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CURRENT ASPECTS OF ORAL SQUAMOUS CELL CARCINOMA IN PAKISTAN: A REVIEW

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Abstract
Oral squamous cell carcinoma (OSCC) is a public health burden worldwide due to its transience and fatality rate. The incidence of oral squamous cell carcinoma varies around the globe due to demographic and genetic differences. Oral cancer is the second most prevalent oral pathology in Pakistan which ultimately leads to death. Recent study divulged that the Pakistan has the increasing trend towards the OSCC, and the incidence rate of Pakistan is like Iran and India. Human papilloma virus and betel nut are the root causes for the development of oral cancer. Oral squamous cell carcinoma occur in the oral cavity. OSSC may present as a well-established to ambiguous lesion like exophytic lesion, endophytic lesion, or sometimes in erythroleucoplastic pattern. In current situation, the use of advance technologies for early detection and prevention can overcome this burden from the population. Due to lack of local literature we rally to review the published literature on Pakistan. The collection of published studies was made by using PubMed, NCBI and Google Scholar as database search engine. We searched and include only Pakistan based population studies during the year between 2016 to 2020. We conclude that OSCC is the highly prevalent oral pathology in Pakistan with male preponderance. Most common risk factor being betel nut followed by tobacco and Grade-II carcinoma is highly prevalent oral cancer in our population.
Keywords: Oral cancer, oral squamous cell carcinoma, risk factors, Pakistani population.

Introduction

Oral squamous cell carcinoma (OSCC) is a public health burden worldwide due to its transience and fatality rate. The incidence of oral squamous cell carcinoma varies around the globe due to demographic and genetic differences. [1] About 657,000 new cases of oral and throat cancer are diagnosed leading to 330,000 deaths annually based on exposure to risk factors. [2] International Agency for Research on Cancer (IARC) reported in 2018 that Asia-Pacific countries poses the top three rates of mouth cancer and betel nut is the most common oral carcinogen.[3] Taiwan ranks highest for the incident of oral cancer 32.46/100,000 subject. [4] it is the type of pathology predominantly found in males than females. [5]

In current situation, the use of advance technologies for early detection and prevention can overcome this burden from the population. Alongside diagnostic modes and treatment plan, there is education of the patient regarding risk factors or the cessation of habits which is the basic cause of this disease is also mandatory. [6] Oral hygiene is the one of the major prevention tools for oral cancers. However, we observed that there is lack of compendious studies or review on the prevalence of oral squamous cell carcinoma in Pakistan. Therefor we gathered the published literature on Pakistani population for the last five years, 2016-2020.

Discussion

Oral cancer is the second most prevalent type of oral pathology in Pakistan which ultimately leads to death. [7] Recent study divulged that the Pakistan has the increasing trend towards the OSCC, and the incidence rate of Pakistan is like Iran and India.[8]

This review is steered according to the guidelines of preferred reporting items for the systematic reviews. The collection of published studies was made by using PubMed, NCBI and Google Scholar as database search engine. We searched and reviewed total 33 only Pakistan based population studies during the year between 2016 to 2020 by using the key words “oral cancer, oral squamous cell carcinoma, Pakistani population”.

We included, Studies present only in English. We also inspected the bibliographies of the studies, contain minimum 40 subjects, studies only reporting oral squamous cell carcinoma. We excluded, all the studies reported on population other than Pakistan and whose major focus on co-

morbid conditions. The appropriate data was retrieved by reviewing the full text articles. Data collection included the frequency and grades of OSCC, age, sex, region of the study and year of publication.

Risk Factors

Human papilloma virus, betel nut, tobacco, ultraviolet radiation, and alcohol consumption are the root causes for the development of oral cancer.[9] According to World Health Organization (WHO), due to the consumption of tobacco the death rate is approximately 6.4 million per year and the 100 of billion dollars of economic mutilation around the world. [10] Oncogenic virus like Human papilloma virus infection possess the burden up to 30% for the development of the oral cancer. [11] Risk for the development of oral squamous cell carcinoma is increasing with increment of age due to prolong exposure to the risk factor and the probability of mutations and epigenetic changes which causes inhibition of many of the normal immune functions and modification of the epithelial cells of the host causing oxidative stress which aids the development the OSCC. [12-13]

