

PREVALENCE OF LEUKOPLAKIA AMONG PATIENTS VISITING A PRIVATE DENTAL HOSPITAL-AN INSTITUTIONAL STUDY

Running title: Prevalence of leukoplakia in a private dental hospital

ABSTRACT

Background: The oral mucous membrane is an integral part of the oral cavity and oral premalignancy plays an intermediate stage. Oral leukoplakia otherwise called smoker's keratosis is a potential premalignant disorder ~~but~~ and if not diagnosed early has a risk of causing oral morbidity and cancer. It is a non-scrapable white patch or plaque which might be homogeneous or nonhomogeneous and is strongly associated with smoking, tobacco, alcohol consumption, chronic irritation, infections, and ultraviolet exposure. The etiology is idiopathic. The main aim of the study was to assess the prevalence of leukoplakia in patients reporting to a university dental hospital.

Methodology: The present study was a retrospective observational study wherein 239 leukoplakia cases were reported to a private dental hospital located in Chennai from June 2020 to April 2021. Data was collected from DIAS and was tabulated in Excel. Data analysis was done in SPSS software Version 20.0. Descriptive statistics and the relation between variables were determined using the chi-square test where done. $p < 0.05$ was considered statistically significant.

Results: The results of this study reveal that oral premalignant leukoplakia has a strong male predilection (95.4%) and the age group of 50-60 years (29.71%) was ~~the~~ most commonly affected when compared to the other age groups. This study further results that homogenous type (75.5%) of oral leukoplakia was commonly prevalent in the right buccal mucosa (29.29%) followed by the left buccal mucosa (23.43%) of the oral cavity associated with the history of excess smoking (38.08%). Pearson chi-square test shows p-value is 0.00, ($p\text{-value} < 0.05$). Hence, it is statistically significant. When association was done between the site of the

lesion in the oral cavity by the number of participants, 28.03% of the male participants were presented with the lesion on the right buccal mucosa. Pearson chi-square test shows p-value is 0.99, (p-value > 0.05). Hence, it is statistically not significant.

Conclusion: The results of this study reveal that oral premalignant leukoplakia has a strong male predilection and the age group of 50-60 years was most commonly affected when compared to the other age groups. This study further results that homogenous type of oral leukoplakia was commonly prevalent in the right buccal mucosa followed by the left buccal mucosa of the oral cavity associated with the history of excess smoking.

Keywords: oral leukoplakia, prevalence, smoking, tobacco chewing, innovative technology, novel method.

INTRODUCTION

The oral mucous membrane is an integral part of the oral cavity (1). Oral premalignancy is considered an intermediate stage. A premalignant lesion is defined as “a morphologically reformed tissue in which oral cancer is more likely to occur than in its seemingly normal counterpart”. Oral leukoplakia is considered a potential premalignant disorder (2) and is graded histologically as mild, moderate, and severe dysplasia depending on the level of involvement of the epithelium by the WHO (3). If not diagnosed early has a risk of causing oral morbidity and cancer (4). Oral leukoplakia is a non-scrapable white patch or plaque which might be homogeneous or nonhomogeneous and is strongly associated with smoking. Risk factors include all forms of tobacco, including cigars, cigarette, beedi, and pipe (5). Other synergistic risk factors include alcohol consumption, chronic irritation, fungal infections such as candidiasis, oral galvanism due to restorations, bacterial infections, sexually transmitted lesions like syphilis, combined micronutrient deficiency, viral infections,

hormonal disturbances, and ultraviolet exposure (6,7). The etiology of oral leukoplakia is multifactorial, and many causes are idiopathic. A well-defined leukoplakia is said to be associated with various factors such as poor diet, poor oral hygiene, local irritants such as caries, sharp teeth, alcohol, and tobacco (8,9). The prevalence of leukoplakia varies among scientific studies. According to a global review point, there is a prevalence of 2.6% and a malignancy conversion rate ranging from 0.1% to 17.5%. The statistical analysis from several studies concluded the prevalence of leukoplakia ranging from 0.2% to 5.2% and the malignant transformation of 0.13% to 10% in India. This alarming increase in the prevalence of leukoplakia in India could be mainly due to its cultural, ethnic, and geographic factors(10). When a tissue cell is exposed to any type of carcinogen, it tries to adapt to it. In the oral epithelium, a hastened growth phase (hyperplasia) is the earlier sequelae(11). When the irritant persists further, the epithelium shows features of cellular degeneration, a well-characterized feature of adaptation (atrophy). When the stage of adaptation and revocable cell damage ends, the cells gradually reach a stage of irrevocable cell damage, manifesting as either apoptosis or malignant transformation via tumor suppressor genes (p53). As an adaptive response, the hastened pace of cell division noted at the earlier stages of transformation facilitates further genetic damage, thereby forcefully pushing the cells further along the path to malignant transformation(12). Our team has extensive knowledge and research experience that has translated into high-quality publications (13–16)(5)(17,18)(19–21)(22–24)(25,26)(27–29)(30,31). The main aim of the study was to assess the prevalence of leukoplakia among patients visiting a private dental hospital.

MATERIALS AND METHODS

This was a university dental hospital-based retrospective cross-sectional study conducted among the patients visiting a private dental hospital in Chennai from June 2020 to April 2021. The data were collected by reviewing the patients' records from Dental Information Archiving Software (DIAS). Patients with leukoplakia were included in the study and patients reported with other

oral lesions were excluded. 239 oral leukoplakia cases were reported at the specified time. The data was cross verified with photographs and was compiled in Excel Sheet. The tabulated data and the parameters were exported to SPSS software Version 20.0. Descriptive statistics and the relation between variables were determined using the chi-square test. $p < 0.05$ was considered statistically significant.

RESULTS

In this study, 239 patients reported leukoplakia in our hospital. Data from the current study revealed that 29.71% of patients reported with oral leukoplakia aged between 50-60 years (**Figure 1**). Among them, 95.4% were males and 4.6% were females (**Figure 2**). 79.5% of the patient population presented with the homogeneous and 20.5% with non-homogenous type of leukoplakia (**Figure 3**). Among the reported cases, 38.08% of the patients gave a history of smoking (**Figure 4**). Right buccal mucosa was the most commonly affected site in the oral cavity with 29.29% followed by left buccal mucosa with 23.43% (**Figure 5**). When association was done between the site of the lesion in the oral cavity by the number of participants, 28.03% of the male participants were presented with the lesion on the right buccal mucosa (**Figure 6**).

