THE INCIDENCE OF ORAL CANDIDIASIS IN PATIENTS WITH DIABETES MELLITUS: A CROSS-SECTIONAL STUDY IN SOUTHERN VIETNAM

Thoai Dang Nguyen1,2*, Tram Thi Huyen Nguyen2,2*, Quang Vinh Tran1

1 Faculty of Pharmacy, Pham Ngoc Thach University of Medicine, Ho Chi Minh City 700000, Vietnam.
2 Department of Pharmacy, Ear-Nose-Throat Hospital in Ho Chi Minh city, Ho Chi Minh City 700000, Vietnam.
2* These authors contributed equally to this work and are co-first author.

*Corresponding Author: Thoai Dang Nguyen (PhD.)
Faculty of Pharmacy, Pham Ngoc Thach University of Medicine, Ho Chi Minh City 700000, Vietnam.
Email: thoaind@pnt.edu.vn

Received: 17.12.2019 Revised: 19.01.2020 Accepted: 21.02.2020

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder marked by elevated levels of blood sugar. There are currently 2 main etiologies of diabetes i.e. the hypo-secretion of insulin from pancreas and the reduced sensitivity of body cell toward insulin [1]. Diabetes has three main subtypes. Type 1 DM (juvenile diabetes) mostly occurred in young people below the age of 30 years. This is due to hypo secretion of insulin from the beta cell of pancreas. Type 2 DM (adult onset diabetes) often occurred in obese patient above the age of 30 years. This is due to decrease sensitivity of body cells toward the insulin. Gestational diabetes occurred in the pregnant women without the prior history of diabetes. In 2017, the prevalence of adult-onset diabetes globally (20–79 years) was equal to 425 million, and by 2045 the World Health Organization and the International Diabetes Federation predicted that the percentage of adults with diabetes worldwide will rise by approximately 629 million [2, 3]. Studies carried out in 2015 have shown that 415 million people worldwide had diabetes with type 2 diabetes affecting 90 percent of people [4]. Comparison of recent research reveals that diabetes prevalence continues to rise quickly. Diabetes raises death risk by 2-fold. Between 2012 to 2015, there were about 1.5 to 5.0 million mortality due to diabetes each year [5]. Diabetes increased the risk of complication including both micro and macro vascular complications. Macro vascular complications involve diabetic neuropathy, diabetic nephropathy, heart diseases, stroke and peripheral arterial disease. In micro vascular complications patient cutaneous manifestation are much important and in above group infection especially fungal infection are more frequent. Oral candidiasis is the most severe fungal infection of diabetic patients, found in the oral cavity with the wipeable white plaques, i.e. tongue buccal mucosa, palate, gingivae and mouth surface [6].

Different studies conducted nationally and internationally to find out the different factors for oral fungal infection in the diabetic patients. The connection between hyperglycemia and Candida’s infection has been studied extensively. However, this issue is underexplored in Vietnamese context. This study aimed to investigate the incidence of oral candidiasis among patients with type-II diabetes admitted to hospitals in southern Vietnam.

PATIENTS AND METHODS

Study design
A cross-sectional study was conducted in five healthcare centers, including primary medical centers, clinics and hospital, which were located in Long An province in southern Vietnam.

Results:
There were significant associated of age and duration of diabetes on the risk of candida infection. The older the patient is and the longer they suffered from diabetes, the higher probability they get candidiasis (p<0.05).

Conclusion:
The incidence of oral fungal infection especially candidiasis increased with the duration of diabetes along with poor glycemic control and with the higher age group of the patients.

Keywords: Candidiasis, diabetes mellitus, oral hypoglycemic, insulin.

© 2019 by Advance Scientific Research. This is an open-access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/)
DOI: http://dx.doi.org/10.31838/jcr.07.04.17
The incidence of oral candidiasis in patients with diabetes mellitus: A cross-sectional study in southern Vietnam

Study subjects
Patients with diabetes mellitus, including all types, were enrolled for the data collection. From July 2019 to December 2019, total sampling method was applied. Patients who previously diagnosed with diabetes, hospitalized due to all-cause, and volunteer to participated was included. Exclusion criteria was infection with other fungi not Candida sp. Interviewers invited the patients join the study when they are waiting for their prescription or for their pharmaceuticals. The questionnaire was self-design, including characteristics of patients with discrete choice. Clinical information was extracted from their medical records.

