



## **Prevalence of Oropharyngeal Candidiasis among HIV Patients Attending ART Clinic, Infectious Disease Hospital (IDH) Kano - Nigeria**

**N. M. Sani<sup>1\*</sup>, I. B. Yusuf<sup>2</sup> and N. S. Mujahid<sup>1</sup>**

<sup>1</sup>Department of Microbiology and Biotechnology, Federal University Dutse, Jigawa State, Nigeria.

<sup>2</sup>Department of Microbiology, Kano University of Science and Technology, Wudil, Kano State, Nigeria.

### **Authors' contributions**

*This work was carried out in collaboration between all authors. Authors NMS and IBY designed the study, participated in data collection and designed the manuscript. Author IBY participated in data collection while author NSM provided critical advice on data analysis and manuscript writing. Authors NMS and NSM reviewed files and participated in designing the manuscript. Author NMS critically reviewed the manuscript. All authors read and approved the final manuscript.*

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### **ABSTRACT**

**Aims:** To determine the prevalence of oral candida infection among HIV positive patients attending ART clinic of infectious disease hospital Kano and to establish the relationship between oral manifestations and the level of immunosuppression.

**Study Design:** The study design comprised of pre-test counselling, informed consent, collection of oral swab and sputum, clinical evaluation and recording of demographic information (such as age, sex, marital status, occupation, present address and smoking).

**Place and Duration of Study:** A total of 120 HIV positive patients attending ART clinic of infectious disease hospital (IDH) Fagge, Kano State-Nigeria were used for the study between October 2016 to January 31, 2017.

**Methodology:** 120 HIV positive patients were examined for candida infection by direct and laboratory based methods. CD4 T-cell counts were also done using flow cytometry.

\*Corresponding author: E-mail: [nuramuhamsani@gmail.com](mailto:nuramuhamsani@gmail.com);

**Statistical Analysis:** Results were subjected to correlation and chi-square test using statistical package for social sciences (SPSS) version 22.

**Results:** Chi square test shows that 30 out of the 120 (25%) samples were positive for the infection. The distribution of patients with oral candida infection in relation to gender shows that more males were infected than females 20 (41.7%) and 10 (13.8%) respectively. Findings from this research have shown that, ART usage was 23 (22.5%) out of 102(100%) among patients with candida infection and 81(77.5%) out of 102(100%) among patients without candida infection. A significantly higher prevalence of candida infection, 7(53.8%) out of 13 was observed among patients with CD4 count of  $\leq 200$  cells/  $\mu\text{L}$  followed by 13(27.7%) out of 47 among patients with 200-500 cells/ $\mu\text{L}$  and 16.7% (10 out of 60) among patients with  $>500$  cells/ $\mu\text{L}$ , respectively ( $p < 0.001$ ).

**Conclusion:** Treatment of opportunistic infections is key to successful ART program and in mitigating the impact of HIV/AIDS in resource constraint settings.

**Keywords:** Oropharyngeal candidiasis; CD4 cell count; ART use; HIV positive patients; Infectious Diseases Hospital (IDH); Highly Active Antiretroviral Therapy (HAART).

## 1. INTRODUCTION

Yeasts are fungi that grow as single cells and reproduce by budding. They are distinguished from one another on the basis of the presence or absence of capsules, their size and shape, the mechanism of daughter formation, the formation of true hyphae or pseudohyphae, and the presence or absence of sexual spores, along with physiologic data from biochemical test. *Candida albicans* is the predominant causative agent of all forms of mucocutaneous candidiasis. Less frequently, *Candida glabrata*, *C. parapsilosis*, *C. tropicalis*, *C. krusei*, and several other species may cause disease. *C. dubliniensis*, a species that is phenotypically similar to *C. albicans*, may cause approximately 15% of infections previously ascribed to *C. albicans*. Although they are often present as benign commensal organisms in the digestive tract of healthy individuals, *Candida* species produce a broad range of serious illnesses in compromised hosts. Such infections are clearly on the rise. Data from the ongoing National Nosocomial Infections Surveillance System conducted in the United States showed a 487 percent increase in *Candida* bloodstream infections between 1980 and 1989 [1], while oropharyngeal candidiasis is the most common fungal infection in patients with human immunodeficiency virus (HIV) infection.