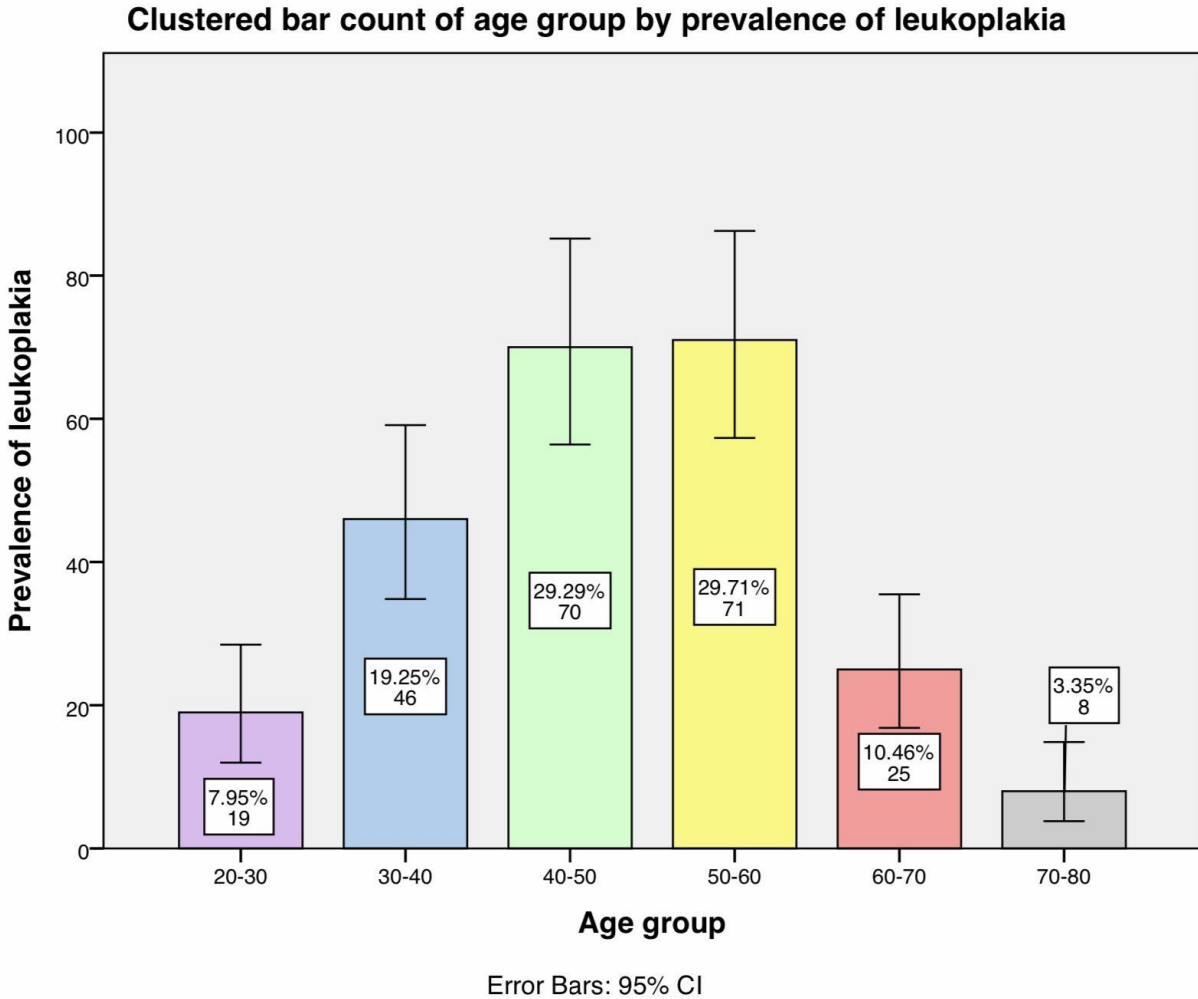


Figure 1:The above bar graph represents the association between the prevalence of leukoplakia among different age groups. X-axis represents the age group while Y-axis represents the percentage of prevalence of leukoplakia. Purple denotes 20-30 years old, blue denotes 30-40 years old, green denotes 40-50 years old, yellow denotes 50-60 years old, red denotes 60-70 year olds and grey denotes 70-80 years old. The highest prevalence was commonly seen in people aged between 50-60 years (29.71%).Pearson chi-square test shows p-value is 0.00, (p-value < 0.05).Hence, it is statistically significant.