Data analysis
Microsoft Excel for Window version 2010 was used for data management. Descriptive statistics and logistics regression was performed by SPSS version 20.0. The independent variables were patients demographical and clinical characteristics. The dependent variable was the probability of candidiasis (with or without Candida sp. infection).

RESULTS
Total 305 patients were recruited in the study, out of which 190 were male and 115 were female. Mean age of the patients was 56.82±5.64 (Table 1).

Table 1. Characteristics of diabetes patients (N=305)

| Characteristic                      | N(%)        |
|------------------------------------|-------------|
| **Age (years old)**                |             |
| Mean (standard deviation)          | 56.8±5.6    |
| Median (interquartile range)       | 55 (50-66)  |
| Min-Max                            | 39-80       |
| <45                                | 89 (29.2)   |
| 45-60                              | 135 (44.3)  |
| ≥60                                | 81 (26.6)   |
| **Gender**                         |             |
| Male                               | 190 (62.3)  |
| Female                             | 115 (37.7)  |
| **Residence**                      |             |
| Rural                              | 136 (44.6)  |
| Urban                              | 169 (55.4)  |
| **Type of diabetes**               |             |
| Type 1                             | 67 (22.0)   |
| Type 2                             | 238 (78.0)  |
| **Therapies**                      |             |
| Lifestyle change only              | 7 (2.3)     |
| Oral hypoglycemia agents           | 145 (47.5)  |
| Insulin                            | 111 (36.4)  |
| OHAs + insulin                     | 42 (13.8)   |
| **History of diabetes (year(s))** |             |
| <5                                 | 69 (22.6)   |
| 5-10                               | 67 (22)     |
| 10-15                              | 117 (38.4)  |
| ≥15                                | 52 (17.0)   |
| **Comorbidity**                    |             |
| None                               | 4 (1.3)     |
| Respiratory diseases               | 15 (4.9)    |
| Cardiovascular diseases            | 124 (40.7)  |
| Psychology diseases                | 7 (2.3)     |
| Gastrointestinal diseases          | 59 (19.3)   |
| Kidney diseases                    | 98 (32.1)   |
| Other discomforts                  | 9 (3.0)     |

Note: Data presented as n (%) unless state otherwise
The incidence of oral candidiasis in patients with diabetes mellitus: a cross-sectional study in Southern Vietnam

Figure 1 shows the difference in demographical and clinical characteristics of patients between two groups. The contribution of these factors on the probability to be candidiasis is tabulated in Table 2. There were significant associated of age and duration of diabetes on the risk of candida infection. The older the patient is and the longer they suffered from diabetes, the higher probability they get candidiasis (P<0.05).

Table 2. Logistic regression

| Category                                | OR (95% CI)   | P-value |
|-----------------------------------------|--------------|---------|
| Age (years old)                         |              |         |
| <45                                     | 1            |         |
| 45-60                                   | 1.56 (1.23 – 1.89) | 0.002  |
| ≥60                                     | 1.73 (1.58 – 2.45) | 0.014  |
| Gender                                  |              |         |
| Male                                    | 1            |         |
| Female                                  | 1.56 (0.97 – 2.09) | 0.073  |
| Residence                               |              |         |
| Rural                                   | 1            |         |
| Urban                                   | 0.89 (0.54 – 2.32) | 0.127  |
| Type of diabetes                        |              |         |
| Type 1                                  | 1            |         |
| Type 2                                  | 0.23 (0.02 – 1.03) | 0.089  |
| Therapies                               |              |         |
| Lifestyle change only                   | 1            |         |
| Oral hypoglycemia agents                | 1.23 (1.04 – 2.45) | 0.065  |
| Insulin                                 | 1.45 (0.98 – 1.98) | 0.102  |
| OHAs + insulin                          | 1.23 (0.73 – 1.49) | 0.003  |
| History of diabetes (year(s))           |              |         |
| <5                                      | 1            |         |
| 5-10                                    | 1.12 (1.02 – 1.98) | 0.045  |
| 10-15                                   | 1.45 (1.34 – 1.65) | 0.001  |
| ≥15                                     | 1.78 (1.39 – 2.03) | 0.007  |
| Comorbidity                             |              |         |
| None                                    | 1            |         |
| Respiratory diseases                    | 2.45 (2.03 – 3.09) | 0.003  |
| Cardiovascular diseases                 | 0.99 (0.56 – 1.43) | 0.236  |
| Psychology diseases                     | 1.01 (0.65 – 3.04) | 0.346  |
| Gastrointestinal diseases               | 0.56 (0.23 – 0.97) | 0.098  |
| Kidney diseases                         | 4.01 (3.04 – 5.60) | 0.005  |
| Other discomforts                       | 0.12 (0.01 – 1.34) | 0.128  |