There are two main forms of candidiasis - mucosal and disseminated. As with other opportunistic infections, the introduction of highly active antiretroviral therapy (HAART) has led to a decreased incidence of oral and oesophageal candidiasis [2].

Mucosal candidiasis, in the form of oral, oesophageal or vaginal infections, is common in HIV/AIDS. The incidence of oral candidiasis in HIV infection varies from 7% to 93%, depending on patient mix, diagnostic criteria and study methods. A review of local HIV-infected women showed that the prevalence of oral candidiasis was 9% and that of vaginal candidiasis 28%. In an early study of HIV-infected women, *Candida* vaginitis was the commonest HIV-associated clinical condition in women. Infections tend to persist and are associated with a lower CD4 count and higher HIV viral load [3]. In the revised 1993 CDC case definition [4] vaginal candidiasis that was persistent, frequent or poorly responsive to therapy, as well as oral candidiasis, became a designated HIV-associated category B condition. In recent years, however, the status of recurrent vaginal candidiasis as a sentinel of HIV infection has been called into question, as it has never been supported by prospective controlled studies. In the current classification, oesophageal candidiasis is an AIDS-defining condition, occurring with a  $\text{CD4} < 200/\mu\text{L}$  and usually in conjunction with oral candidiasis. Rarely, oral candidiasis may occur in the setting of primary HIV infection when the CD4 count is significantly reduced.

Unlike mucosal candidiasis, disseminated candidiasis is remarkably uncommon in AIDS. This is likely due to relatively inadequate neutrophil function in most HIV-infected individuals. Although *Candidaemia* has been reported in AIDS, it usually occurs in the presence of other risk factors such as neutropenia, parenteral nutrition, abdominal surgery, broad spectrum antibiotics, cancer and corticosteroid use [5].

## 2. MATERIALS AND METHODS

### 2.1 Study Area

The study was conducted at the Microbiology laboratory, infectious diseases hospital Kano, Nigeria during a 4 months period (October 2016 to Jan2017). Ethical approval for the study was given by the ethical committee, ministry of health. HIV patients on ART were examined to ascertain the presence of candida infection. Clinical signs and symptoms suggestive of oral candidiasis like presence of white plaque, erythematous lesion, ulcerative lesion, dryness of the mouth, pain, altered taste sensation, and halitosis were included in the study.

### 2.2 Study Population / Sample Size

A total of 120 HIV positive patients were included that attend ART clinic of Infectious Diseases Hospital (IDH), Fagge LGA of Kano State-Nigeria from October 2016 to January 31, 2017. Observations included only periods of hospitalization i.e. patients record after discharge from hospital was not investigated. The patients included in the study were from different locations. Their HIV status was confirmed by three ERS (Enzyme linked immune sorbent assay, ELISA), an ELISA (VIZ: HIV ELISA, Rapid test and western blot).

### 2.3 Sample Collection

The study method comprised of pre-test counselling, informed consent, collection of oral swab and sputum, clinical evaluation and recording of demographic information (such as age, sex, marital status, occupation, present address and smoking). For the diagnosis of oral candidiasis, routine microbiology smears were performed. Different samples were collected depending on the patient's symptoms and clinical presentation. Samples were collected under universal aseptic precautions in suitable sterile containers for the routine diagnosis. The CD4+ count of the HIV-seropositive subjects (n=120) was done at the discretion of the treating physicians. The CD4 cell count and CD4+ T cells were estimated by the use of Cyflow cytometry.

Where an accessible and defined lesion is evident on the oral cavity, a direct sampling approach was used by taking the oral swab of the patient as this will provide information on the organisms present in the lesions itself. In cases where there are no obvious lesions or instances

where the lesion is difficult to access, an indirect sample based on collection of saliva was used.

