

Epidemiological Profile of Oral Cancer Patients Attending at B.P . Koirala Memorial Cancer Hospital, Chitwan, Nepal

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Received: June 11, 2024; Revised & Accepted: August 22, 2024

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Abstract

Background: Oral cancer is one of the most prevalent and leading causes of mortality in certain regions, like South-Central Asia. The incidence of oral cancer in Nepal is also increasing. Oral cancer is preventable and treatable if diagnosed in an early stage. The study conducted at B.P. Koirala Memorial Cancer Hospital (BPKMCH) in Bharatpur, Nepal, was aimed at assessing the epidemiological profile of oral cancer patients attending BPKMCH.

Methods: A descriptive cross-sectional study design was used to assess the epidemiological profile of oral cancer, and 50 patients were included in this study during January to July 2023. A semi-structured interview schedule was developed, which has 3 parts, viz., i. socio-demographic variables, ii. Lifestyle-related factors and iii. Clinical profile of oral cancer, to obtain the information from the respondents.

Results: The study findings revealed that out of 50 majorities of respondents (88%) were male. According to the religion, most of them (84%) were Hindu, and likewise, according to ethnicity, about half of them (40%) belong to Madeshi, followed by 30% Brahmin/Chhetri. Similarly, most of the respondents (90%) were married. Regarding the exposure to risk factors, half of the respondents (50%) had habits of smoking consumption, More than half (68%) had the habit of tobacco consumption, near to half (40%) had the habit of Gudka consumption, and 68% had the



habit of alcohol consumption. None of the respondents had the habits of oral sex or a family history of oral cancer. Similarly, about one-third (30%) of respondents had stage IV, followed by 28% stage II, 26% stage I, and only a few (14%) stages in III disease; all the oral cancer was OSCC. Concerning the treatment modalities, 36% of respondents had surgery, near to one quarter (20%) received chemotherapy, 10% received radiation therapy, and 30% of respondents had surgery with adjuvant therapy.

Conclusion: The study found that the majority of oral cancer patients attending BPKMCH were between the ages of 30 and 45 and were predominantly male. Smoking, tobacco, and Gudka consumption are the main risk factors for oral cancer. The risk assessment approach and screening program should be focused on preventing oral cancer.

Keywords: Cancer, Dentistry, Oral Health, Oncology, Oral Cancer, Nepal

Introduction

Background

Cancer is a major public health problem, and the overall burden of cancer is speedily increasing worldwide. According to GLOBOCAN, 2020, an estimated 19.3 million new cancer cases and 10 million cancer deaths occurred globally. Oral cancer (OC) is the sixth most common cancer worldwide, it accounts for 2% of all cancers, with an estimated 377,713 new cases in 2020 and 177,384 deaths worldwide.¹

The trend of oral cavity cancer is rising in developing countries. OC is one of the highly prevalent and leading causes of mortality in certain regions like South-Central Asia. OC is major public health problem in the Indian subcontinent, where it ranks among the top three types of cancer in the country.² The incidence of OC in Nepal is also increasing trends in both men and women. A three years trend analysis revealed that the OC is the second highest cancer among men and 10th in women.³

The hospital record survey study conducted at BPKMCH during the period of 2009 to 2013, showed that more than half (52.9%) cancer patients were from Terai and near to half (47.1%) from Hill region. Similarly and about of half (50.7%) was from age group 41 to 60 years. OC was found in more than one third (39.5%) and tobacco chewing habit in an about near to half (44.4%) cancer patients. Likewise, risk of OC was 4.6 times more in tobacco chewers than non-chewers with highly significant association.¹²

OC is a malignant neoplasia which arises on the lip or oral cavity. It can be defined as a malignant cancer occurring in the oral cavity. The five most common sites for OC are tongue (25.4%), labial/buccal mucosa (21.7%), gingiva (14.0%), palate (9.9%), and alveolar mucosa (7.9%).⁴

The incidence of OC is two to three times higher in men than women. Overall, the lifetime risk of developing oral cavity is about one in sixty for men, and one in one-hundred and forty-one for women.⁵ The risk factors of Oral Squamous Cell Carcinoma (OSCC) include smoking, alcohol,



chewing tobacco habits, and infection with high-risk human papillomaviruses (HPVs). Tobacco smoking and alcohol intake are well established risk factors for oral cancer.⁶ OC is preventable and treatable if diagnosed in early stage. Oral cavity cancer is one of the most common preventable cancers in the world.⁷

This study assessed the epidemiological profile of oral cancer patients attending BPKMCH. This will be helpful to the clinician to incorporate various contributing factors and treatment plans regarding oral cancer. Moreover, the study might be helpful as baseline information for future researchers.