Site of Lesion

Oral squamous cell carcinoma occur in the oral cavity, may involve only the tongue, lips, gums, oral mucosa, pharynx or larynx.[14]Oral cancer may present as a well-established to ambiguous lesion like exophytic lesion, endophytic lesion, erythroplastic, leucoplastic or sometimes in erythroleucoplastic pattern.[15]

TNM Stage Classification

The most huge and prescient factor which will decide the endurance rate is the phase of the tumor during the determination. The TNM arrangement is an overall known strategy for oral malignant growths organizing which is utilized by medical services professionals, for example, specialists, scientists and disease enlistment offices. The initials, T represents tumor, N for lymph nodes and M for metastases, depend on the estimations of the sickness before therapy. The primary job is to give an anatomical characterization and to appropriately portray the improvement of the malignancy. Explicit portrayal is the key for the choice of a right technique for treatment, the conceivable result and restriction for certain activities. [16-17]

Diagnostic Methods

Analysis of a dicey injury regularly starts with the customary oral assessment, which incorporates clinical assessment and palpation of the mucosa of the oral cavity under the lighting of the dental seat. [18] The capacity to make an analysis at a beginning phase of OSCC is significant so as to diminish the high pace of infection and passing among the patients. The most well-known strategies utilized for determination of PMDs and OSCC in a beginning phase are recorded underneath. [19]

Indispensable Staining

Strategies, for example, Toluidine blue (TB), Lugol's iodine staining, Methylene blue staining, Rose bengal staining. Recoloring with TB is a known strategy for the distinguishing proof of precancerous and cancerous lesions, which is prescribed to be as a feature of the clinical assessment of tissue of oral mucosa, particularly in high-hazard patients. Those strategies are not costly, very simple to apply and successful. The staining executed by different sorts of stains over the mucosa so as to check the neoplastic cells, cells with a high conceptive movement and to demonstrate the particular territories for assessment and biopsy. [20]

Light-based Detection

So as to distinguish oral PMDs and OSCC in their underlying stage, a few light-based gadgets have been created. Those particular gadgets can emanate certain light which will mirror the anomalous tissue and improve the clinical assessment. [21]

Histological Techniques

Incisional and additionally excisional biopsies are the most precise demonstrative strategies and along with the histopathological tests, stay as the most solid techniques for OSCC conclusion. Before the system of excisional biopsy, it is significant that the edges and profundity of the tissue will be checked of being free from the disease. The most prognostic indication of any threat is dysplasia of the epithelium. WHO have characterized the dysplasia as mild, moderate and severe.

Cytological Techniques

Those are techniques that uses magnifying instrument a microscope as to assess the cells which were gotten from smears, scratching and needle goal over different depts of the mucosa. The basic discoveries are a run of the mill mucosal injury which from the outset sight looks typical, yet the readied example will introduce atypical cells. The cytological tests which have been taken from the oral depression may assist with recognizing and determine tissues to have a high-hazard or even threat. [22]

Imaging Analytic Techniques

Those strategies incorporate neighborhood dental radiographs, orthopantomogram (OPG), attractive reverberation imaging (MRI), figured tomography perfusion (CTP), C-arm CT, atomic medication, for example, single-photon discharge processed tomography (SPECT), ultrasonography and blend of barely any techniques, for example, PET, CT/MRI and SPECT/C. [23-24]

