



Original article

# Oral Candida Colonization among Adult Cancer Patients at National Cancer Institute in Misurata

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## Abstract

*Candida species is a common colonizer in the human oral cavity and in many times is considered as part of its microbata. However, Candida species can become opportunistic pathogens, particularly in immune-compromised patients. This study was conducted to evaluate the frequency of yeasts oral colonization among cancer patients at the National Cancer Institute (NCI) in Misurata, Libya. The participants in this study were 102 adults. They were 51 cancer patients and same number of controls. From each participant, three swabs' samples were collected from different sites of intra oral cavity including tongue, buccal mucosa and palate. The swabs were inoculated onto Sabouraud dextrose agar and incubated at 35°C for 24-48 hours. Yeast-like colonies were subjected to further speciation by the colony's morphological characteristics on the agar. A germ tube test was done to detect pseudo-hyphae and distinguish *C. albicans*. The results showed that the total colonization of *Candida spp.* was significantly higher in cancer patients than in the control group ( $P < 0.05$ ). All the isolates were capable to form germ tube. *Candida* colonization was the highest in head and neck cancer patients (100%) followed by lung cancer patients. The total number of *Candida* colonization was the highest in the patients who received chemotherapy and radiotherapy. Patients who received nystatin as antifungal treatment, 50% of them were colonized by *Candida* strains. The most colonized age group was 41-50 years (88%). The most colonized intra oral site was tongue among cancer and control groups. Oral *Candida* infections occurred more frequent in patients with cancer and especially those who were receiving chemotherapy.*

**Keywords:** *Candida spp*, yeasts, cancer, chemotherapy and oral colonization.

## Introduction

*Candida species are common asymptomatic colonizers of the oral cavity that may cause opportunistic infections in immune debilitated hosts [1]. Among of them, C. albicans is the most common species has been detected in the oral cavity of both healthy and medically compromised individuals [2].*

*Oral candida colonization is defined as the presence of yeast cells in the oral cavity with or without clinical signs and symptoms, while oral candidiasis is defined as the demonstration of gram-positive yeast cells and pseudo-hyphae along with clinical signs and symptoms. Candida colonization in the oral cavity may lead to the development of oral candidiasis, which is a major problem in the world, especially among cancer patients who are on cytotoxic therapy. It has been estimated that among cancer patients, oral colonization and infection occur at rates of 43%–90% and 13%–52%, respectively [3]. Its symptoms (discomfort, taste changes burning sensation) can have a significant impact on the quality of life and can*

impair human nutritional intake, which can particularly harm systemic outcomes of cancer therapy [4]. Moreover, the oral *Candida* colonizers can invade the underlying mucosal membrane and enter the bloodstream, leading to disseminated candidemia, which may present as sepsis and lead to septic shock with considerable morbidity and mortality rates if not treated promptly [5]. Recent studies have also shown that oropharyngeal colonization with *Candida* species and other yeasts may pose a threat to the respiratory system, like increasing the occurrence of pneumonia in general and aspiration pneumonia in particular [6]. In addition to the role of candidal infection as a significant factor in the development of potentially malignant oral disorders (PMD) [7]. It is critical that cancer patients should be evaluated clinically and microbiologically for the presence of yeasts in the oral cavity on the regular basis. There has not been much-discussed data on the etiological importance of yeasts in the oral colonization of cancer patients in Libya. Therefore, this study was conducted to investigate the frequency of oral colonization by yeasts among cancer patients at the National Cancer Institute (N.C.I) in Misrata.

### **Methods**

This study was conducted on 102 adult (18 years or older) participants. They were 51 cancer patients and same number of healthy individuals as controls. This was a prospective study performed at N.C.I. in the period of six months (from November 2020 to May 2021). The patients were those who were admitted to Departments of Medical Oncology, Clinical Hematology and Radiotherapy. Most of these patients had either solid tumors, head and neck cancer or hematological malignancy. Healthy individuals were adult volunteers who did not have any disease and did not take any medication. The experimental work was performed in the Microbiology Department at N.C.I.

### **Data collection**

Detailed information pertinent to the demographic and health status (age, sex, use of antibiotics, any chronic ailments, type of cancer, surgical procedure in the preceding two months, recent history of oral fungal infections, treatment taken for that and use of dentures of the participants were documented using a questioner form.

