Indian J Otolaryngol Head Neck Surg
(Jan–Mar 2019) 71(1):124–127; https://doi.org/10.1007/s12070-018-1342-3

ORIGINAL ARTICLE

Prevalence of Oral Candidiasis in Indian HIV Sero-Positive Patients with $CD4^+$ Cell Count Correlation

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Received: 27 March 2018 / Accepted: 30 March 2018 / Published online: 7 April 2018
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Abstract The objective of this study was to investigate the prevalence of oral candidiasis in human immunodeficiency virus/acquired immunodeficiency syndrome patients in India. A descriptive cross-sectional study. To compare the occurrence of candidiasis with the levels of $CD4^+$ (cluster of differentiation) cell counts. A total of 100 patients infected with HIV were included. Oral lesions were observed, only patients with oral candidiasis were studied and classified. Standard methods were used for collection of oral specimens, culturing and identifying Candida species. Potential correlations between the presence and severity of oral lesions and $CD4^+$ cells counts were analysed. Candidiasis was detected in 20% of the patients with an mean $CD4^+$ count being 188. All the patients were on highly active antiretroviral therapy except one. There was pseudomembranous candidiasis in 9, erythematous type in 3, angular chelitis in 2, chronic hyperplastic in 4, and median rhomboid glossitis in 2. Candidiasis is an indicator of low $CD4^+$ cell count but may be seen at different levels of the disease. In HIV sero-positive patients it is an indicator of falling $CD4^+$ cell count generally below 200, indicating onset of AIDS. Many a times the patient does not have specific complaints but, it is picked up only on examination. Hence oral cavity examination should be a must in seropositive patients at every clinical follow up.

Keywords Oral candidiasis · HIV/AIDS · $CD4^+$ cell counts

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Introduction

Candida albicans is an opportunistic fungal pathogen usually found in the human gastrointestinal and female lower genital tracts. It is only one of its kind parasite capable of colonizing, infecting and persisting on mucosal surfaces, and motivating mucosal immune responses [1].

C. Albicans, is naturally there in the oral cavity in a non-pathogenic state in about one-half of healthy individuals but under favourable situations, has the ability to transform into a pathogenic hyphal form. Conditions that favour this transformation includes extremes in age, broad-spectrum antibiotic therapy, corticosteroids, xerostomia, immune dysfunction (especially of cell-mediated immunity), diabetes mellitus, nutritional deficiencies, or the presence of removable prostheses [2, 3].

Human immuno-deficiency virus (HIV) has immerged as a major cause for loss of cell mediated immunity. Candida is commonly seen in immuno-compromised subjects.

HIV has been given this name because of its long-term effect, to attack the immune system of the body, making it weak and deficient. HIV infects vital cells in the human immune system such as helper T cells (specifically CD 4^+ T cells) (CD-cluster of differentiation), macrophages, and dendritic cells [4]. HIV infection leads to low levels of $CD4^+$ cells through a number of mechanisms including: apoptosis of uninfected bystander cells [5], direct viral killing of infected cells, and killing of infected CD 4^+ T cells by CD 8^+ cytotoxic lymphocytes that recognize infected cells [6]. When CD 4^+ T cell numbers decline below a critical level, cell-mediated immunity is lost, and the body becomes progressively more susceptible to opportunistic infections. Hence $CD4^+$ cell count is used as a parameter for assessing disease progression. As the $CD4^+$

cell count drops below 200cells/mm3, patients become vulnerable to many of the processes associated with AIDS (Acquired immune deficiency syndrome).

This study was under taken to observe the relationship of $CD4^+$ cell count and opportunistic infection namely candida in the oral cavity.

Materials and Methods

This clinical cross sectional study was conducted from July 2008 to November 2011, wherein 100 patients attending ART clinic, were randomly selected. After consent and maintaining complete secrecy of the identity of the patient, a full otorhinolaryngological examination was done. All patients who were confirmed to be HIV positive on treatment (HAART—highly active anti-retroviral therapy) or without treatment were included in the study. A through ENT examination was done. Data was collected, tabulated and analysed.

Observations

A total of 100 patients were examined. Clinical examination revealed otorhinolaryngological manifestations in (76%) of patients. Oropharyngeal manifestations were the commonest at (48%) in the 100 patients examined. Oral candidiasis was seen in (20%) of the 100 patients with a mean $CD4^+$ cell count of 188 (Table 1).

