DOI: *http://dx.doi.org/10.22122/johoe.v10i1.1109* *Published by Vesnu Publications*

Received: 20 Sep. 2020 **Accepted: 15 Nov. 2020**

Periodontal status and patient characteristics in oral mucosal malignant and benign lesions: A preliminary study

Ceyda Gurhan[1], Ozgun Ozcaka PhD[2], Pelin Guneri PhD[3], Hayal Boyacioglu PhD[4]

Original Article

Abstract

BACKGROUND AND AIM: Head and neck cancers are the sixth most common type of cancers in the world and it has been emphasized that chronic inflammation may be associated with carcinogenesis in recent years. In the present study, the purpose is to investigate the patient characteristics and the periodontal health status of patients with malignant and benign oral mucosal lesions.

METHODS: 34 patients with suspicious mucosal lesions were registered. The patients' demographic variables, tobacco use, and clinical periodontal measurements such as probing pocket depth (PD), plaque index (PI), and bleeding on probing (BOP) were established for statistical analysis. All lesions were stained using Toluidine blue solution in order to determine the biopsy site and punch biopsy was performed prior to the histological examination. The patients' test parameters including demographic variables, tobacco use, and clinical periodontal measurements were statistically analyzed for benign and malignant groups. T-test, chi square, and Fisher's exact tests and logistic regression test were utilized for data analyses using SPSS program. The level of significance was set at P = 0.050.

RESULTS: 34 patients [15 (44.0%) females and 19 (56.0%) males] with suspicious oral mucosal lesions were enrolled into the study. Of the 34 lesions, 8 (23.5%) were histologically diagnosed as malignant whereas 26 (76.5%) were benign. Although periodontal parameters and tobacco use were clearly granted higher scores in the malignant group, the logistic regression analysis revealed that none of the variables were influential on the diagnosis of the lesions [gender (P = 0.487), age (P = 0.891), duration of the lesion (P = 0.526), lesion localization (P = 0.356), tobacco use (P = 0.873), pocket depth (P = 0.741), plaque index (P = 0.672), bleeding index (P = 0.707)].

CONCLUSION: Despite the fact that the present study did not report statistically significant results, meaningful values related to tobacco use and periodontal measurements were observed in the patients with malignant mucosal lesions when compared to those with benign mucosal lesions.

KEYWORDS: Carcinogenesis; Head and Neck; Neoplasms; Inflammation; Oral Cancer; Periodontal Diseases

Citation: Gurhan C, Ozcaka O, Guneri P, Boyacioglu H. **Periodontal status and patient characteristics in oral mucosal malignant and benign lesions: A preliminary study.** J Oral Health Oral Epidemiol 2021; 10(1): 37-42.

One of the of malignancies, which have a highest global incidence rate, is head and neck cancers and it has been conveyed as a major global health problem.[1,2] Moreover, this health problem was included among the prior action plans of the World Health Organization (WHO).[3] Although the most known etiologic factors related to oral cancers are classically tobacco use, alcohol consumption, and poor diet, it has been emphasized that chronic inflammation may be associated with carcinogenesis in recent years.[4,5] Periodontitis is a chronic inflammation of the supporting structures around the teeth which causes the connective tissue, attachment, and alveolar bone loss and globally, it affects approximately 50% of the population.[6] Many

1- Department of Oral and Maxillofacial Radiology, School of Dentistry, Ege University, Izmir, Turkey
2- Professor, Department of Periodontology, School of Dentistry, Ege University, Izmir, Turkey
3- Professor, Department of Oral and Maxillofacial Radiology, School of Dentistry, Ege University, Izmir, Turkey
4- Associate Professor, Department of Statistics, School of Science, Ege University, Izmir, Turkey
Address for correspondence: Ceyda Gurhan; Department of Oral and Maxillofacial Radiology, School of Dentistry, Ege University, Izmir, Turkey; Email: cydgrhn@gmail.com

factors such as socioeconomic level, income status of individuals, access to health services, and level of education are directly associated with the individual oral hygiene level, as well as incidence and prevalence of oral diseases such as dental caries, periodontal diseases, tooth loss, and oral cancer.[7] Moreover, the stated prevalence rates vary in accordance with the level of development of nations, and not surprisingly, there is a higher prevalence of periodontal and gingival disease among developing nations compared to the developed countries.[7]