Management

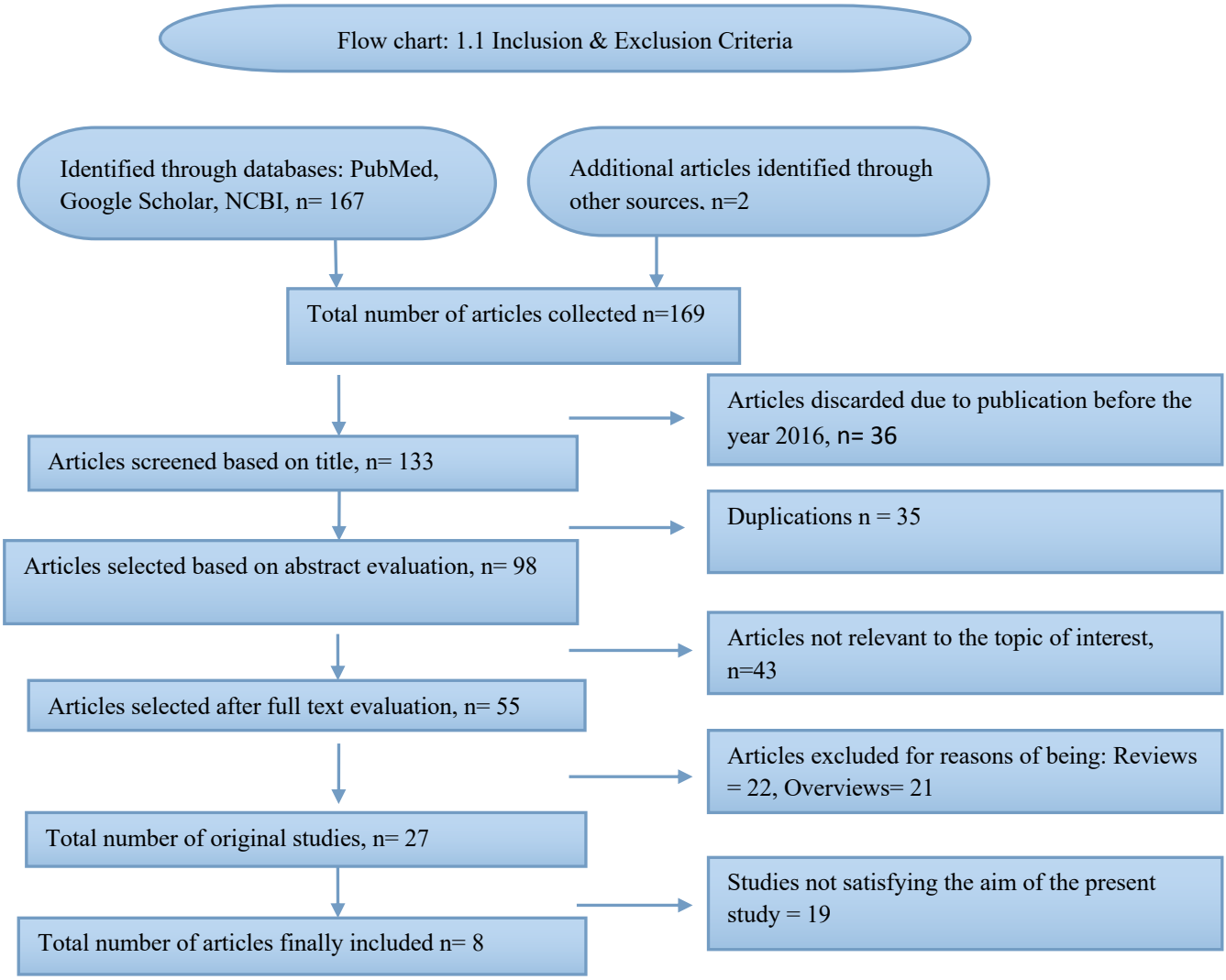
The most widely recognized therapy strategies for oral malignancy can be noninvasive, for example, radiotherapy in a large portion of the cases or can be intrusive, for example, medical procedure, which is typically the primary alternative

of therapy in spite of the way that radiotherapy endurance rate and control of the anatomical site are comparable. Those strategies can be given independently or as a blend. [25]

Radiotherapy might be furnished independently or as a blend with chemotherapy so as to treat the underlying tumor. It might be given as neo-adjuvant treatment, which will diminish the tumor size before the underlying medical procedure. Radiotherapy may likewise be given as adjuvant treatment, which will improve the effectiveness of the underlying treatment and by doing so will drag out the endurance rate, decline the difference in conceivable repeat and even improve the indications of a late stage oral disease. [26] Radiotherapy has some significant downsides, for example, xerostomia, osteoradionecrosis, mucositis and long length of treatment which in instances of closeness deep down as well as youthful patients are not ideal. The therapy techniques for oral disease, for example, medical procedure, radiotherapy and chemotherapy majorly affect the patient's personal satisfaction and considered as cruel because of the area and the prominent methods of therapy. [27] The point of OSCC treatment techniques are to treat the underlying tumor and to safeguard however much as could be expected the shape and capacity with an appropriate reclamation. [28-29]

Prevention

So as to decrease the OSCC mortality among everyone, scarcely any means ought to be advanced. To start with, if there should be an occurrence of patients with high danger, the mortality might be decreased by advancing way of life changes and apply clinical assessment as an aspect of a wide demonstrative program among the populace. [30] Second, an instructive program with the essential information with respect to the OSCC ought to be installed in the populace while a successive expert demonstrative and pathologic information ought to be given to the medical services professionals. Third, the continuous and future investigates with respect to the OSCC must proceed so as to characterize the specific etiological components and biomarkers of the sickness. [31]



Only eight studies meeting the eligibility criteria were included in this systematic review.