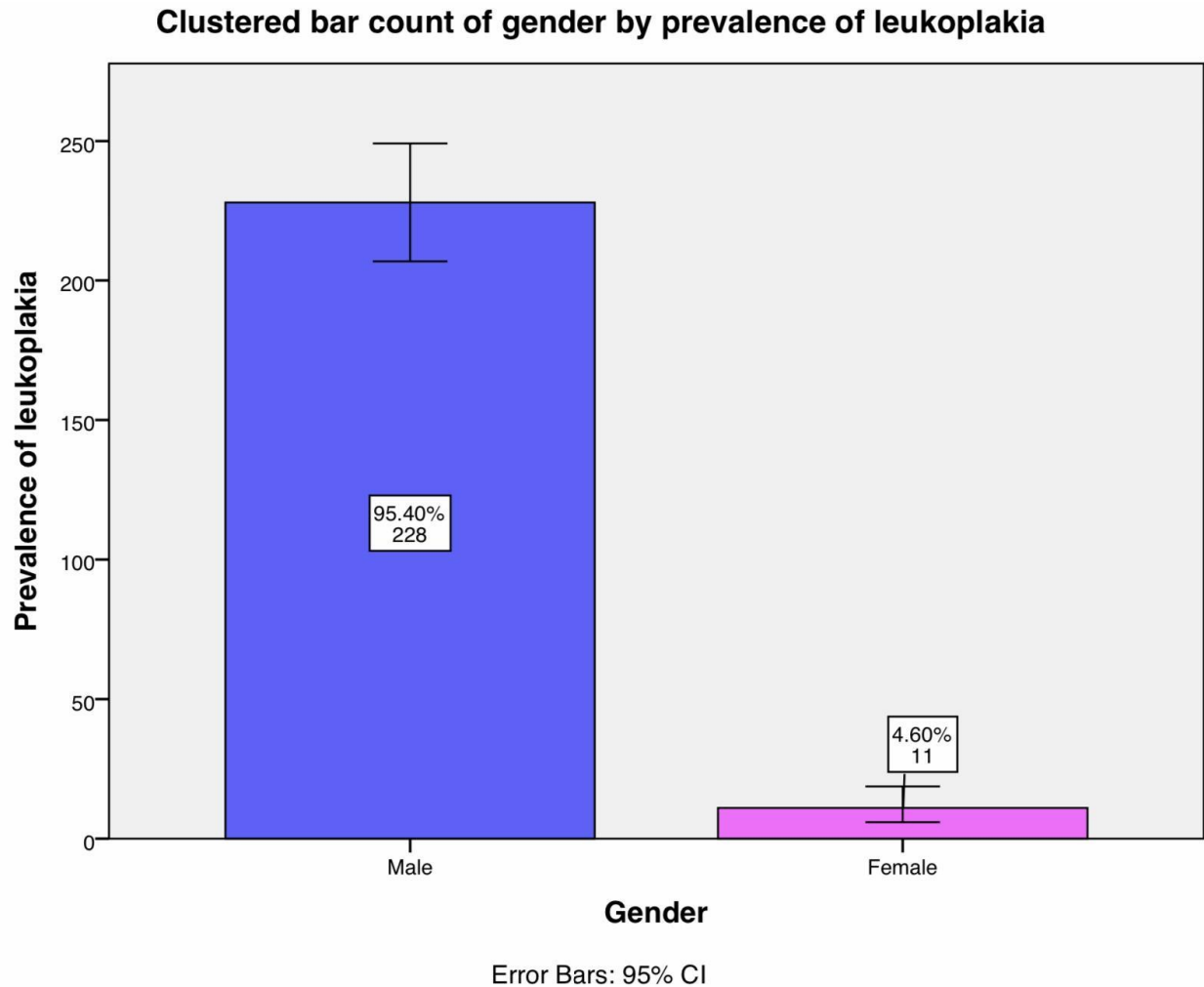


Figure 2:The above bar graph represents the association between the prevalence of leukoplakia among males and females. X-axis represents the gender while Y-axis represents the percentage of prevalence of leukoplakia. Pink denotes female population while blue denotes male population. The prevalence of males with leukoplakia (95.4%) was greater than females (4.6%). Pearson chi-square test shows p-value is 0.00, (p-value < 0.05). Hence, it is statistically significant.

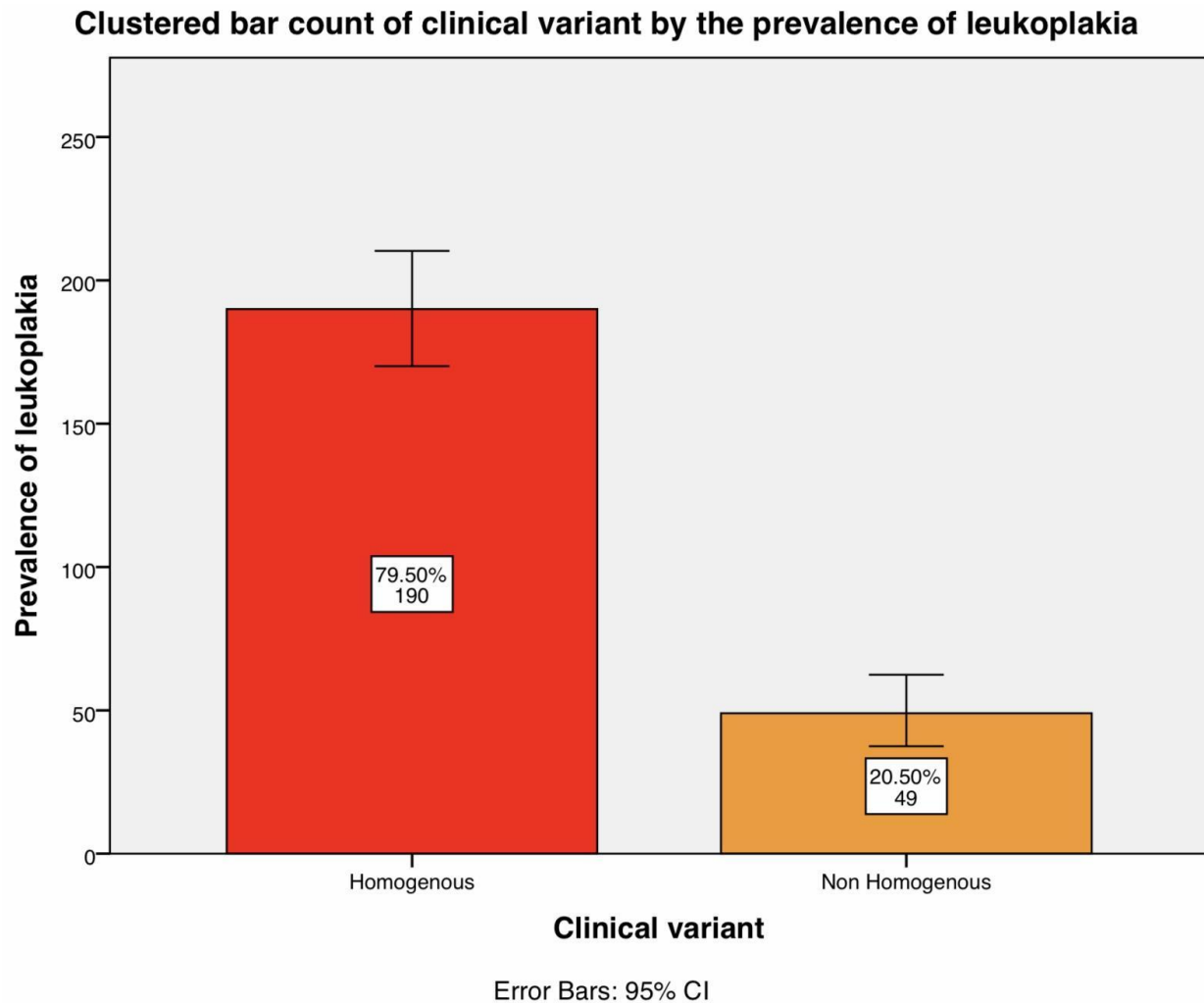


Figure 3:The above bar graph represents the association between the prevalence of leukoplakia with different clinical variants. X-axis represents the clinical variant of leukoplakia while Y-axis represents the percentage of prevalence of leukoplakia. Red denotes homogeneous type of clinical variant and orange denotes non-homogenous type of clinical variant. Higher population of people was affected with homogenous type (79.5%) and the rest of the population was affected with non-homogenous type (20.5%). Pearson chi-square test shows p-value is 0.00, (p-value < 0.05). Hence, it is statistically significant.

