

Evaluation Of Clinical Presentation Of Oral Squamous Cell Carcinoma In A Private Dental Institution

Research Article

Abarna Jawahar¹, G. Maragathavalli^{2*}, Manjari Chaudhary³

¹ Department of Oral Medicine and Radiology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai, India.

² Professor, Department of Oral Medicine and Radiology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai, India.

³ Senior Lecturer, Department of Oral Medicine and Radiology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai, India.

Abstract

Oral cancer is the second most common disease in India with a mortality rate of about 0.3 million deaths per year. Oral squamous cell carcinoma (OSCC) contributes to 95% of all forms of head and neck cancer. The aim of the study is to evaluate the clinical presentation of oral squamous cell carcinoma in a private dental institution. A retrospective study was conducted on patients who visited the Department of Oral Medicine and Oral Oncology during the period June 2019 to March 2020. Case records of 31 patients who were diagnosed with oral squamous cell carcinoma histopathologically were reviewed. Descriptive statistics and chi square test was used to evaluate the clinical association between OSCC and age, sex, site and duration of habit. From the study we found that maximum patients belonged to the age group of 40-50 years (37.50%) and males (71.88%) were predominantly affected than females (28.13%). About 37.50% of the patients had a habit of smoking or chewing tobacco over a duration of about 1-5 years and 37.50% had a habit for a duration of about 5-10 years. Ulceroproliferative type (62.50%) was the most commonly seen clinical type of oral squamous cell carcinoma followed by the ulcerative type (34.38%). The most commonly affected sites were left buccal mucosa (21.88%), right lower posterior alveolar mucosa (21.88%) and right buccal mucosa (18.75%). There was statistically no significant association between oral squamous cell carcinoma with age, sex, site and duration of habit (p value > 0.05).

Keywords: Oral Cancer; Oral Carcinoma; Oral Squamous Cell Carcinoma; OSCC.

Introduction

Oral cancer can be defined as a neoplasm involving the oral cavity which begins at lips and ends at anterior pillar of fauces. Oral cancer is a seriously growing problem in many parts of the world. Oral and pharyngeal cancer grouped together is the sixth most common cancer in the world [38]. Oral cancer is the second most common disease in India with mortality rate of about 0.3 million deaths per year [11]. Oral squamous cell carcinoma (OSCC) represents 95% of all forms of head and neck cancer. Its incidence has increased by 50% in the last decade [23]. Primary oral squamous cell carcinoma is the most prevalent oral malignancy, but secondary malignancy from distant sites have also been reported [18, 20].

Majority of the oral carcinomas are related to the use of tobacco and tobacco products [35, 19]. Smoking or chewing tobacco combined with alcohol results in increased cancer incidence has an additive effect because of their synergistic action [37, 30].

Pain may be one of the initial symptoms in oral cancer and is a common complaint in these patients [32]. The pathognomonic sign of oral squamous cell carcinoma is the presence of induration of the margin and the base of the tumour. The high risk sites for the development of oral squamous cell carcinoma are the lower buccal sulcus or posterior buccal mucosa followed by lateral border of tongue and floor of the mouth due to placement of tobacco containing quid and pooling of tobacco fluid [5,

*Corresponding Author:

G. Maragathavalli,

Professor, Department of Oral Medicine and Radiology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai, India.

Tel: 9445171146

E-mail: maragathavalli@saveetha.com

Received: August 11, 2020

Accepted: August 29, 2020

Published: August 30, 2020

Citation: Abarna Jawahar, G. Maragathavalli, Manjari Chaudhary. Evaluation Of Clinical Presentation Of Oral Squamous Cell Carcinoma In A Private Dental Institution. *Int J Dentistry Oral Sci.* 2020;S4:02:0013:69-74. doi: <http://dx.doi.org/10.19070/2377-8075-SI02-040013>

Copyright: G. Maragathavalli©2020. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.

21]. Radiographically the changes caused due to oral squamous cell carcinoma may or may not be seen. If there is involvement of bone, radiographic changes such as bone resorption with ill-defined margins or well-defined margins may be seen [6]. CBCT has been found to show higher sensitivity for detection of cortical bone invasion and with a significantly lower exposure dose [24].