A correlational retrospectively study carried out on demographic and clinic-pathological variables of head and neck cancer in ENT, department, BPKMCH. The findings revealed that, during the periods of 11 years, total 3,452 cases were included, among them 1,111 cases were oral cancer. Out of 1,111 cases, (97.3%) were OSCC. Majority (73.0%) males, and, tongue was the most common site, (42.8%) followed by buccal mucosa (27.2%). Similarly, majority (49.7%) were diagnosed at advanced stage in Stage IV and received a combination therapy (42.0%).⁸

A cross-sectional study among the 340 oral cancer patients from January 2019 to December 2019 was carried out in Department of oncology & radiotherapy at Medical Gwalior, Madhya Pradesh India. The study findings showed that, the mean age of patient was 46.45 ± 12.09 years. Out of 340 patients (91.47%) were males. Based on socio-economic status, majority (41.5%) belonged to lower middle and lower socio-economic class. Similarly, (25.58%) were advised surgery + radio therapy followed by (20%) chemo therapy alone. Majority of patients come for treatment at advanced stage of oral cancer i.e., TNT stage III & TNT stage IV. The prevalence of oral cancer was significantly (p < 0.001) higher in males (91.5.9%) than females (8.5%). In both the sexes, most affected sites were the buccal mucosa and gingiva-buccal sulcus.⁹

Oral cancer (OC) is the most frequent type of head and neck cancer and can be cured if detected and treated early. Squamous cells account for approximately 90% of all mouth cancers. The frequency of OC was higher in males and economically disadvantaged populations. The majority of patients arrived at the hospital in advance. Tobacco and alcohol usage, human papillomavirus (HPV) infections, poor diet, and UV light exposure are all risk factors for OC.

Rational of the study

Oral cavity cancer is easily preventable and treatable if diagnosed early. Due to a lack of proper preventive strategies, its burden is likely to increase worldwide.⁸ OC has been one of the public health issues in Nepal. The incidence of OC is increasing trends in both men and women in Nepal. OC can be preventable by focusing on modifying habits, educational programs, counseling for those who are willing to take the modifying risk, early screening, and early detection and referral.¹⁰ Numerous studies have been conducted in Nepal regarding oral health. However, very limited studies have been conducted on the epidemiological profile of oral cancer in Nepal. This study, entitled Epidemiological Profile of OC Patients Attending at BPKMCH, Chitwan, Nepal, focused



on describing the epidemiological profile of oral cancer patients, and provides the evidence for the stakeholders to manage, treat, and future research in the domain of epidemiology and the theme of oral health and the umbrella of oncology. Moreover, researcher tried to contribute to sustainable development goal (SDG) and the objectives of the national planning of Nepal by provide the evidence based information on OC.

Materials and Methods

Study design and setting

A descriptive cross-sectional study was used to assess the epidemiological profile among OC patients at BPKMCH, Chitwan, Nepal in January 2023.

Participants, sampling and sample size

The population of the study was all the patients with oral cancer attending at BPKMCH and a non-probability, purposive sampling technique was used to select the sample. The number participants for the study was 50 OC patients who atended in BPKMCH chitawan. A semi-structured interview schedule was developed in English and translated into Nepali language to collect the information. The instruments consisted of three parts; i. Question-related to socio-demographic variables, ii. Question-related to life style related factors, and iii. Question related to clinical profile of oral cancer.

Statistical consideration

Administrative approval for data collection was obtained from BPKMCH. Ethical approval obtained from IRC BPKMCH. Written informed consent was taken from all the respondents by explaining the objectives of the study. The data was collected by using a semi-structured interview schedule. Interview was taken by using Nepali version of semi-structure interview schedule. Each respondent was given 20 -25 minutes time for interview. Data was collected within two weeks periods.

All the collected data was checked, reviewed, organized for its completeness. Then the data was coded, classified, entered, and analyzed in Statistical Package for Social Science (SPSS) version 22. All the collected data was analyzed and interpreted in terms of descriptive statistics (frequency, mean, percentage and standard deviation). Finding of the study were presented in different tables.