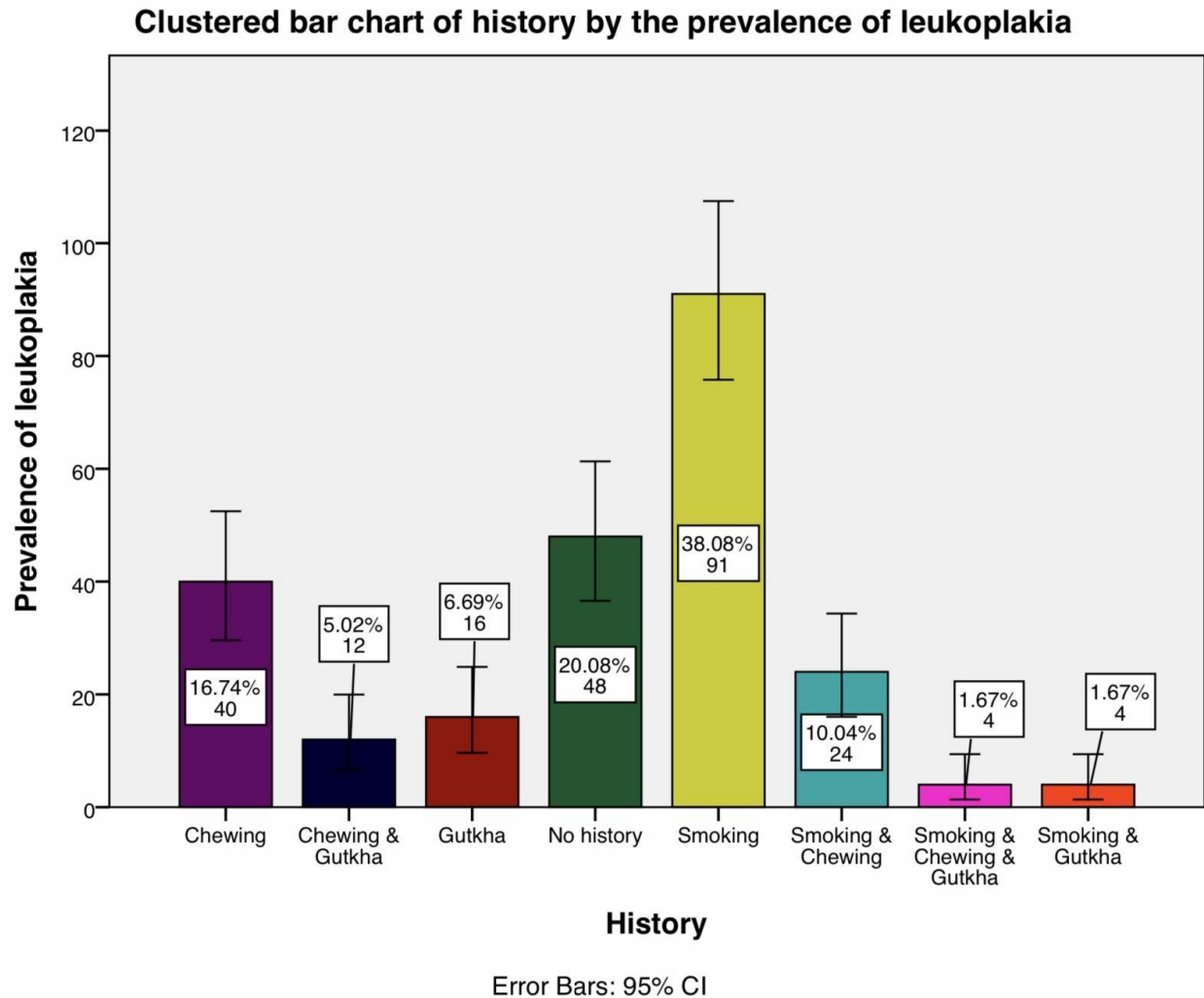


Figure 4:The above bar graph represents the association between the prevalence of leukoplakia with the history of the habit of the patient. X-axis represents the history of the patient while Y-axis represents the percentage of prevalence of leukoplakia. Purple denotes the history of chewing, dark blue denotes the history of chewing & gutkha, red denotes the history of gutkha, green denotes no history, yellow denotes the history of smoking, turquoise denotes the history of smoking & chewing, pink denotes the history of smoking & chewing & gutkha and orange denotes the history of smoking & gutkha. People with the most common history of smoking reported to the dental hospital with a higher prevalence (38.08%). Pearson chi-square test shows p-value is 0.00, (p-value < 0.05). Hence, it is statistically significant.

