A Case–Control Study to Evaluate Candidal Parameters in the Oral Cavity of Patients with Type 2 Diabetes Mellitus

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Aim: The aim of this study was to evaluate candidal parameters in the oral cavity of patients with type 2 diabetes mellitus (DM). Materials and Methods: The samples included in the study were divided into two groups: group A, comprises 50 patients with type 2 DM, and group B, comprises 30 subjects who were nondiabetic. A nonrandom consecutive sampling technique was used to enroll the subjects for the study. The $\chi^2$ test was used to examine the characteristics of the samples. Results: The results found that there is a significant difference in saliva and swab for Candida growth between patients with type 2 DM and normal healthy individuals. Swab had shown slightly more Candida growth than saliva in group A (type 2 DM). No significant variation in Candida growth was found. Candida krusei was seen in normal healthy individuals alone. In antifungal susceptibility pattern to various antifungal agents, Candida tropicalis has shown a significant result for various antifungal agents whereas Candida albicans and Candida dubliniensis did not show any significant result for various antifungal agents used in group A (patients with type 2 DM). Conclusion: Diabetic individuals who are prone to a hyperglycemic state favors the growth and establishment of Candida species. Although a smaller percentage of multidrug-resistant Candida species has been observed in the saliva of patients with type 2 DM.

KEYWORDS: Antifungal, Candida, patients with type 2 diabetic mellitus

INTRODUCTION

Diabetes mellitus (DM) is an endocrine disorder that is characterized by a relative or absolute insufficiency of insulin secretion and/or concomitant resistance to the metabolic action of insulin on target tissues. The prevalence of type 2 diabetes and impaired glucose tolerance was greater in the urban areas, which indicates the presence of a genetic basis for type 2 diabetes in the ethnic Indian population.[¹]
The studies show that diabetic patients had a higher candidal carriage rate and a variety of candidal species that were resistant to azole antifungal agents. Oral candidal colonization was significantly associated with glycemic control, type of diabetes, and pH of saliva. Although *Candida albicans* was the predominant isolate, a variety of other candidal species, with less susceptibility to azole antifungal agents, were identified in diabetics.[5]

Oral thrush is the term used to refer pseudomembranous candidiasis. Under normal circumstances, the body’s immune system keeps *C. albicans* growth under control. The candidal growth is exaggerated in immunocompromised patients. Uncontrolled diabetes and candidal infections can make life extremely uncomfortable, and in some cases, can produce serious infections.[3]

Controversy still exists whether the *Candida* species is more common in the oral cavity of diabetic patients than in nondiabetic controls and whether this is related to the oral and systemic factors. It has been unanimously seen that patients with type 2 DM have a poor oral health status, which leads to an increase in morbidity and poor glycemic control, leading to an increase in the severity of DM. Our hypothesis is that an increase in candidal load is seen in diabetic patients, which may contribute to the deterioration of oral health.[4]

**Materials and Methods**

**Study objectives**

The objectives of the study were as follows:

1. To estimate and compare the microbial parameters, namely
   a. *Candida* prevalence
   b. *Candida* load
   c. *Candida* species
   in the salivary samples of patients with type 2 DM with controls
2. To determine the susceptibility pattern of *Candida* species to various antifungal agents

**Sample and its characteristics**

The study population including patients with type 2 DM and normal healthy subjects was selected from the patients attending the outpatient department in Rajah Muthiah Dental College and Hospital and Department of Diabetology, Rajah Muthiah Medical College and Hospital, Annamalai University, Annamalai Nagar, Tamil Nadu, India.

The samples included in the study were divided into two groups: group A, comprises 50 patients with type 2 DM, and group B, comprises 30 nondiabetic subjects.

**Sampling technique**

A nonrandom consecutive sampling technique was used to collect the subjects for the study. Consecutive patients with type 2 DM visiting the outpatient department of Oral Medicine and Radiology, Rajah Muthiah Dental College and Hospital and Department of Diabetology, Rajah Muthiah Medical College and Hospital, Annamalai University, Annamalai Nagar, who qualified the diagnostic criteria, were enrolled in the study.

**Statistical tools**

In this study, the χ² test was used to analyses the collected data. The study results were derived from the *P* values obtained. The software used was Statistical Package for Social Sciences (SPSS, IBM, New York, USA), version 16.0.

**Results and Discussion**

The statistical result *P* < 0.001, which is significant, shows that there is an association in total culture, saliva, and significant *Candida* growth between type 2 DM group and normal healthy group [Table 1, Figure 1].

Table 2 shows that the *Candida* species identified 51% *C. albicans*, 38% *Candida tropicalis*, and 10% *Candida dubliniensis*, which shows that the *P* value is not significant, that is, *P* > 0.001 proves that there is a no statistically significant variation in the *Candida* species.

Table 3 and Figure 2 focusing only Candida strains belongs to type 2 DM cases and its susceptibility pattern to the antifungal all Candida strains belongs to the control group shown sensitivity to all the drugs the result is not included.