Results

Table 1 shows the socio-demographic characteristics of the study participants. Out of 50, 30% of the respondents belong to the 35-45 year age group, followed by 26% of the 46-55 year age group, and a similar percentage also belongs to the 66-75 year age group, and a few of (18%) belong to the 56-65 year age group. The mean of age was \pm SD: 54.75 \pm 11.754 54. Concerning the gender, more than three-fourths (88%) were male. Likewise, 26% of the respondents were from Madesh



province, followed by 24% from Lumbini province, and only 4% from Gandaki province. Regarding the religion, majority (84%) were belongs to Hindu. Concerning the ethnicity, 40% belongs to Madeshi, followed by 30% Brahmin/Chhetri and few of (6%) were Dalit. Similarly, almost all the of respondents (90%) were married.

Table 1: socio-demographical characteristics of the respondents

Variables		Frequency	Percentage
Age group	35-45	15	30
	46-55	13	26
	56-65	9	18
	66-75	13	26
	<i>Mean</i> ± <i>SD</i> : 54.75±11.754		
	Mini / max: 35/75		
Gender	Male	44	88
	Female	6	12
Provinces	Koshi province	10	20
	Madesh province	13	26
	Bagmati province	3	6
	Gandaki province	2	4
	Lumbini province	12	24
	Karnali province	5	10
	Sadurpachhim province	5	10
Religion	Hindu	42	84
	Buddhist	3	6
	Muslim	3	6
	Christian	1	2
	Kirat	1	2
Ethnicity	Brahmin/Chhetri	15	30
	Janajati	12	24
	Dalit	3	6
	Madeshi	20	40
Marital Status	Unmarried	2	4
	Married	45	90
	Widow/widower	3	6
Educational Status	No formal education	21	42
	Primary	11	22



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Educational status: out of 50 respondents, 42% did not have any formal education, whereas 16% of respondents completed a school-level certificate and above. Similarly, 38% of respondents were involved in agriculture as their occupation, followed by 32% in service, 18% in business, 10% in house making, and 2% in other professions not mentioned above. Likewise, the income of the family: about half (48%) of respondents had income to maintain sufficiently for 6 to 12 months, followed by 40% having sufficient to run a family throughout the year, and a few (10%) had income just to run the family for 3 to 6 months, as shown in Table 1.

Table 2 shows the risk behavior of respondents for this study. According to the table, the fourth (68%) had the habit of chewing tobacco and had the habit of alcohol consumption; likewise, half of the (50%) respondents had the habit of smoking, and 40% of the respondents had the habit of Gudka consumption. None of the respondents reported that they don't have habits of oral sex, and none of the respondents had a family history of oral cancer.

The smoking habits of respondents are shown in Table 2. Out of 25 smokers from cancer patients, the majority of respondents (88%) had cigarette smoking habits, and only a few of them (12%) had the habit of smoking Bidi. Regarding the time of smoking habits per day, one-third (32%) of respondents consumed 2-4 times in a day; a similar percentage of respondents also consumed 4-6 times, followed by 20% had 7-10 times, and a few (16%) were chain smokers. In relation to the duration of smoking, the majority (52%) had a habit of more than 15 years, followed by 24% having 10-15 years, and only a few (8%) of respondents had 5 to 10 years of smoking habits.



NPRC Journal of Multidisciplinary Research

Vol. 1, No. 3, August 2024. Pages: 15-27 ISSN: 3059-9148 (Online)



