“Antifungal Susceptibility Pattern of Oropharyngeal Candidiasis in Cancer Patients”

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Abstract

Introduction: Fungal infections like oral candidiasis is prevalent in cancer patients as their immune systems were compromised.

Material and Methods: 377 cancer patients who were clinically diagnosed with oropharyngeal candidiasis were included in the study. Isolation and identification of Candida species was based on standard microbiological procedures. CLSI (2021) recommendations were followed when determining antifungal susceptibility.

Results: Among the total 377 cases included, the highest number of instances was reported in those aged 41 to 50 years (30.23%). Candida albicans (21.98%) was the most frequent followed by Candida tropicalis (18.84%), Candida parapsilosis (17.80%). Monomicrobial growth was observed in 77.63% patients whereas polymicrobial growth was observed in 22.36% patients. Candida albicans (24.59%) and Candida tropicalis (20.49%) were the most frequent isolates among patients who underwent chemotherapy while Candida albicans (40%) and Candida Parapsilosis (26.66%) were the most frequent isolates among patients undergoing radiotherapy. Miconazole was found to be more susceptible than Fluconazole, Itraconazole, Clotrimazole among the antifungals.

Conclusion: Due to the risk of a systemic infection, it is important to recognise candidiasis as soon as possible for the clinical management of seriously unwell cancer patients. It may also aid the clinician in selecting antifungals for empirical treatment.

Keywords: Oropharyngeal, Candidiasis, Oral cancer.

INTRODUCTION

In recent years, the prevalence of mycotic infections has progressively climbed. Fungus that was originally thought to be non-pathogenic or less virulent are now recognized as an important contributor to mortality and morbidity in immunocompromised and critically ill individuals.

However, there has recently been a movement toward Candida species that are not Candida albicans. These non albicans Candida species have a lower susceptibility to antifungals than other Candida species. Emerging Candida glabrata, Candida parapsilosis, Candida tropicalis and Candida krusei are non-albicans Candida spp. can lead to both superficial infections of the oral and vaginal mucosa and more severe systemic and localized infections of deeper tissues.

The prevalence of oropharyngeal candidiasis varies around the world and it has been found to range from 20 to 75% depending on region, age of the patients and other factors.

The greater prevalence of NCA species in disease could also be due to their naturally higher level of antifungal treatment resistance. Thus the goal of the current study was to detect and isolate Candida species as well as determine antifungal susceptibility pattern among oropharyngeal cancer patients.
MATERIAL AND METHODS

Oral swabs were collected from 377 patients during the period from January 2019 to February 2021. Mouth tissue (the tongue and roof) was gently rubbed with a sterile cotton swab which was then divided into two smears: one was examined under a microscope right away for direct examination while the other was cultured on SDA medium supplemented with antibiotics (chloramphenicol) to prevent bacterial overgrowth.

The presence of yeast and pseudohyphae of Candida spp. was determined by direct examination in KOH wet mount and Gram’s staining. Standard procedures for identifying the isolated species were performed which included germ tube test, corn meal agar morphology, colony colour on Hi-crome Candida differential agar, carbohydrate assimilation technique, urea hydrolysis and growth at 45°C.

RESULTS

In the present study of the total 377 patients highest number of cases (30.23%) were observed in the age group of 41-50 years while minimum number of cases (2.65%) were within the age range of 71-80 years.

![Graph 1. Age and Gender Wise Distribution Oropharyngeal Cancer Patients.](image)

Of the total 377 samples 152(40%) samples showed growth on Sabouraud’s Dextrose agar (SDA) while 225(60%) did not show any growth on the culture media. Maximum number of patients belonged to the age group of 41-50 years (40%) and were culture positive.
Of the total 191 Candida species that were isolated majority of cases showed monomicrobial growth (77.63%) while polymicrobial growth was observed among 22.36% cases. Candida albicans (21.98%) was the prevalent isolate followed by Candida tropicalis (18.84%), Candida parapsilosis (17.80%), Candida dubliniensis (15.70%), Candida krusei (15.70%) and Candida glabrata (9.94%).

Predisposing factors like pan-masala (Tobacco), smoking and diabetes were correlated with Candida infection in oropharyngeal cancer patients. Among the pan-masala (Tobacco) eaters Candida albicans (30.61%) was the prevalent isolate followed by Candida tropicalis (22.24%), Candida parapsilosis (14.28%), Candida dubliniensis (12.24%), Candida krusei (12.24%) and the least common being Candida glabrata (8.16%). In cases among smokers Candida krusei (22.85%) was predominant followed by Candida tropicalis (20%), Candida albicans & Candida dubliniensis (17.14%), and lesser common were Candida parapsilosis and Candida glabrata (11.42%). Among the 13 diabetic patients Candida parapsilosis and Candida dubliniensis (30.76%) were the most common species isolated followed by Candida albicans and Candida krusei (15.38%) with Candida tropicalis (7.69) being the least common. Candida albicans (50%) followed by Candida parapsilosis (25%), Candida dubliniensis (12.5%) and Candida krusei (12.5%) were the common species isolated among the thyroid patients (08 patients).