In recent years, numerous comprehensive studies have been accomplished that explored the relationship between periodontal diseases and malignancy such as prostate, breast, and head and neck cancers.[4,5,7-19] A lot of these studies have reported that there may be a linkage between periodontal disease and oral cancer, especially due to the presence of similar inflammatory mediators between these two pathologies.[4,5,9-19]

Messenger mediators such as interleukin-1 beta (IL1-ß) and necrosis factor-alpha (TNF-α), which organize the inflammatory response, have been similarly released in both inflammation and the first phase of carcinogenesis. Additionally, deep gingival pockets and excessive plaque accumulation may serve as host for possible oncogenic bacterial (e.g. porphyromonas gingivalis) and viral pathogens [e.g. uman papillomavirus (HPV)]. It has been noticed that reactive oxygen species (ROS) and reactive nitrogen species (RNS) emerging during inflammation process may cause mutagenic deoxyribonucleic acid (DNA) damages. In summary, comprehensive studies investigating a possible relationship between periodontal diseases and oral cancer concluded that infections may increase this risk via triggering cell proliferation, inhibiting apoptosis, interfering with cellular signaling mechanisms, and up-regulating tumor promoters.[4,5,9-19]

The goal of this study is to assess the periodontal health status of patients with suspicious oral mucosal lesions who were referred for evaluation of their oral lesions.

Methods

The case-control study protocol was accepted by the Ethics Committee, School of Medicine, Ege University, Izmir, Turkey (protocol no. 16-2/47). Full accordance to Declaration of Helsinki (DoH) as revised in 2008 was provided throughout the study. The patients who applied to Outpatient Clinic, School of Dentistry, Ege University between January 2019 and March 2019 were involved in the present study. The 34 individuals with suspicious oral lesions clinically diagnosed as oral potentially malignant disorders (OPMDs) or malignant lesions or lesions that required an incisional biopsy for definitive diagnosis were included into the study. The study protocol was explained to the subjects and an informed written consent was received from them before enrollment. The subjects who reported a history of local or systemic treatment for the lesion (topical or systemic medications, radiation therapy, chemotherapy) and a systemic contraindication for punch biopsy, and patients with periodontal treatment within six months were excluded from the study.

The patients' demographic data and duration and location of the lesions were recorded. Thorough extra- and intra-oral examinations of the patients were performed by an expert on oral mucosal lesions [pyoderma gangrenosum (PG)] using dental unit light and routine dental instruments.

Bleeding on probing (BOP), plaque index (PI), and probing pocket depth (PD) were measured at four sites (mesio-buccal, mid-buccal, disto-buccal, mid-lingual) of each tooth present, excluding the third molars. BOP was deemed positive if it occurred within 15 seconds following periodontal probing. Visible plaque accumulation was recorded dichotomously. Periodontal measurements were recorded using a manual Williams periodontal probe that has circumferential lines at 1, 2, 3, 5, 7, 8, 9, and

10 mm. All clinical measurements were assessed by a single periodontologist (OO).

After two weeks from removal of potential relevant agents (factors that might be associated with traumatic and inflammatory alterations including ill-fitting dentures, non-hygienic restorations, orthodontic brackets, cheek biting), all lesions were re-examined and were stained with 1% toluidine blue solution to determine the biopsy site, as described previously[20] by a clinician experienced in vital staining procedures (CG). The punch biopsy samples were obtained from the dark stained areas of the lesion.