The majority of the oral squamous cell carcinoma are diagnosed at late stage due to lack of awareness which markedly decreases the chances of their survival and also leads to a significant deterioration in patient's quality of life [33, 13]. Treatment options for oral cancer includes surgery, radiation therapy, targeted drug therapy and chemotherapy (International Journal of Research in Pharmaceutical Sciences, no date). Due to the diversity of the anatomic sites in the neck region and proximity of tumour to the important vital structures that may be present in that region, makes the treatment of OSCC more challenging. The dental care of these patients often requires a multidisciplinary team of surgeons, radiation oncologists, medical oncologists, nutritionists, gastroenterologists, speech and swallowing therapists [36]. Despite the currently available advanced diagnostic and therapeutic strategies, the disease still remains a challenge for medical and dental professionals. In some patients there might be poor response to the treatment and might have recurrence [1]. The five-year survival rate is only 53% and has not improved in the past decade [34, 29].

Oral cancer and its treatment can cause a range of problems in patients including difficulty in maintaining their routine oral hygiene [8, 31]. The management of postoperative pain remains a hideous task for health-care providers [5]. The main complication of non surgical treatment of oral cancer is development of oral mucositis. It is considered as an inherent outcome of chemotherapy or radiotherapy to the head and neck region in oral cancer patients. Patients treated with radiotherapy have the oral mucositis prevalence of about 100 % when compared to those in chemotherapy treated ones which is about 40% [4]. Radiotherapy (RT) to the head and neck region can cause salivary gland dysfunction and xerostomia which increases the risk of dental caries. Hence every steps should be taken to prevent and manage patients with severe caries. This can be accomplished through preoperative dental treatment along with frequent dental evaluation and additional home care that includes self-applied fluoride [25].

Recently several biomarkers have been identified which can be used as a diagnostic tool for screening and early detection of oral cancer. It can also be used to indicate the prognosis of the disease. Serum lactate dehydrogenase (LDH) levels are significantly increased in OSCC patients [2, 14]. A range of salivary metabolites are found to be significantly altered in oral premalignant condition and in oral squamous cell carcinoma. Salivary biomarkers such as micro RNA, MMP-9, chemerin, glutathione, malondialdehyde and tumour necrosis factor (TNF) alpha can be used for early detection of oral squamous cell carcinoma [15, 16, 9, 26, 28].

The prevalence of oral cancer is higher among elderly males predominantly with risk habits of betel quid/tobacco chewing and smoking. Ishiyama et al. (1994) conducted a study on papillary squamous neoplasm of head and neck, which reported that the papillary type of squamous neoplasms was highest in age group of 50-59 years and 60-69 years, males were affected more than females. Alveolar ridge was the most commonly involved site fol-

lowed by buccal mucosa and use of tobacco being the most common habit [12, 22].

Hence the aim of the study is to evaluate the clinical presentation of oral squamous cell carcinoma in a private dental institution.

Materials and Methods

A retrospective study was conducted on patients who visited the Department of Oral Medicine and Oral Oncology during the period June 2019 to March 2020. Ethical clearance was obtained from the research committee and the ethical approval number is SDC/SIHEC/2020/DIASDATA/0619-0320. A primary researcher and a reviewer were involved in this retrospective study. Case records of 31 patients who were diagnosed with oral squamous cell carcinoma histopathologically were reviewed and cross verification of the case records were done by the primary researcher and reviewer. In order to minimise the sampling bias, all the available data on histopathologically confirmed cases of oral squamous cell carcinoma were included in the study. The following criteria were followed for the selection of patients.

Inclusion Criteria:

Histopathologically diagnosed oral squamous cell carcinoma patients who were above the age of 35 years and lesions that were clinically visible in the oral cavity only were included.

Exclusion Criteria:

Oral squamous cell carcinoma not histopathologically diagnosed and patients below the age of 35 years were excluded from the study. Lesions that were not clinically visible in the oral cavity and patients who had already undergone treatment for oral cancer were excluded.