The χ² test proves that there is a significant variation and association among the various drugs related to *C. tropicalis* (*P* < 0.05), but there is no significant variation among the various drugs related to *C. albicans* and *C. dubliniensis*.

**Findings**

- Results show that there is a significant difference in saliva and swab for *Candida* growth between patients

**Table 1: The total culture result of Candida**

| S. no. | Individuals       | Total *Candida* culture positive |
|-------|-------------------|---------------------------------|
|       |                   | Saliva | Swab  |
| 1.    | Type 2 DM (*N* = 50) | 74%    | 84%   |
| 2.    | Normal healthy individuals (*N* = 30) | 60%    | 28%   |

Calculated χ² value = 39.56, degrees of freedom = 3, *P* value = 0.0000 (significant)
Discussion

DM is a metabolic disease commonly manifested in adults and frequently associated with many risk factors. Various factors have been associated with oral carriage of yeast in diabetic patients, such as the type and duration of disease and the degree of glycemic control. In patients with uncontrolled type 2 DM, salivary flow and pH contribute to yeast colonization, which leads to an increase in the candidal carriage rate. Some controversy still remains regarding the role of diabetes in the colonization of the oral cavity by yeasts.

To the best of our knowledge, the research carried out in India, especially in South India, pertaining to the oral Candida carriage rate among individuals with diabetes seem to be rare. So, with the available research information, after performing a thorough discussion, we selected the current topic “A Case–Control Study to Evaluate Candidal Parameters in the Oral Cavity of Type 2 Diabetes Mellitus Patients” in view of evaluating the oral Candida carriage rate in the patients with type 2 DM in and around Chidambaram.

According to the criteria for the evaluation of the infective nature of the Candida species, the formation or the presence of pseudohyphae is considered as the
infective status of *Candida*. In this study, we could not predict the infective nature of the *Candida* species in patients with type 2 DM because they were clinically normal and did not show any signs and symptoms of candidiasis. So, to have a better vision in this field, a more detailed future study is essential.

From our constant study performed in patients with type 2 DM (50 samples), we found that the saliva of 74% of patients with DM contains *Candida*, which was proved by *Candida* culture, whereas saliva of 23% from nondiabetic healthy controls contains *Candida*. So for research with *Candida* carriage rate with normal healthy individuals were not touched high-level percentage, which we could be able to record. The reason could be the number of subjects in normal control population may show the higher percentage of *Candida* carriage rate, which may again account individuals’ geographic *Candida* distribution and food habit.

As *Candida* is the normal inhabitant of the oral cavity, we must evaluate the colonization or the infective status of the *Candida* in patients with type 2 DM to rule out the *Candida* carriage rate. Because of the presence of *Candida* as a normal oral flora, *Candida* colonization and asymptomatic carriage were determined by analyzing the *Candida* load. In this study, the colony-forming efficiency was assessed by *Candida* growth with respect to the number of colonies [Table 2]. Again the number of CFU of *Candida* was expressed as significant if it was >10 colonies, and if it was <10 colonies, it was considered as insignificant growth. Of the 50 patients with type 2 DM, 16 yielded significant *Candida* growth; among 16 patients, 4 (25%) showed 100 colonies, 5 (31%) showed heavy growth, and 7 (44%) showed confluent growth. Whereas of the four controls, three (17%) showed 10 colonies and one (5%) showed 10–25 colonies. The *Candida* load between patients with DM and the controls was found to be statistically significant with a *P*-value of <0.01.

Kadir *et al.*[^6^] have reported that the oral *Candida* carriage rate and density of *Candida* species were comparatively higher in the patients with diabetes than in the control participants. In our study, we have neither investigated nor included the aforementioned local etiologic and systemic factors.

We also found that *C. krusei* was isolated only from the normal healthy individuals and not from the patients with type 2 DM. This may be due to the nature of *C. krusei* affinity toward the normal salivary pH or the normal condition of the saliva (nonhyperglycemic).

Sashikumar *et al.*[^7^] concluded that salivary glucose concentration is a potentially useful noninvasive tool to monitor glycemic control in diabetic patients. The presence of increased oral *Candida* is common in patients with higher salivary glucose level.

Al-Attas and Amro[^2^] identified a variety of other *Candida* species, with less susceptibility to azole antifungal agents, in patients with diabetes.
Bhuyan and Hassan\textsuperscript{[8]} reported that a comparatively low number of non-albicans were seen in healthy individuals. \textit{Candida albicans} showed increased resistance to fluconazole in patients with DM. Other species showed a variable sensitivity pattern.

Mathew Fenn \textit{et al.}\textsuperscript{[8]} showed that a higher candidal CFU is common in the uncontrolled diabetic patients group.

**CONCLUSION**

This study concludes that diabetic individuals are prone to a hyperglycemic state, which in turn favors the growth and establishment of \textit{Candida} species. Although a smaller percentage of multidrug-resistant \textit{Candida} species has been observed in the saliva of patients with type 2 DM, it is prudent to consider prophylactic measures in such patients. We suggest extensive and elaborative studies in the future to either support or refute our results.

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**Conflicts of interest**

There are no conflicts of interest.

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