Candida albicans (24.59%) followed by Candida tropicalis (20.49%) were the most common species isolated among patients undergoing Chemotherapy. Among the patients undergoing Radiotherapy Candida albicans (40%) was predominant followed by Candida parapsilosis (26.66%).
Antifungal susceptibility showed maximum sensitivity to Miconazole (69.44%) for Candida parapsilosis (70.58%) and Candida dubliniensis (86.66%) followed by Itraconazole (58.33%) for Candida tropicalis isolates. Maximum sensitivity to Ketoconazole (86.66%) was observed with Candida krusei while Candida glabrata was 100% sensitive to Amphotericin-B.

**DISCUSSION**

Candida an opportunistic pathogen is becoming a deadly illness, especially in immunocompromised patients. Oropharyngeal candidiasis is the most prevalent fungus among cancer patients and it's now known to be the most prevalent fungal infection in humans. Radiotherapy and Chemotherapy could damage immune system and create neutropenia in cancer patients resulting in Candida species colonisation in mucosal tissue, especially the oral cavity, where it can spread and produce invasive candidiasis. As a result, these patients have a greater chance of developing invasive candidiasis than the general population.

In the present study of the oral cancer cases undertaken in the study highest numbers of instances were reported in those aged 41 to 50 years. Candida albicans (21.98%) was most prevalent species isolated and among non albicans Candida, Candida
tropicalis (18.84%) was the predominant organism followed by Candida parapsilosis (17.80%), Candida dubliniensis (15.70%), Candida krusei (15.70%) and Candida glabrata (9.94%). Similar results were found in a study conducted by Betts et al., who reported non-albicans Candida tropicalis (37%) and Candida krusei (11%) to be the predominant. In another study conducted by Mehroush Maheronnaghsh, non-albicans yeasts that occurred most frequently was Candida tropicalis (9.4%), followed by Candida krusei (7%), Candida glabrata (5.4%) and Candida kefyr (2.7%). The most prominent non-albicans Candida spp. isolated are Candida glabrata followed by Candida tropicalis, Candida parapsilosis, Candida krusei and Candida kefyr are consistent with earlier studies. The non-albicans Candida spp. isolated in the study conducted by Andrew N. Davies included Candida glabrata, Candida krusei, Candida tropicalis, S. cerevisiae, Candida parapsilosis, Candida rugosa, Candida dubliniensis and Candida famata.

In our study 118 (77.63%) patients showed monomicrobial growth whereas 34 (22.36%) patients showed polymicrobial growth. However, in a study by Andrew N. Davies in most of cases (63%), a single species of yeast was isolated while in 31 (36%) cases, two species of yeast isolated and in only one (1%) case three species of yeast were obtained.

Antifungal susceptibility showed maximum sensitivity to Miconazole (69.44%) for Candida parapsilosis (70.58%) and Candida dubliniensis (86.66%) followed by Itraconazole (58.33%) for Candida tropicalis isolates. Maximum sensitivity to Ketoconazole (86.66%) was observed with Candida krusei while Candida glabrata was 100% sensitive to Amphotericin-B.

Fluconazole and Amphotericin B sensitivity of Candida albicans and non-albicans spp. like Candida tropicalis, Candida krusei and Candida glabrata has gradually reduced in recent decades according to reports. Miconazole is more vulnerable in this study than other antifungal such as Fluconazole, Itraconazole, Clotirconazole, and others which have a sensitivity pattern of less than 50% for most non albicans Candida.

Resistance to Amphotericin B was found in Candida albicans, Candida krusei and Candida glabrata spp. according to Haddadi and colleagues.

Fluconazole and Amphotericin B resistance is increasing necessitating the development of new antifungal medicines with a distinct function. Furthermore, to achieve optimal treatment response it is recommended that epidemiological trends be monitored and drug susceptibility in diverse Candida species be assessed.

Radiotherapy and Chemotherapy side effects include the establishment of antifungal resistance spp. and a hike in oral colonisation by non-albicans Candida strains.

Tolerance to azole category of antifungal medications (e.g., Fluconazole, Itraconazole) is related with non-albicans Candida species. In patients with advanced cancer several investigations have observed significant levels of isolation of non-albicans Candida spp. as well as equivalent levels of isolation of numerous yeast species.

CONCLUSION

This study has highlighted that risk factors such as immunocompromised condition, hypothyroidism, diabetes mellitus, chewing tobacco (pan-masala) and smoking were associated with oropharyngeal cancer which might also influence the growth and virulence of Candida species contributing to infection in oral cancer.

Oropharyngeal cancer patients have multisystem abnormalities and require a well systematic and executed treatment plan; thus, such preparatory methods can help progress oral cancer patient's survival rates by early diagnosis and treatment of Candida infection.

DECLARATIONS

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None.
Conflict of Interest

The authors declare that there is no conflict of interest.

Authors’ Contribution

All authors listed have made a substantial, direct, and intellectual contribution to the work, and approved it for publication.

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None.

Data Availability

All datasets analyzed in the study are included in the manuscript and presented as charts.

Ethics Statement

The study protocol was approved by the Ethics Committee, Santosh Deemed to Be University (SU/2018/528(4) and VarunArjun Medical College and Rohilkhand Hospital (VAMC&RH/655/2019).

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