After selection of the patient, further information on age, sex, duration of the tobacco habit, site of the lesion, histopathological grading of OSCC and clinical presentation was obtained from an electronic database. The retrieved data was tabulated in SPSS software and analysed statistically. Descriptive statistics and chi square test was used to assess the clinical correlation between oral squamous cell carcinoma with age, sex, site and duration of habit.

Results And Discussion

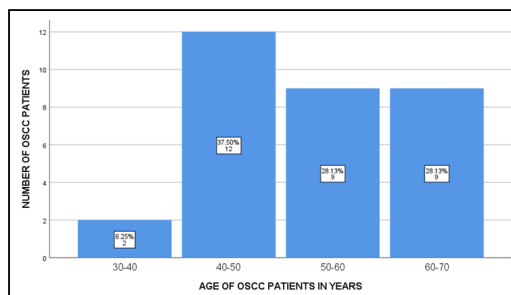
The study was conducted on 31 patients who were diagnosed with oral squamous cell carcinoma.

From the study we observe that maximum patients belong to the age group of 40-50 years (37.50%) (graph 1) and males (71.88%) were predominantly affected than females (28.13%) (graph 2).

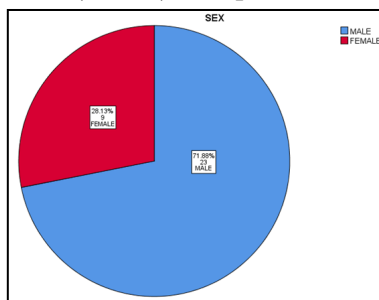
About 37.50% of the patients had a habit of smoking or chewing tobacco over a duration of about 1-5 years, 37.50% had a habit for a duration of about 5-10 years and 15.63% had the habit for a duration of more than 10 years (graph 3).

Ulceroproliferative type (62.50%) was the most commonly seen clinical type of oral squamous cell carcinoma followed by the ulcerative type (34.38%) (graph 4).

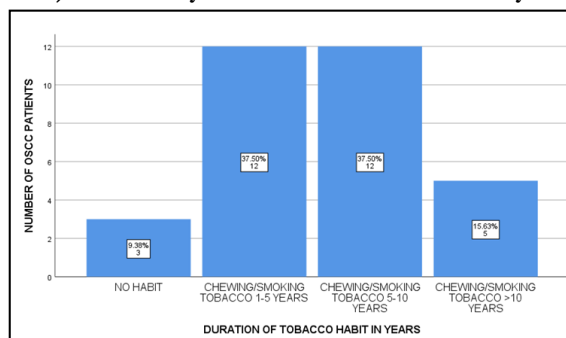
Graph 1. This bar graph shows age distribution of the study population. X axis denotes age of OSCC patients in years and Y axis denotes number of OSCC patients. The maximum patients belonged to the age group of 40-50 years(37.50%) followed by 50-60 years(28.13%) and 60-70 years(28.13%) in the study population.



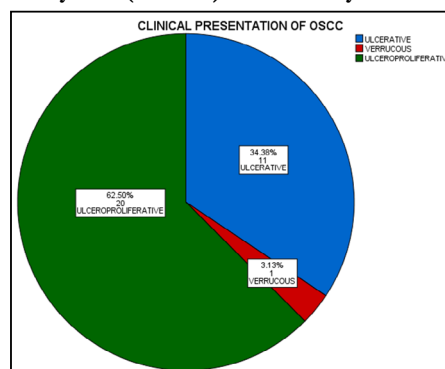
Graph 2. This pie-chart shows sex distribution of the study population. Blue colour denotes male and red colour denotes female. In the present study the males (71.88%) were predominantly affected than females (28.13%).



Graph 3. This bar graph shows the frequency distribution of duration of chewing/smoking tobacco habit in the OSCC patients. X axis denotes the duration of tobacco consumption habit in years and Y axis denotes the number of OSCC patients. The majority of patients had the habit of chewing/smoking tobacco for a duration of 1-5 years (37.50%) and 5-10 years (37.50%) followed by a duration of more than 10 years (15.63%).



