

Correlation between demographic and clinical variables and the incidence of oral *Candida* colonization in cancer patients

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ABSTRACT

Introduction: Cancer patients are highly vulnerable to *Candida* infections due to their impaired immunity, as the over-colonization of *Candida* is common among immunocompromised individuals. The occurrence of *Candida* overgrowth is influenced by several factors that can weaken the host's immune system and promote the growth of opportunistic fungal pathogens. Comorbidities, use of certain medications, lifestyle habits such as smoking and alcohol consumption, as well as oral hygiene and overall oral health, can all affect *Candida* proliferation in the mouth. These factors may cause dysbiosis in the oral cavity, creating conditions favourable for the overgrowth of *Candida*. This study assessed these variables to determine their potential as contributing factors for the carriage of *Candida* in the oral cavity.

Methods: Oral rinse samples and swab samples were obtained from cancer patients attending Oncology Clinics, Teaching Hospital Karapitiya (National Hospital Galle), from December 2021 to March 2022. Each sample was screened for *Candida* using a selective medium, followed by morphological and biochemical identification. The demographic and clinical data were obtained from all the study participants. The association between the oral *Candida* colonization and the demographic and clinical data of the study population was assessed using the *chi-square* test.

Results: *Candida* in the oral cavity was substantially correlated with denture wear ($p=0.041$). Remarkably, no statistically significant correlations were found between comorbid factors, use of oral and inhaled corticosteroid therapy, frequency of tooth brushing, smoking, alcohol consumption, betel chewing, dental caries and oral *Candida* carriage.

Conclusions: Wearing dentures was significantly associated with oral *Candida* carriage among the selected group of cancer patients while there were no other significant associations were found with the other factors tested.

Keywords: Associations, *Candida* colonization, Oral cavity.

Introduction

Colonization of the oral cavity by *Candida* species dates back to the times of Hippocrates, as early as 377 BCE, as the oral lesions that Hippocrates had reported were probably caused by *Candida* (1). *Candida* is a type of yeast that belongs to the class Ascomycetes of the Kingdom Fungi (2). Only 20 of the 200 identified species of *Candida* are human pathogens; the majority are benign commensals or endosymbionts (3). *Candida albicans* is the most prevalent pathogenic fungal species in the human microbiota, mostly colonizing the skin and mucosal surfaces (4). *C. albicans* can remain without causing any symptoms as a commensal of humans. No environmental reservoirs are understood. It is usually transmitted congenitally to neonates and by nosocomial infection. Approximately 70% of healthy individuals carry at least one species of *Candida* as commensals (5). However, it can cause superficial and invasive candidiasis if the host immunity is impaired. Candidiasis is an umbrella term encompassing cutaneous, mucosal, and invasive infections caused by *Candida* species. Invasive candidiasis denotes bloodstream infections caused by *Candida* spp., also known as candidemia (6).

Oral candidiasis is one of the most common opportunistic infections among immunocompromised individuals caused by the overcolonization of *Candida* species in the oral cavity (7). Oral *Candida* colonization denotes a significant clinical challenge in patients with cancer; the impaired immunity that is induced by both the malignancy and its associated treatment modalities is solely responsible (8). The patient's health and quality of life may be significantly impacted by the variety of negative consequences that this condition may cause, such as mucosal infections, discomfort, and possible systemic invasion (9). Numerous clinical and demographic parameters, such as age, sex, cancer type, treatment modalities such as radiation therapy and chemotherapy, and the existence of concomitant diseases, affect the occurrence of oral *Candida* carriage (10). Further, the occurrence of *Candida* in the oral cavity may be dependent on several predisposing factors like lifestyle, taking immunosuppressive drugs, alcohol consumption, betel chewing, personal hygiene, etc. (11, 12).