Abidi et al., 2020 conducted their study at Ziauddin University Hospital (ZUH), Karachi. Total 140 cases of OSCC were taken, 110 males and 30 females. The mean age of cases was 46.99 years. Unemployment was present in approximately 38.9% cases. Most prevalent risk factor in 77% of total cases was habit of smokeless tobacco. The most common site of lesion was buccal mucosa in 66.4% cases followed by tongue and 89% cases were suffering from moderately differentiated carcinoma (Grade-II).

Asif et al., 2020 carried out this research study at Liaquat College of Medicine and Dentistry, Karachi. Comprising of total 60 participants. 35 males and 25 females. The mean age of participants was 50.87 years. Most of the cases belonged to lower middle class and 54% suffered from unemployment. Buccal mucosa was found to be the most common site of tumor in 51.67% of patients. Frequently reported risk factor was betel nut and betel quid chewing around 43.45% of total included subjects. Moderately differentiated carcinoma (Grade II) was found in 50% cases.

Anwar et al., 2020 performed study at Aga khan University Hospital (AKUH) Karachi. Included total 146 cases of OSCC, 149 males and 37 females. Mean age of cases was 47.6 years. The maximum number of cases over 30.1% were laborer. The most common risk factor was habit of betel nut chewing in any form around 77.4%. The frequent site of lesion was buccal mucosa and highest number about 79% patient diagnosed with poorly differentiated carcinoma (Grade-III).

Khalid et al., 2019 conducted their research at Post Graduate Medical Institute, Lahore. Covering total 71 patients of OSCC. 46 males and 25 females. Mean age of patients was 50 years. Highest number of the cases belonged to lower middle-class category. Frequently noted risk factor was tobacco chewing 54.1%. More often reported site of lesion was oral mucosa 42% cases. 43.66% cases were diagnosed as moderately differentiated carcinoma (Grade II).

Ahmed et al., 2019 carried out this research study at the Institute of Radiotherapy and Nuclear Medicine, Peshawar, Pakistan. Comprising of total 60 participants. 341 males and 210 females. The mean age of participants was 55.0 years. Most of the cases belonged to lower middle class and 54% suffered from unemployment. Buccal mucosa was found to be the most common site of tumor in 61% of patients. Frequently reported risk factor was smokless tobacco around 72% of total included subjects. Moderately differentiated carcinoma (Grade II) was found in 52% cases.

Mahmood et al., 2018 conducted their work at Ziauddin University Hospital (ZUH), Karachi. Involved 115 subjects. 82 males and 33 females. Mean age of subjects was 45.6 years. Excessive number of subjects belonged to lower socioeconomic class. Commonest risk factor was reported to be smokeless tobacco and betel nut. Buccal mucosa was the frequently observed site of cancerous lesion. 60.6% cases were suffering from moderately differentiated carcinoma (Grade II).

Sahaf et al., 2017 worked for their research study at three (Mayo hospital, Sheikh Zaid Hospital and AllamaIqbal Medical College/ Jinnah Hospital) tertiary care hospitals at Lahore. They included 89 patients. 52 males and 37 females. The mean age of total included population was 53.13 years. Most of the participants belonged to lower to middle socioeconomic class. The highest number about 33.7% patients reported idiopathic etiology followed by smoking 22.5%. Highly reported site of oral lesion was tongue in 37.0% patients. There was no comment found on the grading of OSCC.

Mirza et al., 2016 undertook their research work at Hamdard University Dental Hospital, Karachi by incorporating 80 cases, 53 males and 27 females. The mean age of the total cases was 42.12 years. Commonly mentioned risk factor was betel nut chewing. Most observed site of lesion was hard palate with alveolar mucosa. Moderately differentiated carcinoma (Grade II) was noted in highest number of 44.3%.

