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A MULTICENTER STUDY ON THE PREVALENCE AND PREVENTION OF ORAL CANCER

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Abstract:

Background: *To find out the incidence of science and cellular features of mouth cancer patients.*

Material and Method: *Oral cancer cases diagnosed from 2018 to 2019, their biopsy records of the participated institution were reviewed. Site of lesions and analytical data were collected. Mandible and maxilla, palate, buccal/labial mucosa, alveolar mucosa, floor of the mouth, lip, tongue, were the subdivision of the site of lesions. Seven categories of oral cancer are: Salivary gland tumors, epithelial tumors, Hematologic tumors, Bone tumors, Odontogenic tumors and mesenchymal tumors. SPSS SOFTWARE and descriptive statistics were used for analyzing data.*

Results: *Of the 474,850 assumed cases, 6150 cases [1.29%] were diagnosed with oral cancer. 58.36 ± 15.76 years was the mean age of the patients. A total of 4236 cases [68.80%] were diagnosed in males, whereas 1910 cases [31.06%] were diagnosed in females. The male to female ratio was 2.23:1.Alveolar mucosa, palate, gingiva, labial/buccal mucosa, are the sites of prepossession for oral cancer. In descending order of frequency the three most common oral cancer were Squamous cell carcinoma, non-Hodgkin lymphoma and mucoepidermoid carcinoma.*

Conclusion: *As compared to other, the prevalence of oral cancer is not high as compared to other entities, when discovered late in the course of disease, oral cancer pose significant mortality and morbidity in the patients. Anatomical locations where oral cancer are frequently encountered, are highlighted by this study. In the high prevalence area, clinicians should pay an attention to not only teeth but oral mucosa. The chance of patients being cured and great reduction in the mortality and morbidity increases when there is early detections of precancerous lesions in the early stage. Difference between pediatric and elderly oral cancer patients as well as between Asian and non- Asian oral cancer patients are also showed by this study.*

Key Words: *Prevalence, oral cancer, clinic-pathologic features and retrospective study.*

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INTRODUCTION:

Sixth most common malignancy worldwide is oral cancer. Four hundred thousand patients (3.1% of the total cancer cases) were affiliated with cancer of lip and oral cavity in 2014. By the cancer of oral cavity and lip, two-hundred-thousand patients passed away. The principle factors for the development of oral cancer are tobacco and alcohol consumptions. Different other factors such as viral infections, malnutrition, low fruits and vegetable diets, genetic factors are also susceptible causes of oral cancer. Tobacco use and alcohol abuse which have synergistic effect are the most important risk factors for squamous cell carcinoma. According to international agency for research on cancer, cigarette smoke contains 80 carcinogens. In experimental animals, factors that have been demonstrated to cause cancer are, Tobacco specific N-nitrosamines specially 4- (mehtylnitrosamino) -1-(3-pyridyl)-1-butanone (NNK) and N'-nitrosonornicotine (NNN). Cytochromes P450 to DNA-reactive metabolites which induce methylation as well as pyridyloxobutylation of nucleobases in DNA and from DNA adducts are the metabolically activating factors for NNK. Major pathways that lead to the formation of DNA adducts are 2'- and 5'- **α** hydroxylation pathways. Deleterious mutations in oncogenes and tumor suppressor genes can be induced by resulting DNA adducts, which could be considered as tumor initiation. Increased risk for oral cancer is associated with the use of betel quads containing areca nut and lime, in the Indian subcontinent, some parts of Southeast Asia and Taiwan. Independent risk factor for development of cancer in the dose dependent manner is alcohol consumption, as shown in the previous study. By alcohol dehydrogenase (ADH) alcohol is first oxidized to acetaldehyde. According to International Agency for Research on Cancer (IARC), acetaldehyde is considered as group 1 carcinogen. By aldehyde dehydrogenase (ALDH) , acetaldehyde is further metabolized to acetate. Carcinogenesis by alcohol may be influenced by any defect in these enzymes (ADH and ALDH). Basal cell proliferation and generates free radical can be induced by alcohol, which have the deleterious effects on DNA. Further carcinogenesis may be promoted by alcohol associated impairment of the body's ability to breakdown and absorb nutrients.

Human papilloma virus has recently received special attention, apart from tobacco use and alcohol abuse. Etiological agent for the development of subset of squamous cell carcinoma, is Human papilloma virus. Proportion of HPV- positive oropharyngeal cancer was 55% in North America , 51%in Japan , 44% in Australia, 33% in Northern and Western Europe,36% in Eastern Europe , 16% in southern Europe and 12% in rest of the world.

Prevalence of oral cancer in different regions of the world or even within the same countries from the minorities or sub-populations, has wide variation. To report the prevalence as well as clinicopathologic features of the oral cancer patients from different parts of Asia and Canada and to compare them with patients from other parts of the world was the main aim of this research.