### **Collection of biological samples**

An examination of the oral cavity and sample collection of the participants were performed by dentists. Intra oral cavity swabs were collected from three different sites including tongue, buccal mucosa and palate. All samples were processed for yeast isolation and identification in Microbiology Laboratory at N.C.I on the same day.

### **Isolation and identification of *Candida* species**

The collected swabs were inoculated onto Sabouraud's dextrose agar and incubated at 35 Co for 24-48 hours. Yeast-like colonies were subjected to further speciation by the colonies morphological characteristics on the agar. In addition, characteristics of yeast cells were studied under a light microscope. A germ tube test was performed to detect pseudo-hyphae and distinguish *C. albicans*.

### **Statistical analysis**

All the collected data was analyzed using the Statistical Package for Social Sciences software (SPSS, version 2021).

### **Results**

This study was conducted on 102 participants. 51 cancer patients and 51 healthy controls. The patients involved in this study had various malignancies, and they were undergoing to chemotherapy, radiotherapy, or surgery therapy.

There were no significant differences between the patients' genders (47% males and 53% females). The age of the patients ranged from 20 to 80 years. Healthy individuals were 17 males and 32 females. The age of controls also ranged from 20 to 60 years. The numbers and the percentage of patients for each type of cancer are summarized in Figure (1). Among patient group, twenty of them had gastrointestinal cancer and eight patients had breast cancer. They were the most frequent cancer in the studied group, accounting for 40% and 16%, respectively followed by seven cases of hemopoietic cancer. Six patients had head and neck tumors and genital cancer; the last four patients had lung cancer (Figure 1).

Six cases have not begun cancer treatment in the study group, forty patients were treated with chemotherapy, and the last four patients had taken both chemotherapy and radiotherapy. All cancer patients had received antibiotic as adjunctive treatment. There were 14 cancer patients regularly using nystatin orally as antifungal treatment.

Total colonization of *Candida* spp. was significantly more prevalent in cancer patients (76%) than in the control group (27%),  $P < 0.05$ . All candidial isolates were capable to form germ tube. Total number of candidial colonization was the highest in head and neck cancer patients (100%) followed by lung cancer (Figure 2). Total number of candidial colonization was the highest in of the patients who received chemotherapy alone (80%) and of patients who had both radiotherapy and chemotherapy treatment 75% were colonized as it is shown in Figure 4.

Patients who received nystatin as antifungal treatment, 50% of them were colonized by candidial strains. The most colonized age group was 41-50 years (88%) as it shows in Figure 3. The most colonized intra oral site was tongue among cancer patients and control groups as can be seen in Figure 5.

