Epidemiological and clinical analysis of potentially malignant disorders

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Abstract

Potentially malignant diseases of the oral mucosa that have a risk of conversion to oral squamous cell carcinoma, are described as precancer, premalignant, intraepithelial neoplasia, and potentially malignant disorders. The etiology includes oral habits associated with tobacco, heavy alcohol, betel nut chewing, and human papilloma virus (HPV) infection. Diagnosis of OPLs typically relies on visual observation by experienced practitioners followed by biopsy and analysis under a microscope. The main purpose of this study was epidemiological and clinical analysis of patients with oral premalignant lesions diagnosed and treated in our collaborative healthcare structures. Oral premalignant lesions were more common in men than women. Buccal mucosa was the most common location of oral premalignant lesions in our study (31.03%), followed by floor of the mouth (22.4%). Homogenous leukoplakia was the most common type of leukoplakia (present in 44.8% of patients), followed by lichen planus (25.8%). The degree of dysplasia was associated with the type of oral premalignant lesions but not significantly with their size.

Keywords: oral premalignant lesion, leukoplakia, epidemiology.

Introduction

Potentially malignant diseases of the oral mucosa that have a risk of conversion to oral squamous cell carcinoma, are described in the literature as precancer, premalignant, intraepithelial neoplasia, and potentially malignant disorders. According to the World Health Organization, conditions of oral mucosa, which may undergo malignant transformation, are defined as a potentially malignant disorders (1). There are 5 conditions described in literature as potentially malignant disorders: erythroplakia, lichen planus, oral submucous fibrosis, actinic cheilitis and leukoplakia. Oral cancer is the 18th (out of 36) most common cancer worldwide, with an annual incidence of 377,713 and a mortality of 177,757 in 2020 (2) and is the 8th and 15th most common cancer for males and females in the US, respectively (3). The etiology includes oral habits associated with tobacco, heavy alcohol, and betel nut chewing; human papilloma virus (HPV) infection and in some cases no known risk factor at all. HPV-negative and nonsmokers represent only a small group of oral cancer patients (4). Dysplastic changes of oral keratinocytes start in the basal cell layers, showing hyperchromatism, pleomorphism, increased nuclear-cytoplasmic ratio, large and prominent nucleoli, increased mitotic activity, abnormal mitotic figures, and altered epithelial architecture and maturation pattern. Oral epithelial dysplasia is classified either as low-grade, including mild and

How to Cite

D. Kostandini, E. Qorri, S. Rastelli, G. Botticelli, G. Falisi.
Epidemiological and clinical analysis of potentially malignant disorders.
Annali Di Stomatologia, 16(1), 42-48.
https://doi.org/10.59987/ads/2025.1.42-48

moderate dysplasia, when cytomorphological changes are confined to the lower half of the epithelium, or as high-grade (severe dysplasia) when changes involve more than half of the epithelial thickness according to the 2017 WHO criteria (5). This classification was recently challenged for its ability to predict risks, and, as a result, other grading systems are proposed (6). Oral premalignant lesions may be asymptomatic or cause irritation, such as pain, burning sensation, and difficulty swallowing (7). Diagnosis of oral premalignant lesions typically relies on visual observation by experienced practitioners followed by biopsy and analysis under a microscope. The lesion biopsy remains the "Gold standard" in detecting the oral premalignant lesions. However, recent developments have introduced new methods for diagnosing, which can be more accurate and cost-effective than traditional methods. These include immunocytochemistry, vital staining tests, fluorescence imaging, and laser confocal microscopy (8). The timely identification and management of oral premalignant lesions is crucial in enhancing patient outcomes and modifying mortality risk (9).

Material and methods

This is a cohort-prospective type of study conducted in the clinical files of patients. Basic criteria for inclusion in the study was a clinical diagnosis or definitive diagnosis with oral premalignant lesion. The main purpose of this study was epidemiological and clinical analysis of patients with oral premalignant lesion diagnosed and treated in the Department of Oro-maxillo-facial surgery, Medical University of Tirana; Department of Dentistry, Albanian University Tirana; and private dental clinics. We examined the clinical data of 58 patients diagnosed with oral premalignant lesions clinically and histologically from 2013 to 2023. In this study we analyzed factors thought to influence malignant transformation of oral precancerous lesions. For statistical analysis, the "Chi-square test" was used (with a fixed value of P statistically valid: $P<0.05$). This test reveals the connection between two categories of variables. For this test, a randomly selected sample is required, the variables to be independent of each other (no quotations between them), the calculation is done in tables with 5 constituent parts (rows/columns) or less in a built-in table 2x2.