Less expensive treatment, less morbidity and a greater probability of surviving can be achieved when the cancer is identified early. Furthermore cancer is more likely to respond to effective treatment when it is identified at an early stage. Three steps of early diagnosis that must be integrated in a timely manner:

1. Awareness and accessing care
2. Diagnosis, staging and clinical evaluation
3. Easy access to treatment.

Curative treatment may no longer be an option, in absence of early diagnosis. Educational programs and cancer awareness aids in helping adult learners or secondary school students to reduce the risk of cancer. By engaging students with its age appropriate, interactive and informative material, the program makes cancer less frightening. UN organisations within the UN interagency task force collaborate with WHO and IARC on the prevention and control of noncommunicable disease and partners to:

1.Research are conducted on the causes of human cancer and the mechanism on carcinogenesis.
2.Cancer burden is monitored.
3. Political commitment of cancer prevention and control is increased.

MATERIALS AND METHODS:

The oral cancer cases diagnosed from 2018 to 2019were reviewed by biopsy records of the Department of Oral Pathology , Chulalongkorn University , Gangneung-Wonju national university and Kyungpook National university, Department of Oral biology and diagnostic sciences, Chiangmai University , Department of oral Diagnosis , Khon kean university, Department of Stomatology , Prince of Songkla University, Department of oral and Maxillofacial Pathology , Tehran university of Medical sciences , Department of Pathology and laboratory medicine , Western university and department of oral pathology and oral diagnosis , School of Dentistry , National Taiwan university .Sites of lesion and demographic data were also collected . Subdivision of Sites of lesion were : Lip , Tongue , floor of the mouth , alveolar mucosa , palate , gingiva , buccal mucosa , maxilla and mandible . Subdivision of oral cancer into 7 categories was: Salivary gland tumors, Hematologic tumors, Bone tumors, Mesenchymal tumors,

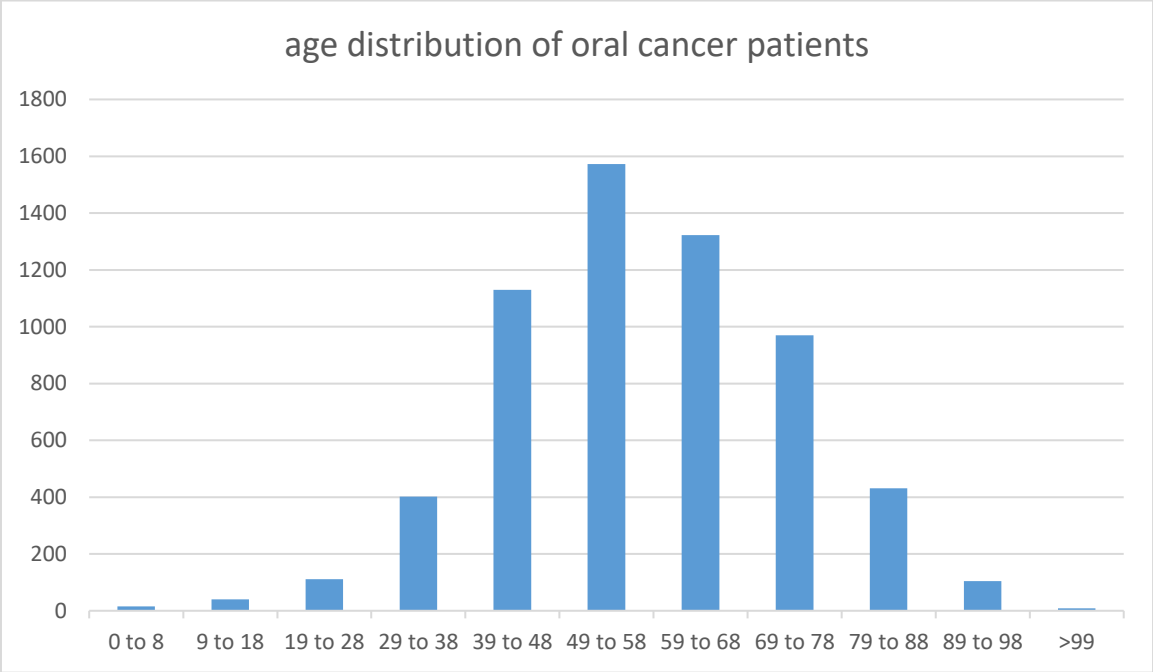
Odontogenic tumors, epithelial tumors and others. Appropriate statistics used to analyze data collection were SPSS statistics for Windows, Version 17.0 .Statistical significant value of Chicago: SPSS Inc. A P would be less than .04 .Ethical committee of the Faculty of Dentistry, Chulalongkorn University (no. 70/2019) approved this research.