DOI: <u>https://doi.org/10.3126/nprcjmr.v1i3.70061</u>

Variables		Frequency	Percentage
Distribution of tobacco	Smoking	25	50
consumption	Chewing tobacco	34	68
	Gudka consumption	20	40
	Alcohol consumption	34	68
Oral sex habits	No	50	100
Family history of oral cancer	No	50	100
Type of smoke	Cigarette	22	88
	Bidi	3	12
Smoke time per day	2-4	8	32
	4-6	8	32
	7-10	5	20
	Chain smoker	4	16
Duration of Smoking	1-5 years	4	16
	5-10 years	2	8
	10-15 years	6	24
	>15 years	13	52
Tobacco consumption times	1-3	3	8.8
(per day)	4-6	15	44.1
	7-10	7	20.6
	>10	9	26.5
Duration of Tobacco	1-5 years	5	14.7
consumption	6-10 years	3	8.8
	11-15 years	6	17.6
	>15 years	20	58.8
Gudka consumption time	1-3	8	40
(per day)	4-6	6	30
	7-10	4	20
	>10	2	10
Period of consumption (in	1-5	9	45
years)	6-10	5	25
	11-15	1	5
	>15	5	25
Distribution of Respondents	Hypertension		
by Co- morbidities	Yes	7	14
	No	43	86
	Diabetic Mellitus		
	Yes	5	10
	No	45	90
Time duration of Oral	Diagnosis Time (in months)		
Cancer Diagnosis	1-12	42	84
	13-24	4	8
	25-36	3	6
	>36	1	2

Table 2: Distribution of Respondents by Risk Factor



Regarding the times of chewing tobacco per day, nearly half (44.1%) of respondents consumed 4-6 times per day, followed by 26.5% more than 10 times per day, and few of them (8.8%) had consumed 1-3 times per day. Likewise, duration of chewing tobacco consumption, an about more than half (58.8%) had habit of more than 15 years of durations followed by 17.6% had 11-15 years, and few of them (8.8%) had 6-10 years period of chewing tobacco consumption. Shown in table 2.

Table 2 shows distribution of respondents by co-morbidity, very few (14%) of the respondents' ad high Blood Pressure and (10%) had history of Diabetic Mellitus (DM).

Table 3 presents the epidemiological profiles of oral cancer of the participants of the study. Out of 50 oral cancer patients majority (84%) respondents were diagnosed of oral cancer in time period of 1 to 12 months followed by (8%) in 13-24 months, and (2%) was diagnoses in a period of more than 36 months. Eventually, majority (80%) had reported pain followed by (70%) had speech problem and similar percentage of respondents also had white and red patches, similarly (32%) had bleeding from oral cavity and (36%) had loosen teeth.

Anatomical site of oral cancer shown that 36% had cancer of Tongue, followed by 32% Gum, 12(24%) Cheek and only 1(2%) had cancer of Lips.

Variable		Frequency (n)	Percentage
			(%)
Diagnosis Time (in	1-12	42	84
months)	13-24	4	8
	25-36	3	6
	>36	1	2
Sign and Symptoms	Pain	40	80
of Oral Cancer	Speech problem	35	70
	Bleeding from oral cavity	16	32
	White and red patch	35	70
	Losing teeth	18	36
Anatomical Site of	Tongue	18	36
Oral Cancer	Gum	16	32
	Lips	1	2
	Cheek	12	24
	Roof and floor of mouth	3	6
	Stage I	13	26
	Stage II	14	28
	Stage III	8	16

Table 3: Epidemiological Profile of Oral Cancer.



NPRC Journal of Multidisciplinary Research Vol. 1, No. 3, August 2024. Pages: 15-27 OP



ISSN: 3059-9148 (Online) DOI: https://doi.org/10.3126/nprcjmr.v1i3.70061

Staging and	Stage IV	15	30
Metastasis of Oral	I ymph node metastasis	14	28
Cancer		17	20
Treatment	Surgery	18	36
Modalities	Chemotherapy therapy	10	20
	Radiation	5	10
	Radiation and chemotherapy	2	4
	Surgery and adjuvant therapy	15	30
Classification of	Histological classification		
Oral Cancer			
	Undifferentiated	2	4
	Well differentiated	30	60
	Moderately differentiated	15	30
	Poorly differentiated	3	6
	Morphological classification		
	oral squamous cell carcinoma		
	(OSCC)	50	100

According to the table 3 staging and metastasis of the cancer patents in this study shown, among them 30% of respondent had stage IV, followed by 28% stage II, 26% stage I and 14% stage III disease. Regarding the site of metastasis, 28% of respondent had lymph nodes metastasis. According to treatments modalities, an about of one third (36%) respondents had treated with surgery only, followed by 30% had treated with surgery and adjuvant therapy. Similarly, 20% were treated with chemotherapy only. Likewise, 10% of the respondent received radiation therapy only and very few (4%) of respondent were treated with radiation and chemotherapy.