Results and statistical analysis

Oral premalignant lesions were more common in men than women (62.06% vs. 37.93%), which corresponded to a 1.63:1 man-to-woman ratio. Statistically not significant ($p>0.05$). The patient's age ranged from 31 to 78 years old.

Most patients lived in urban areas (60% of them in the last 15-20 years) and 31% lived in rural areas. A previous history of cancer was found in 10% of patients,

Table 1. Distribution of oral premalignant lesions (age and gender).

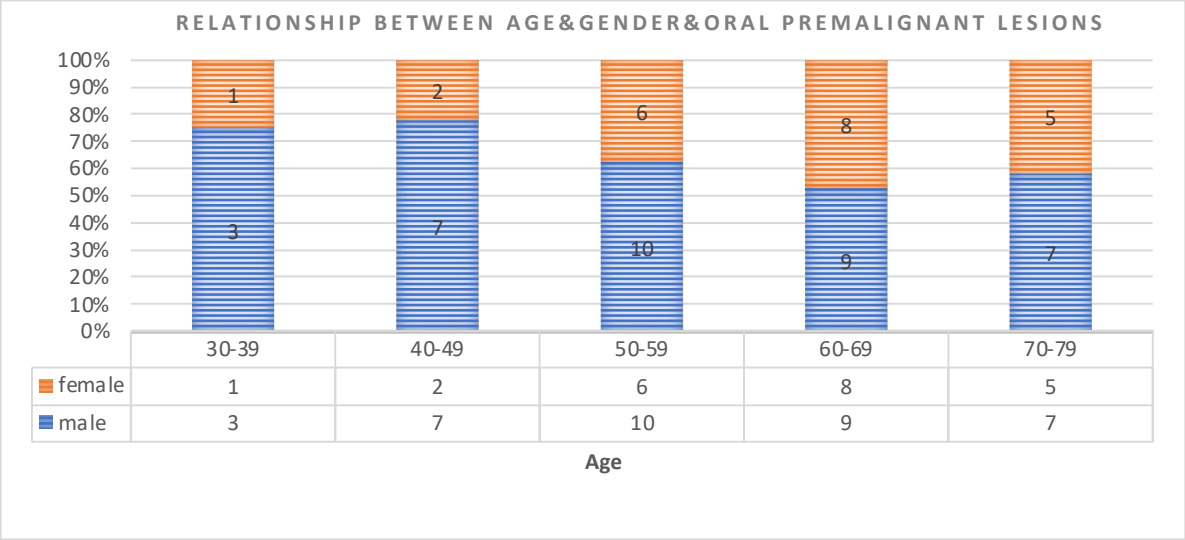
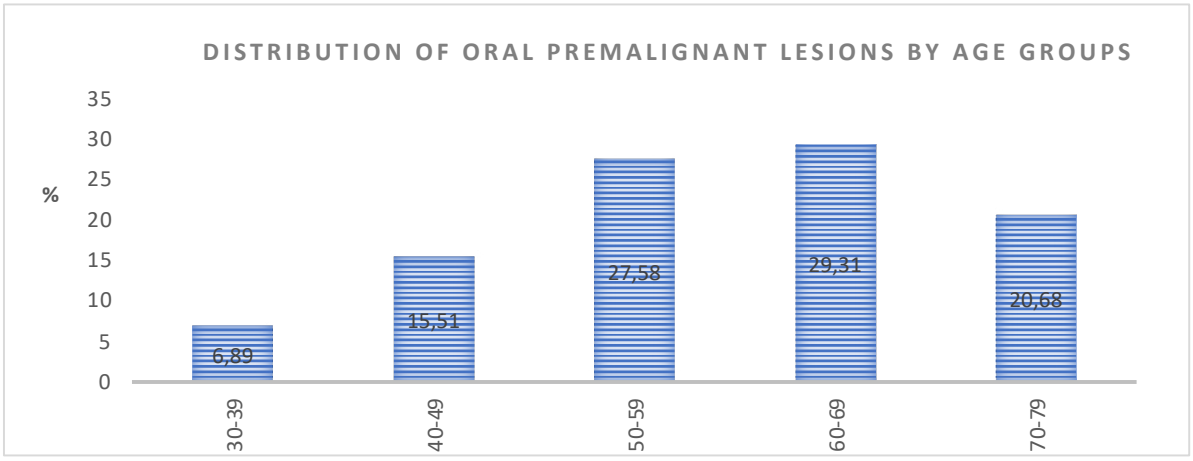


Table 2. Statistic correlation of oral premalignant lesions (age and gender).