Graph 4. This pie-chart shows the frequency distribution of clinical presentation OSCC in the study population. Green colour denotes ulceroproliferative, blue colour denotes ulcerative and red colour denotes verrucous type. The most commonly seen clinical presentation was ulceroproliferative (62.50%) followed by the ulcerative (34.8%). The verrucous type (3.13%) was least seen in the study population.

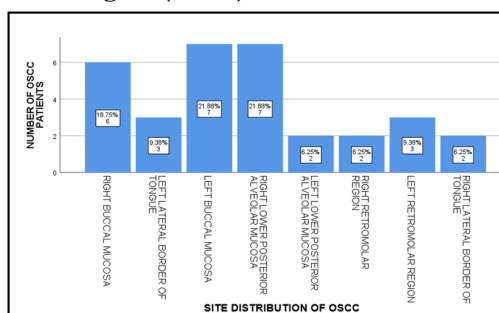


of tongue (6.25%) (graph 5).

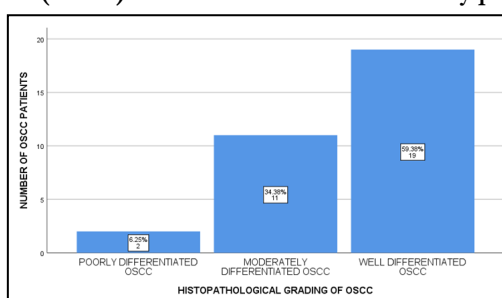
The most commonly affected sites are left buccal mucosa (21.88%), right lower posterior alveolar mucosa (21.88%) and right buccal mucosa (18.75%). Other sites which were affected are left retromolar region (9.38%), left lateral border of tongue (9.38%), right retromolar region (6.25%) and right lateral border

Well-differentiated oral squamous cell carcinoma contributed to the majority of the study population (59.38%) followed by moderately differentiated oral squamous cell carcinoma (34.38%) (graph 6).

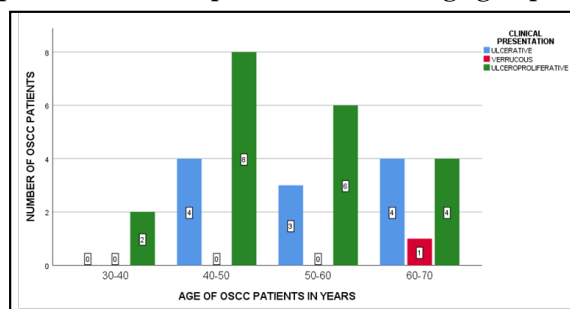
Graph 5. This graph shows the frequency of site-distribution of OSCC in the oral mucosa. X axis denotes the site distribution of OSCC in the oral mucosa and Y axis denotes the number of OSCC patients. The most commonly affected sites were right lower posterior alveolar mucosa (21.88%) and left buccal mucosa (21.8%) followed by the right buccal mucosa (18.75%), left retromolar region (9.38%) and left lateral border of tongue (9.38%).



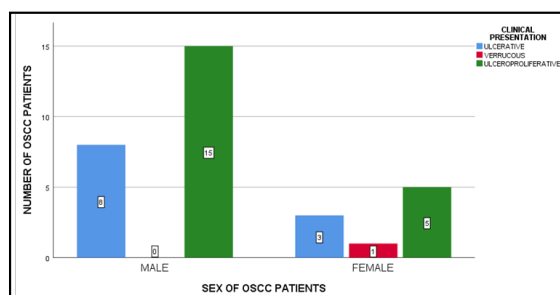
Graph 6. This graph shows the frequency distribution of histopathological grading of OSCC in the study population. X axis denotes the histopathological grading of OSCC and Y axis denotes the number of OSCC patients. The well-differentiated OSCC(59.38%) was most commonly reported followed by moderately differentiated OSCC(34.38%).The poorly differentiated OSCC(6.25%) was seen the least in the study population.