Under local anesthesia, the punch biopsy was executed with a 5 mm punch (Kai Europe GmbH, Solingen, Germany) by the periodontologist (OO). The biopsy sample was placed in 10% formalin glass tube and the material was transferred to the pathology laboratory. The diagnoses of severe dysplasia, carcinoma-in-situ, or squamous cell carcinoma (SCC) were classified as malignant, whereas no, mild, and moderate dysplasia were considered as benign.[21]

Quantitative variables were analysed by t-test as mean ± standard deviation (SD), and for qualitative variables, chi-square and Fisher's exact tests were peformed. The differences between the test parameters of the patients and the lesions in malignant and benign groups were determined with logistic regression test. P = 0.050 was adopted as the significance level.

Results

A total of 34 individuals, 15 (44.0%) females and 19 (56.0%) males were enrolled. Of the 34 lesions, 8 (23.5%) were histologically diagnosed as malignant, whereas 26 (76.5%) were benign. The patient and lesion characteristics and histological diagnoses of the lesions in the study are outlined in table 1.

The mean age of the patients with malignant and benign lesions was 54.3 ± 19.6 and 55.9 ± 14.5 years, respectively. Nevertheless, this difference was not significant (P = 0.827). Both in benign and malignant groups, males presented more lesions (53.3% and 62.5%, respectively), but the gender variation did not reach statistical significance (P = 0.735).

Of the 34 patients, the lesion duration was more than 4 weeks in 23 (67.6%) patients, whereas it was between 2 to 4 weeks in 7 (20.6%) cases. Unfortunately, 4 (11.8%) individuals were unaware of their lesions. The duration was more than 4 weeks in 83.30% of the malignant lesions, whereas this was 70.83% in the benign group, but this difference was not statistically significant (P = 0.084) (Table 1).

Lesions were observed similarly both at the non-keratinized and keratinized mucosa: 17 were reported at the non-keratinized tissues [9 (26.5%) at the buccal mucosa, 4 (11.8%) at the floor of the mouth, 1 (2.9%) at the fornix, and 3 (8.8%) at the lateral tongue]. The remaining 17 were observed at the keratinized mucosa; 5 (14.7%) were at the alveolar mucosa, 3 (8.8%) at the palatal, 3 (8.8%) at retromolar mucosa, and 6 (17.6%) at the tongue.

Most of the benign lesions (53.8%) were located at the keratinized oral mucosa, whereas 62.5% of malignant lesions were observed at the non-keratinized oral mucosa; however, no significant differences were observed between the location of the lesions and diagnosis (P = 0.263) (Table1).

The patients with malignant lesions used more tobacco (14.4 ± 12.9 per day) than those with benign lesions (7.69 ± 7.9 per day), but without statistical significance (P = 0.164). In the malignant group, the mean pocket depth, plaque index, and bleeding index were 4.16 ± 0.79 mm, 59.62 ± 26.56, and 63.13 ± 28.77, respectively. In the benign lesions group, the mean pocket depth, plaque index, and bleeding index were 3.70 ± 1.18 mm, 47.96 ± 21.32, and 50.38 ± 23.19, respectively. Although higher scores for periodontal parameters were assessed in the malignant group, the differences were not significant ($P_{\text{pocket depth (mm)}} = 0.327$, $P_{\text{plaque index}} = 0.110$, $P_{\text{bleeding index}} = 0.120$) (Table 2).