	30-39	**40-49**	**50-59**	**60-69**	**70-79**	*Total*
M	3 (2.48) (0.11)	7 (5.59) (0.36)	10 (9.93) (0.00)	9 (10.55) (0.23)	7 (7.45) (0.03)	36
F	1 (1.52) (0.18)	2 (3.41) (0.59)	6 (6.07) (0.00)	8 (6.45) (0.37)	5 (4.55) (0.04)	22
Total	4	9	16	17	12	**58**

Chi-square = 1.9014; p value = 0.753886. The result is not statistically significant, $p > 0.05$.
Most of the patients (77.57%) were between 50 and 79 years old. There is a tendency for these lesions to appear earlier in men than in women.

Table 3. Distribution of oral premalignant lesions by age groups.



and a family history of cancer in 50% of patients. In this study 39.65% of patients were non-smokers, 46.55% were smokers, and 13.79% were former smokers. Within the group of smokers, 18.51% smoked tobacco wrapped by themselves, and in this group 3 patients admitted that they chew tobacco sometimes. Most smokers smoked 10-20 cigarettes a day. Only 33.33% of smokers smoked less than 10 cigarettes a day. Most former smokers smoked 10-20 cigarettes a day. All smokers have been smokers for more than 10 years.

Table 4. Oral premalignant lesions and smoking.

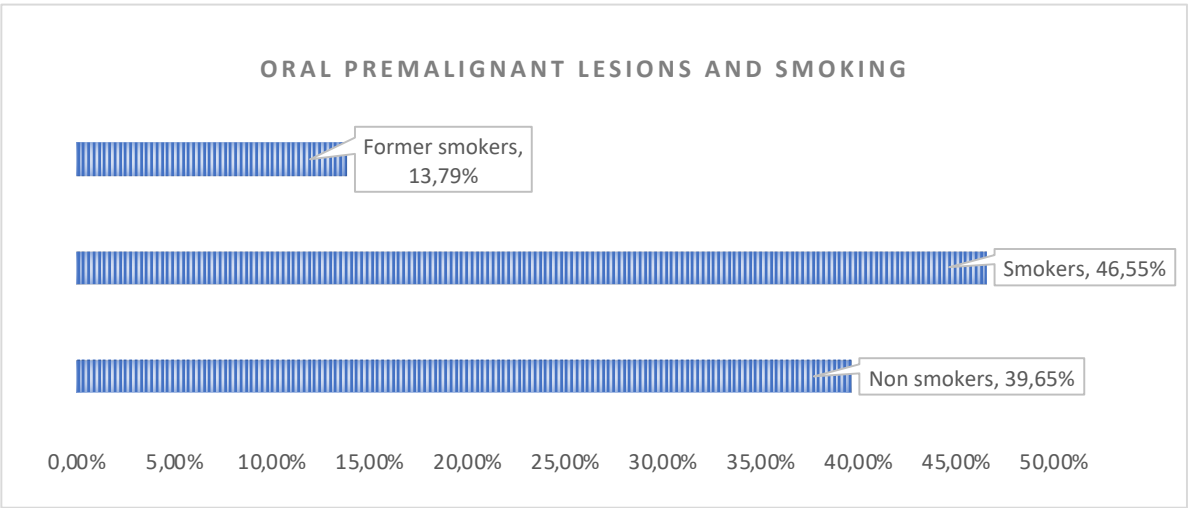
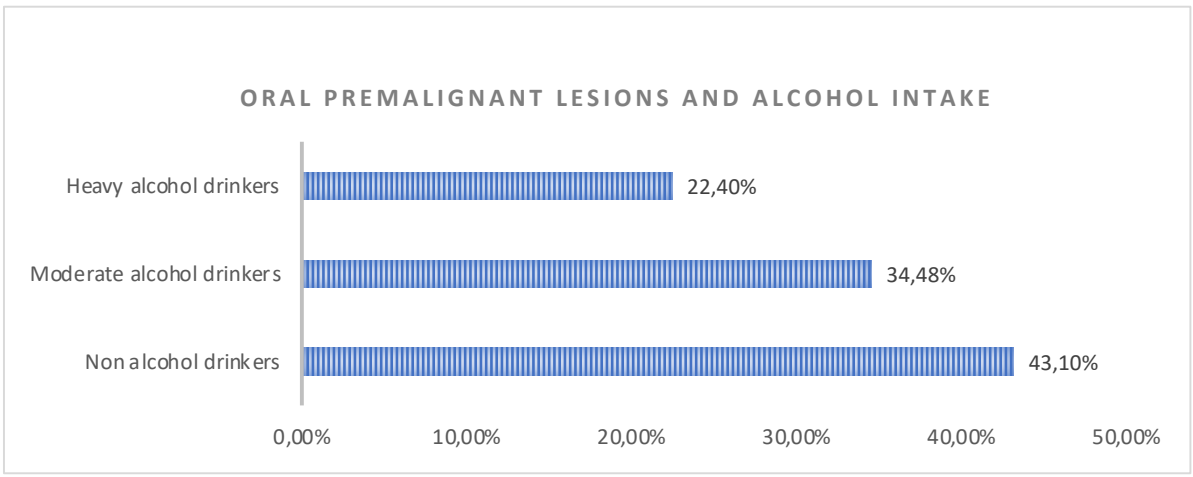


Table 5. Oral premalignant lesions and alcohol intake.



