Study of Oral Candidiasis in HIV / AIDS Patients and Their Antifungal Susceptibility Pattern

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ABSTRACT

BACKGROUND

Oral candidiasis (also known as oral thrush) is a common opportunistic mycotic infection of *Candida* species on the mucous membranes of the mouth. It is one of the most common, treatable oral mucosal infections seen in persons with Human Immunodeficiency Virus (HIV) infection or acquired immune deficiency syndrome (AIDS). *Candida* is a normal inhabitant of the body & it changes from a harmless saprophyte to become a true pathogen especially in immune-compromised individuals. The worldwide prevalence of OPC (Oropharyngeal Candidiasis) among HIV patients is 80 % to 95 % with *C. albicans* being the most common causative agent.

METHODS

50 sero-positive patients clinically suspected to have oropharyngeal candidiasis were included in the study, from whom two swabs each were collected after a written consent was taken. These swabs were inoculated on appropriate medias and *Candida* was isolated and identified up to species level using standard phenotypic methods. All the *Candida* isolates were subjected to antifungal testing following CLSI guidelines.

RESULTS

22 out of 50 patients tested positive for *Candida* spp. The study reported higher incidence in females (55 %) than males (45 %). The incidence was reported maximum between the age group of 31 - 50. The etiological agent for most species was found to be *C. albicans*, with a growth of 73 % while the remaining were *C. tropicalis* (22 %). The study also confirmed that maximum HIV patients who were reported with oropharyngeal candidiasis showed a CD4+ count of ≤ 200 . Based on our anti-fungal resistance study, Fluconazole & Ketoconazole were the mostly resistant, while Amphotericin-B & Voriconazole were the most sensitive antifungal drugs for *Candida* spp.

CONCLUSIONS

The vast majority of cases of oral candidiasis are not life-threatening and readily respond to appropriately administered antifungal agents. It must always be remembered, however, that the organism has the capacity to produce fulminating fatal infection by hematogenous dissemination from seemingly innocuous oral infections that serve as a portal of entry to the systemic circulation. Consequently, all oral Candidal infections in compromised patients must be treated vigorously and effectively.

KEY WORDS

HIV, AIDS, Oropharyngeal Candidiasis (OPC), *Candida* spp, Anti-Fungal Resistance

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BACKGROUND

Oral candidiasis, also known as oral thrush, is seen to affect the mucous membrane of the oral cavity. It's an opportunistic infection caused by *Candida* species. It can also be a mark of systemic disease such as diabetes mellitus and is a common problem among the immunocompromised. *C. albicans* is the most common species of yeast isolated from patients with oral candidiasis.¹ Oral candidiasis results from yeast overgrowth and penetration of the oral tissues when the host's physical and immunological defences have been undermined. Tissue invasion may be assisted by secreted hydrolytic enzymes, hyphal formation, and contact sensing. While these and other phenotypic characteristics may endow certain *Candida* species or strains with a competitive advantage in the oral cavity, it is the host's immune competence that ultimately determines whether clearance, colonization, or candidiasis occurs.² Oral candidiasis is the most common HIV related oral lesion and most patients infected with a strain originally present as a commensal of the oral cavity.³ Oral candidiasis is one of the commonest infections related to HIV. The risk of acquiring this opportunistic pathogen is directly related to the immune status of the individual which can be assessed by estimating the CD4 counts and HIV RNA levels in the patient.⁴ Appropriate Anti-Retroviral Therapy (ART) goes a long way in controlling these complications.⁵ The low absolute CD4 + T-lymphocyte count has traditionally been cited as the greatest risk factor for the development of OPC. The risks are considered to be higher in patients with a CD4+ cell count of less than 200 cells / mm. During the course of HIV infection, the rate of *Candida* infection is inversely related to the CD4 counts of the patient which in turn depends on the use of anti-retroviral treatment.⁶ Although the introduction of Highly Active Antiretroviral Therapy (HAART) has dramatically reduced the incidence of opportunistic infections in HIV-positive individuals who have received antifungal drugs, OPC with a shift in the spectrum of *Candida* species remains the most frequent HIV associated oral lesion including developing countries.

METHODS

Study design: This was a descriptive and prospective study. The study was carried out in a period of one year at Department of Microbiology, MGM Medical College & Hospital, Navi Mumbai, India. Approval of Institutional Ethical Committee was obtained for the study. Two oropharyngeal swabs each were collected from 50 HIV infected patients who were clinically suspected of having oral candidiasis, after taking a written consent from them. Out of the two swabs collected from each patient, one was used for Gram's staining and the other was inoculated on SDA (Sabouraud Dextrose Agar) slant and incubated at 37° C, it was observed for fungal growth after 48 hours. Isolates were identified using combination of microscopic examination, colony characteristics, germ tube test, morphology on cornmeal agar, species identification on CHROM agar, and sugar assimilation test. All the yeast isolated were subjected to susceptibility testing against antifungals. The testing was done on Mueller Hinton agar supplemented with 2 % glucose and 0.5 µg / mL

methylene blue (as per CLSI guidelines M 44-A) using the colonies directly from the CHROMagar plates.