However, data on association between the demographic and clinical factors with oral *Candida* colonization among cancer patients is scarce in the Sri Lankan setting. Therefore, this study was planned to examine the relationship between oral *Candida* colonization and various demographic and clinical factors in cancer patients. It seeks to assess the prevalence of *Candida* carriage in this vulnerable population and explore how factors such as age, gender, oral hygiene practices (including tooth brushing frequency, denture use, and mouthwash use), and underlying health conditions (such as diabetes, anaemia and asthma) influence colonization. Additionally, the study investigates the potential impact of lifestyle habits like smoking, alcohol consumption, and betel chewing, as well as the use of corticosteroids (inhaled and oral) and the presence of dental caries. By identifying statistically significant associations, the study focuses on highlighting modifiable and non-modifiable risk factors that contribute to *Candida* colonization. The ultimate goal was to provide evidence that can inform early detection strategies, preventive measures, and more tailored therapeutic interventions, thereby enhancing oral health management and overall patient care in oncology settings.

Methods

Study Setting

The clinical samples and the patient data were obtained from the Oncology Unit at the National Hospital, Galle, Sri Lanka, and the laboratory component was performed at the Department of Microbiology and Department of Biochemistry of the Faculty of Medicine, University of Ruhuna, Galle, Sri Lanka.

Study Population

Cancer patients who were admitted or attending outpatient oncology clinics from December 2021 to March 2022 were studied for oral colonization of *Candida*. Adult cancer patients (over 18 years old) who were admitted or attending outpatient oncology clinics at the National Hospital Galle and who had given consent to participate were

included in the study. All children and adults who were not willing to participate, patients on antifungal therapy for the past four weeks, and terminally ill patients from whom an oral rinse sample could not be taken were excluded.

Sample Size Calculation

According to a previous study done at the National Hospital, Galle, by Navaratne, 2005, the prevalence rate of oral *Candida* infection among cancer patients was 34 (13). The sample size was calculated according to a descriptive cross-sectional study conducted by Hully *et al.*, (14) with a 95% confidence interval and a total width of the confidence interval of 0.15; the calculated sample size was 153. With a 10% correction for dropouts, the final sample of cancer patients to be screened was 169.

Clinical Sample Collection

An oral swab sample and oral rinse solution taken from each patient were separately inoculated on Candida Chrome Agar (CCA) and incubated at 25°C and 37°C for 48 hours. Obtained isolates on CCA were subjected to preliminary morphological identification and identified by *Biometriux API*TM 20°C identification kits, and confirmed as *Candida*.

Questionnaire Survey

Demographic data, age, sex, use of mouthwashes, alcohol consumption, betel chewing, smoking, tooth brushing frequency, present and past clinical history co-morbid factors such as diabetes, anaemia, asthma, use of oral and inhaled corticosteroids were documented with the help of a pre-prepared interviewer-administered questionnaire from each patient. Informed consent was obtained from study subjects before enrollment.

Data Analysis

The statistical analysis was performed using IBM-SPSSTM (V27.0). The Chi-Square (χ^2) test was used to evaluate the association between oral *Candida* colonization of cancer patients and socio-demographic and clinical characteristics. The statistical approach provided a comprehensive

analysis of how different clinical and socio-demographic factors correlate with oral *Candida* carriage among the test population.

Results

A total of 170 patients were included in the study. Of the 170 cancer patients, 103 carried *Candida* in their oral cavities, while 67 in the test population did not. The association between demographic/clinical data and oral *Candida* colonization among cancer patients is given in Table 1.

Discussion

This study focuses on the association between demographic/clinical factors and oral *Candida* colonization among the cancer patients who participated in the study. Overall, the only factor associated with oral candidiasis was wearing dentures. Surprisingly, all other factors were not associated with oral *Candida* carriage.

In certain published studies by Bartholomew *et al.*, 1987; Soysa *et al.*, 2006, and Lamster *et al.*, 2008 (15-17), diabetes was recognised as a risk factor associated with oral candidiasis. In contrast, in this population, diabetes was found to be an independent parameter from oral *Candida* colonization, as it exceeded the statistical significance limit.

According to Wyk and Steenkamp, the metabolism and, consequently, the kinetics of the rapidly dividing oral epithelial cells may be affected by iron deficiency anaemia due to the impairment of iron-dependent enzyme systems (18). These changes may make the epithelial surface more favourable for *Candida* adherence, growth, and invasion (18). However, the *p*-value obtained for the association analysis of anaemia and oral candidiasis produced a greater *p*-value than the significance interval ($p > 0.05$), indicating anaemia is not associated with oral *Candida* colonization in the sample studied.

