dr_priya_nagar@yahoo.com

Madhumita Naithani
Postgraduate Student, Department of Pedodontics and Preventive
Dentistry, Krishnadevaraya College of Dental Sciences and Hospital
Bengaluru, Karnataka, India

Dhanu Ganesh Rao
Professor and Head, Department of Pedodontics and Preventive
Dentistry, Krishnadevaraya College of Dental Sciences and Hospital
Bengaluru, Karnataka, India

Rashmi Jayanna
Professor, Department of Pedodontics and Preventive Dentistry
Krishnadevaraya College of Dental Sciences and Hospital, Bengaluru
Karnataka, India