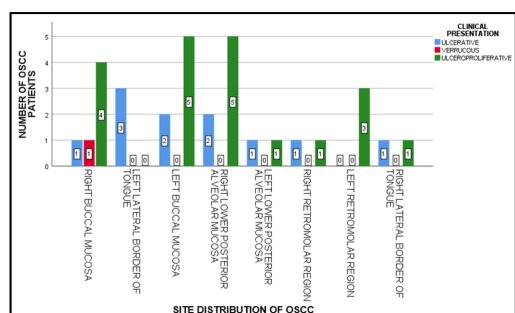
Graph 7. This bar graph depicts the association between clinical presentation of OSCC and age. Blue colour denotes ulcerative, red colour denotes verrucous and green colour denotes ulceroproliferative type. X axis denotes age of the patients in number and Y axis denotes number of OSCC patients. The 40-50 years group (12) was the most affected age group, with maximum presentation of ulceroproliferative type(8) followed by ulcerative type(4). In 60-70 years group ulceroproliferative type(4) and ulcerative(4) was seen equally with one patient presenting with verrucous type. In the 30-40 years group only ulceroproliferative type(2) was seen. Chi-square analysis was done [Pearson $\chi^2 = 4.493$ a p value = 0.61(>0.05)] and there was statistically no significant association between OSCC and age. Hence the ulceroproliferative was the most commonly reported type with maximum presentation in the age group of 40-50 years.



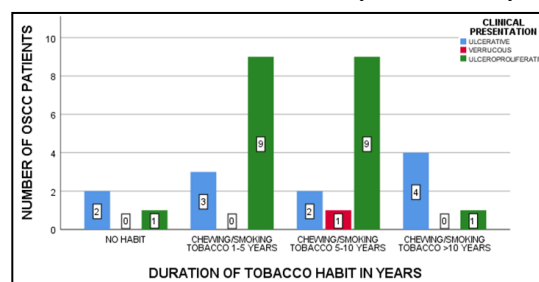
Graph 8. This bar graph shows the association between clinical presentation of OSCC and sex. Blue colour denotes ulcerative, red colour denotes verrucous and green colour denotes ulceroproliferative type. X axis denotes sex and Y axis denotes number of OSCC patients. The males (23) were more commonly affected than females (9). In males the ulceroproliferative type(15) was predominantly seen followed by ulcerative type(8). Similarly in females also the ulceroproliferative type(5) was predominantly seen followed by ulcerative(3) and one patient presented with a verrucous type. The males did not report a verrucous type of OSCC. Chi-square analysis was done [Pearson $\chi^2 = 2.656$ a p value = 0.265 (>0.05)] and there was statistically no significant association between OSCC and sex. Hence the ulceroproliferative was the commonly reported type with maximum presentation in the males.



Graph 9. This bar graph shows the association between clinical presentation of OSCC and site. Blue colour denotes ulcerative, red colour denotes verrucous and green colour denotes ulceroproliferative type. X axis denotes site distribution of OSCC in the oral mucosa and Y axis denotes the number of OSCC patients. The most commonly affected sites were right lower posterior alveolar mucosa(7) and left buccal mucosa(7). In both these sites the ulceroproliferative type (5) was predominantly seen followed by ulcerative (2). Chi square analysis was done [Pearson $\chi^2=13.129$ a p value= $0.516(>0.05)$] and there was no statistically significant association between OSCC and site. Hence the ulceroproliferative type was the commonly reported type with maximum presentation in the sites right posterior alveolar mucosa and left buccal mucosa.



Graph 10. This bar graph shows the association between clinical presentation of OSCC and duration of tobacco habit. Blue colour denotes ulcerative, red colour denotes verrucous and green colour denotes ulceroproliferative type. X axis denotes the duration of tobacco habit in years and Y axis denotes number of OSCC patients. Most of the patients had a duration of tobacco habit of 1-5 years(12) and 5-10 years (12). In patients with a duration of habit for 1-5 years the ulceroproliferative type(9) was reported the maximum followed by ulcerative (3). In patients with a duration of habit for 5-10 years the ulceroproliferative type(9) was reported the maximum followed by ulcerative(2) and one verrucous type. 2 patients of ulcerative type and 1 patient of ulceroproliferative had no tobacco habit. Chi-square analysis was done [Pearson $\chi^2= 9.459$ a p value= $0.149 (>0.05)$] and there was no statistically significant association between OSCC and duration of tobacco habit. Hence the ulceroproliferative was the commonly reported type with maximum presentation in patients who had a duration of tobacco habit 1-5 years and 5-10 years.