Table 1. A summary of demografic variables, patient characteristics, and histological diagnoses of the lesions

Gender	Age (year)	Duration	Lesion region	Histology (gold standard)
Male	55	> 4 weeks	Fornix mucosa	Lupus erythematosus
Male	67	> 4 weeks	Buccal mucosa	Squamous hyperplasia
Male	52	> 4 weeks	x	Carcinoma in situ
Female	65	> 4 weeks	FOM	Carcinoma in situ
Female	72	> 4 weeks	x	SCC
Female	69	x	x	SCC
Male	22	2-4 weeks	Lateral tongue	SCC
Female	55	> 4 weeks	x	Squamous metaplasia
Male	40	x	x	Verrucous hyperplasia
Male	47	x	x	Adenoid cystic carcinoma
Female	61	> 4 weeks	FOM	Squamous hyperplasia
Male	55	> 4 weeks	Alveolar crest	SCC
Female	35	2-4 weeks	Buccal mucosa	Erosive lichen planus
Female	73	x	Alveolar crest	Carcinoma in situ
Male	40	> 4 weeks	Lateral tongue	Squamous hyperplasia
Male	22	> 4 weeks	Tongue, buccal mucosa	Squamous hyperplasia
Male	61	> 4 weeks	Alveolar crest	Squamous hyperplasia
Female	66	> 4 weeks	Palatine mucosa	Lichenoid reaction
Female	68	> 4 weeks	Tongue	Lichen planus
Female	78	> 4 weeks	Tongue, buccal mucosa	Lichen planus
Male	60	2-4 weeks	Tongue	Ulcerous inflammation
Male	64	2-4 weeks	Palatine mucosa	Nonspecific ulcerous inflammation
Male	55	> 4 weeks	Tongue	Erosive lichen planus
Female	51	> 4 weeks	Retromolar region	Squamous intraepithelial neoplasia 1
Male	73	2-4 weeks	FOM	Squamous intraepithelial neoplasia 2
Male	59	2-4 weeks	Tongue	Non-specific (lymphocyte infiltration+mildfibrosis)
Female	57	> 4 weeks	Buccal mucosa	Squamous hyperplasia
Male	68	> 4 weeks	Buccal mucosa	Lichen planus
Female	60	> 4 weeks	FOM	Squamous hyperplasia
Male	36	> 4 weeks	Buccal mucosa	SCC
Female	81	> 4 weeks	Retromolar region	SCC
Male	29	2-4 weeks	Buccal mucosa	Squamous hyperplasia
Male	32	> 4 weeks	Retromolar region	Squamous hyperplasia

FOM: Floor of the mouth; SCC: Squamous cell carcinoma

All tested parameters were placed in a statistical model to determine the factors which were significantly important on the diagnostic efficacy of the test methods. The logistic regression analysis revealed that none of the variables were influential on the diagnosis of the lesions: [gender (P = 0.487), age (P = 0.891), duration of the lesion (P = 0.526), lesion localization (P = 0.356), tobacco use (P = 0.873), pocket depth (P = 0.741), plaque index (P = 0.672), bleeding index (P = 0.707)].

Table 2. Statistical analyses of age, tobacco use, and clinical periodontal measurements including probing pocket depth (PD), plaque index (PI), and bleeding on probing (BOP)

		Age	Tobacco (per day)	PD (mm)	PI	Bleeding index
Malignant	n	8	8	8	8	8
	Mean ± SD	54.30 ± 19.56	14.38 ± 12.94	4.16 ± 0.79	59.62 ± 26.56	63.13 ± 28.77
Benign	n	26	26	26	26	26
	Mean ± SD	55.92 ± 14.51	7.69 ± 7.90	3.70 ± 1.18	47.96 ± 21.32	50.38 ± 23.19
P		0.827	0.164	0.327	0.110	0.120
Total	n	34	34	34	34	34
	Mean ± SD	55.53 ± 15.53	9.26 ± 9.55	3.81 ± 1.11	50.71 ± 22.78	53.38 ± 24.76

PD: Pocket depth; PI: Plaque index

Discussion

The results of the present study revealed that distribution of age and gender was nearly homogeneous in malignant and benign groups. In contrast to the basic concept that "oral malignant lesions are more common among older patients and males", age and gender have not been observed as the predictors in assessment of the nature of oral mucosal lesions in some recent studies, and it has been emphasized that the frequency of oral cancer has been increased both among young populations and female individuals.[22,23] So, it can be claimed that our results are associated with this changing trend regarding patients' age and gender.