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Most former smokers quit 5-10 years ago.

From the total, 43.1% of patients did not drink alcohol; 34.48% drank occasionally (moderate alcohol drinkers) and 22.4% were heavy alcohol drinkers. Patients who were more likely to smoke were also more regular drinkers of alcohol. The most common systemic diseases were hypercholesterolemia in 18.9% of patients, followed by cardiovascular disease and rheumatic disease and diabetes.

Buccal mucosa was the most common location of oral premalignant lesions in our study (31.03%), followed by floor of the mouth (22.4%), gingiva (17.2%), lateral and dorsal aspect of the tongue (each 7.75%), palatum, lips, commissura areas and the ventral surface of the tongue (each 3.42%). The most common location in younger patients were in palatum (median age, 51) and lips (median age, 40). In older patients, the most common locations were buccal mucosa (median age, 70), floor of the mouth (64), and tongue (median age, 59). The most common locations in men were buccal mucosa and the floor of the mouth. In women the most common locations were the tongue and the areas around the commissura.

In this study, 70.6% of patients had a single lesion and 29.3% had multiple lesions. Most patients (60.3%) were unaware when the lesion appeared; 20.8% reported being aware of the lesion in a period of 3 to 6 months, and 18.9% reported being aware of the lesion in a period of more than 12 months. Homogenous leukoplakia was the most common type of leukoplakia (present in 44.8% of patients), followed by lichen planus (25.8%), erythroleukoplakia (6.8%), and nodular leukoplakia (1.7%), palatal lesions of reverse cigar smoking (3,4%), nicotine stomatitis (8.6%), keratosis from tobacco (5.1%), squamous-cell carcinoma (3.4% or present in 2 patients). White lesions such as linea alba, leukoedema,

Table 6. Distribution of oral premalignant lesions by location.

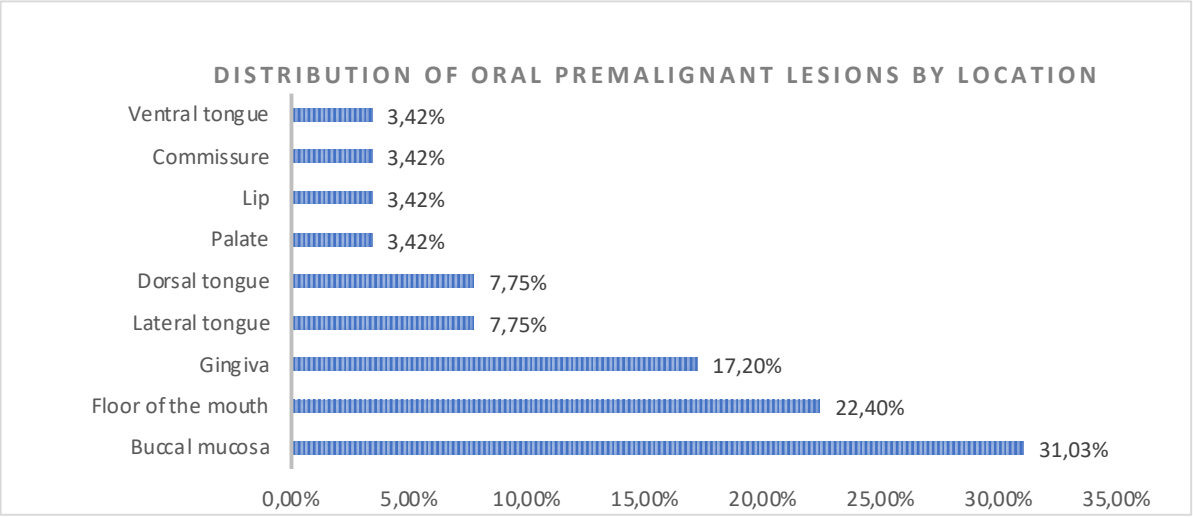
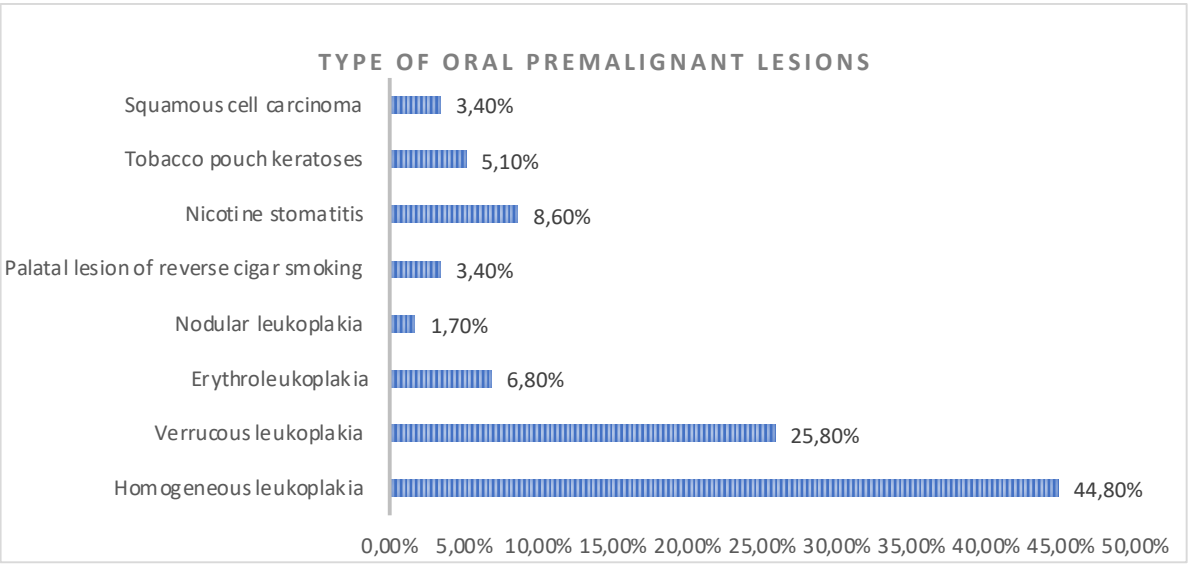