Despite the high the prevalence of this oral pathology there is lot of lacunae regarding prevention, control, early diagnosis, and appropriate treatment plan. The histomorphological parameters and other diagnostic tool with TNM staging on time can prevent the pathology and increases the survival rate of the patient. Oral hygiene and public awareness program can be the better step towards the prevention and control of the oral cancer. Our study will provide the plat form for future research in local territory as well as at international level to make better health care programs.

Table 1.1: Oral Squamous Cell Carcinoma In Pakistan

Studies	Region	Male/Female	MCSL	MCRF	Grade
Abidi et al., 2020	Karachi	110/30	Buccal Mucosa	Tobacco	II
Asif et al., 2020	Karachi	35/25	Buccal Mucosa	Betel Nut	II
Anwar et al., 2020	Lahore	149/37	Buccal Mucosa	Betel Nut	III
Khalid et al., 2019	Lahore	46/25	Buccal mucosa	Tobacco	II
Ahmed et al., 2019	Peshawar	341/210	Buccal Mucosa	Tobacco	NC
Mahmood et al., 2018	Karachi	53/27	Hard Palate	Betel Nut	II
Sahaf et al., 2017	Lahore	52/37	NC	Idiopathic	NC
Mirza et al., 2016	Karachi	53/27	Hard Palate	Betel Nut	II

NC : No Comments
MCSL : Most Common Site of Lesion
MCRF : Most Common Risk Factor

Conclusion

We conclude that OSCC is the highly prevalent oral pathology in Pakistan with male preponderance. Most common causative agent is betel nut followed by tobacco and Grade-II carcinoma is highly prevalent oral cancer in our population. This research area demands the special attention due to its high prevalence and low survival rate. However due to scarcity of local literature regarding OSCC we were not able to cover major population of Pakistan.