In patients with candidiasis, epistaxis and otitis externa the $CD4^+$ cell counts were below 200 which is considered to define AIDS as per CDC (centres for disease control) classification [7].

The $CD4^+$ cell counts in 100 patients were analysed which ranged from 685 to lowest being 44. The patients with oral candidiasis were analysed. There was pseudomembranous candidiasis in 9, erythematous type in 3, angular chelitis in 2 (Fig. 1), chronic hyperplastic in 4, and median rhomboid glossitis in 2 (Table 2). All the patients had $CD4^+$ cell counts below 500 majority being less than 100 (Fig. 2) Candidiasis was also seen in patients already receiving HAART, hence starting antiretroviral therapy did not prevent infection but only maintained the $CD4^+$ cell counts. Therefore HAART helped in delaying the onset of AIDS. Hence candidiasis was an indicator to look for other opportunistic infections and low $CD4^+$ cell count.

Table 1 $CD4^+$ cell count correlation with oropharyngeal findings

Oropharyngeal findings	Number of cases	Mean $CD4^+$ cell count
Leukoplakia/ erythroplakia	7	263
Apthous ulceration	17	218
Oral candidiasis	20	188
Laryngitis/pharyngitis	17	235
Oesophageal candidiasis	5	238

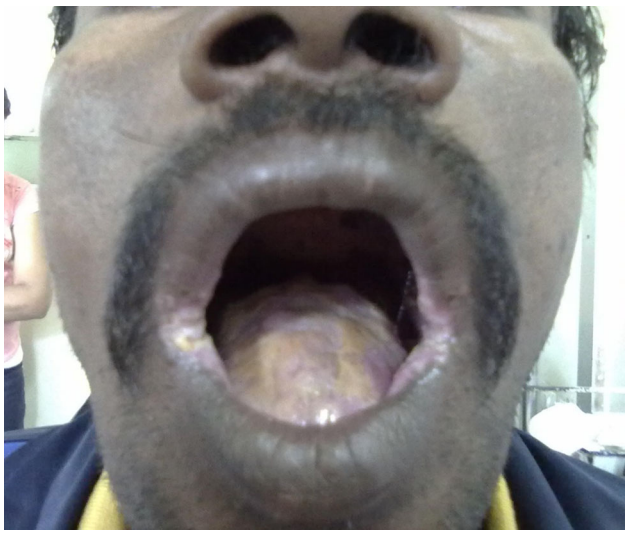

Fig. 1 Angular stomatitis

Table 2 Types of oral candidiasis

Type of candidiasis	Number of patients
Acute pseudomembranous candidiasis (thrush)	9
Chronic hyperplastic candidiasis	4
Acute atrophic (erythematous) candidiasis	3
Chronic atrophic candidiasis	0
Angular stomatitis	2
Median rhomboid glossitis	2

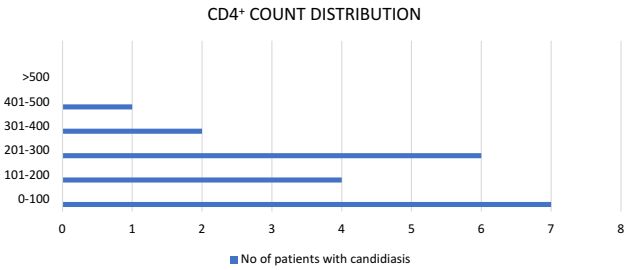

Fig. 2 $CD4^+$ cell count distribution in patients with oral candidiasis

Discussion

Candida yeasts are generally present in healthy humans, frequently part of the human body's normal oral and intestinal flora, and particularly on the skin; however, their

growth is normally limited by the human immune system and by competition of other micro-organisms.

Candidiasis in the mouth and throat can have many different symptoms, including: White patches on the inner cheeks, tongue, roof of the mouth, and throat redness or soreness cottony feeling in the mouth, loss of taste, pain while eating or swallowing, cracking and redness at the corners of the mouth [7].

