

Oral candidiasis and AIDS

Monica.B¹, Mogit Gupta.Y²

Final year BDS, Saveetha Dental College, India1

MDS, Department of oral medicine and radiology, Saveetha Dental College, India2

Abstract: Human immune deficiency virus [HIV] infected seropositive patient suffer from a lot of opportunistic infection because of defective immune response. The defective immune response in HIV seropositive patient is due to the depletion of CD4 lymphocytes with advancing stages of HIV infections. Oral candidiasis is commonly affecting opportunistic infections in patients. The predominant species affecting is candida albicans. Oral candidiasis is seen in increasing frequency in reduced CD4 counts. This article gives an attempt to an over view of oral candidiasis in HIV relationship of oral candidiasis with CD4 count. Various modalities of diagnosis and treatment of oral candidiasis.

Keywords: candidiasis, candida albicans, fungal infection, HIV, opportunistic infection,

I. Introduction

Acquired immune deficiency syndrome (AIDS) a disease of the human immune system which is caused by the human immune deficiency virus (HIV) has emerged as a global crisis since its discovery in the summer of 1981 in the United States. Patients with defective cellular immunity associated with AIDS are under the risk for variety of opportunistic infection [1]. Oral candidiasis an opportunistic infection is a frequent and early manifestation of disease associated with the AIDS [2,3]. Candida albicans produces an opportunistic fungal infections which occurs in favorable conditions [1], including broad spectrum antibiotic therapy, xerostomia, presence of removable prosthesis, immune dysfunction such as diabetes or use of immune suppressant drugs [4].

II. Causative organism:

Among the fungal pathogens Candida species are the most predominant causes for the invasive infection [4] more than 95% of candidiasis is caused by 5 major species: Candida albicans, Candida glabrata, Candida parapsilosis, Candida tropicalis and Candida krusei [5,6,7,8]. Candida albicans is a dimorphic fungi which is typically present in the oral cavity in a nonpathogenic state in one half of healthy individual but they transform to pathogenic hyphal form under favorable environment [1]. Candida parapsilosis occur with high frequency in premature neonates and in patients with vascular catheters [9,10]. Candida glabrata occur common in elderly people and rarely in infant and children [11]. Candida tropicalis plays an important role as a cause of invasive disease in patients with hematological malignancy [12]. Candida glabrata and Candida krusei species have received attention due to their enhanced resistance to certain antifungal agents. Candida dubliniensis is recently identified pathogenic species [13].

III. Classification:

Samaranayake [14, 15] proposed a classification in which Group-1 (Primary oral candidiasis) is confined to lesions localized to the oral cavity with no involvement of skin or other oral mucosa and Group-2 (Secondary oral candidiasis) lesions are present on the oral as well as extra oral sites

Classification Of Candidiasis

| Primary oral candidiasis (group-1) | Secondary oral candidiasis (group-2) | Sub group |
|------------------------------------|--|-----------|
| Pseudo membranous (mainly acute) | Familial chronic mucocutaneous candidiasis | |
| Erythematous (acute \chronic) | Diffuse chronic mucocutaneous candidiasis | 1 |
| Hyperplastic (mainly chronic) | Candidiasis endocrinopathy syndrome | |
| i) plaque like | Familial mucocutaneous candidiasis | 2 |
| ii) nodular/speckled | Severe combined immunodeficiency | 3 |
| Candida associated lesion | Digeorge syndrome | 4 |
| Denture stomatitis | Chronic granulomatous disease | 5a |
| Angular cheilitis | Acquired immune deficiency syndrome | 5b |
| Median rhomboid glossitis | | 5c |
| Linear gingival erythema | | 6 |

Table .1 [14, 15]

IV. Pathogenesis of Oral Candidiasis in HIV infected individual:

Transition of *Candida* from a harmless commensal to the pathogenic organism is complex and is related to the environmental changes which lead to the expression of various virulence factors [16]. The ability of *Candida* species to persist on the oral mucosal surface of a healthy individual is an important virulence factor [16]. This can be inhibited by saliva [17] and enhanced by dietary carbohydrates [18]. Increased frequency of Oral Candidiasis has been seen in patients with cell-mediated immunodeficiency in a non-HIV-infected population also [19,20]. The effect of HIV on the immune system is depletion of CD4 lymphocytes, with disease progression there is a drop in the absolute count and a reversal of CD4 counts ratio [21,22,23]. It has been found that HIV-related oral candidiasis occurs in patients with CD4 counts less than 300 cells/mm³. Frequency of Oral Candidiasis also increased with reversal of CD4/CD8 cells ratio [24,25]. Severe Oral Candidiasis is also found in the patient with low CD4 counts with no HIV infection [26]. Torrsander et al [24] noted a decreased number of CD4 counts in HIV-infected patients with smears from the oral mucosa that showed pseudo mycelia forms of yeast, compared with other HIV-infected patients with no pseudo mycelia forms of yeast. Sindrup et al [25] found HIV-related mucocutaneous lesions occurred twice as frequently in patients with CD4 counts of less than 200/mm³.