### 2.4 Sample Preparation

The swab was used for direct examination of yeast. The laboratory method was by direct microscopy with 10% potassium hydroxide (KOH) preparation. KOH serves to digest the protein debris and clears keratinized tissues thereby increasing visibility. Potassium hydroxide preparation (KOH) revealed non pigmented septate hypha.

For sputum, samples were inoculated onto Sabouraud's dextrose agar and incubated at 240C for 48 hours. The growth of creamy white colonies were subjected to gram's staining for presence of gram positive budding yeast cells. After gram's staining, young candida organisms appeared as Gram positive, oval or round in shape showing yeast cells, pseudohyphae and short elements of true hyphae with characteristic dichotomous branching (at an angle of approximately 45°). Using this method candida yeast and hyphae appeared dark blue.

### 2.5 Statistical Analysis

The CD4 cell count of all the patients was estimated and correlated with the presence/absence of candidiasis. Clinical signs and symptoms of patients were also recorded. Candida infection or oral candidiasis is defined as the demonstration of gram positive hyphae/pseudohyphae and yeast cells microbiologically along with clinical signs and symptoms.

The positive and negative predictive value of direct staining versus clinical symptoms in identifying *Candida albicans* was calculated. The significance of association between the symptoms / signs and the isolation of candida was analyzed using chi-square test, where a two-sided p value less than 0.05 was considered statistically significant. Statistical package for social sciences (SPSS) version 22 was used for the analysis.

## 3. RESULTS AND DISCUSSION

Oral candidiasis is a major problem in the world especially among HIV seropositive patients. The prevalence of oral candidiasis in the present study was lower than that previously reported in Daresalaam, Tanzania [6] and in Nigeria [7]. The

**Table 1. Sex-wise distribution of candida infection**

Sex	No. of infected patients (%)	Positive (%)	Negative (%)
Male	48(40)	20(41.7)	28(58.3)
Female	72(60)	10(13.8)	62(45.9)
Total	120(100)	30(25)	90(75)

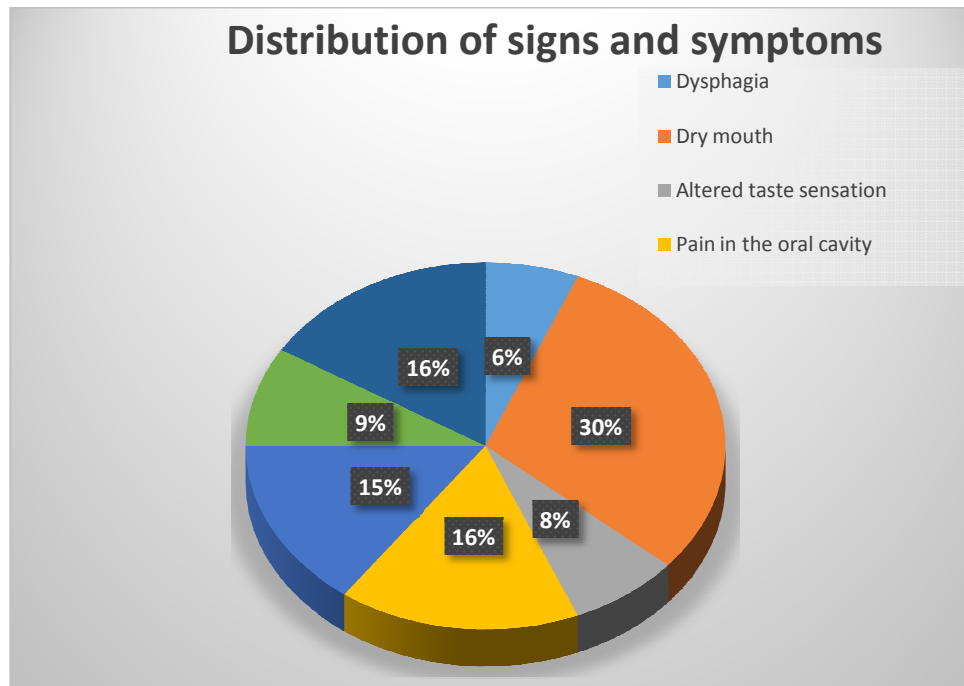
observed differences in the prevalence are likely to be due to different study designs and population. The study by [6] excluded individuals ≤18 years old. On the other hand, the study in Nigeria [7] compared candida colonization in asymptomatic HIV patients and control.