The present paper reported that the lesion duration was more than 4 weeks in 67.6% of all patients and in 83.3% of the malignant lesions. It was assumed that delays in diagnosis of oral malignant lesions may occur when the severity of the patient's pain is low or the frequency of individual's dental visits is rare.[24]

For 90% of head and neck cancer; tobacco use, poor diet, and alcohol consumption have been revealed as predisposing factors in literature,[25] and it has been emphasized that 75% of patients with oral cancer in the United States of America smoke.[26] Based on the results, tobacco use that is well established etiologic factors for the development of oral cancer in literature was nearly 2-times higher in malignant group and this finding was consistent with the literature.

Pocket depth, plaque index, and bleeding index were measured in both benign and malignant groups in the present study. Even though no statistically significant differences were observed between the periodontal measurements of the patients with benign lesions and oral cancer, higher periodontal measurements were established in the malignant group. This finding was in agreement with the literature and has shown that periodontal diseases may be increased among the patients with oral cancer. Beside alcohol consumption, tobacco use, and inadequate diet, poor oral hygiene and periodontal disease may contribute to the development of oral cancers.[4,5,9-19] Unfortunately, the number of our patients was too small to reach a statistical conclusion, and the sample size needs to be increased in further investigations.

Despite the small sample size which was the main limitation of the present study, there were some strengths. Firstly, staining mucosal lesion with toluidine blue solution before punch biopsy positively affected the determination of the biopsy site, and consequently, the accuracy of diagnosis and histological examination. In addition, performing clinical periodontal measurements at four different sites of each tooth (mesio-buccal, mid-buccal, disto-buccal, mid-lingual) by single experienced periodontologist was another advantage of the study.

Conclusion

Despite the fact that the present study did not report statistically significant results, meaningful values related to tobacco use and periodontal measurements were observed in the patients with malignant oral mucosal lesions when compared to those with benign oral mucosal lesions.

Conflict of Interests

Authors have no conflict of interest.

Acknowledgments

The authors were not supported by any organization.

References

1. Rivera C, Venegas B. Histological and molecular aspects of oral squamous cell carcinoma (Review). Oncol Lett 2014; 8(1): 7-11.
2. Guneri P, Gurhan C, Karaca B. The role of the human papilloma virus in head and neck squamous cell carcinoma. Ege Univ Dis Hekim Fak Derg 2018; 39(3), 123-4.