Table 7. Type of oral premalignant lesions.



and friction keratosis were found present in our patients, but these lesions have no tendency for malignant transformation. The most common location of oral premalignant lesions was in lateral part of the tongue for homogeneous leukoplakia; gingiva and buccal mucosa for lichen planus; gingiva and commissura for nodular leukoplakia, tobacco pouch keratoses and nicotine stomatitis; lateral part of the tongue and floor of the mouth for squamous-cell carcinoma. Analyzing the histopathological results, we found that 75% of the lesions had no dysplasic characteristics. Of the 76.4% of the affected dysplasic features, 11.76% had moderate dysplasic characteristics to severe dysplasic characteristics; 2 patients (11.76% of the lesions) had a carcinoma.

The degree of dysplasia was associated with the type of oral premalignant lesions but not significantly with their size (Table 8; P<0.05). Dysplasia was significantly more common in patients with a family history of cancer and with a personal history of cancer. We, also saw a presence of dysplastic characteristics, slightly more in older patients and in women. In this study we found no significant association between the location of lesion and the degree of dysplasia (Table 9; p>0.05). We also found no association between clinical surface area and degree of dysplasia.

Discussion

Oral premalignant lesions and especially leukoplakia, the most common precancerous condition of the oral cavity, is quite often the subject of research investigations. According to the literature, leukoplakia affects from 0.2% to 11.7% of the population (10). Such significant differences are due to dissimilarities in the incidence of pathology in the defined age, ethnic and social group. Axell (11) conducted epidemiological studies on a group of 20 333 people aged over 15 years old; leukoplakia was found in 3.6%. In the material of Hogewind and van der Waal (12), the percentage was 1.4% (1000 patients). In the material of Campisi et al. (13), was diagnosed in 13.8% of men over 40 years old. Cebeci et al. (14), after analyzing the results of 5000 routine dental examinations, diagnosed oral premalignant lesions only in 0.4% cases. Tokajuk et al. (15) conducted research among 591 patients aged over 55, oral premalignant lesions were diagnosed in 7.4% of cases. The literature emphasizes a three times higher incidence of oral premalignant lesions in men; in the material of Cebeci et al. (14). In our results, oral premalignant lesions were more common in men than women (62.06% vs. 37.93%), which corresponded to a 1.63:1 man-to-woman ratio. Most of the patients

Table 8. Histopathological characteristics in correlation with the type of oral premalignant lesions.

