

REVIEW ARTICLE

An Updated Review on HIV Disease in India & Oral Manifestations associated with HIV Infection & AIDS

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ABSTRACT

Acquired Immuno Deficiency Syndrome (AIDS) associated with HIV infection is undoubtedly the most rapidly advancing epidemics in recent times. It is a multisystem disease with numerous manifestations. The prominent features are cachexia, unexplained fever, unexplained diarrhoea and malnutrition – all of which are found in abundance as a result of poverty prevalent in India as well as majority of South East Asian countries. Hence it becomes difficult to rule out or rule in HIV as a cause of any disease syndrome. The fear of stigmatizing the patient by a wrong diagnosis being as great as the fear of missing a diagnosis.

A strong association is being established between the development of oral lesions and immune suppression. Orofacial manifestations serve as early markers for immune deterioration and disease progression.

This paper reviews orofacial lesions associated with HIV infection and current treatment modalities for management of oral lesions to justify role of oral medicine experts in providing oral health for overall health for patients living with HIV / AIDS.

Keywords: AIDS, HIV Infection, orofacial manifestations, management.

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INTRODUCTION

As per the consensus for the year 2013-2014, an estimated

number of populations living with human immunodeficiency virus (HIV) were over two million in India. However, Global epidemiology of adults and adolescents living with HIV estimates to be approximately 32 million people.¹

The Acquired Immunodeficiency Syndrome (AIDS) pandemic, caused by infection with human immunodeficiency virus (HIV) illustrates the varied transmission capabilities of disease and is capable of mounting resistance that brings about the complete destruction of the invading pathogen. Spread by blood borne and sexual contact HIV has infected over 36.1 million people in the world and according to joint United Nations Programme on HIV / AIDS (UNAIDS) and World Health Organization (WHO) 1600 new cases are coming up every day.²

With advancement in medical management of HIV infection among adult and pediatric patients, prolonged survival is possible, though associated with longer duration of immune suppression.³ Recent investigators have genetically disrupted HIV Receptor *CCR5* in patients with HIV, the role of Oral Medicine experts in diagnosing orofacial manifestations as clinical markers for disease progression is of paramount importance and significant, thereby helping oro-dental diagnosticians relating to treatment, disease progression and survival.⁴

The likelihood of developing oral manifestations has always been multifactorial in HIV infected and oral manifestations are among the earliest and most common clinical signs of adult and pediatric HIV disease.⁵ Some oral lesions are also indicators of the disease's progression.

The present paper reviews the recent classification, oral manifestations and treatment associated with HIV infection and AIDS.

CDC CLASSIFICATION

A “CD4 percentage” is the percentage of total T-lymphocytes represented by CD4 cells. HIV-infected individuals should have a CD4 cell count / percentage performed every three months.

The most recently revised CDC classification (shown in the Table 1) employs three ranges of CD₄ cell counts and uses a matrix of nine mutually exclusive categories. All patients in categories A3, B3, C1-3 are reported as AIDS.

Undiagnosed or untreated infection with HIV, results in progressive loss of immune function marked by depletion of the CD4⁺T lymphocytes (CD4), leading to opportunistic infec-

CD4+ T cell Count (cells/ μ L)(CD4%)	Clinical Categories		
	A Asymptomatic acute (Primary) HIV/PGL	B Symptomatic (not A or C conditions)	C AIDS-indicator conditions
>500 (28%)	A1	B1	C1
200-499 (15-28%)	A2	B2	C2
<200 (14%)	A3	B3	C3

Category A: asymptomatic HIV infection, persistent generalized lymphadenopathy (PGL). Category B: Oropharyngeal and vulvovaginal candidiasis, constitutional symptoms such as fever (38.5°C) or diarrhea lasting >1 month, herpes zoster (shingles). Category C: *Mycobacterium tuberculosis* (pulmonary and disseminated), *Pneumocystis carinii* pneumonia, candidiasis of bronchi;trachea or lungs, extrapulmonary cryptococcosis, CMV, HIV-related encephalopathy, Kaposi's sarcoma, wasting syndrome due to HIV.

Table-1: Revised Classification system for HIV Disease based on CD4 Cell Count and Percentage.⁶

Group I Lesions strongly associated with HIV infection
a) Candidiasis – Erythematous, Pseudomembranous
b) Hairy leukoplakia
c) Kaposi's sarcoma
d) Non-Hodgkin's lymphoma
e) Periodontal disease
Linear gingival erythema
Necrotizing (ulcerative) gingivitis
Necrotizing (ulcerative) Periodontitis
Group II Lesions less commonly associated with HIV infection
a) Bacterial infections
Mycobacterium aviumintracellulare
Mycobacterium tuberculosis
b) Melanotic hyperpigmentation
c) Necrotizing (ulcerative) stomatitis
d) Salivary gland disease
Dry mouth due to decreased salivary flow rate
Unilateral or Bilateral swelling of major salivary glands
e) Thrombocytopenic purpura
f) Ulceration NOS (not otherwise specific)
g) Viral infections
Herpes simplex virus
Human papilloma virus (warty-like lesions)
-Condylomaacuminatum
- Focal epithelial hyperplasia
-Verucca vulgaris
Varicella – Zoster virus
-Herpes zoster
-Varicella
Group III Lesions seen in HIV infection
a) Bacterial infection
Actinomycesisraelii
Escherichia colli
Klebsiellapneumoniae
b) Cat – scratch disease
c) Drug reactions (Ulceration, Erythema multiforme, Lichenoid, Toxic epidermolysis)
d) Fungal infections other than candidiasis
Cryptococcus neoformans
Geotrichumcandidum
Histoplasmaacapsulatum
Mucoraceae (Mucormycosis/Zygomycosis)
Aspergillusflavus
e) Neurologic disturbances
Facial palsy
Trigeminal neuralgia
f) Recurrent aphthous stomatitis
g) Viral infections
Cytomegalovirus Molluscumcontagiosum
Table-2: Revised Classification of Orofacial lesions associated with HIV Infection



