ASSESSMENT ON THE DEMOGRAPHIC DATA AND RISK FACTORS OF ORAL SQUAMOUS CELL CARCINOMA PATIENTS IN TERTIARY CARE SETTING

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ABSTRACT

The epidemiological study on oral squamous cell carcinoma (OSCC) differs significantly among continents. Smoking, betel quid chewing and alcohol consumption are the most important risk factors. This is a hospital based retrospective study. Medical record of 55 confirmed OSCC patients was reviewed. The mean age of OSCC patients was 58 years old (SD 14.87) with female predominates. Patients of Indian ethnicity were the highest associated with OSCC. Betel quid chewing was the major risk factor for the development of OSCC followed by alcohol consumption and smoking. The most common site of tumor was in buccal mucosa region, followed by tongue, gingiva, floor of the mouth, palate region and lip. Majority of the patients (45.5%) was diagnosed at stage IV. There was correlation between age and stage of cancer, p<0.005. No significant correlation (p> 0.05) was noted between two variables among age, gender, ethnic, habits, staging, site of tumor, history of head and neck cancer and family history of cancer. OSCC was predominantly found in elderly female with habits of betel quid chewing. It was found within buccal region and the majority of the cases presented were at advanced stage.

Keywords: Demographic data, risk factor, oral cancer, oral squamous cell carcinoma.

1. INTRODUCTION

Etiologically, oral carcinoma may arise afresh or from different pre-malignant lesions with different malignancy potentials likes leukoplakia, erythroplakia or a mix of the two (erythroleukoplakia) with an ulcer (Yardimci *et al.*, 2014). Despite the vital role played by genetic factors, oral carcinoma is tremendously influenced by environmental and behavioural risk factors (Antunes *et al.*, 2013). Chronic exposure by carcinogens like tobacco or alcohol will inactivating tumor suppressor genes and causing over expression of oncogenes (Kerawala *et al.*, 2016, Sousa *et al.*, 2014). In addition, betel quid chewing, chronic exposure to sunlight

and human papillomavirus are among well-known risk factor for oral squamous cell carcinoma (OSCC) (Kaminagakura *et al.*, 2012, Lee *et al.*, 2012, Shenoi *et al.*, 2012, Vargas-Ferreira *et al.*, 2012). OSCC is an invasive lesion with the manifestation of perineural growth. Approximately, 90% of epithelial malignancy found within oral mucosa is squamous cell carcinoma (SCC) (Paul, 2012). It is one of the most difficult malignancies to control and has been associated with poor prognosis that may be explained by frequent lymph node metastases and local invasion characteristic (Noguti *et al.*, 2012).

According to the latest World Health Organization (WHO) data published in May 2014, oral cancer deaths in Malaysia reached 1,060 or 0.83% of total deaths (WHO, 2014). Malaysia population comprises many ethnic groups, the largest being the Malays followed by the Chinese, the indigenous peoples of Borneo and the Indians (Department of Statistics Malaysia, 2014). Of these ethnic, the highest prevalence of oral cancer are Indians and indigenous groups. A traditional stimulant mixture of areca nut and/or tobacco with the betel leaf (Piper betel) is common in Malaysia found associated in these ethnic groups (Razak *et al.*, 2010). Among the Chinese and Malays, where mouth cancer is less prevalent, the major risk factors are tobacco smoking for Malays and alcohol consumption for Chinese (*e*cancer, 2010).

Above all, oral cancer is a preventable disease. The malignant lesions that occur in an anatomic region is easily accessed and reachable during physical examination. The lesion can be easily explored visually and tactilely (Sousa *et al.*, 2014). Hence, knowledge on the risk factors and lesion malignancy will aid health care professionals in determining the extent of the disease together with decision making in health policy.

2. MATERIALS AND METHOD

This is a hospital based retrospective study, conducted at Oral Cancer Research & Coordinating Centre (OCRCC) Universiti Malaya, from January 2006 to December 2014. Written informed consent was obtained from all participants prior to data collection. This study was approved by the Ethics Committee (Human) of Universiti Malaya (UM) [OI DF1601/0072 (P)]. All 55 patients were confirmed cases of OSCC by histopathological staining. Patients medical record were reviewed to obtain the information regarding the oral cancer status. This included medical history, age, gender, habits of tobacco ingestion, and alcohol intake, site of the primary tumor and size of tumor (TNM staging).

All data were analysed using SPSS version 22.0 (SPSS Inc, Chicago, IL, USA). Descriptive analysis was calculated and was expressed as mean and median. The correlation between categorical variables were analysed using chi-square test between the two variables, i.e., site to habits, staging to site involved, staging to history of the disease, staging to habits, and staging to age of the patient were done. The significant level was set at p<0.05 at 95% Confidence Interval (CI).

