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Oral manifestations of HIV infected children undergoing highly active antiretroviral therapy

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ABSTRACT

Oral manifestations in paediatric HIV infection are diverse and show differences in clinical presentation and severity from that of adults. Very little data exist for oral lesions in paediatric population in India. We aimed to evaluate the oral manifestations of Paediatric HIV seropositive patients undergoing highly active antiretroviral therapy (HAART). The cross sectional study was conducted on forty four HIV positive children in the age group of 8–14 years undergoing HAART at NGO centres in Salem district were included in the study. Children were examined for oral lesions and diagnosed in accordance with European council Clearinghouse-World Health Organization. Patients were classified with respect to their immune status based on CD4 count. The common oral manifestations associated with HIV were found to be reduced with the introduction of HAART.

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1. Introduction

The global estimate of children living with HIV infection in 2009 amounts to 2.5 million, of which India has an estimated 220,000 children. It is estimated that 55,000–60,000 children were born every year to mothers who are HIV positive. These newborns whose mothers did not take any treatment have an estimated 30% chance of becoming infected during the mother's pregnancy, labour or through breastfeeding after six months.[1] The HIV transmission in children is predominantly vertical and through blood transfusion. In India the main mode of HIV transmission in children is through the vertical route. The vertical transmission includes: transplacentally, during pregnancy, during delivery or postnatally during breastfeeding.[2]Though the disease process in paediatric HIV infection is similar to adults, certain lesions are typical in the paediatric population.[3] Oral manifestations are useful in monitoring HIV disease progression.[4]

The introduction of antiretroviral therapy (ART), especially the combination therapy, which is a highly active antiretroviral therapy (HAART), has led to dramatic reduction in HIV morbidity and mortality in developed countries. Protease inhibitors of HIV-1 introduced in the ART against HIV in the middle of 90's and their later combination with reverse transcriptase inhibitors established the highly active antiretroviral treatment (HAART). Although HAART does not cure HIV infection, the decrease in the viral load and the improvement in immunological status brought about by the use of these drugs have changed HIV/AIDS from a "virtual death sentence" to a "chronic manageable disease".[5]The purpose of this study was to evaluate the oral

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Table 1 – EC-Clearinghouse and the World Health Organization classification of oral manifestations of paediatric HIV disease (1993).

Group 1 lesions commonly associated with paediatric HIV infection	Group 2 lesions less commonly associated with paediatric HIV infection	Group 3 lesions strongly associated with paediatric HIV infection
Candidosis (Erythematous ,Pseudomembranous, Angular chelitis)	Seborrhoeic dermatitis	Kaposi's sarcoma Non Hodgkin's lymphoma
Herpes simplex viral infection	Necrotizing ulcerative stomatitis	Oral hairy leukoplakia
Linear gingival erythema	Necrotizing ulcerative gingivitis	Tuberculosis – related ulcers
Parotid enlargement	Necrotizing ulcerative periodontitis	
Recurrent aphthous ulcers	Viral infections (CMV, HPV, Varicella zoster)	
	Xerostomia	

manifestations in paediatric HIV seropositive children undergoing highly active antiretroviral therapy (HAART).

2. Materials and methods

A cross sectional study includes, 44 HIV seropositive children between the age group of 8 and 14 years undergoing HAART for at least 6 months at NGO centres in Salem district. Informed consent as approved by the institutional review board was obtained from NGO Centre authority for clinical examination and photographic documentation. All the clinical details were noted in preformatted case sheet. The oral examination was carried out by a qualified dental surgeon specialized in Paediatric dentistry based on the EC-Clearinghouse diagnostic criteria for paediatric patients (Table 1).[6]

The information recorded for each patient includes: age, gender, previous antiretroviral therapy, scheme of current antiretroviral therapy and CD4+ lymphocyte cell count/ml. The CD4 cell count/ml in peripheral blood recorded within 2 months before the oral examination served as a baseline. Children's immune status was classified using revised classification system for paediatric HIV disease (1994).[7]

Statistical analysis was done with Univariate Chi-square test using SPSS_ version 11.0.5.