Figure-1: Pseudo membranous Candidiasis as creamy white plaque in HIV Patient



Figure-2: Solitary large Herpes Simplex Virus (HSV) ulcer involving palate

tions and malignancies characteristic of Acquired Immuno-deficiency Syndrome (AIDS).⁷

OROFACIAL MANIFESTATIONS

As with HIV-infected adults and children, the likelihood of developing oral manifestations depend on several factors. Presentation of orofacial disorders in patients with HIV disease (HIVD) is strongly associated with immune suppression.⁸

Current classification of many oral lesions of HIV disease is

Common disease	Salient clinical features	Diagnosis	<u>Treatment</u>
Pseudomembranous Candidosis.	Soft white/yellow, curd-like plaques on oral mucosa. Deposits easily removable by gentle scraping.	Clinical grounds; smear stained by Gram's or PAS stain show candidal hyphae; candidal culture	<ol style="list-style-type: none"> 1. Topical antifungals: Mycostatin Pastilles: Dissolve 1 tablet in mouth until gone, 4-5x q.d x 14 days. 2. Mycostatin Oral Suspension: Use 1 teaspoon 4-5x q.d, rinse and hold in mouth as long as possible before swallowing or spitting out (approximately 2 minutes). 3. Mycostatin Ointment or Cream: Contains nystatin 100,000 units/g. Denture-wearers should apply to re denture surface prior to each insertion. For edentulous patients, mycostatin powder can be sprinkled on the denture. Apply liberally to affected areas 4-5x q.d. 4. Mycelex Troche: Contains clotrimazole. Tablets contain sucrose; risk of dental caries with prolonged use (>3 months); care must be exercised in diabetic patients. 10mg: dissolve 1 tablet in the mouth 5x q.d x 2 weeks. 5. Nizoral: Contains ketoconazole. To be taken if Candida infection does not respond to Mycostatin. Potential for liver toxicity exists. LET should be monitored with long term use (>3 months)" 200mg: take 1 tablet q.d x 10-14 days. 6. Nystatin: Contains nystatin (100,000 units) vaginal tablet dissolved in the mouth t.l.d x 2 weeks. 7. Diflucan: Contains fluconazole. 100mg: 2 tablets the first day and 1 tablet q.d x 10-14 days. 8. Mycolog Cream: Contains nystatin and triamcinolone 9. Fungizone Oral Suspension: Contains amphotericin B. 1ml swish and swallow q.i.d between meals.
Erythematous Candidosis	Flat red patches on the dorsal surface of the tongue and hard palate.	As Above	As Above
Candidal Angular Cheilitis	Red, ulcerated, and fissured lesion at the angle of the mouth.	As Above	Mycolog Cream: Occasionally this may be caused by a mixed infection (See above.)
Hairy Leukoplakia (Oral Hairy Leukoplakia)	Asymptomatic bilateral, vertically corrugated or hairy white lesions on the lateral borders of the tongue.	Clinical and histological; demonstration of the virus; (EBV) by in situ hybridisation techniques or PCR	Zovirax Acyclovir: Systemic administration causes some regression of HE HL is not a premalignant lesion. 200mg: 1 capsule q.6h x 7 weeks.
Linear Gingival Erythema	Well-demarcated, linear band of intense redness along the gingival margins	Clinical	No treatment is necessary. Does not respond to oral prophylaxis
Necrotising Ulcerative Gingivitis	Painful ulceration of the interdental papillae associated with halitosis and spontaneous gingival bleeding.	Clinical; smear for identification of fusospirochetal organisms	Metronidazole: 500mg: t.l.d x 7 days. Oral prophylaxis (scaling and debridement) is needed for these patients.
Necrotising Ulcerative Periodontitis (NUP)	Rapidly progressive periodontal disease resulting in bone loss.	Clinical; radiological	As Above