V. Clinical features in candidiasis infection:

Oral candidiasis infection has different clinical presentations which include pseudo membranous candidiasis, erythematous candidiasis, hyperplastic candidiasis and atrophic candidiasis. Among the different clinical varieties of Oral Candidiasis, erythematous type is most frequent, pseudo membranous candidiasis and angular cheilitis are the next common types. While hyperplastic candidiasis is the least common type [3, 18].

5.1 Pseudo membranous candidiasis:

Pseudo membranous candidiasis is commonly known as "thrush" and it is often seen in neonates and in people receiving corticosteroid therapy. It is usually present as multiple white plaques resembling cottage cheese that can easily be wiped away leaving bleeding spots. It is usually asymptomatic with minimal slight tingling sensation or foul taste [4].

5.2 Erythematous candidiasis:

Erythematous candidiasis, as the name implies, clinically appears red or erythematous [4]. It appears as the mucosal erythema and depapillated patches on the dorsum surface of the tongue and may be painful. Erythematous candidiasis is the most frequent with approximately 50% of individuals with HIV infections. It may occur independently or simultaneously with pseudo membranous types [29].

5.3 Hyperplastic candidiasis:

Hyperplastic candidiasis is the least common type [29]. This form has been referred to as "candidal leukoplakia" like leukoplakia, hyperplastic candidiasis will present as a white plaque that cannot be wiped away by the clinician [4]. It is often confused with hairy leukoplakia which is another lesion commonly seen in AIDS [29].

5.4 Angular cheilitis:

The final clinical presentation of Oral Candidiasis infection is angular cheilitis. This form presents as cracking, peeling or ulcerations involving the corner of the mouth. It is due to increased folding of soft tissue that is frequently seen at the corners of the mouth [4].

VI. Diagnosis:

Diagnosis of Oral Candidiasis can often be made on the nature of clinical presenting features [26]. The various methods for isolating the *Candida* species are culture of whole saliva, swab, imprint culture, smear, concentrated oral rinse, biopsy, direct microscopy. Culture of whole saliva has the advantage of being sensitive and isolates the viable organism. But it's not site specific and there is a problem with sample collection [30].

Biopsy is used in case of chronic hyperplastic candidiasis. Drawbacks are invasive and it's not suitable for other types of candidiasis [13].

In Direct microscopy a smear taken from the lesional site is fixed on to the microscopic slides and then stained either by gram stains or by periodic acid Schiff (PAS) technique [31]. Smear technique has the advantage of being simple while the disadvantage is viable cells cannot be identified [13].

In swab culture a sterile cotton swab is gently rubbed over the lesional tissue and then inoculated with primary isolation medium like SDA (Sabouraud's dextrose agar) the advantage of swab is simple, site specific and viable cells are isolated. Drawback is difficult to standardize [13, 32].

Concentrated oral rinse can be used for isolation by asking the

Patient to hold the sterile phosphate buffer saline for 1min in mouth and the solution is centrifuged and inoculated with agar medium. Advantage is viable cells are isolated while disadvantage are some people has difficulty to use rinse quantitative and it's not site specific [33, 34].

In Imprint culture technique a Sterile foam pad is dipped in an liquid medium like sabourauds broth immediately before use then the pad is placed on the target site for 30 sec and transferred to agar for culture .advantage of imprint culture are quantitative ,viable cells are isolated and site specific. Draw backs with this are some sites are difficult to sample [34, 35].

Most commonly used primary isolation medium for Candida is SDA [36] which although permits the growth of Candida and suppress the growth of other oral bacteria due to low ph. [26].

Identification of Candida species is through morphological criteria [34], physiological criteria [37], serology [38], and molecular based identification method [34]

VII. Management:

Wide variety of agents are available for the treatment of oral candidiasis [39] some of these antifungal drugs are used topically and others are used systemically either topical or ivroutes. Topical agents requires sufficient contact time between the drug and the oral mucosa as well as the presence of adequate saliva to dissolve the medication[40].several topical drugs contain sweetening agents sucrose or dextrose and long term use of these preparation may leads to increase in caries[40].