3. World Health Organization. Oral health: Action plan for promotion and integrated disease prevention (60th world health assembly resolution A16). Geneva, Switzerland: WHO; 2007.
4. Javed F, Warnakulasuriya S. Is there a relationship between periodontal disease and oral cancer? A systematic review of currently available evidence. Crit Rev Oncol Hematol 2016; 97: 197-205.
5. Ye L, Jiang Y, Liu W, Tao H. Correlation between periodontal disease and oral cancer risk: A meta-analysis. J Cancer Res Ther 2016; 12(Supplement): C237-40.
6. Heikkila P, But A, Sorsa T, Haukka J. Periodontitis and cancer mortality: Register-based cohort study of 68,273 adults in 10-year follow-up. Int J Cancer 2018; 142(11): 2244-53.
7. Nazir MA. Prevalence of periodontal disease, its association with systemic diseases and prevention. Int J Health Sci (Qassim) 2017; 11(2): 72-80.
8. Guven DC, Dizdar O, Akman AC, Berker E, Yekeduz E, Ceylan F, et al. Evaluation of cancer risk in patients with periodontal diseases. Turk J Med Sci 2019; 49(3): 826-31.
9. Chung SD, Tsai MC, Huang CC, Kao LT, Chen CH. A population-based study on the associations between chronic periodontitis and the risk of cancer. Int J Clin Oncol 2016; 21(2): 219-23.
10. Michaud DS, Fu Z, Shi J, Chung M. Periodontal disease, tooth loss, and cancer risk. Epidemiol Rev 2017; 39(1): 49-58.
11. Nwizu NN, Marshall JR, Moysich K, Genco RJ, Hovey KM, Mai X, et al. Periodontal disease and incident cancer risk among postmenopausal women: Results from the Women's Health Initiative Observational Cohort. Cancer Epidemiol Biomarkers Prev 2017; 26(8): 1255-65.
12. Dizdar O, Hayran M, Guven DC, Yilmaz TB, Taheri S, Akman AC, et al. Increased cancer risk in patients with periodontitis. Curr Med Res Opin 2017; 33(12): 2195-200.
13. Moraes RC, Dias FL, Figueredo CM, Fischer RG. Association between chronic periodontitis and oral/oropharyngeal cancer. Braz Dent J 2016; 27(3): 261-6.
14. Laprise C, Shahul HP, Madathil SA, Thekkepurakkal AS, Castonguay G, Varghese I, et al. Periodontal diseases and risk of oral cancer in Southern India: Results from the HeNCe Life study. Int J Cancer 2016; 139(7): 1512-9.
15. Tezal M, Sullivan MA, Reid ME, Marshall JR, Hyland A, Loree T, et al. Chronic periodontitis and the risk of tongue cancer. Arch Otolaryngol Head Neck Surg 2007; 133(5): 450-4.
16. Tezal M, Grossi SG, Genco RJ. Is periodontitis associated with oral neoplasms? J Periodontol 2005; 76(3): 406-10.
17. Guha N, Boffetta P, Wunsch FV, Eluf NJ, Shangina O, Zaridze D, et al. Oral health and risk of squamous cell carcinoma of the head and neck and esophagus: Results of two multicentric case-control studies. Am J Epidemiol 2007; 166(10): 1159-73.
18. Divaris K, Olshan AF, Smith J, Bell ME, Weissler MC, Funkhouser WK, et al. Oral health and risk for head and neck squamous cell carcinoma: The Carolina Head and Neck Cancer Study. Cancer Causes Control 2010; 21(4): 567-75.
19. Talamini R, Vaccarella S, Barbone F, Tavani A, La Vecchia C, Herrero R, et al. Oral hygiene, dentition, sexual habits and risk of oral cancer. Br J Cancer 2000; 83(9): 1238-42.
20. Guneri P, Epstein JB, Ilhan B, Kaya A, Boyacioglu H. Clinical application of a digital method to improve the accuracy of color perception in toluidine blue stained oral mucosal lesions. Quintessence Int 2013; 44(8): 619-27.
21. Guneri P, Epstein JB, Kaya A, Veral A, Kazandi A, Boyacioglu H. The utility of toluidine blue staining and brush cytology as adjuncts in clinical examination of suspicious oral mucosal lesions. Int J Oral Maxillofac Surg 2011; 40(2): 155-61.
22. Ribeiro AC, Silva AR, Simonato LE, Salzedas LM, Sundefeld ML, Soubhia AM. Clinical and histopathological analysis of oral squamous cell carcinoma in young people: A descriptive study in Brazilians. Br J Oral Maxillofac Surg 2009; 47(2): 95-8.
23. Speight PM, Khurram SA, Kujan O. Oral potentially malignant disorders: risk of progression to malignancy. Oral Surg Oral Med Oral Pathol Oral Radiol 2018; 125(6): 612-27.
24. Allen K, Farah CS. Patient perspectives of diagnostic delay for suspicious oral mucosal lesions. Aust Dent J 2015; 60(3): 397-403.
25. Johnson N. Tobacco use and oral cancer: A global perspective. J Dent Educ 2001; 65(4): 328-39.
26. Winn DM. Tobacco use and oral disease. J Dent Educ 2001; 65(4): 306-12.