3. Results

The immune status of those children revealed as severe immune suppression in 2 (4%), moderate immune suppression in 10 (22%) and no immune suppression in 32 (72%) according to 1994 revised classification system for paediatric HIV disease, based on their age and CD4 cell count (Table 2). The oral manifestations noticed were aphthous ulcers (4%), linear gingival erythema (2%), gingivitis (9%), hyper pigmentation (15%), depapillation of tongue (4%), and fissured tongue (2%). When it was compared with the immunological status of the study group, high statistical significance ($p < 0.001$) was found between oral manifestation and immune status (Table 3).

4. Discussion

Globally, 94% of paediatric HIV infections acquired vertically with the vast majority being acquired during delivery. The HIV transmission to children by the vertical route includes before birth (20%), during childbirth (40%) and during breastfeeding (40%).[3] In this study also the predominant mode of acquiring HIV infection was found to be vertical.

Cluster of Differentiation 4 (CD4) is a glycoprotein expressed on the surface of T helper cells, monocytes, macrophages and dendritic cells. CD4 counts assess the immune status of HIV patients and helps in determining the initiation of antiretroviral therapy and it can be used in conjunction with clinical assessment. This allows an earlier detection before worsening of HIV disease as CD4 decline usually occurs prior to clinical progression.[8]

Paediatric HIV infection is associated with a wide spectrum of HIV associated oral lesions (HIV-OL). Though the clinical features of HIV infection are similar in adults and children, they may vary in severity.[9–12] In children, oral mucosal lesions are one of the earliest clinical indicators of HIV infection and its progression is strongly associated with immune suppression. In this study 72.7% of children were not immunosuppressed, 22.7% of children were moderately immuno suppressed and only 4.5% of children were severely immunosuppressed. The most common oral manifestation noticed

Table 2 – Immunologic categories based on age-specific CD4+ T-lymphocyte counts and percent of total lymphocytes.

Immunologic category	Age of child		
	<12 months	1–5 years	6–12 years
	uL (%)	uL (%)	uL (%)
No evidence of suppression	≥1500 (≥25)	≥1000 (≥25)	≥500 (≥25)
Evidence of moderate suppression	750–1499 (15–24)	500–999 (15–24)	200–499 (15–24)
Severe suppression	<750 (<15)	<500 (<15)	<200 (<15)

Table 3 – Correlation between oral manifestations and immunological status of the study group.

Oral manifestations	CD4						Total	
	Severely immunosuppressed		Moderately immunosuppressed		Not immunosuppressed			
	n	%	*n*	%	*n*	%	*n*	%
Nil			4	9.09	23	52.27	27	61.36
Gingivitis	1	2.27	2	4.55	1	2.27	4	9.09
Hyperpigmentation			1	2.27	6	13.64	7	15.91
Aphthous ulcer			2	4.55			2	4.55
Depapillation of tongue			1	2.27	1	2.27	2	4.55
Linear gingival erythema	1	2.27					1	2.27
Fissured tongue					1	2.27	1	2.27
Total	2	4.55	10	22.73	32	72.73	44	100.00

$P < 0.001$ highly significant.

was mucosal hyper pigmentation (15.9%) (Fig. 1), followed by conventional gingivitis (9%)(Fig. 2). The higher prevalence of mucosal hyper pigmentation in patients on HAART has been linked with increased melanin production in the epithelium associated with increased release of melanocyte-stimulating hormone (MSH) as a result of systemic ketoconazole and zidovudine therapy.[13,14] Also, two cases of aphthous ulcers (4.5%) in moderately immunosuppressed group (Fig. 3) and one case of linear gingival erythema (2.2%)in severely immunosuppressed group was noted (Fig. 4).

According to EC-Clearinghouse-WHO criteria, Group 1 lesions like candidiasis, parotid enlargement were not found probably due to partial restoration of the immune system by regular use of HAART which suppresses the viral replication. In the present study HIV-OL were found only in few children, this could be due to strict adherence of ART regimen, effectiveness of HAART (1 NNRTI + 2NRTI) and hence an effective immune response.



Fig. 1 – Mucosal hyper pigmentation.



Fig. 2 – Gingivitis.



Fig. 3 – Aphthous ulcer.



Fig. 4 – Linear gingival erythema.

5. Conclusion

According to the present cross sectional study, the oral manifestations are less with HIV/AIDS children undergoing HAART and thereby their quality of life is not compromised. Further longitudinal evaluation in larger group is considered in order to get a better picture about the efficacy of HAART in reducing oral manifestations of HIV/AIDS children.

Conflicts of interest

All authors have none to declare.

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Authors Names

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