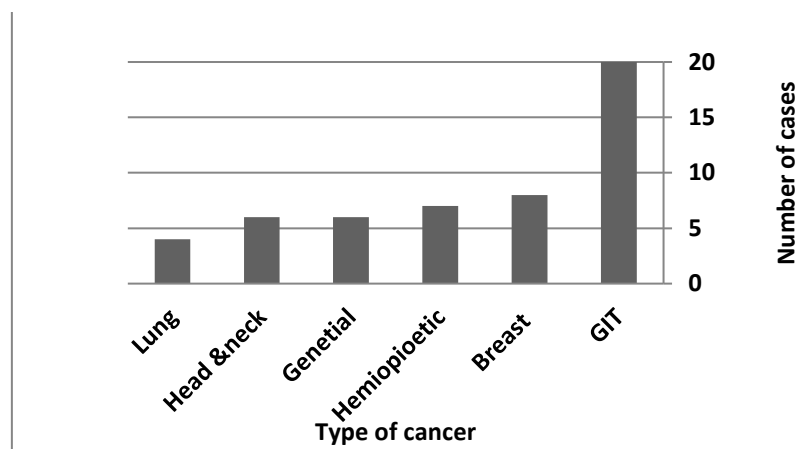


Figure 1: Frequency of cancer types among the patients

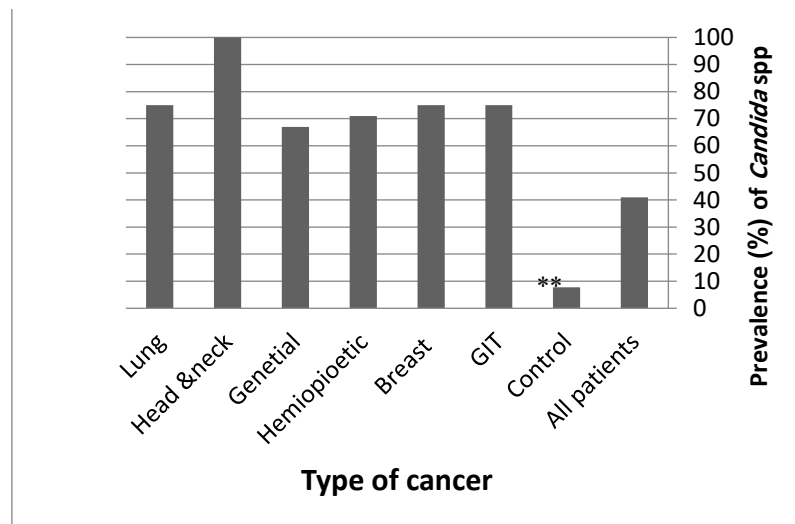


Figure 2: Frequency of *Candida* spp. colonization in the participants

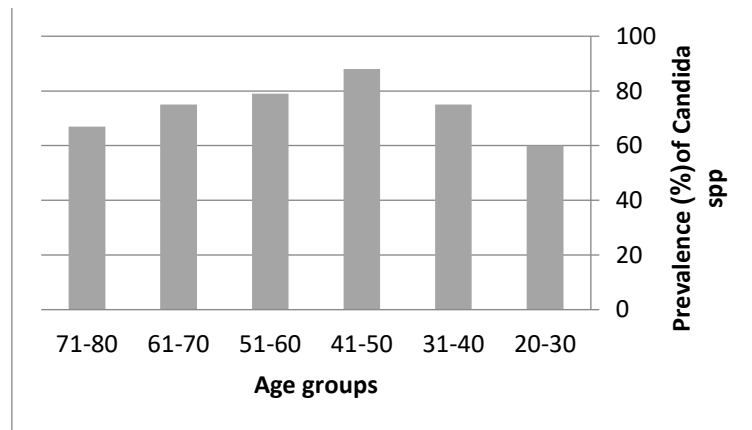


Figure 3: Frequency of Candida spp. colonization in the participants based on the age groups.

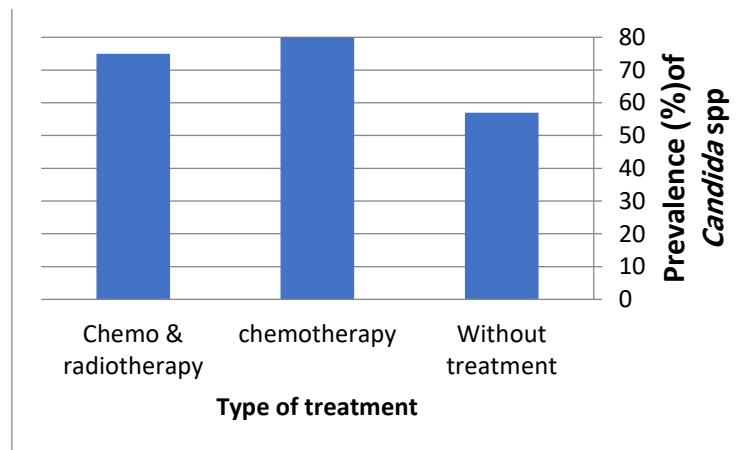


Figure 4: Frequency of Candidial colonization based on the type of treatment used for cancer patients.

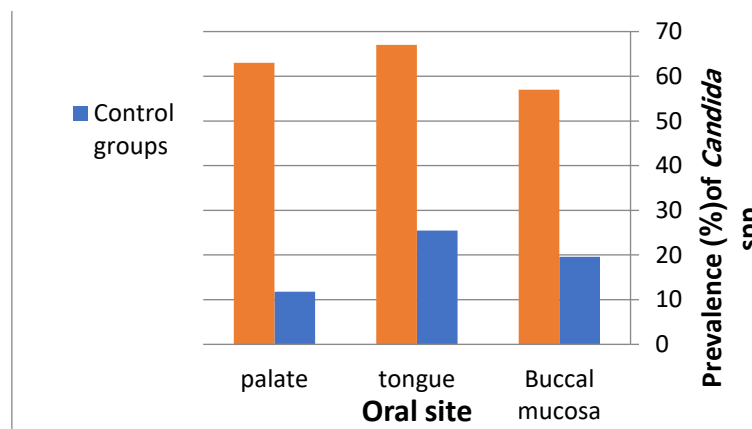


Figure 5: Frequency of Candidial colonization based on intra oral sites.