From the study we find that there is no statistically significant association between oral squamous cell carcinoma with age, sex, site and duration of habit(p value > 0.05) (graph 7-10).

Study done by Rai HC et al. in 2016 and Mathew PT et al. in 2011 found that there was no statistically significant association between age and sex with the clinical type of oral squamous cell carcinoma. This article favours the study findings [7, 17].

According to Soni R et al. there was no statistically significant association between the duration of tobacco chewing or smoking habit with the clinical pattern of oral squamous cell carcinoma. This article supports our study findings [27].

In our study the ulceroproliferative was the most commonly seen clinical presentation of OSCC, affecting the majority of patients in the age group of 40-50 years, with a male predilection. The left buccal mucosa and alveolar mucosa were the most commonly affected site. The duration of the tobacco habit observed in most of the patients were minimum of 1 year to a maximum of 10 years.

The limitation of the present study was a relatively small sample size and study being done retrospectively. Further studies with an increased sample size can be done prospectively in the future.

Conclusion

The present study concludes that there is statistically no significant association between oral squamous cell carcinoma with age, sex and duration of habit. However ulceroproliferative(62.50%) type of oral squamous cell carcinoma was the most predominantly seen clinical presentation. Maximum patients belonged to the age group of 40 to 50 years(37.50%) with male predilection (71.88%). Majority of OSCC patients had a duration of tobacco habit for a minimum of 1 year to a maximum of 10 years (75%). Future studies should concentrate on evaluation of hidden predisposing idiopathic factors associated with oral squamous cell carcinoma.

References

- [1]. Bettendorf O, Piffkò J, Bänkfalvi A. Prognostic and predictive factors in oral squamous cell cancer: important tools for planning individual therapy? *Oral Oncol.* 2004 Feb;40(2):110-9. Pubmed PMID: 14693233.
- [2]. Bharathi, R., N, A. V. and Savitha, G. (2018) 'Assessment of lipid profile status in oral squamous cell carcinoma patients', *International Journal of Research in Pharmaceutical Sciences*. International Journal of Research in Pharmaceutical Sciences, Sponsored by JK Welfare & Pharmascope Foundation, 9(3).
- [3]. Bray F, Sankila R, Ferlay J, Parkin DM. Estimates of cancer incidence and mortality in Europe in 1995. *Eur J Cancer.* 2002 Jan;38(1):99-166. Pubmed PMID: 11750846.
- [4]. Chaitanya NC, Muthukrishnan A, Babu DBG, Kumari CS, Lakshmi MA, Palat G, Alam KS. Role of Vitamin E and Vitamin A in Oral Mucositis Induced by Cancer Chemo/Radiotherapy- A Meta-analysis. *J Clin Diagn Res.*