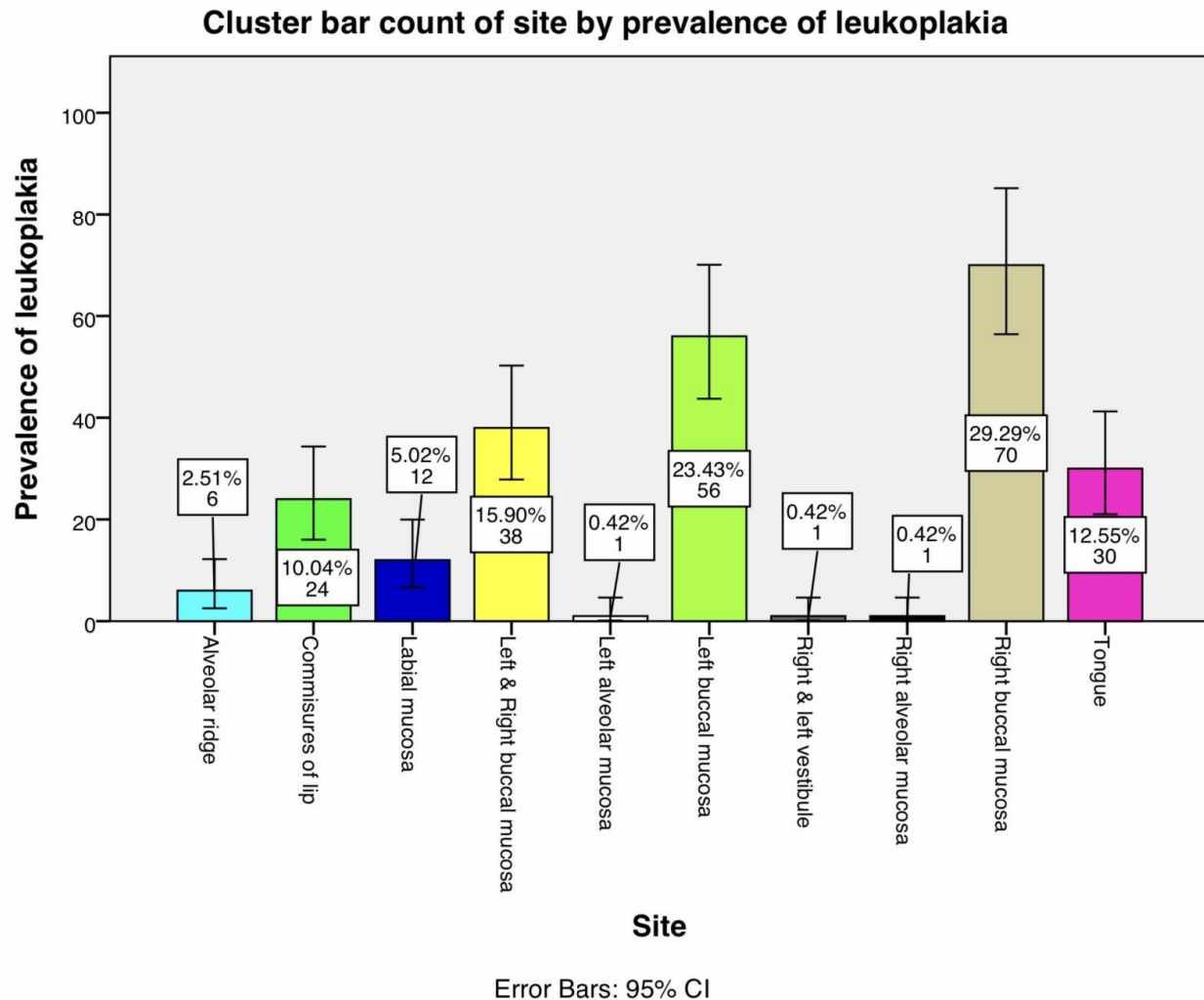


Figure 5:The above bar graph represents the prevalence of leukoplakia in different sites of the oral cavity. X-axis represents the site of the oral cavity while Y-axis represents the percentage of prevalence of leukoplakia. Blue denotes alveolar ridge, green denotes commissures of lip, blue denotes labial mucosa, yellow denotes left & right buccal mucosa, white denotes left alveolar mucosa, lime green denotes left buccal mucosa, grey denotes right & left vestibule, black denotes right alveolar mucosa, sandal denotes right buccal mucosa and pink denotes tongue. Right buccal mucosa was found to have the highest prevalence of leukoplakia (29.29%). Pearson chi-square test shows p-value is 0.00, ($p\text{-value} < 0.05$). Hence, it is statistically significant.

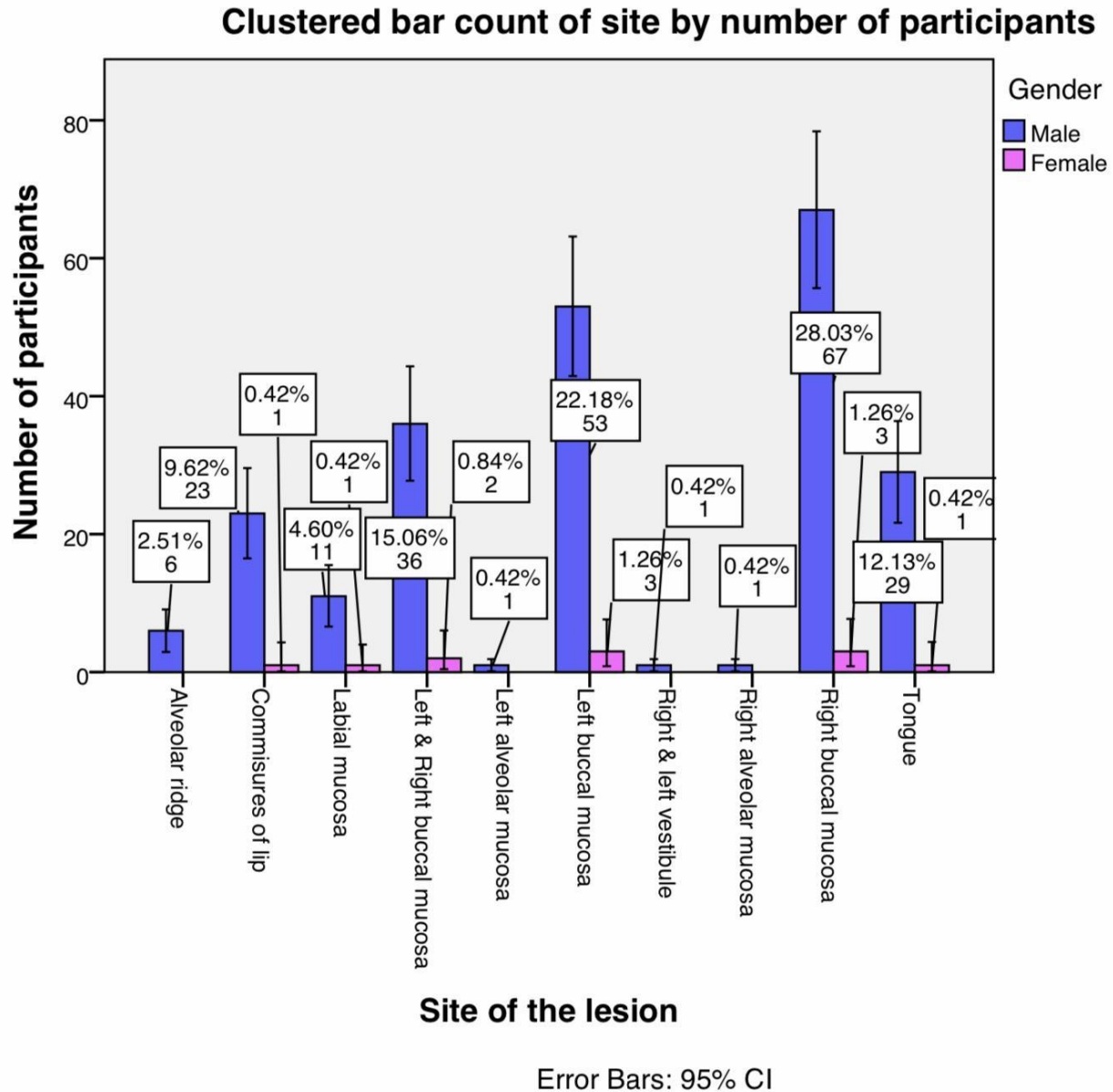


Figure 6:The above bar graph represents the association between the site of the lesion in the oral cavity by the number of population. X-axis represents the site of the lesion in the oral cavity while Y-axis represents the number of participants. Pink denotes female participants & blue denotes male participants. Pearson chi-square test shows p-value is 0.99, (p-value > 0.05).Hence, it is statistically not significant.