RESULTS:

Of the 474,850 accessioned cases, 6150 cases (1.29%) were diagnosed in the category of oral cancer. Oran cancer prevalence range from 0.82% in Taiwan to 6.22% in Thailand. (Table 1). The age of the patients in the present study ranges from 2 to 110 years, with a mean ± SD = 58.36±16.76 years. The cases encountered in the fifth and eighth decades of life were in majority i-e (81.25%). Cases discovered in children aged 15 and below were sixty six (1.08%). In the elderly aged (aged 66 and above) two thousand one hundred and forty seven cases (34.91%) were found. Pediatric patients had mean age of 5.81±6.06, 75.0±7.73 was of elderly patients. Asian patient's ±SD had mean age of 56.36±14.97 years. Non-Asian patients was 69.98±15.50 years. Mean age of the Non-Asian patients was significantly higher than Asian patients. A male predilection was demonstrated in most countries except Thailand. The male to female ratio was 2.21:1. Male to female ratio from Taiwan was as high as 5.61:1, it was noteworthy.

M:F ratio, prevalence and average age of oral cancer patients :

Country	prevalence	Mean age ± SD	M:F ratio
Canada	**1.70**	**69.21±15.50**	**1.27:1**
Korea	**3.42**	**61.40±14.35**	**1.66:1**
Iran	**3.87**	**56.54±19.79**	**1.12:1**
Taiwan	**0.82**	**54.82±12.33**	**5.61:1**
Thailand	**6.22**	**59.12±17.31**	**0.85:1**
total	**1.29**	**58.36±15.76**	**2.21:1**



Five most common sites for Oral Cancer in descending order of frequency regarding the anatomical distribution of oral cancer were: Tongue (25.5%), Labial/buccal mucosa (21.8%), gingiva (14.1%) , palate (9.8%), and alveolar mucosa (7.8%) respectively. The most common site for oral cancer in Taiwan was Labial/buccal mucosa, the site of predilection for oral cancer in Canada and Iran was Tongue and for Korea and Thailand was Gingiva. Five most common sites for oral cancer in descending order of frequency in children below 16(age) were: mandible (17.8%), palate (14.8%) , gingiva (13.5%), alveolar mucosa(11.9%) , maxilla and tongue(10.5% each), respectively. Five most common sites for oral cancer in descending order of frequency in the elderly age 65 and above were: Tongue (20.9%), labial/buccal mucosa (18.3%), Gingiva (16.1%), alveolar mucosa (14.6%) and palate (9.6%) , respectively. The site of predilection of oral cancer for both Asian and Non-Asian patients is Tongue .In Asian patients, the second most common site for oral cancer was labial/buccal mucosa, followed by gingiva and palate respectively, while in Non-Asian patients the second

most common site was alveolar mucosa followed by floor of the mouth and lip respectively.

Epithelial tumor category consist of Salivary gland tumor category (410 cases ,6.67%), Mesenchymal tumor category(74 cases,1.20%), others category(58 cases, 0.94%) ,hematologic tumor category(272 cases ,4.45%), bone tumor category (77 cases, 1.28%) from most of the oral cancer (5235 cases,85.08%) respectively (Table 2, Table 2 continue) and odontogenic tumor category(21 cases,0.34%). According to ranking, the most common oral cancer category in all countries is epithelial tumor category, while almost in all countries except Canada, Salivary gland tumor is ranked second and in most countries except Canada, third most common category was hematologic tumor category. Hematologic tumor category followed by salivary gland tumor category was second most common oral cancer in Canada .Squamous cell carcinoma which constituted 95.09% of all epithelial tumor and 80.06% of all oral cancer cases was the most common oral cancer. Lymphoma which accounted for 86.92% of the hematologic tumors and 3.88% of all oral cancer cases was second most prevalent oral cancer. Mucoepidermoid carcinoma which constituted 46.26% of all salivary gland tumors and 3.03% of all oral cancer cases was third most prevalent oral cancer cases. The most common tumor constituting 40.28% of the cases in this group, followed by muceopidermoid carcinoma (16.43%) and lymphoma (14.94%) respectively in pediatric patient was squamous cell carcinoma. The most universal tumor constituting 80.78% of the cases in the group, followed by verrucous carcinoma (5.43%) and lymphoma (5.28%) respectively in elder patient was squamous cell carcinoma. The most common oral cancer in both Asian (80.24%) and Non-Asian (73.47%) was squamous cell carcinoma. Verrucous carcinoma(3.38%) followed by lymphoma(3.35%), mucoepidermoid carcinoma (2.88%) and adenoid cystic carcinoma(1.86%) respectively was second most common oral cancer in Asian patients, while lymphoma(6.91%) followed by muceopidermoid carcinoma (3.77%), verrucous carcinoma (3.67%) and adenoid cystic carcinoma(2.18%) respectively was second most universal oral cancer in Non-Asian patients. For both Asian and Non-Asian patient's items constituting the top five most universal oral cancer were exactly the same, but with different ranking .Metastatic tumors to the oral cavity which constituted 0.95% of the oral cancer were 59 cases. Patients mean age, ±SD was 61.32±16.34 years. Ratio of Male-to-Female was 1.53:2. The mandible followed by gingiva were the sites of predilection for metastatic tumors. Primary sites for the metastatic tumors to the oral cavity in the present study were lung, thyroid gland, breast, kidney liver, colon, pancreas, bile duct but thyroid gland and the lung were the most common ones.