Note: Data presented as n (%) unless state otherwise

Figure 1. Difference in characteristics of patients with and without candidiasis
DISCUSSION

Oral candidiasis is growing in prevalence, being one of the most serious fungal infections [17]. Differential forms of mucosal alterations such as erythematous, pseudomembranous, and curd-like plaques (biofilms) can be treated with oral candidiasis [18, 19]. In patients with type 1 DM, higher Candida sp. colonization levels were registered relative to patients with type 2 DM (84% vs. 68% respectively), while in non-diabetic patients the figure was about 27% [16]. Candida sp. has particular characteristics. Several studies have identified a correlation between development of hydrolytic enzymes and an increase of Candida’s pathogenic capacity [20, 21]. Biofilms are microorganism populations that are found in extracellular matrix [22, 23]. That confer significant antifungal resistance and improved immune responses of the host [24, 25][26, 27]. Because hydrophobic interactions seem crucial for the promotion of tissue invasion by Candida’s mycelial process.

Benefit factors for the disease are nuanced, but it is known that tongue lesions, tobacco using, denture wearing (e.g. diabetes) directly influence oral Candida sp. delivery and the development of oral candida infection [28-34]. The above results show that the increasing age is the important risk factor of developing oral fungal infection in diabetic patients. However, there are various studies in which this trend is not well appreciated. Relationship among the duration of diabetes and oral infection in not well established [4]. In the study done by Lamey et al. [35] no association was found between the duration of illness and oral fungal infection. However, in the study mentioned above there is significant relation is showed between the duration and frequency of illness. The frequency goes on increasing with the increase in the duration of diabetes.

In this study the type of treatment plans whether the patient is on oral hypoglycemic or using insulin is not well noted. Similarly gender based difference have not been noted in this study. The incidence of oral candidiasis in various studies is noted more in the diabetes type 1 as compared to diabetes type 2. Other contributory factors include the poor glycemic control of patient gender and type of treatment i.e. oral hypoglycemic or insulin, related association was not found is this study.

CONCLUSION

The frequency of oral candidiasis was well associated with the duration of diabetes mellitus and age of the patient. Gender and type of treatment i.e. oral hypoglycemic or insulin, related association was not found is this study.

CONFLICTS OF INTERESTS

The authors have no conflicts of interests to declare.

FUNDING

None.