	No dysplasia	**Mild dysplasia**	**Moderate dysplasia**	**Carcinoma in situ**	**Total**
Leukoplakia	27 (23.13) (0.65)	3 (5.55) (1.17)	0 (1.39) (1.39)	1 (0.93) (0.01)	31
Liken Planus	14 (13.43) (0.02)	4 (3.22) (0.19)	0 (0.81) (0.81)	0 (0.54) (0.54)	18
Erythroplakia	0 (2.99) (2.99)	1 (0.72) (0.11)	2 (0.18) (18.51)	1 (0.12) (6.49)	4
Nodular Leukoplakia	0 (0.75) (0.75)	1 (0.18) (3.76)	0 (0.04) (0.04)	0 (0.03) (0.03)	1
Tobacco pouch keratoses, Nicotine stomatitis	9 (9.70) (0.05)	3 (2.33) (0.19)	1 (0.58) (0.30)	0 (0.39) (0.39)	13
Total	50	12	3	2	**67**

Chi-square = 38.3874; p value = 0.000133; The result is statistically significant, $p < 0.05$.

Table 9. Histopathological characteristics in correlation with the location of oral premalignant lesions.

	No dysplasia	Mild dysplasia	Moderate dysplasia	Carcinoma in situ	**Total**
Buccal mucosa	16 (15.67) (0.01)	5 (3.76) (0.41)	0 (0.94) (0.94)	0 (0.63) (0.63)	21
Floor of the mouth	10 (11.94) (0.32)	4 (2.87) (0.45)	1 (0.72) (0.11)	1 (0.48) (0.57)	16
Gingiva	9 (8.96) (0.00)	3 (2.15) (0.34)	0 (0.54) (0.54)	0 (0.36) (0.36)	12
Tongue	3 (3.73) (0.14)	0 (0.90) (0.90)	1 (0.22) (2.69)	1 (0.15) (4.85)	5
Palate & Lip	12 (9.70) (0.54)	0 (2.33) (2.33)	1 (0.58) (0.30)	0 (0.39) (0.39)	13
Total	50	12	3	2	**67**

Chi-square = 16.8022; p value = 0.157192; The result is not statistically significant, $p > 0.05$.

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(77.57%) were between 50 and 79 years old in this study. There is a tendency for these lesions to appear earlier in men than in women in our study. The impact of smoking on the incidence of oral premalignant lesions is now indisputable. In an east European study, the percentage of smokers was 82–100% (16). Morger et al. (17), in a study of 615 individuals, showed a statistically higher incidence of pathology of the oral mucosa, among smokers and alcohol abusers. In our study 39.65% of patients were non-smokers, 46.55% were smokers, and 13.79% were former smokers. From the total in our study, 43.1% of patients did not drink alcohol; 34.48% drank occasionally (moderate alcohol drinkers) and 22.4% were heavy alcohol drinkers. Patients who were more likely to smoke were also more regular drinkers of alcohol. It is believed that in the carcinogenesis process tobacco acts both at the initiation and promotion stage, however alcohol only acts at the promotion stage. Carcinogenic effects of these two factors do not add up, but multiply (18). The role of alcohol as an independent factor for oral premalignant lesions and cancer development is not as well documented as tobacco. In 2006, Maserejian et al. (19) conducted a prospective study among 41 458 people and proved that the risk of developing oral premalignant lesions is dependent on the amount of alcohol regardless of the tobacco. Homogenous leukoplakia was the most common type of leukoplakia (present in 44.8% of patients), what is compatible with other reports (11, 12). Buccal mucosa was the most common location of oral premalignant lesions in our study (31.03%), followed by floor of the mouth (22.4%), gingiva (17.2%), lateral and dorsal aspects of the tongue (each 7.75%); similar as well, as in other studies (20). In our material, carcinoma in lesions clinically corresponding to oral premalignant lesions was found in 2 patients (11.76% of the lesions). This percentage is somehow lower than that presented in the literature (15.6–39.2%) (21). These differences are probably caused by the small sample of our population. All the patients with carcinoma were smokers. In a study, De Stafani et al. (22) proved that the relative risk of oral cancer development among non-smokers was 1, while among smokers 4.2. These authors also found that the risk among people who have given up smoking is lower in comparison to active smokers. To date, there is no uniform standard of care for patients with diffuse or large-sized low-grade oral dysplasia due to their relatively low malignant transformation rate weighted against the severity of treatment complications. However, for the significant minority that do develop carcinoma, the consequence is grave. The visible appearance of oral premalignant lesions during routine dental visits provides an opportunity to implement risk assessment and cancer-preventative strategies, if only a sensitive and reliable method is available to predict the progressive vs. non-progressive outcome of low-grade oral premalignant lesions, so that unnecessary treatment complications can be avoided. It is of fundamental importance to dissect the mechanisms underlying the malignant progression of oral dysplastic lesions, which may reveal druggable targets for cancer prevention even before the appearance of oral premalignant lesions. There is a clinical need to test the identified prediction models on saliva and/or brushing samples, collected from patients with low-grade oral premalignant lesions, and compare the readouts and their predictive powers to data collected from biopsy samples. Using saliva or brushing cytology samples as surrogates for tissue samples may obviate some practical issues related to multiple biopsies. Several efforts have spearheaded the translational frontiers of salivary diagnostics for carcinomas. For instance, by comparing between oral carcinomas and control, several aberrantly expressed cancer-related mRNAs were observed in oral carcinoma saliva from profiling human salivary transcriptome (23). In addition, salivary proteomic analysis identified elevated levels of salivary proteins compared to normal counterparts. These salivary biomarkers were able to distinguish cancer from benign diseases with high sensitivity and specificity (24,25). Cytological study of oral cells is also a non-invasive technique that has been harnessed into use for detection of disease progression and therapeutic monitoring. By quantifying the DNA amount from collected cells, an image analysis system was developed to classify cells based on DNA ploidy, which, in term, can triage patients based on the levels of abnormality in their lesions (26,27). There is a critical need for a screening method, preferably non-invasive, to predict the risk of oral premalignant lesions in becoming carcinomas, which allows early medical interventions that are more effective and less damaging (28, 29).