DISCUSSION:

Oral leukoplakia has an increased potential for turning into oral squamous cell carcinoma (15,16,26,27)(32)(33). With an overall rise in oral cancers throughout the world, the need for its early diagnosis and management becomes crucial in controlling the situation. The present study was a retrospective observational study wherein 239 leukoplakia cases were reported to a private dental hospital located in Chennai from June 2020 to April 2021. The collected data were subjected to descriptive statistical analysis and chi-square tests in SPSS to find the frequencies of age groups, gender, clinical variants, history of the habit and site of the lesion, and bar graphs were charted.

The present study reveals the gender predilection of the disease. The highest prevalence of leukoplakia among age groups was commonly observed in people aged between 50-60 years (29.7%) with the chi-square test showing a p-value of 0.000 which is considered to be statistically significant (**Figure 1**). According to our study, a higher rate of prevalence was observed in males (95.4%) than females (4.6%) with the chi-square test showing a p-value of 0.000 which is considered to be statistically significant (**Figure 2**). A previous study conducted by *Boker M et al* showed that oral leukoplakia occurred in men over 40 years of age and in women over 50 years of age (34). However, these results were opposite to a study conducted by *Rivera C et al* where females represented the majority of the prevalence (35)

Tobacco smoking is one of the most important etiological factors in the development of oral leukoplakia. Smokers tend to have a six-fold increase in the risk of developing leukoplakia of the oral mucosa in regard to non-smokers. In our study, people with a history of smoking (38.08%) had a higher prevalence than non-smokers or people with mixed habits with the chi-square test showing a p-value of 0.000 which is considered to be statistically significant (**Figure 4**). Comparing our study to the one conducted by *Boker M et al* shows the highest prevalence of leukoplakia among smokers (33.3%) (34). A similar study conducted by *Pratik P et al* revealed that smokers have a higher prevalence of leukoplakia (51.4%) (36). This also corresponds to a study conducted by *Bathi R*

et al where leukoplakia was reported by 8.2% of the patients with smoking habits and in those who chewed betel quid with tobacco (37).

Looking further into the study it reveals that 79.5% of the patients were diagnosed with the homogenous type and the remaining 20.50% of the patients were diagnosed with the non-homogenous type with the chi-square test showing a p-value of 0.000 which is considered to be statistically significant (**Figure 3**).

A previous study conducted by *Macigo FG et al*, reveals that smokers and patients with mixed habits had a higher prevalence of homogenous type of leukoplakia (10%) than the non-homogeneous type of leukoplakia (0.6%) (38). In another study conducted by *Scheifele C et al*, the prevalence estimates were 0.37% for homogeneous leukoplakia and 0.06% for non-homogeneous leukoplakia (39). A similar study conducted by *Nauma H et al* reveals the prevalence of 76.3% of homogenous type leukoplakia followed by 23.7% of non-homogenous type of leukoplakia among the patients (40).

Our current study reveals that the most common site of the prevalence of leukoplakia in the oral cavity was right buccal mucosa (29.29%) followed by the left buccal mucosa (23.43%) with the chi-square test showing a p-value of 0.000 which is considered to be statistically significant (**Figure 5**). This is similar to the previous study conducted by *Alshayeb M et al* which shows the prevalence of leukoplakia in the buccal mucosa (40.5%) and *Priya MK et al* which also revealed the buccal mucosa as the common site of the lesion (41,42). A study conducted by *Patil PB et al*, reveals that 40.2% of the population had the highest prevalence of leukoplakia in buccal mucosa of the oral cavity (37). Limitation of this study was less sample size and homogenous population. Further studies with larger sample size should be done to generalize the results.

CONCLUSION

Within the limits of the study oral premalignant leukoplakia has a strong male predilection and the age group of 50-60 years were most commonly affected

when compared to the other age groups. This study further results that homogenous type of oral leukoplakia was commonly prevalent in the right buccal mucosa followed by the left buccal mucosa of the oral cavity associated with the history of excess smoking. This gives us an idea of the causes specific to the study population and suggests steps that should be taken effectively for early diagnosis, treatment, and prevention of any malignant transformation.

ACKNOWLEDGEMENT

The authors are thankful to Saveetha Dental College for providing a platform to express our knowledge.

REFERENCES

1. Verma S, Sharma H. Prevalence of Oral mucosal lesions and their association with Pattern of tobacco use among patients visiting a dental institution. Indian J Dent Res [Internet]. 2019 Sep;30(5):652–5. Available from: http://dx.doi.org/10.4103/ijdr.IJDR_23_18
2. Ramani P, Gheena S, Karunagaran M, Hannah R. Clear-cell variant of oral squamous cell carcinoma: A rare entity. J Oral Maxillofac Pathol [Internet]. 2021 Mar 1 [cited 2021 May 18];25(4):22. Available from: <https://www.jomfp.in/article.asp?issn=0973-029X;year=2021;volume=25;issue=4;spage=22;epage=26;aulast=Ramani>
3. Narayan TV, Shilpashree S. Meta-analysis on clinicopathologic risk factors of leukoplakias undergoing malignant transformation. J Oral Maxillofac Pathol [Internet]. 2016 Sep;20(3):354–61. Available from: <http://dx.doi.org/10.4103/0973-029X.190900>
4. Analysis of Prevalence of Oral Squamous Cell Carcinoma in Patients with History of Chronic Irritation of Oral Tissues - A Retrospective Study [Internet]. Indian Journal of Forensic Medicine & Toxicology. 2020. Available from: <http://dx.doi.org/10.37506/ijfmt.v14i4.12511>
5. Antony JVM, Ramani P, Ramasubramanian A, Sukumaran G. Particle size penetration rate and effects of smoke and smokeless tobacco products - An invitro analysis. Heliyon [Internet]. 2021 Mar;7(3):e06455. Available from: <http://dx.doi.org/10.1016/j.heliyon.2021.e06455>
6. Mohammed F, Fairozekhan AT. Oral Leukoplakia. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020. Available from:

<https://www.ncbi.nlm.nih.gov/pubmed/28723042>

7. Yamunadevi A, Pratibha R, Rajmohan M, Ganapathy N, Porkodisudha J, Pavithrah D, et al. Molecular Insight into Odontogenesis in Hyperglycemic Environment: A Systematic Review. *J Pharm Bioallied Sci* [Internet]. 2020 Aug;12(Suppl 1):S49–56. Available from: http://dx.doi.org/10.4103/jpbs.JPBS_159_20
8. Pindborg JJ, Kiaer J, Gupta PC, Chawla TN. Studies in oral leukoplakias. Prevalence of leukoplakia among 10,000 persons in Lucknow, India, with special reference to use of tobacco and betel nut. *Bull World Health Organ* [Internet]. 1967;37(1):109–16. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/5300044>
9. Shah S, Dave B, Shah R, Mehta TR, Dave R. Socioeconomic and cultural impact of tobacco in India. *J Family Med Prim Care* [Internet]. 2018 Nov;7(6):1173–6. Available from: http://dx.doi.org/10.4103/jfmprc.jfmprc_36_18
10. Kumar Srivastava V. To Study the Prevalence of Premalignancies in Teenagers having Betel, Gutkha, Khaini, Tobacco Chewing, Beedi and Ganja Smoking Habit and Their Association with Social Class and Education Status. *Int J Clin Pediatr Dent* [Internet]. 2014 May;7(2):86–92. Available from: <http://dx.doi.org/10.5005/jp-journals-10005-1243>
11. Metgud R, Gupta K, Prasad U, Gupta J. Cytomorphometric analysis of oral submucous fibrosis and leukoplakia using methyl green-pyronin Y, Feulgen staining and exfoliative brush cytology [Internet]. Vol. 90, *Biotechnic & Histochemistry*. 2015. p. 8–13. Available from: <http://dx.doi.org/10.3109/10520295.2014.919025>
12. Bastos DB, Sarafim-Silva BAM, Sundfeld MLMM, Ribeiro AA, Brandão JDP, Biasoli ÉR, et al. Circulating catecholamines are associated with biobehavioral factors and anxiety symptoms in head and neck cancer patients. *PLoS One* [Internet]. 2018 Aug 20;13(8):e0202515. Available from: <http://dx.doi.org/10.1371/journal.pone.0202515>
13. Princeton B, Santhakumar P, Prathap L. Awareness on Preventive Measures taken by Health Care Professionals Attending COVID-19 Patients among Dental Students [Internet]. Vol. 14, *European Journal of Dentistry*. 2020. p. S105–9. Available from: <http://dx.doi.org/10.1055/s-0040-1721296>
14. Mathew MG, Samuel SR, Soni AJ, Roopa KB. Evaluation of adhesion of *Streptococcus mutans*, plaque accumulation on zirconia and stainless steel crowns, and surrounding gingival inflammation in primary molars: randomized controlled trial [Internet]. Vol. 24, *Clinical Oral Investigations*. 2020. p. 3275–80. Available from: <http://dx.doi.org/10.1007/s00784-020-03204-9>
15. Sridharan G, Ramani P, Patankar S, Vijayaraghavan R. Evaluation of salivary metabolomics in oral leukoplakia and oral squamous cell carcinoma. *J Oral Pathol Med* [Internet]. 2019 Apr;48(4):299–306. Available from: <http://dx.doi.org/10.1111/jop.12835>
16. R H, Hannah R, Ramani P, Ramanathan A, Jancy MR, Gheena S, et al. CYP2 C9 polymorphism among patients with oral squamous cell carcinoma and its role in altering the

metabolism of benzo[a]pyrene [Internet]. Vol. 130, Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology. 2020. p. 306–12. Available from: <http://dx.doi.org/10.1016/j.oooo.2020.06.021>

17. Sarode SC, Gondivkar S, Sarode GS, Gadbail A, Yuwanati M. Hybrid oral potentially malignant disorder: A neglected fact in oral submucous fibrosis [Internet]. Oral Oncology. 2021. p. 105390. Available from: <http://dx.doi.org/10.1016/j.oraloncology.2021.105390>
18. Hannah R, Ramani P, WM Tilakaratne, Sukumaran G, Ramasubramanian A, Krishnan RP. Author response for “Critical appraisal of different triggering pathways for the pathobiology of pemphigus vulgaris—A review” [Internet]. Wiley; 2021. Available from: <https://publons.com/publon/47643844>
19. Chandrasekar R, Chandrasekhar S, Shantha Sundari KK, Ravi P. Development and validation of a formula for objective assessment of cervical vertebral bone age [Internet]. Vol. 21, Progress in Orthodontics. 2020. Available from: <http://dx.doi.org/10.1186/s40510-020-00338-0>
20. Subramanyam D, Gurunathan D, Gaayathri R, Vishnu Priya V. Comparative evaluation of salivary malondialdehyde levels as a marker of lipid peroxidation in early childhood caries [Internet]. Vol. 12, European Journal of Dentistry. 2018. p. 067–70. Available from: http://dx.doi.org/10.4103/ejd.ejd_266_17
21. Jeevanandan G, Thomas E. Volumetric analysis of hand, reciprocating and rotary instrumentation techniques in primary molars using spiral computed tomography: An in vitro comparative study [Internet]. Vol. 12, European Journal of Dentistry. 2018. p. 021–6. Available from: http://dx.doi.org/10.4103/ejd.ejd_247_17
22. Ponnulakshmi R, Shyamaladevi B, Vijayalakshmi P, Selvaraj J. In silico and in vivo analysis to identify the antidiabetic activity of beta sitosterol in adipose tissue of high fat diet and sucrose induced type-2 diabetic experimental rats [Internet]. Vol. 29, Toxicology Mechanisms and Methods. 2019. p. 276–90. Available from: <http://dx.doi.org/10.1080/15376516.2018.1545815>
23. Sundaram R, Nandhakumar E, Haseena Banu H. Hesperidin, a citrus flavonoid ameliorates hyperglycemia by regulating key enzymes of carbohydrate metabolism in streptozotocin-induced diabetic rats [Internet]. Vol. 29, Toxicology Mechanisms and Methods. 2019. p. 644–53. Available from: <http://dx.doi.org/10.1080/15376516.2019.1646370>
24. Alsawalha M, Rao CV, Al-Subaie AM, Haque SKM, Veeraraghavan VP, Surapaneni KM. Novel mathematical modelling of Saudi Arabian natural diatomite clay. Mater Res Express [Internet]. 2019 Sep 4 [cited 2021 Aug 17];6(10):105531. Available from: <https://iopscience.iop.org/article/10.1088/2053-1591/ab2f9b/meta>
25. Tang X, Yu J, Li M, Zhan D, Shi C, Fang L, et al. Inhibitory effects of triterpenoid betulin on inflammatory mediators inducible nitric oxide synthase, cyclooxygenase-2, tumor necrosis factor- α , interleukin-6, and proliferating cell nuclear antigen in 1,2-dimethylhydrazine-induced rat colon carcinogenesis [Internet]. Vol. 16, Pharmacognosy