Table 2: Histopathologic diagnosis of oral cancer patients.

TUMORS	Canada	Iran	South Korea	Taiwan	Thailand	Total Number (percent of all cancer cases)
Epithelial tumors	**769**	**145**	**344**	**2942**	**1035**	**5235(85.08%)**
Squamous cell carcinoma	712	130	329	2789	963	4923(80.06%)
Verrucous carcinoma	36	5	8	124	37	210(3.42%)
Metastatic carcinoma	12	2	4	17	22	57(0.93%)
Undifferentiated carcinoma	7	7	1	5	5	25(0.38%)
Others	2	1	2	7	7	19(0.28%)
Salivary gland tumors	**94**	**17**	**50**	**92**	**157**	**410(6.67%)**
Mucoepidermoid carcinoma	34	6	21	39	81	181(3.00%)
Adenoid cystic carcinoma	20	4	17	26	47	114(1.89%)
Polymorphous low-grade adenocarcinoma	19	1	3	6	7	36(0.56%)
Adenocarcinoma NOS	7	1	5	8	12	33(0.53%)
Carcinoma ex pleomorphic adenoma	1	3	2	1	4	11(0.17%)
Others	13	2	2	12	6	35(0.56%)
Hematologic tumors	**73**	**4**	**23**	**56**	**116**	**272(4.45%)**
Lymphoma	65	2	23	46	103	239(3.92%)
Myeloma	6	1	0	6	10	23(0.46%)
Leukemia	1	0	0	2	2	5(0.08%)
Myeloid sarcoma	1	1	0	2	1	3(0.08%)
Bone tumors	**5**	**5**	**14**	**13**	**40**	**77(1.28%)**
Osteosarcoma	2	2	10	11	28	53(0.95%)
Chondrosarcoma	1	2	3	1	7	14(0.23%)
Ewing's sarcoma	2	1	1	1	5	10(0.15%)

Table 2 continue
Histopathologic diagnosis of oral cancer patients

Tumors	Canada	Iran	South Korea	Taiwan	Thailand	Total number(percent of all cancer cases
Mesenchymal tumors	**5**	**5**	**16**	**23**	**25**	**74(1.20%)**
Fibrosarcoma	3	1	3	3	5	15(0.25%)
Spindle cell sarcoma	1	3	2	0	3	9(0.15%)
Kaposi's sarcoma	0	0	1	2	3	6(0.12%)
Post-radiation sarcoma	0	0	0	3	0	3(0.03%)
Leiomyosarcoma	0	0	0	6	4	10(0.08%)
Malignant fibrous histiocytoma	0	0	5	3	0	8(0.13%)
Rhabdomyosarcoma	0	0	2	0	3	5(0.08%)
Others	1	0	2	4	4	11(0.20%)
Odontogenic tumors	**2**	**3**	**1**	**1**	**13**	**21(0.34%)**
Clear cell odontogenic carcinoma	0	0	0	0	6	**6(0.10%)**
Ameloblastic carcinoma Primary intraosseous carcinoma	1	1	0	0	1	**3(0.05%)**
Odontogenic ghost cell carcinoma	0	0	1	1	2	**4(0.06%)**
Ameloblastic fibroscroma	1	0	0	0	1	**2(0.03%)**
	0	1	0	0	2	**3(0.05%)**
	0	1	0	0	1	**1(0.02%)**
Others	**6**	**8**	**14**	**12**	**18**	**58(0.94%)**
Melanoma	4	4	13	6	10	37(0.60%)
Others	2	4	1	6	8	21(0.32%)

CONCLUSIONS:

Oral cancer poses significant mortality and morbidity in the patients when discovered late in the course of the disease although prevalence of oral cancer is not high as compared to other items. Anatomical location is highlighted where oral cancers are frequently encountered in this study.Clinicians should pay attention to not only teeth but oral mucosa especially in the high prevalence area as well since early detection of precancerous lesions or cancers in early stage thr chance of patient being cured and greatly reduce mortality and morbidity. Some difference between pediatric and elderly oral cancer patients as well as between Asian and non asain oral cancer patients is shown in this study. Through an integrated approach the World Health Organization passed the resolution for cancer prevention and control and to achieve the targets specified in the global action plan to reduce premature mortality of cancers for sustainable development.

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