The various risk factors were use of antibacterial agents and steroids, comorbid illness like diabetes poor oral hygiene and tobacco usage.

**Table 2. Distribution of patients by age**

Age group (years)	Number (%)
0-20	19(15.83)
21-40	67(55.83)
≥41	34(28.30)

The first step in the development of candida infection is colonization of the mucocutaneous surfaces. HIV infection is not only associated



**Fig. 1. Distribution of signs and symptoms presented by patients with oral candida infection**

**Table 3. Prevalence of candida infection in relation to ART usage and CD4+T-cell count**

Variables	Response	Number(n)	Oral candida infection		P- value
			Positive % (n)	Negative % (n)	
ART use	Yes	102	22.5(23)	77.5(81)	0.12
	No	18	38.9(7)	61.1(11)	
CD4+ T- cells category (cells/ µl)	≤ 200	13	53.8(7)	46.2(6)	<0.001
	201-500	47	27.7(13)	72.3(34)	
	>500	60	16.7(10)	83.3(50)	

with increased colonization rates but also with the development of overt disease. 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. The present study analysed the spectrum and the prevalence of Candida infection and its association with the immunological markers and Anti-retroviral treatment status. Candida infection in patients with malignant diseases can lead to invasive infection and Candidaemia.

Dryness of mouth and pain in the oral cavity are the most frequently encountered symptoms (Fig. 1).

Although in this Study the prevalence of candida infection was found to be more in males (20%) than females (Table 1) in contrast to a study by [8] where it was reported that more females were infected with oral candida than males. Although there are evidences that the use of ART in HIV patients decreases the prevalence of oral candidiasis [9], the findings of this research indicates that 23 out of 81 patients on ART were infected (Table 3). Similarly, a study by [7] reported that 30% of patients who were on ART were infected with oral candida infection. Reasons for this high prevalence of oral candida infection among patients on ART is probably due to lack of ART adherence [10].

A recent research by [11] has reported that during the course of HIV infection, the rate of candida infection is associated to the CD4 T-cells counts of the patients (<200cells/ $\mu$ l) CD4+ T cells. In the present study, a significant association between oral candidiasis and CD4 cell count was found. The prevalence of candida infection was significantly higher in patients with CD4 count less than 200 cells/ $\mu$ l (Table 3), this is in line with previous reports by [12] which showed that CD4+ T cells counts < 200 cells/ $\mu$ l were more frequent in patients with oral candidiasis.

Studies by [13] have showed a gram staining positivity rate of 75% compared to 30% in the present study. Direct gram staining of the specimens along with the clinical signs and symptoms of oral candidiasis can be a valuable tool in differentiating colonization from infection.

The prevalence of oral candidiasis was seen higher among HIV patients not on ART. In the present study, data for the duration of ART use

was not available which would have given a clear picture in associating occurrence of candida infection. Although present study is only limited to one hospital, it reports a high prevalence of oral candida among HIV patients attending ART clinic infectious disease hospital Kano.

#### 4. CONCLUSION

Treatment of opportunistic infections is key to successful ART program and in mitigating the impact of HIV/AIDS in resource constraint settings.

#### CONSENT

All authors declare that written informed consent was obtained from the patient (or other approved parties) for publication of this paper.

#### ETHICAL APPROVAL

Ethical approval was obtained from the ethics committee of the state ministry of health and hospitals management board before embarking on the research.

#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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