Management of Candidiasis Infection

| Topical agents | Method of use |
|---------------------------------|--|
| Clotrimazole solution 1% | 1 tea spoon (5ml) rinse and expectorate 4 times daily after meals at bed times |
| Clotrimazole (1%) cream | Apply to affected mucosa/skin twice daily |
| Nystatin(mycostatin)1:100000 ml | 1 teaspoon (5ml) rinsed and swallowed 5 times daily |
| Ketoconazole (2% cream) | Apply to affected mucosa/skin after meals and bed time |
| Chlorhexidine (0.2% to 0.12%) | 3 spoon rinse and expectorate twice daily after meals or bed times |
| Systemic agents | |
| Flucanazole 50-100mg | 2 tablets orally followed by 1 |
| Ketoconazole 200-400 | 1 tablet once daily |

Table.2 [41]

VIII. Conclusion:

In view of present global crisis of AIDS causing great amounts of mortality and morbidity where candidiasis infection in such AIDS individual has a high prevalence rate. It is imperative that there is regular monitoring of the patient suffering from AIDS for opportunistic infection like candidiasis which can serve as marker for progression of disease. Oral candidiasis in AIDS individual can be easily diagnosed using the technique described above. And should be treated to reduce the discomfort of the patients.

References

[1]. Aravindshetti, Ishitagupta et al “oral candidiasis aiding in diagnosis of HIV”case reports in dentistry 2001, pg 4(article id-929616).
 [2]. Greenspan d, Greenspanjs et al “AIDS and the dental team”. Copenhagen: munksgaard, 1986.
 [3]. SamaranayakeLP, Holmstrupp. “oral candidiasis and hiv virus infection”j oral pathol med 1989; 18: pg 554-64.
 [4]. Yuvrajasingh dang, Murarilalsoni, Kamta Prasad Namedo “oral candidiasis” review international journal of pharmacy and pharamaceuticals science.vol-2, issue 4, 2010.
 [5]. Pfaller ma, Pappas pg, WingarJR.”Invasive fungal pathogens: current epidemiological trends.clin infect dis 2006; 43(sup-1) S 3-14.
 [6]. Tortorano AM, Kibbler c, Peman J, bernhardt H et al,”Candidaemia in Europe: epidemiology and resistance.int j antimicrob agents 2006; 27:359-66.
 [7]. Pfaller ma, DiekemaDJ.”Rareand emerging opportunistic fungal pathogens: concern for resistance beyond candida albicans and aspergillusfumigates”jclin microbial 2004; 42:4419-31.
 [8]. Hajjeh RA, sofair an, HarrisonLH, etal.”incidence of blood stream infection due to candida species and in vitro susceptibilities of isolates collected from 1998 to 2000 in a population-based active surveillance program”.jclin microbiology 2004;42;1519-27.
 [9]. Kuhn DM, Mikherjipk, Clark TA, etal “candida parapsilosis characterization in outbreak setting .EmerginfecDis 2004; 10; 1074-81.