**Discussion**

Candidal infections are caused by Candida species and are common in immunocompromised patients. The incidence has dramatically been increasing during the last decades. Several virulence factors may contribute in the pathogenicity of Candida albicans, which is one of the main causes of systemic infection in individuals with cancer that can lead to high mortality rates of these patients. The epidemiology of C. albicans and other yeasts infections in the oral cavity of patients with cancer is quite varied ranging from 43% - 90% depending greatly on the type of cancer, type of treatment and advance stages of the disease.

In this study, the total prevalence of oral colonization was significantly higher in cancer patients (76%) than in the control group (27%). These findings were in consistent with Jham et al and Al-Abeid et al studies [11,12]. The significantly increased of Candidal carriage in this study may be due to compromised defense system of host because of underlying disease and usage of cytotoxic treatments (chemotherapy and radiotherapy) of malignancy, as can lead to mucositis, xerostomia and damage of the cell immunity. Thus, the patients became susceptible to fungal colonization.

All patients with cancer involved in this study were treated with antibiotics in turn emphasis that antibiotics are important risk factor in Candidal colonization, which has also been attributed to increased yeast colonization in the gut and oro-pharynx [13]. In the current study, it was found that the oral colonization rate was the highest in the patients with head and neck cancer (100%), the reason beyond that was likely to be local tissue damage due to cancer itself or therapy-induced oral mucositis [14]. Consequently, the reduction of the ability to maintain oral hygiene and poor nutrition will increase the rates of oral colonization in GIT. The candida oral colonization rates in patients with breast (75%), lung (75%) cancer, hematological malignancies (71%) and genital malignancies (67%); which were in agreement with other studies findings [15-17].

The results obtained from this study showed that patients who were being treated with chemotherapy had the highest candidal colonization rate (80%) compared to those were being treated with radiotherapy (75%) or have not receive any treatment (57%). This outcomes could be due to the fact that most of the patients (40/52) involved in this study were on only chemotherapy.

Our study showed that the most colonized age group was 41-50 years. This finding was in contrast with Bashiret al (2014) finding at tertiary care center in Northern India, where the most colonized age group was over 60 years [17]. It might be the elderly are one of the risks factors but not a major cause for candidal colonization. Only seven (29%) of the 14 cancer patients were receiving antifungal therapy had candidal colonization, which may be related to the medication transitional effect on the oral mucosa, and it can be impacted by saliva flushing or could develop resistance to the antifungal treatment (nystatin).

A higher prevalence of total candida colonization in cancer patients was seen in males (41%) higher than in females (35%), that could be because males are not cautious as females about their oral [18]; whereas in the control group, total colonization was higher in females (20%) compared to males (8%) and that could be due to the number of females patients included in present study were higher than male participants.

The most colonized intra oral site for both groups were tongue, it is presumed that the ragged construction of the dorsal tongue surface contributes to the candida invasion process [19,20]. The findings of our study strongly suggest that oral candidal colonization is frequent among cancer patients in NCI. In the oral cavity, the occurrence of candidal colonization can cause infection and then disseminate leading to severe infection with increased morbidity and mortality, oral colonization with Candida poses a threat to the respiratory system and increase incidence of pneumonia particularly aspiration pneumonia in immunocompromised patients. Therefore, particular attention must be given to cancer patients such as periodic examination prior to and during anticancer treatment to manage any underline disease.

The problem may be minimized by using prophylaxis and having regular dental check-up, additional daily oral care methods are necessary taking into consideration tongue cleaning. Seek assessment from a nutritionist to avoid foods and drinks that could increase the risk of candida overgrowth might also be a helpful measure. Further studies with a larger sample size are needed to determine the relationship between cancer patients and candida colonization. Additional investigations are needed to clarify possible risk factors that predispose subjects to systemic candida infections in oral Candida occurrences.

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