Conclusions

gIn this study, oral premalignant lesions were more common in men than women. There is a tendency in recent years for this difference between the genders to be equalized. Most patients were between 50 to 79 years of age. Oral premalignant lesions appeared at a younger age in men than in women in our study. Homogeneous leukoplakia was the most frequent clinical form. The degree of dysplasia was seen to be more related to the type of oral premalignant lesions, than to its size. Dysplasia was most common in patients with a family history of cancer or a personal history of cancer development. Also, a mild predominance of dysplastic characteristics was observed in older patients. In this study, we did not find a possible link between the location of oral premalignant lesions and the degree of dysplasia. Likewise, there was no link between the clinical size of lesion and the degree of dysplasia.

References

1. Warnakulasuriya S, Johnson NW, van der Waal I. Nomenclature and classification of potentially malignant disorders of the oral mucosa. J Oral Pathol Med 2007; 36: 575-80.
2. Sung, H.; Ferlay, J.; Siegel, R.L.; Laversanne, M.; Soerjomataram, I.; Jemal, A.; Bray, F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J. Clin. 2021, 71, 209–249. (CrossRef)
3. Neville, B.W.; Damm, D.D.; Allen, C.M.; Bouquot, J.E. Squamous cell carcinoma. In Oral and Maxillofacial Pathology; Saunders Elsevier: St. Louis, MO, USA, 2016; pp.