The histological classification shown in table 3, 60% respondents' disease was classified as well differentiated, followed by 30% moderately differentiated, and 4% undifferentiated. Regarding the morphological classification all 100% of the respondents' disease was diagnosed as OSCC.

Discussion

This study was conducted to assess the epidemiological profile of oral cancer patients. Altogether 50 patients with oral cancer were included in the study. Study findings are discussed in relation to socio-demographic variables, lifestyle related factors and clinical profile of oral cancer patients attending at BPKMCH during the study period.



Out of 50 respondents of this study, 30% of respondents are belongs to 35-45 years and mean age of respondents is 54.75 ± 11.754 . This finding was similar to the findings of retrospective study conducted in King George's Medical University, Lucknow, India, where common age group was also 35 to 45 years and mean age was also 47.84 year.¹⁰

The findings of this study show, majority of respondents was male (88%). This finding was also supported by the study conducted in department of oncology & radiotherapy, Madhya Pradesh India where the finding was male 76.0% and female 24.0%^{.11}

Regarding the life style factors related to oral cancer, this present study findings shows that majority (68%) had the habits of chewing tobacco and similar percent of respondent also had habit of alcohol consumption. Likewise, an about of half (50 %) respondents had habits of smoking. Similarly, 40% of respondent had the habits of Gudka consumption. This finding was consistent with the findings of the retrospective study done among 295 in VSPM Dental College and Research Centre and Rashtrasant Tukdoji Cancer Institute, which showed, 31.86% were tobacco chewers, followed by 18.64% those who had the habit of both tobacco chewing and smoking, and 15.03% had habit of all the three - smoking, tobacco chewing and consumption of alcohol.¹⁰ Similarly, another study carried out in department of oncology & radiotherapy, Madhya Pradesh India also supported the findings.¹¹

The habit of oral sex is one of the risk factors of oral cancer, however none of the respondents the habits of oral sex in this study. This finding is supported with the findings of meta-analysis carried out in 2015. The results showed that there was no significant association between oral sex and risk of oral cancer.¹³ Moreover, there is no family history of oral cancer among cancer patients, whereas the finding was contrast with the retrospective study conducted in Rome, in which findings showed family history was related with oral cancer.¹⁴

Regarding the clinical profile of oral cancer patients, majority of the patients 60% had well differentiated and 30% are moderately differentiated. The finding of the study from northern Portugal in 2016 and Maharashtra, India in 2012. The majority of both studies were well differentiated and moderately differentiated.¹⁵

Regarding the sites of oral cancer, in this study, tongue was common site (36%), followed by gum 32%, cheeks 24%, roof of mouth 6% and lips 2%. This finding is consistent with the findings with the studies carried in India 2015. The majority of study site of oral cancer tongue, cheek, gum and root of mouth and lips respectively.¹⁵ In current study all the oral cancers were squamous cell carcinoma, similar findings seen in the Risk assessment of smokeless tobacco among oral precancer and cancer patients in eastern developmental region of Nepal in 2019. The majority were oral squamous cell carcinoma.¹⁶

Regarding the stages of cancer, findings in this study, shows 30% of in stage IV, followed by 28% in stage II, 26% in stage I and 14% in stage III disease. This finding is similar to the retrospective study conducted among 295 in VSPM Dental College and Research Centre and Rashtrasant



Tukdoji Cancer Institute and Research Centre from January 2008 to September 2010. These study shows majority in stage IV.¹⁰

Regarding the sign and symptoms majority (80%) had reported of pain followed by 70% had speech problem and similar percentage of respondents also had white and red patches. Likewise, 32% had bleeding from oral cavity and 36% had loosen teeth which is comparable to the study in warning signs and symptoms of oral cancer and its differential diagnosis in India 2018.¹⁷

Conclusion

Based on the findings of the study, it is concluded that oral cancer is most common in male, majority oral cancer was seen at 30-45 years. Smoking, tobacco and Gudka consumption are main risk factor of oral cancer. Pain and speech problem are the main clinical features of oral cancer. Therefore, risk assessment approach and screening program should be focused timely.

Acknowledgements

The authors would like to thank all individuals who rendered help and participated during the study period.

Funding

Self.

Competing interest

The authors declare no competing interests

Author Contributions

Concept and design: PP and MG; statistical analysis and SKP; writing of the manuscript: PP and MG; revision and editing the manuscript: SKP and MG. All authors read and agreed with the contents of the final manuscript.