On clinical examination candidiasis can have varied appearance as pseudomembranous candidiasis or thrush being the most common. White patches on the surface of the oral mucosa, tongue, or other parts of the body characterize thrush. Lesions develop into confluent plaques that resemble milk curds that when removed, reveal a raw, erythematous, and sometimes bleeding base. Acute atrophic (erythematous) candidiasis: Lesions on the dorsum of the tongue present as depapillated areas. Angular cheilitis: This is a subset of erythematous candidiasis. Lesions affect the angles of the mouth, causing soreness, erythema, and fissuring (Fig. 1). Median rhomboid glossitis: This is also a subset of erythematous candidiasis. Median rhomboid glossitis is an erythematous, atrophic lesion on the dorsum of posterior tongue. Chronic hyperplastic candidiasis: This is characterized by thick, white plaques on the buccal mucosa or the tongue that are hard or rough to the touch. Chronic atrophic candidiasis: erythema and oedema of the mucosa that is in contact with the fitting surface of the denture are characteristic, causing soreness and burning [8]. In our study the commonest lesion seen was oral thrush.

HIV infects primarily vital cells in the human immune system such as helper T cells, macrophages and dendritic cells. HIV leads to fall in $CD4^+$ cell counts. $CD4^+$ cell numbers decline below a critical level of 200 cells per μL, cell-mediated immunity is lost, and infections with a variety of opportunistic microbes appear.

The first symptoms often include moderate and unexplained weight loss, recurring respiratory tract infections (such as sinusitis, bronchitis, otitis media, and pharyngitis), skin rashes, and oral ulcerations. CDC has classified HIV on the basis of the lowest recorded $CD4^+$ cell count and the presence of symptoms into A, B, C categories is used for treatment purposes [9]. Where $CD4^+$ cell counts are not possible WHO (world health organisation) classification based on clinical features is used to classify patients in 1–4 clinical stages [10]. All these classification systems are to make the treatment protocols simpler depending on the level of strength of the immune system.

The timing of when to initiate therapy has continued to be a core controversy within the medical community. The WHO recommendations (2013) [10] are to start Highly active antiretroviral therapy (HAART) in WHO clinical stage 3 and 4 patients, or if the $CD4^+$ cell count is below ≤ 500, co infection with Hepatitis B Virus (HBV), active tuberculosis and sero-discordant couples, all pregnant women, all children below 5 years of age. In our study of the 100 patients 75 were on HAART, with majority of patients being on treatment the incidence of infection was lesser. Patients with candidiasis receiving HAART were 19. One patient was newly diagnosed not on treatment.

In our study the $CD4^+$ cell counts of the 100 patients examined, ranged from a highest being 685 and lowest recorded as 44. Normal $CD4^+$ cell count are between 500 and 1500/μl. The oral lesions were studied. The $CD4^+$ cell counts in patients with oral candidiasis were compared (Fig. 2). Majority of these patients were on HAART at different stages of the disease. Candidiasis was seen in patients with $CD4^+$ cell count as high as 446. Majority of the patients had $CD4^+$ cell count below 200. Hence candidiasis can be generally seen in patients with $CD4^+$ cell count below 500, also it is an indicator of falling cell mediated immunity. Whenever oral candidiasis is seen in a patient a definite cause of immune deficiency needs to be identified. If the patient is HIV positive the $CD4^+$ cell counts need to be assessed to know the progression of the retrovirus.

Many severely ill patients are unable to give clear history/complaints. Hence all patients with $CD4^+$ cell count below 200, their oral cavity needs to be examined at every follow up. Oral candidiasis patients were treated with clotrimazole mouth paint & chlorhexidine mouth wash, in severe or persistent cases oral fluconazole tablet was added for 14 days.

In our study the prevalence of oral candidiasis was 20%. Prasad et al. [11] in a study done in Mangalore, India reported candidiasis in 39% of the patients. Our lower prevalence could be attributed to the fact that majority of the patients were receiving Anti-retroviral therapy. Deb et al. [12] in his study done in Imphal, Manipur, India reported oral candidiasis in 22.5% of the patients.

There is a definite correlation between falling CD4 count and the prevalence of oral candidiasis (Fig. 2). The incidence is variable in different parts of India, may be because of environmental differences.

Conclusion

Candida is present in the oral cavity in a non-pathogenic state. Frank candidiasis either pseudomembranous or erythematous type when seen is an indicator of immune deficiency. In HIV sero-positive patients it is an indicator of falling $CD4^+$ cell count generally below 200, indicating onset of AIDS. The HIV positive patients should be regularly followed with the otorhinolaryngologist. As early changes in the ear, nose, pharynx and neck can be detected.

Eminent fall in $CD4^+$ cell count can be anticipated in view of the clinical presentation, and timely HAART can be started, before further worsening takes place.

Compliance with Ethical Standards

Conflict of interest Author declares that there is no conflict of interest.

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