409–421.
4. Katzel, J.A.; Merchant, M.; Chaturvedi, A.K.; Silverberg, M.J. Contribution of demographic and behavioral factors on the changing incidence rates of oropharyngeal and oral cavity cancers in northern California. Cancer Epidemiol. Biomark. Prev. 2015, 24, 978–984. (CrossRef) (PubMed)
5. Reibel, J.; Gale, N.; Hille, J.; Hunt, J.L.; Lingen, M.; Muller, S.; Sloan, P.; Tilakarante, W.M.; Westra, W.H.; Williams, M.D.; et al. Oral potentially malignant disorders and oral epithelial dysplasia. WHO/IARC Classif. Head Neck Tumours 2017, 4, 112–115.
6. Odell, E.; Kujan, O.; Warnakulasuriya, S.; Sloan, P. Oral epithelial dysplasia: Recognition, grading, and clinical significance. Oral Dis. 2021, 27, 1947–1976. (CrossRef)
7. Abati S, Bramati C, Bondi S, Lissoni A, Trimarchi M. Oral Cancer and Precancer: A Narrative Review on the Relevance of Early Diagnosis. Int J Environ Res Public Health. 2020 Dec 8;17(24):9160. DOI: 10.3390/ijerph17249160; PMID: 33302498; PMCID: PMC7764090.
8. Walsh T, Warnakulasuriya S, Lingen MW, Kerr AR, Ogden GR, Glenny AM, Macey R. Clinical assessment for the detection of oral cavity cancer and potentially malignant disorders in apparently healthy adults. Cochrane Database Syst Rev. 2021 Dec 10;12(12):CD010173. DOI: 10.1002/14651858.CD010173.pub3; PMID: 34891214; PMCID: PMC8664456.
9. Omar E. Current concepts and future of noninvasive procedures for diagnosing oral squamous cell carcinoma-a systematic review. Head Face Med. 2015 Mar 25; 11:6. DOI: 10.1186/s13005-015-0063-z; PMID: 25889859; PMCID: PMC4396078.
10. Silverman S, Bhargava K, Smith LW, Malaowalla AM. Malignant transformation, and natural history of oral leukoplakia in 55518 industrial workers of Gujarat, India. Cancer 1976; 38: 1790-5.
11. Axell T. Occurrence of leukoplakia and some other oral white lesions among 20333 adult Swedish people. Community Dent Oral Epidemiol 1987; 15: 46-51.
12. Hogewind WF, van der Waal I. Prevalence study of oral leukoplakia in a selected population of 1000 patients from the Netherlands. Community Dent Oral Epidemiol 1988; 16: 302-5.
13. Campisi G, Margiotta V. Oral mucosal lesions and risk habits among men in an Italian study population. J Oral Pathol Med 2001; 30: 22-8.
14. Cebeci AI, Gulsahi A, Kamburoglu K, et al. Prevalence and distribution of oral lesions an adult Turkish population. Med Oral Patol Oral Cir Bucal 2009; 14: 272-7.
15. Tokajuk G, Stokowska W, Miksza-Żyłkiewicz R. Occurrence of lesions of the oral cavity mucosa among patients after 55 years old in North-Eastern region of Poland (Polish). Gerontol Pol 2002; 10: 178-81.
16. Banoczy J, Ginter Z, Dombi C. Tobacco use and oral leukoplakia. J Dent Educ 2001; 65: 322-7.
17. Morger R, Ramseier CA, Rees TD, et al. Oral mucosal findings related to tobacco use and alcohol consumption: a study on Swiss army recruits involving self-reported and clinical data. Oral Health Prev Dent 2010; 8: 143-51.
18. Kruk-Zagajewska A, Wierzbicka M. The tongue and floor of the mouth cancer – diagnosis and advances in treatment (Polish). Contemp Onkol 2003; 7: 264-74.
19. Maserejian NN, Joshipura KJ, Rosner BA, et al. Prospective study of alcohol consumption and risk of oral premalignant lesions in men. Cancer Epidemiol Biomarkers Prev 2006; 15: 774-81.
20. Garcia-Pola Vallejo MJ, Martinez Diaz-Canel AI, Garcia Martin JM, et al. Risk factors for oral soft tissue lesions in an adult Spanish population. Community Dent Oral Epidemiol 2002; 30: 277-85.
21. Neville BW, Day TA. Oral cancer and precancerous lesions. CA Cancer J Clin 2002; 52: 195-215.
22. De Stafani E, Boffetta P, Oreggia F, et al. Smoking patterns and cancer of the oral cavity and pharynx: a case control study in Uruguay. Oral Oncol 1998; 34: 340-6.
23. Li, Y.; St John, M.A.; Zhou, X.; Kim, Y.; Sinha, U.; Jordan, R.C.; Eisele, D.; Abemayor, E.; Elashoff, D.; Park, N.H.; et al. Salivary transcriptome diagnostics for oral cancer detection. Clin. Cancer Res. 2004, 10, 8442–8450. (CrossRef) (PubMed)
24. Xie, H.; Onsongo, G.; Popko, J.; de Jong, E.P.; Cao, J.; Carlis, J.V.; Griffin, R.J.; Rhodus, N.L.; Griffin, T.J. Proteomics analysis of cells in whole saliva from oral cancer patients via value-added three-dimensional peptide fractionation and tandem mass spectrometry. Mol. Cell. Proteom. 2008, 7, 486–498. (CrossRef) (PubMed)
25. Nagler, R.; Bahar, G.; Shpitzer, T.; Feinmesser, R. Concomitant analysis of salivary tumor markers–a new diagnostic tool for oral cancer. Clin. Cancer Res. 2006, 12, 3979–3984. (CrossRef) (PubMed)
26. Macaulay, C.; Poh, C.F.; Guillaud, M.; Michele Williams, P.; Laronde, D.M.; Zhang, L.; Rosin, M.P. High throughput image cytometry for detection of suspicious lesions in the oral cavity. J. Biomed. Opt. 2012, 17, 086004. (CrossRef)
27. Parfenova, E.; Liu, K.Y.P.; Harrison, A.; MacAulay, C.; Guillaud, M.; Poh, C.F. An improved algorithm using a Health Canada- approved DNA-image cytometry system for non-invasive screening of high-grade oral lesions. J. Oral Pathol. Med. 2021, 50, 502–509. (CrossRef) (PubMed)
28. Kostandini D, Eriksen N, Qorri E. The Importance of Knowledge of Risk Factors and Clinical Evaluation for Oral Precancerous Lesions and Oral Cancer in Dentists Community of Tirana. European Journal of Natural Sciences and Medicine. 2023 Aug 10;6(2):138-47.
29. Miele, M. T., Qorri, E., Borshi, X., Avantaggiato, P., & Candotto, V. Circulating tumor cells of oral cancer: a narrative review. JOURNAL OF BIOLOGICAL REGULATORS AND HOMEOSTATIC AGENTS, 2022, 36(2), 95-101.

10.59987/ads/2025.1. 42-48