REFERENCES

1. Alanazi, N.H., et al., Prevalence of diabetes and its relation with age and sex in Turaf city, northern Saudi Arabia in 2016–2017. Electronic physician, 2017. 9(9): p. 5294.
2. King, H., R.E. Aubert, and W.H. Herman, Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. Diabetes care, 1998. 21(9): p. 1414-1431.
3. Agarwal, S., et al., Sankara Nethralaya—Diabetic Retinopathy Epidemiology and Molecular Genetic Study (SN—DREAMS 1): Study Design and Research Methodology. Ophthalmic epidemiology, 2005. 12(2): p. 143-153.
4. World Health Oranganization, Diabetes Fact sheet N°312. 2014, World Health Oraganization: Geneva.
5. World Health Oraganization, About diabetes. 2019, World Health Oraganization: Geneva.
6. Shi, Y. and F.B. Hu, The global implications of diabetes and cancer. Lancet (London, England), 2014. 383(9933): p. 1947.
7. Davenport, J., The oral distribution of candida in denture stomatitis. Brit. dent. J., 1970. 129(4): p. 151-156.
8. International Diabetes Federation, Annual Report 2014. 2014.
9. Darwazeh, A., et al., The relationship between colonisation, secretor status and in-vitro adhesion of Candida albicans to buccal epithelial cells from diabetics. Journal of medical microbiology, 1990. 33(1): p. 43-49.
10. Brownlee, M., A. Cerami, and H. Vlassara, Advanced glycosylation end products in tissue and the biochemical basis of diabetic complications. New England Journal of Medicine, 1988. 318(20): p. 1315-1321.
11. Kadir, T., et al., Mycological and cytological examination of oral candidal carriage in diabetic patients and non-diabetic control subjects: thorough analysis of local aetiologic and systemic factors. Journal of oral rehabilitation, 2002. 29(5): p. 452-457.
12. Tang, H.J., et al., Epidemiology and prognostic factors of candidemia in elderly patients. Geriatrics & gerontology international, 2015. 15(6): p. 688-693.
13. Belazi, M., et al., Candidal overgrowth in diabetic patients: potential predisposing factors. Mycoses, 2005. 48(3): p. 192-196.
14. Gonçalves, R.H.P., et al., Species diversity of yeast in oral colonization of insulin-treated diabetes mellitus patients. Mycopathologia, 2006. 162(2): p. 83-89.
15. Gullauxooue, O., et al., Attributable mortality of nosocomial candidemia, revisited. Clinical Infectious Diseases, 2003. 37(9): p. 1172-1177.
16. Kumar, B., et al., Prevalence of Candida in the oral cavity of diabetic subjects. The Journal of the Association of Physicians of India, 2005. 53: p. 599-602.
17. Akpan, A. and R. Morgan, Oral candidiasis. Postgraduate medical journal, 2002. 78(922): p. 455-459.
18. Neville, B., et al., Fungal and protozoal diseases. Oral & Maxillofacial pathology: Filadélia, 1995.
19. Rajendran, R., Shafter's textbook of oral pathology. 2009: Elsevier India.
20. Bramono, K., et al., Comparison of proteinase, lipase and alpha-glucosidase activities from the clinical isolates of Candida species. Japanese journal of infectious diseases, 2006. 59(2): p. 73.
21. Ingham, C., et al., Rapid susceptibility testing and microcolony analysis of Candida spp. cultured and imaged on porous aluminum oxide. PLoS One, 2012. 7(3).
22. Constorton, J.W., et al., Microbial biofilms. Annual review of microbiology, 1995. 49(1): p. 711-745.
23. Donlan, R.M. and J.W. Constorton, Biofilms: survival mechanisms of clinically relevant microorganisms. Clinical microbiology reviews, 2002. 15(2): p. 167-193.
24. Forseea, E., et al., Effects of fluconazole on Candida glabrata biofilms and its relationship with ABC transporter gene expression. Biofouling, 2014. 30(4): p. 447-457.
25. Rodrigues, C.F., S. Silva, and M. Henriques, Candida glabrata: a review of its features and resistance. European journal of clinical microbiology & infectious diseases, 2014. 33(5): p. 673-688.
26. Silva-Dias, A., et al., Adhesion, biofilm formation, cell surface hydrophobicity, and antifungal planktonic susceptibility: relationship among Candida spp. Frontiers in microbiology, 2015. 6: p. 205.
27. De Groot, P.W., et al., The cell wall of the human pathogen Candida glabrata: differential incorporation of novel
adhesin-like wall proteins. Eukaryotic cell, 2008. 7(11): p. 1951-1964.

28. Al Mubarak, S., et al., The prevalence of oral Candida infections in periodontitis patients with type 2 diabetes mellitus. Journal of infection and public health, 2013. 6(4): p. 296-301.

29. Javed, F., et al., Periodontal conditions, oral Candida albicans and salivary proteins in type 2 diabetic subjects with emphasis on gender. BMC Oral Health, 2009. 9(1): p. 12.

30. Lamey, P.J., et al., Secretor status, candidal carriage and candidal infection in patients with diabetes mellitus. Journal of Oral Pathology & Medicine, 1988. 17(7): p. 354-357.

31. Mulu, A., et al., Frequent detection of 'azole resistant Candida species among late presenting AIDS patients in northwest Ethiopia. BMC infectious diseases, 2013. 13(1): p. 82.

32. Goregen, M., et al., Median rhomboid glossitis: a clinical and microbiological study. European Journal of dentistry, 2011. 5(04): p. 367-372.

33. Arendorf, T. and D. Walker, Tobacco smoking and denture wearing as local aetiological factors in median rhomboid glossitis. International journal of oral surgery, 1984. 13(5): p. 411-415.

34. Flaitz, C., C. Nichols, and M. Hicks, An overview of the oral manifestations of AIDS-related Kaposi's sarcoma. Compendium of continuing education in dentistry (Jamesburg, NJ: 1995), 1995. 16(2): p. 136-8, 140, 142 passim; quiz 148.

35. Rodrigues, C.F., M.E. Rodrigues, and M. Henriques, Candida sp. Infections in patients with diabetes mellitus. Journal of clinical medicine, 2019. 8(1): p. 76.