Kaposi's Sarcoma	Painless purple/haemorrhagic lesion on palatal/ anterior gingival mucosa; later becomes raised and ulcerated.	Clinical	<ol style="list-style-type: none"> 1. Nystatin: 100mg: 2 tablets the first day and 1 tablet (Id x 10-14 days. 2. Mycolog Cream: Contains nystatin and triamcinolone Apply to affected area after each meal and before bedtime. 3. Fungizone Oral Suspension: Contains amphotericin B. 1ml swish and swallow q.i.d between meals.
Erythematous Candidosis	Flat red patches on the dorsal surface of the tongue and hard palate	As above	As above
Candidal Angular Cheilitis	Red, ulcerated, and fissured lesion at the angle of the mouth	As Above	Mycolog Cream – See Above
Non-Hodgkin's Sarcoma	Rapidly enlarging rubbery mass in the tonsillar fossa, palate, or gingival	Clinical; histological	Surgery Radiotherapy Chemotherapy Referral to an oncologist.
Herpes Simplex (HSV)	Clusters of painful, small vesicles/ulcers on palate or gingivae. Most cases of HSV infections are recurrent	Clinical; smear for viral inclusion bodies	<ol style="list-style-type: none"> 1. Zovirax (Acyclovir): 200mg: 1 capsule q.6h x 2 weeks 2. DenavirL (Penciclovir) 1% Cream: Apply locally q.2h x 4 days. Vira-A 1% (Vidarabine) Ointment: 3. Carbamazepine (for post-herpetic neuralgia): 200mg: b.id to start; 800-1,200mg q.d (in divided doses) x 2 weeks.
Condyloma Acuminata (Verruca Vulgaris)	Warts are nodular or cauliflower-like in appearance, often multiple	Clinical; histological	Surgery CO2 Laser surgery
Xerostomia	Dry mouth, often with fissured tongue. Promotes dental caries.	Clinical	Artificial saliva Sodium Carboxymethylcellulose 0.5% Aqueous Solution
Salivary Gland Swelling	Unilateral/ Bilateral salivary gland swellings	Clinical	If xerostomia is present, See above
Thrombocytopenic Purpura	Bleeding tendencies; petechiae on oral mucosa.	Clinical	Platelet transfusions in severe platelet deficiency. No dental surgical intervention unless platelet numbers are restored.
Melanotic Hypopigmentation	Melanotic linear lesions on the gingivae	Clinical	No treatment is necessary
Cryptococcosis	Necrotic ulcerative lesion	Clinical	Antifungal treatment. Oral involvement is rare.
Erythema Multiforme	Ulcerative lip and intra-oral lesions	Clinical	Referral to a specialist
Lichenoid Reactions	White lace-like lesions on the oral mucosa	Clinical; histological	Topical steroid application. Kenalog (triamcinolone acetamide) in Orabase cream 3-4x q.d x 1 week
Tuberculous Ulcers	Ulcerative lesions usually on the tongue or gingivae. Usually patient has pulmonary TB.	Clinical; histological (APB stain); chest x-ray, tests for TB	Treat the systemic disease with anti-TB drugs
Trigeminal Neuralgia	Shock-like pain along the distribution of the trigeminal nerve	History	Carbamazepine
Facial Palsy	Unilateral paresthesia of the face	History; clinical	Sometimes antiviral medications help.
Dental caries	Dental decay	Clinical	Early detection and appropriate treatment.

Table-3: Summary of Oral Manifestations of HIV / AIDS and Treatment Modalities for Oral Lesions



Figure-3: Unilateral Herpetic Zoster (shingles) involving face extending to peri-oral mucosa.

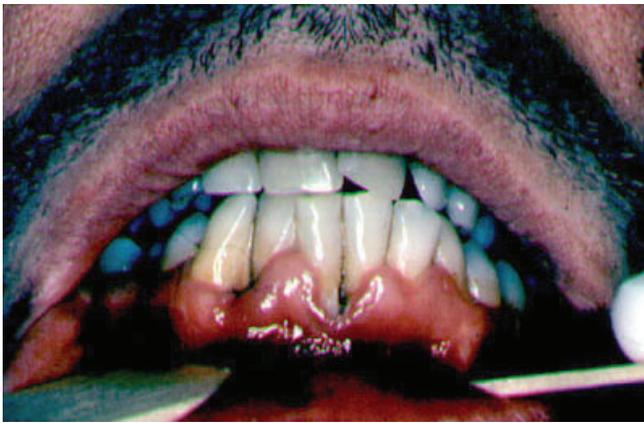


Figure-4: Necrotizing Ulcerative Periodontitis (NUP) with loss of attachment and alveolar bone in AIDS Patient.

based on their strength of association with HIV infection as depicted in Table 2.^{9,10}

The salient features of oral lesions, clinical presentation and treatment protocol for oral lesions in HIV and AIDS patients is being tabulated in Table 3.¹¹⁻¹⁸

CONCLUSION

“Mouth is the Mirror of the Body that reflects the systemic diseases.”

This seems to be quite true as Oral manifestations and lesions are seen in early as well as in advanced stage of HIV infection and disease. Oral lesions are undoubtedly important indicators of HIV infection. Early recognition, careful diagnosis of oral manifestations allows prompt institution of maintenance of optimal, “*Oral Health for Overall Health*” in HIV and AIDS patients.

Nevertheless, with prompt identification and appropriate understanding of oral manifestations of a systemic disease, the oral diagnostician and dental surgeon correlates with disease progression, survival and treatment of HIV infected patients.

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