Based on the findings of the studies carried out by Reichart *et al.*, and Javed *et al.*, betel chewing is not associated with oral colonization of *Candida* (19, 20). Our study results regarding betel chewing among cancer patients and the prevalence of *Candida* in the oral cavity agree with their findings, as betel chewing was found to be an independent factor from oral *Candida* carriage.

Table 1: Association between demographic/ clinical data and oral *Candida* colonization among cancer patients

Variable	Number of Patients	Oral <i>Candida</i> carriage		χ^2	<i>p</i> -value
		Yes	No		
Gender					
Male	49	31	18	0.203	0.652
Female	121	72	49		
Age group					
18-25 years	0	0	0	4.020	0.545
26-35 years	03	02	01		
36-45 years	36	20	16		
46-55 years	42	25	17		
56-65 years	46	25	21		
66-75 years	32	24	08		
76-85 years	11	07	04		
Co-morbid factors					
Diabetes	65	38	27	0.199	0.655
Anaemia	60	36	24	0.013	0.910
Asthma	14	08	06	0.075	0.780
Alcohol consumption					
Smoking	25	17	08	0.672	0.412
Betel chewing	11	09	02	2.230	0.135
Presence of dental caries	27	17	10	0.078	0.780
Wearing dentures	53	32	21	0.001	0.970
Use of mouthwashes					
Use of corticosteroid inhalers	17	14	03	4.17	0.041
Use of oral corticosteroids	16	09	07	0.137	0.710
Frequency of brushing teeth	11	05	06	1.130	0.288
	02	0	02	3.110	0.078
Once	02	02	0	1.680	0.641
Twice	160	97	63		
Thrice	06	03	03		
Other	02	01	01		

Studies conducted by Alnuaimi *et al.*, and Epstein *et al.*, have revealed that smoking and alcohol consumption are risk factors for oral candidiasis (21, 22). However, heavy consumption of alcohol and other associated factors like HIV and HPV triggered the oral colonization of *Candida* (23, 24). Since no HIV and HPV patients participated in our study and the amount of alcohol intake was not assessed, the result might have been obtained as alcohol consumption and smoking were not associated factors.

The use of corticosteroids was found as an independent factor with no association with oral candidiasis in our study. Yet, Boven *et al.*, have shown that in the first year following the start of inhaled corticosteroid therapy, there was a large and clinically significant rise in the number of patients receiving treatment for oral candidiasis (25). The first three months were when the relative risk was at its peak, but it continued to rise for at least a year after the therapy was started (25). Although they revealed an association between corticosteroid therapy and the prevalence of oral *Candida* carriage, it was basically time-dependent and the duration of the regimen.

When the frequencies of brushing teeth were considered, interestingly, 94.12% of the study population brushed teeth twice a day, and this was found to be independent of oral *Candida* colonization. Sun *et al.*, found that tooth-brushing less than once might be linked with excessive oral colonization of *Candida* (26). Since there were no such participants with extremely poor oral hygiene habits, the result was not statistically significant.

In our sample, the presence of dental caries was not associated with oral candidiasis. This finding is not in accordance with the findings of Raja *et al.*, and Al-Amad *et al.*, (23, 24). Nevertheless, wearing dentures was found to be a risk factor for the presence of *Candida* in the oral cavity in our study sample. A similar published study supports our finding of the association between the risk of developing oral candidiasis among denture-wearers (27).

Our findings regarding the association between the age of the host and oral *Candida* colonization do not agree with the work done by Akpan *et al.*,

and Nishimaki *et al.*, who stated that age is a predisposing factor for *Candida* colonization in the oral cavity (28,29).

Limitations

The relatively small sample size is one of the limitations of this study that resulted in smaller number of people in each category to compare. When association between social habits such as alcohol and smoking were considered, the frequency or the severity of the habit has not been considered to get a precise assessment.

Conclusions

Based on the results, it can be concluded that wearing dentures is associated with oral *Candida* carriage among cancer patients. Gender, age, diabetes, anaemia, asthma, the presence of dental caries, the frequency of brushing teeth, the use of mouthwashes, alcohol consumption, betel chewing, smoking, steroid therapy are not associated with oral *Candida* colonization in the sample of patients studied.

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