References

- Sung H, Ferlay J, Siegel RL, 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: a cancer journal for clinicians. 2021 May;71(3):209-49. DOI: 10.3322/caac.21660
- 2. Elango JK, Gangadharan P, Sumithra S, Kuriakose MA. Trends of head and neck cancers in urban and rural India. Asian Pacific Journal of Cancer Prevention. 2006 Jan 25;7(1):108.
- 3. Shrestha G, Neupane P, Lamicchane N, Acharya BC, Siwakoti B, Subedi KP, Kumar K, Pradhananga RM. Cancer Incidence in Nepal: A Three-Year Trend Analysis



- 4. Dhanuthai K, Rojanawatsirivej S, Thosaporn W, Kintarak S, Subarnbhesaj A, Darling M, Kryshtalskyj E, Chiang CP, Shin HI, Choi SY, Lee SS. Oral cancer: A multicenter study. Medicina oral, patologia oral y cirugia bucal. 2018 Jan;23(1):e23.
- 5. ACS. Key Statistics for Oral Cavity and Oropharyngeal Cancers
- 6. Radoï L, Luce D. A review of risk factors for oral cavity cancer: the importance of a standardized case definition. Community dentistry and oral epidemiology. 2013 Apr;41(2):97-109.
- 7. Shrestha G, Maharjan L. Mouth self-examination for prevention and control of oral cavity cancer. JNMA: Journal of the Nepal Medical Association. 2020 May;58(225):360.
- Shrestha G, Siwakoti B, Mulmi R, Gautam D. Trend of Head and Neck Cancers in a National Tertiary Cancer Hospital of Nepal from 2012 to 2017. South Asian Journal of Cancer. 2021 Dec 31;10(04):236-40
- Gajurel R, Gautam DK, Pun CB, Dhakal HP, Petrovski BÉ, Costea DE, Sapkota D. Trends and clinicopathological characteristics of oral squamous cell carcinomas reported at a tertiary cancer hospital in Nepal during 1999 to 2009. Clinical and Experimental Dental Research. 2020 Jun;6(3):356-62.
- 10. Singh MP, Kumar V, Agarwal A, Kumar R, Bhatt ML, Misra S. Clinico-epidemiological study of oral squamous cell carcinoma: A tertiary care centre study in North India. Journal of oral biology and craniofacial research. 2016 Jan 1;6(1):32-5.
- 11. Agarwal AK, Mahore R, Bhadoriya SS, Tripathi A, Saraswat S. A clinico-epidemiological hospital-based study of oral cancer patients in Gwalior district. Indian J Forensic & Community Med. 2021;8(2):132-8
- 12. Shenoi R, Devrukhkar V, Sharma BK, Sapre SB, Chikhale A. Demographic and clinical profile of oral squamous cell carcinoma patients: A retrospective study. Indian journal of cancer. 2012 Jan 1;49(1):21-6
- Li S, Ni XB, Xu C, Wang XH, Zhang C, Zeng XT. Oral sex and risk of oral cancer: a metaanalysis of observational studies. Journal of Evidence-Based Medicine. 2015 Aug;8(3):126-33.
- Tenore G, Nuvoli A, Mohsen A, Cassoni A, Battisti A, Terenzi V, Della Monaca M, Raponi I, Brauner E, De Felice F, Musio D. Tobacco, alcohol and family history of cancer as risk factors of Oral Squamous Cell Carcinoma: Case-control retrospective study. Applied Sciences. 2020 Jun 4;10(11):3896.
- 15. Tavares C, Guimarães J, Lopes O, Felino A, Coimbra F. Epidemiological profile of malignant oral cancers in a population of northern Portugal. Revista Portuguesa de Estomatologia, Medicina Dentária e Cirurgia Maxilofacial. 2016 Oct 1;57(4):229-35.
- 16. Rimal J, Shrestha A, Maharjan IK, Shrestha S, Shah P. Risk assessment of smokeless tobacco among oral precancer and cancer patients in eastern developmental region of Nepal. Asian



Pacific journal of cancer prevention: APJCP. 2019;20(2):411.

17. Muthu K, Vaishnavi V, Sivadas G. Warning signs and symptoms of oral cancer and its differential diagnosis. Journal of Young Pharmacists. 2018;10(2):138.