Following Antifungals were Tested against the Isolates

Fluconazole (Flu), Itraconazole (Itr), Ketoconazole (Keto), Voriconazole (Vori), Amphotericin B (Amp), and Clotrimazole (Ctr)

RESULTS

Microbiological analysis of 50 sero-positive patients with clinically suspected oropharyngeal candidiasis was done. Out of the 50 sero-positive patients, *Candida* was isolated from 22 patients. Hence, the incidence of OPC in our study was 44 %. Male to female ratio was found to be 1.2:1. The age group most commonly affected was 31 - 50 years (Figure 1) with a mean of 40 years.

Figure 1. Age Wise Distribution of Patients Having Oral Candidiasis

Figure 2. Species Distribution of Candida in Oral Candidiasis Patients

Figure 3. CD4 Counts in Oral Candidiasis Patients

The number of women screened in this study were found to be 176, while men were 64. *Candida albicans* was the most frequently isolated spp. (72.7 %) which was followed by *Candida tropicalis* (22 %) in our study (Figure 2). Our study showed that 59 % of sero-positive patients who developed OPC had low CD4 counts < 200 cells / mm³ (Figure 3). It was also seen that 1 (4.5 %) patient with CD4 + count > 500 and 3 patients > 400 (13.6 %) also suffered from oral candidiasis. Our study showed that 90 % of *Candida* isolates were resistant to fluconazole, whereas 100 % sensitivity was seen for voriconazole and amphotericin B (Figure 4)

DISCUSSION

The incidence of oral candidiasis is a most common manifestation in HIV infected population. Lower CD4 counts between 200 - 300μ / dL, age and gender are considered as predisposing factors for the increasing incidence rate. During the course of HIV infection, the rate of *Candida* infection is inversely related to the CD4 counts of the patient which in turn depends on the use of antiretroviral treatment.⁷ In this study, the age distribution of the patients having OPC infection ranges from 31 - 50 years with a mean of 40 years. These results are in agreement with previous study from Inés María Bravo et al.⁸ Berhanu Yitayew. et al.⁹ also studied oral *Candida* carriage with an age distribution of 19 - 70 years old; comprising 29.8 % males and 70.2 % of females. In another study, Okonkwo E. C. et al.¹⁰

Candida albicans was the most frequently isolated spp. (72.7 %) which was followed by *Candida tropicalis* (22 %). This correlates to the study by Antoine Berberi et al.,¹¹ 2014 who found that *C. albicans* (73 %) continues to be the most frequently isolated species in OPC. Shobha D Nadagir et al.,¹² also showed in their study that the predominantly isolated species was *C. albicans* (90.66 %). A study by Francis Kwamintet at., also showed that the most predominant *Candida* species isolated was *C. albicans* (68.5 %) followed by *C. tropicalis* (7.4 %).¹³

A low CD4 cell count of < 200 cell / mm³ is directly related to oral *Candidal* colonization and infection in immunocompromised individuals. Our study showed that 59 % of sero-positive patients who developed OPC had low CD4 counts < 200 cells / mm³ same as Shiva Kumar K.L et al., 2013,¹⁴ who found that patients with lower CD4 counts were

more exposed to the incidence of oral candidiasis. During the course of HIV infection, the rate of *Candida* infection is inversely related to the CD4 counts of the patient. A study carried out by Antoine Berberi et al.,¹¹ showed that among distribution of OPC lesions and CD4 + cell counts, 73 % was associated with < 200 cells / mm³.

Fluconazole is widely used as a prophylactic drug because of its high oral bioavailability, minimal drug interaction and minimal adverse effects.¹⁵ However, our study showed that 90 % of *Candida* isolates were resistant to fluconazole. Whereas, minimum resistance was shown to voriconazole and amphotericin B (100 % sensitivity). A study from Ethiopia also reported 11.9 % resistance rate of *C. albicans* to fluconazole. Based on our results, it was observed that voriconazole and amphotericin B were most effective against the isolated yeast species which can be considered as good options against fluconazole.

Antifungal susceptibility testing is receiving an increased attention with the advent of newer antifungal drugs.⁷ In-vitro susceptibility testing provides a measure of the activities of two or more drugs and monitors the development of resistance. It also provides a means to co-relate clinically the in-vitro activity with the outcome of therapy.

CONCLUSIONS

Although cases of oral candidiasis are quite often cured with antifungal agents and are not life threatening, it is also a fact that we are seeing increasing resistance in *Candida* against commonly used antifungal agents. Resistant *Candidal* infection can result in severe complications which can prolong the hospital stay and increase the days of morbidity especially in immunosuppressed patients. Hence it is necessary that oral candidiasis in HIV patients need to be tested for antifungal susceptibility so that appropriate antifungals can be administered for effective treatment of the patient.

Data sharing statement provided by the authors is available with the full text of this article at jemds.com.

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