- 2017 May;11(5):ZE06-ZE09. Pubmed PMID: 28658926.
- [5]. Chaitanya NC, Muthukrishnan A, Krishnaprasad CMS, Sanjuprasanna G, Pillay P, Mounika B. An Insight and Update on the Analgesic Properties of Vitamin C. *J Pharm Bioallied Sci.* 2018 Jul-Sep;10(3):119-125. Pubmed PMID: 30237682.
- [6]. Choudhury P, Panigrahi RG, Maragathavalli, Panigrahi A, Patra PC. Vanishing roots: first case report of idiopathic multiple cervico-apical external root resorption. *J Clin Diagn Res.* 2015 Mar;9(3):ZD17-9. Pubmed PMID: 25954713.
- [7]. Rai HC, Ahmed J. Clinicopathological Correlation Study of Oral Squamous Cell Carcinoma in a Local Indian Population. *Asian Pac J Cancer Prev.* 2016;17(3):1251-4. Pubmed PMID: 27039755.
- [8]. Dharman S, Muthukrishnan A. Oral mucous membrane pemphigoid - Two case reports with varied clinical presentation. *J Indian Soc Periodontol.* 2016 Nov-Dec;20(6):630-634. Pubmed PMID: 29238145.
- [9]. Hema Shree K, Ramani P, Sherlin H, Sukumaran G, Jeyaraj G, Don KR, Santhanam A, Ramasubramanian A, Sundar R. Saliva as a Diagnostic Tool in Oral Squamous Cell Carcinoma - a Systematic Review with Meta Analysis. *Pathol Oncol Res.* 2019 Apr;25(2):447-453. Pubmed PMID: 30712193.
- [10]. Neralla M, Jones Jayabalan RG, Rajan J, MP SK, Haque AE, Balasubramanian A, Christopher PJ. INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACEUTICAL SCIENCES.
- [11]. Kadiyala SV. A study of salivary lactate dehydrogenase (Ldh) levels in oral cancer and oral submucosal fibrosis patients among the normal individuals. *Journal of Pharmaceutical Sciences and Research.* 2015 Jul 1;7(7):455.
- [12]. Khanolkar VR. Oral cancer in Bombay, India. A review of 1,000 consecutive cases. *Cancer Research.* 1944 May 1;4(5):313-9.
- [13]. Kumar, R. P., Thenmozhi, S. and Thangavelu, L. (2019) 'Awareness about oral cancer among tobacco users visiting a private dental hospital in Chennai', *Drug Invention Today*, 12(3).
- [14]. Madhumithaa, S., N, A. V. and Savitha, G. (2018) 'Serum LDH levels in oral squamous cell carcinoma patients', *International Journal of Research in Pharmaceutical Sciences*, Sponsored by JK Welfare & Pharmascope Foundation, 9(3).
- [15]. Maheswari TNU, Venugopal A, Sureshbabu NM, Ramani P. Salivary micro RNA as a potential biomarker in oral potentially malignant disorders: A systematic review. *Ci Ji Yi Xue Za Zhi.* 2018 Apr-Jun;30(2):55-60. Pubmed PMID: 29875583.
- [16]. Mariyam Niyas, F. and Savitha, G. (2018) 'Metabolic Antioxidant Status in Oral Squamous Cell Carcinoma', *Research Journal of Pharmacy and Technology.* *Research Journal of Pharmacy and Technology*, 11(10), pp. 4362-4364.
- [17]. Mathur, P. T., Dayal, P. K. and Pai, K. M. (2011) 'Correlation of Clinical Patterns of Oral Squamous Cell Carcinoma with Age, Site Sex and Habits'. *unknown*, 23(2), pp. 81-85.
- [18]. Misra SR, Shankar YU, Rastogi V, Maragathavalli G. Metastatic hepatocellular carcinoma in the maxilla and mandible, an extremely rare presentation. *Contemp Clin Dent.* 2015 Mar;6(Suppl 1):S117-21. Pubmed PMID: 25821363.
- [19]. Muthukrishnan A, Bijai Kumar L. Actinic cheilosis: early intervention prevents malignant transformation. *BMJ Case Rep.* 2017 Mar 20;2017:bcr2016218654. Pubmed PMID: 28320702.
- [20]. Muthukrishnan A, Bijai Kumar L, Ramalingam G. Medication-related osteonecrosis of the jaw: a dentist's nightmare. *BMJ Case Rep.* 2016 Apr 6;2016:bcr2016214626. Pubmed PMID: 27053542.
- [21]. Muthukrishnan A, Warnakulasuriya S. Oral health consequences of smokeless tobacco use. *Indian J Med Res.* 2018 Jul;148(1):35-40. Pubmed PMID: 30264752.