Magazine. 2020. p. 841. Available from: http://dx.doi.org/10.4103/pm.pm_516_19

26. Hema Shree K, Ramani P, Sherlin H, Sukumaran G, Jeyaraj G, Don KR, et al. Saliva as a Diagnostic Tool in Oral Squamous Cell Carcinoma - a Systematic Review with Meta Analysis. *Pathol Oncol Res* [Internet]. 2019 Apr;25(2):447–53. Available from: <http://dx.doi.org/10.1007/s12253-019-00588-2>
27. Zafar A, Sherlin HJ, Jayaraj G, Ramani P, Don KR, Santhanam A. Diagnostic utility of touch imprint cytology for intraoperative assessment of surgical margins and sentinel lymph nodes in oral squamous cell carcinoma patients using four different cytological stains. *Diagn Cytopathol* [Internet]. 2020 Feb;48(2):101–10. Available from: <https://onlinelibrary.wiley.com/doi/10.1002/dc.24329>
28. Karunagaran M, Murali P, Palaniappan V, Sivapathasundharam B. Expression and distribution pattern of podoplanin in oral submucous fibrosis with varying degrees of dysplasia – an immunohistochemical study [Internet]. Vol. 42, *Journal of Histotechnology*. 2019. p. 80–6. Available from: <http://dx.doi.org/10.1080/01478885.2019.1594543>
29. Sarode SC, Gondivkar S, Gadbail A, Sarode GS, Yuwanati M. Oral submucous fibrosis and heterogeneity in outcome measures: a critical viewpoint. *Future Oncol* [Internet]. 2021 Jun;17(17):2123–6. Available from: <http://dx.doi.org/10.2217/fon-2021-0287>
30. Preeth DR, Saravanan S, Shairam M, Selvakumar N, Raja IS, Dhanasekaran A, et al. Bioactive Zinc(II) complex incorporated PCL/gelatin electrospun nanofiber enhanced bone tissue regeneration [Internet]. Vol. 160, *European Journal of Pharmaceutical Sciences*. 2021. p. 105768. Available from: <http://dx.doi.org/10.1016/j.ejps.2021.105768>
31. Prithiviraj N, Yang GE, Thangavelu L, Yan J. Anticancer Compounds From Starfish Regenerating Tissues and Their Antioxidant Properties on Human Oral Epidermoid Carcinoma KB Cells. In: *PANCREAS. LIPPINCOTT WILLIAMS & WILKINS TWO COMMERCE SQ, 2001 MARKET ST, PHILADELPHIA ...*; 2020. p. 155–6.
32. Sinduja P, Ramani P, Gheena S, Ramasubramanian A. Expression of metallothionein in oral squamous cell carcinoma: A systematic review. *J Oral Maxillofac Pathol* [Internet]. 2020 Jan;24(1):143–7. Available from: http://dx.doi.org/10.4103/jomfp.JOMFP_137_19
33. Thamilselvan S, Abilasha R, Ramani P, Gheena S, Hannah R. Evaluation of Accuracy between Habit History and Incidence of Oral Squamous Cell Carcinoma [Internet]. *International Journal of Current Research and Review*. 2020. p. 30–5. Available from: <http://dx.doi.org/10.31782/ijcrr.2020.122503>
34. Bokor-Bratic M. Prevalence of oral leukoplakia [Internet]. Vol. 56, *Medical review*. 2003. p. 552–5. Available from: <http://dx.doi.org/10.2298/mpns0312552b>
35. Rivera C, Jones-Herrera C, Vargas P, Venegas B, Droguett D. Oral diseases: a 14-year experience of a Chilean institution with a systematic review from eight countries. *Med Oral Patol Oral Cir Bucal* [Internet]. 2017 May 1;22(3):e297–306. Available from: <http://dx.doi.org/10.4317/medoral.21665>

36. Pratik P, Desai VD. Prevalence of habits and oral mucosal lesions in Jaipur, Rajasthan. *Indian J Dent Res* [Internet]. 2015 Mar;26(2):196–9. Available from: <http://dx.doi.org/10.4103/0970-9290.159166>
37. Patil PB, Bathi R, Chaudhari S. Prevalence of oral mucosal lesions in dental patients with tobacco smoking, chewing, and mixed habits: A cross-sectional study in South India. *J Family Community Med* [Internet]. 2013 May;20(2):130–5. Available from: <http://dx.doi.org/10.4103/2230-8229.114777>
38. Macigo FG, Mwaniki DL, Guthua SW. Prevalence of oral mucosal lesions in a Kenyan population with special reference to oral leukoplakia. *East Afr Med J* [Internet]. 1995 Dec;72(12):778–82. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/8689976>
39. Scheifele C, Reichart PA, Dietrich T. Low prevalence of oral leukoplakia in a representative sample of the US population [Internet]. Vol. 39, *Oral Oncology*. 2003. p. 619–25. Available from: [http://dx.doi.org/10.1016/s1368-8375\(03\)00050-2](http://dx.doi.org/10.1016/s1368-8375(03)00050-2)
40. Hafeez N, Uma Maheshwari TN. PREVALENCE OF CLINICAL TYPES OF ORAL LEUKOPLAKIA REPORTED IN A PRIVATE DENTAL INSTITUTION : A RETROSPECTIVE STUDY. *J ArchEgyptol* [Internet]. 2020 Nov 28 [cited 2021 May 14];17(7):3191–200. Available from: <https://archives.palarch.nl/index.php/jae/article/view/1859>
41. Priya MK, Krishna Priya M, Srinivas P, Devaki T. Evaluation of the prevalence of oral mucosal lesions in a population of eastern coast of South India [Internet]. Vol. 8, *Journal of International Society of Preventive and Community Dentistry*. 2018. p. 396. Available from: http://dx.doi.org/10.4103/jispcd.jispcd_207_17
42. Alshayeb M, Mathew A, Varma S, Elkaseh A, Kuduruthullah S, Ashekhi A, et al. Prevalence and distribution of oral mucosal lesions associated with tobacco use in patients visiting a dental school in Ajman. 2019 [cited 2021 May 14]; Available from: <https://www.semanticscholar.org/paper/9caa076a8f746a923fd1eba7eb17ef242b0a5264>