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References

1. García-Martín JM, Varela-Centelles P, González M, Seoane-Romero JM, Seoane J, García-Pola MJ. Epidemiology of oral cancer. InOral Cancer Detection 2019 (pp. 81-93). Springer, Cham.
2. WHO Cancer Prevention. Available online: https://www.who.int/cancer/prevention/diagnosis-screening/oral-cancer/en/ (accessed on 20 January 2020)
3. WHO Global Oral Health Programme. Available online: https://www.who.int/oral_health/objectives/en/ (accessed on 20 January 2020)
4. Hung LC, Kung PT, Lung CH, Tsai MH, Liu SA, Chiu LT, Huang KH, Tsai WC. Assessment of the risk of oral cancer incidence in a high-risk population and establishment of a predictive model for oral cancer incidence using a population-based cohort in Taiwan. International Journal of Environmental Research and Public Health. 2020 Jan;17(2):665.
5. Siewchaisakul P, Sarakarn P, Vatanasapt P, Chen SL, Yen AM. Sex Differences in the Heterogeneous Dynamic Incidence of Oral Cancer: A Comparison between Taiwan and Thailand. BioMed Research International. 2020 Sep 15;2020.
6. . Patil S, Arakeri G, Alamir AW, Patil S, Awan KH, Baeshen H, Raj T, Fonseca FP, Brennan PA. Is Toombak a risk factor for oral leukoplakia and oral squamous cell carcinoma? A systematic review. Journal of Oral Pathology & Medicine. 2020 Feb;49(2):103-9.
7. Muhammad RehanSarwar&AnumSaqib | Udo Schumacher (Reviewing Editor) (2017) Cancer prevalence, incidence and mortality rates in Pakistan in 2012, Cogent Medicine, 4:1, DOI: 10.1080/2331205X.2017.1288773
8. Yosefof, E., Hilly, O., Stern, S., Bachar, G., Shpitzer, T. and Mizrachi, A., 2020. Squamous cell carcinoma of the oral tongue: Distinct epidemiological profile disease. Head & Neck.
9. Kumar GK, Abidullah M, Elbadawi L, Dakhil S, Mawardi H. Epidemiological profile and clinical characteristics of oral potentially malignant disorders and oral squamous cell carcinoma: A pilot study in Bidar and Gulbarga Districts, Karnataka, India. Journal of Oral and Maxillofacial Pathology: JOMFP. 2019 Jan;23(1):90.
10. Jiang X, Wu J, Wang J, Huang R. Tobacco and oral squamous cell carcinoma: A review of carcinogenic pathways. Tobacco induced diseases. 2019;17.
11. Naqvi SU, Khan S, Ahmed A, Lail A, Gul S, Ahmed S. Prevalence of EBV, CMV, and HPV in oral squamous cell carcinoma patients in the Pakistani population. Journal of Medical Virology. 2020 Mar 26.
12. Ahmed R, Malik S, Khan MF, Khattak MR. Epidemiological and clinical correlates of oral squamous cell carcinoma in patients from north-west Pakistan. JPMA. The Journal of the Pakistan Medical Association. 2019 Aug;69(8):1074-8.
13. Araghi M, Galanti MR, Lundberg M, Liu Z, Ye W, Lager A, Engström G, Alfredsson L, Knutsson A, Norberg M, Wennberg P. No association between moist oral snuff (snus) use and oral cancer: pooled analysis of nine prospective observational studies. Scandinavian Journal of Public Health. 2020 May 28:1403494820919572.
14. Paraguassu EC, Ramos PF, Oliveira LB, Gentil LM, Santo AM, da SILVA SR. Systematic review of the epidemiology of oral cancer in Brazil. International Journal of Innovation Education and Research. 2019;7(4):366-74.
15. Lin NC, Hsu JT, Tsai KY. Survival and clinicopathological characteristics of different histological grades of oral cavity squamous cell carcinoma: A single-center retrospective study. PloS one. 2020 Aug 25;15(8):e0238103.
16. Mattavelli D, Ferrari M, Taboni S, Morello R, Paderno A, Rampinelli V, Del Bon F, Lombardi D, Grammatica A, Bossi P, Deganello A. The 8th TNM classification for oral squamous cell carcinoma: What is gained, what is lost, and what is missing. Oral Oncology. 2020 Dec 1;111:104937.
17. Adeoye J, Thomson P, Choi SW. Prognostic significance of multi-positive invasive histopathology in oral cancer. Journal of Oral Pathology & Medicine. 2020 Aug 2.
18. daConceição MG, Figueiró AC, Luiza VL. Non-Invasive Methods for Early Diagnosis of Oral Cancer. Oral Diseases. 2019 Nov 28.
19. Di Stadio A, Amadori M, Dipietro L, Colangeli R, Falcioni M, Ricci G, Frezza D. Seborrheic Keratosis or Squamous Carcinoma? Clinical Examination versus Biopsy: The Importance of Criticism. The Journal of International Advanced Otology. 2019 Aug;15(2):326.
20. Jayasinghe RD, Hettiarachchi PV, Amugoda D, Kumaraarachchi M, Liyanage RL, Siriwardena BS, Gunasena R, Karunatilake AH, Amarasinghe HK. Validity of Toluidine Blue test as a diagnostic tool for

high risk oral potentially malignant disorders-a multicentre study in Sri Lanka. Journal of Oral Biology and Craniofacial Research. 2020 Oct 1;10(4):547-51.

21. Arora KS, Nayyar A, Kaur P, Arora KS, Goel A, Singh S. Evaluation of collagen in leukoplakia, oral submucous fibrosis and oral squamous cell carcinomas using polarizing microscopy and immunohistochemistry. Asian Pacific journal of cancer prevention: APJCP. 2018;19(4):1075.

22. Jairajpuri ZS, Rana S, Hajela A, Jetley S. Toward early diagnosis of oral cancer: Diagnostic utility of cytomorphological features, a pilot study. National journal of maxillofacial surgery. 2019 Jan;10(1):20.

23. Lupu M, Căruntu A, Moraru L, Voiculescu VM, Boda D, Tănase C, Căruntu CO. Non-invasive imaging techniques for early diagnosis of radiation-induced squamous cell carcinoma of the lip. Rom. J. Morphol. Embryol. 2018 Jan 1;59(3).

24. Keshavarzi M, Darijani M, Momeni F, Moradi P, Ebrahimnejad H, Masoudifar A, Mirzaei H. Molecular imaging and oral cancer diagnosis and therapy. Journal of Cellular Biochemistry. 2017 Oct;118(10):3055-60.