- [22]. Nandhini, T. and Narayan, V. (2019) 'Prevalence of oral cancer among patients using different forms of tobacco-A retrospective study', *Drug Invention Today*, 11(2).
- [23]. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin.* 2005 Mar-Apr;55(2):74-108. Pubmed PMID: 15761078.
- [24]. Patil, S. R. et al. (2018) 'Three-Rooted Mandibular First Molars in a Saudi Arabian Population: A CBCT Study', *Pesquisa brasileira em odontopediatria e clinica integrada*, 18(1), p. 4133.
- [25]. Rohini, S. and Kumar, V. J. (2017) 'Incidence of dental caries and pericoronitis associated with impacted mandibular third molar-A radiographic study', *Journal of advanced pharmaceutical technology & research*, 10(4), p. 1081.
- [26]. Sabarathinam, J., Selvaraj, J. and Devi, S. (2019) 'Estimation of Levels of Glutathione Peroxidase (Gpx), Malondialdehyde (Mda), Tumor Necrosis Factor Alpha (Tnf Alpha) and Alpha FetoProtein (Afp) In Saliva of Potentially Malignant Disorders and Oral Squamous Cell Carcinoma', *Biomedical and Pharmacology Journal*, 12(04), pp. 1881-1886.
- [27]. Shenoir R, Devrukhkar V; Chaudhuri, Sharma BK, Sapre SB, Chikhale A. Demographic and clinical profile of oral squamous cell carcinoma patients: a retrospective study. *Indian J Cancer.* 2012 Jan-Mar;49(1):21-6. Pubmed PMID: 22842164.
- [28]. Sridharan G, Ramani P, Patankar S, Vijayaraghavan R. Evaluation of salivary metabolomics in oral leukoplakia and oral squamous cell carcinoma. *J Oral Pathol Med.* 2019 Apr;48(4):299-306. Pubmed PMID: 30714209.
- [29]. Sridharan G, Ramani P, Patankar S. Serum metabolomics in oral leukoplakia and oral squamous cell carcinoma. *J Cancer Res Ther.* 2017 Jul-Sep;13(3):556-561. Pubmed PMID: 28862226.
- [30]. Steele JC, Clark HJ, Hong CH, Jurge S, Muthukrishnan A, Kerr AR, Wray D, Prescott-Clements L, Felix DH, Sollecito TP. World Workshop on Oral Medicine VI: an international validation study of clinical competencies for advanced training in oral medicine. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2015 Aug;120(2):143-51.e7. Pubmed PMID: 25861956.
- [31]. Subashri, A. and Maheshwari, T. N. (2016) 'Knowledge and attitude of oral hygiene practice among dental students', *Research Journal of Pharmacy and Technology.* A & V Publications, 9(11), pp. 1840-1842.
- [32]. Subha, M. and Arvind, M. (2019) 'Role of magnetic resonance imaging in evaluation of trigeminal neuralgia with its anatomical correlation', *Biomedical and Pharmacology Journal*, 12(1), pp. 289-296.
- [33]. Sunar, S., Gayathri, R. and Vishnu Priya, V. (no date) 'Awareness of smoking and oral cancer among economically backward society - A survey'.
- [34]. Varshitha, A. (no date) 'Prevalence of Oral Cancer in India'.
- [35]. Venugopal A, Uma Maheswari TN. Expression of matrix metalloproteinase-9 in oral potentially malignant disorders: A systematic review. *J Oral Maxillofac Pathol.* 2016 Sep-Dec;20(3):474-479. Pubmed PMID: 27721614.
- [36]. Wahab, A. P. U. et al. (2017) 'Comparisons of Clinicopathologic Characteristics among Early and Late Stage of Oral Squamous Cell Carcinoma', *Research journal of pharmaceutical, biological and chemical sciences.* *Journal of Pharmaceutical Sciences and Research*, 9(11), pp. 2147-2150.
- [37]. Wangsa D, Ryott M, Avall-Lundqvist E, Petersson F, Elmberger G, Luo J, Ried T, Auer G, Munck-Wikland E. Ki-67 expression predicts locoregional recurrence in stage I oral tongue carcinoma. *Br J Cancer.* 2008 Oct 7;99(7):1121-8. Pubmed PMID: 18766188.
- [38]. Warnakulasuriya S. Global epidemiology of oral and oropharyngeal cancer. *Oral Oncol.* 2009 Apr-May;45(4-5):309-16. Pubmed PMID: 18804401.