- [10]. Sarvikivi E, Lyytikäinen O, Soll DR, et al. "Emergence of fluconazole resistance in a candida parapsilosis strain that caused infection in a neonatal intensive care unit". *J Clin Microbiol* 2005; 43, 27 29-35.
- [11]. Malani A, Hmoud J, Chiu L, Carver PL, et al "candida glabrata fungemia: experience in a tertiary care centre" *Clin Infect Disease* 2005; 41:975-81.
- [12]. Marr KA, Seidel K, Whitte et al "Candidemia in allogeneic blood and marrow transplant recipients: evolution of risk factors after the adoption of prophylactic fluconazole" *J Infect Dis* 2000; 181:309-16.
- [13]. P.D.Marsh and M.Martin "Oral fungal infection" in *oral microbiology* pg 166-179, Churchill living stone, Edinburgh, UK, 2009.
- [14]. L.P. Samaranayake, "Superficial fungal infection" in *current opinions dentistry*, c.Scully, Ed, pp,415-422, current science, Philadelphia, pa, USA, 1991.
- [15]. P. holmstrup and M.Bessermann, "Clinical therapeutic, and pathogenic aspects of chronic multifocal candidiasis" *oral surgery oral medicine and oral pathology*, vol.56, no-4, pg 388-395-1983.
- [16]. Smitha Byadarahally Raju and Shashanka Rajappa "Isolation and Identification of candida from the oral cavity" *ISRN Dentistry* volume 2011, pg 7 (article id 487921).
- [17]. Olsen L. "Oral adhesion of yeast" *Acta Odontol Scand* 1990; 48; 45-53.
- [18]. Samaranayake LP, Macfarlane TW "The Effect of dietary carbohydrates on the invitro adhesion of candida albicans to epithelial cells" *J med microbial* 1982; 15; 511-7.
- [19]. Odds FC. "Candida and candidosis 2nd ed. London: Bathere Tindall, 1988.
- [20]. Budtz-Jørgensen E. "Histopathology, immunology and serology of oral yeast infection: diagnosis of oral candidosis." *Acta Odontol Scand* 1990; 48:37-43.
- [21]. Challacombe S. "Immunology of oral candidiasis. In: Samaranayake LP, Macfarlane TW, eds, *oral candidosis*. London: Wright, 1990:104-23.
- [22]. Scully C, Cawson RA. "Medical Problems in Dentistry". 2nd Ed Bristol: wright, 1987.
- [23]. Flob PI, Trounce JR, "Immunological aspects of candida infection complicating steroid and immune suppressive drug therapy". *Lancet* 1970; 2:1112-4.
- [24]. Kaplan MH, Sadick N, McNutt NS, Meltzer M, et al. "Dermatological findings and manifestation of AIDS". *J Am. Acad Dermatol* 1987; 16:485-506.
- [25]. Korting HC, Ollert M, Georgii A, Froschl M. "In vitro susceptibilities and bio types of c.albicans isolates from the oral cavities of patient infected with HIV" *J Clin Microbiology* 1988-26:2626-31.
- [26]. Pankhurst C, Peak man M. "Reduced CD4+ cells and severe oral candidiasis in absence of HIV infection." *Lancet* 1989; 1:672.
- [27]. Torssander J, Morefeldt-Manson L, et al "Oral Candida albicans in HIV infection". *Scand J Infect Dis* ; 1987; 19:291-5.
- [28]. Sindrup JH, Weismann K, Peterson CS et al. "skin and oral mucosal changes in patient infected with human immunodeficiency virus" *Acta Derm Venerol (stockh)* 1988; 68:440-3.
- [29]. Anil S, Nair R.G, Beena V.T "oral candidiasis a potential expression of HIV infection" *carc calling* vol-7, no-2, apr, jun-1994.
- [30]. D.E. Oliver and E.J. Shillito, "Effects of smoking on the prevalence and intra oral distribution of Candida albicans" *journal of oral pathology*, vol-13, no-3, 265, 270, 1984.
- [31]. J.C Davenport, "the oral distribution of Candida in denture stomatitis" *The British Dental Journal*, vol-129, no-4 pg-151-156 (1970).
- [32]. L.P. Samaranayake T.W. Macfarlane, P-J Lamey and M.M. Ferguson "A comparison of oral rinse and imprint sampling techniques for detection of yeast, coliform and staphylococcus aureus carriage in oral cavity" *journal of oral pathology*, vol-15, no-7, 386-388 (1986).
- [33]. J.C Davenport and J.M.A. Wilton "Incidence of immediate and delayed hypersensitivity to Candida albicans in denture stomatitis" *Journal of Dental Research*, vol-50, no-4, pg 892-896 (1971).
- [34]. T. Axell, T. Simonsson, D. Birkhed, J. Rosenborg and S. Edwardsson, "Evaluation of simplified diagnostic aid coricult-n for detection of oral candidiasis" *Scandinavian Journal of Dental Research*, vol-93 no-1 pg 52-55, 1985.
- [35]. D.W Williams and M.A.O Lewis "Isolation and Identification of candida from oral cavity" *Oral Disease*, vol-6, no-1, pg 3-11, 2000.
- [36]. F.C. odds "Sabouraud's agar" *Journal of Medical and Veterinary mycology*, vol-29, 355-359' 1991.
- [37]. A.N. Bellepola and C.J. Morrison "laboratory diagnosis of invasive candidiasis" *The journal of microbiology* volume-43, pg 65-84, 2005.
- [38]. D. Aabert, D. Pygaulthier-Toubas, P. Leonetal, "characterization of specific anti-candida Igm, Iga and Ige; diagnostic value in deep-seated infection mycoses" *vol-39, no-5-6, 169-176, 1996.*
- [39]. Epstein JB. "Antifungal therapy in oropharyngeal mycosis infection." *Oral surgery, oral medicine and oral pathology* 1990; 69:32-41.
- [40]. Deborah Greenspan, BDS, Dsc, ScD (hc), San Francisco, Calif. "Treatment of oral candidiasis in HIV infection" *oral surgery, oral medicine, oral pathology* 1994, 78, 211-5.
- [41]. Lancey PJ, Samaranayake L.P "oral candidiasis diagnosis and management." *dental update* 15:328-331, 1988.