25. Hosni A, Chiu K, Huang SH, Xu W, Huang J, Bayley A, Bratman SV, Cho J, Giuliani M, Kim J, O'Sullivan B. Non-operative management for oral cavity carcinoma: Definitive radiation therapy as a potential alternative treatment approach. Radiotherapy and Oncology. 2020;154:70-5.

26. Huang SH, Hahn E, Chiosea SI, Xu ZY, Li JS, Shen L, O'Sullivan B. The role of adjuvant (chemo-) radiotherapy in oral cancers in the contemporary era. Oral Oncology. 2020 Mar 1;102:104563.

27. Kucha N, SoniTp, Jakhotia N, Patni N, Singh Dk, Gupta Ak, Sharma Lm, Goyal J. A Prospective, Comparative Analysis Of Acute Toxicity Profile Between Three-Dimensional Conformal Radiotherapy (3dcrt) And Intensity-Modulated Radiotherapy (Imrt) In Locally Advanced Head And Neck Cancer Patients. Cancer Treatment And Research Communications. 2020 Oct 21:100223.

28. Hirakawa H, Hanai N, Suzuki H, Nishikawa D, Matayoshi S, Hasegawa Y, Suzuki M. Prognostic importance of pathological response to neoadjuvant chemotherapy followed by definitive surgery in advanced oral squamous cell carcinoma. Japanese journal of clinical oncology. 2017 Nov 1;47(11):1038-46.

29. de Souza ML, Branco IV, Matos FC, Júnior BC, de Lacerda Vidal AK. Prevention, early diagnosis and treatment of oral cancer in the Brazilian Unified Health System. Revista Journal of Health-ISSN 2178-3594. 2020 Jun 29;1(1).

30. Thomson PJ. Perspectives on oral squamous cell carcinoma prevention—proliferation, position, progression and prediction. Journal of Oral Pathology & Medicine. 2018 Oct;47(9):803-7.

31. Roi A, Roi CI, Negruțiu ML, Riviș M, Sinescu C, Rusu LC. The Challenges of OSCC Diagnosis: Salivary Cytokines as Potential Biomarkers. Journal of Clinical Medicine. 2020 Sep;9(9):2866.

32. Abidi F, Hosein M, Butt SA, Zaidi AB, Anjum A, Fatima S. Association of Clinicopathological Features with Lymph Node Metastasis: A Cross Sectional Study of Oral Squamous Cell Carcinoma Patients. Journal of Advances in Medicine and Medical Research. 2020 Feb 25:46-53.

33. Asif S, Kanwal S, Ayub T, Abbas Z, Vazir B, Qureshi NR. Clinicopathological profile of squamous cell carcinoma presenting in Tertiary Care Hospital, Karachi. The Professional Medical Journal. 2020 May 10;27(05):939-43.

34. Anwar N, Pervez S, Chundriger Q, Awan S, Moatter T, Ali TS. Oral cancer: Clinicopathological features and associated risk factors in a high-risk population presenting to a major tertiary care center in Pakistan. Plos one. 2020 Aug 6;15(8): e0236359.

35. Khalid W, Farooq U, Lail RA, Hassan M. Clinicopathological profile of Oral squamous cell carcinoma cases in a tertiary care hospital of Lahore during 2014-15. Pakistan Postgraduate Medical Journal. 2019;30(01):27-31.

36. Ahmed R, Malik S, Khan MF, Khattak MR. Epidemiological and clinical correlates of oral squamous cell carcinoma in patients from north-west Pakistan. J Pak Med Assoc. 2019 Aug 1;69(8):1074-8.

37. Mahmood N, Hanif M, Ahmed A, Jamal Q. Impact of age at diagnosis on clinicopathological outcomes of oral squamous cell carcinoma patients. Pakistan Journal of Medical Sciences. 2018 May;34(3):595.

38. Sahaf R, Naseem N, Anjum R, Nagi AH, Path FR. A study of 89 cases of oral squamous cell carcinoma presenting at Teaching Hospitals of Lahore, Pakistan. JPDA. 2017 Jan; 26(01):27.

39. Mirza D, Raza G, Basit A, Naqvi K, Ahmed S, AbassiZa. Oral Squamous Cell Carcinoma (Oscc) In Karachi City--A Retrospective Study. Pakistan Oral & Dental Journal. 2016 Sep 30; 36(3).