3. RESULTS

There were 55 cases of OSCC confirmed by biopsy from 2006 to 2015. Table 1 showed the demographic data of the OSCC patients. Thirty-four patients (61.8%) were females and 21 (38.2%) were males. The largest number of patients in the study were seen in the age group 51-60 (25.5%). The youngest of all patients affected was 20 years old and the oldest was 90 years old. The least number of patients were in the age group 20-30 (5.5%) and the mean age of OSCC patients was 58 years old. Indian ethnic dominates with 33 cases (60.0%) and the least were from Iban and Bidayuh ethnic. Table 2 showed the habits of OSCC patients. By

looking at personal habits, most patients were betel quid chewer (47.3%). Both smoking and alcohol consumption represented 14 cases each (25.5%). Table 3 showed the relationship and history of cancer. Among 55 OSCC cases, 11 (20.0%) of the patients have family history of cancer while four patients (7.3%) were previously diagnosed with head and neck cancer. Table 4 showed the site distribution of the lesions in oral cavity. The buccal mucosa was the most frequently involved site, accounting for 22 cases (40.0%), followed by tongue for 14 cases (25.5%). Gingiva was involved in 11 cases (20.0%) and floor of the mouth in 4 cases (7.3%) patients. The least site affected was in palate region represented only 2 cases (3.6%). Table 5 showed the staging of the tumor during diagnosis. Majority of patients, 25 (45.5%) were in stage IV. Fourteen patients (25.5%) presented in stage III. Nine patients (16.4%) were in stage I and seven (12.7%) in stage II.

Correlation using chi-square test between the two variables, i.e., site to habits, staging to site involved, staging to ethnic, staging to habits, and staging to age of the patient were done. All the above-said correlation was found to be statistically nonsignificant (p>0.05). Although, it was seen that patients with older age (>40 years old) were at diagnosed at stage IV [Table 6] and younger age (<40 years old) were diagnosed at stage I.

Demographic data	No of patients	Percentage	
Gender			
Male	21	38.2%	
Female	34	61.8%	
Age group (years)			
20-30	3	5.5%	
31-40	5	9.1%	
41-50	7	12.7%	
51-60	14	25.5%	
61-70	13	23.6%	
> 70	13	23.6%	
Ethnic			
Malay	10	18.2%	
Chinese	10	18.2%	
Indian	33	60.0%	
Other	2	3.6%	

Table 1: Demographic data

Table	2:	Personal	habits
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Habits	No of patients	Percentage
Smoking	14	25.5%
Alcohol consumption	14	25.5%
Betel quid chewing	26	47.3%
No habits	3	5.5%

Table 3: History of cancer

History	No of patients	Percentage
History of Head and neck cancer	4	7.3%
Family history of cancer	11	20.0%

Table 4: Primary site

Site	No of patients	Percentage
Gingiva	11	20.0%
Lip	1	1.8%
Buccal mucosa	22	40.0%
Floor of the mouth	4	7.3%
Tongue	14	25.5%
Palate	2	3.6%

Table 5: Staging

Staging	No of patients	Percentage
Stage I	9	16.4%
Stage II	7	12.7%
Stage III	14	25.5%
Stage IV	25	45.5%

		<	40	>4	0	
		n	%	n	%	p-value
Site	Buccal mucosa	2	3.6	20	36.4	0.349
	Gingiva	1	1.8	10	18.2	0.566
	Tongue	5	9.1	9	16.4	0.321
	Floor of the mouth	0	0	4	7.3	0.349
	Palate	0	0	2	3.6	0.552
	Lip	0	0	1	1.8	0.677
Habits	Smoking	4	7.3	12	22.2	0.159
	Alcohol	4	7.3	12	22.2	0.159
	Betel quid chewing	2	3.8	25	45.5	0.140
Stage	Stage I	5	9.1	4	7.3	0.000*
	Stage II	0	0	7	12.7	0.243
	Stage III	2	3.6	12	21.8	0.975
	Stage IV	1	1.8	24	43.6	0.043*
Cancer	Previous head & neck cancer	1	1.8	3	5.5	0.538
history	Family history of cancer	1	1.8	9	16.4	0.65

Table 6: Correlation between the variable

4. DISCUSSION

Of Asia continent, Bangladesh being the highest in prevalence of oral cancer (WHO, 2016). Early identification and prompt treatment are important as it pilot to early institution of therapy that translates in a better prognosis (Shenoi *et al.*, 2012). The OSCC cases in this study were found higher in female than male. Sex distribution or the male-to-female (M:F) ratio in the present study is 1:1.6. This is disagreement with the result of previous studies where males were more often affected than females because males were more likely indulge in major risk habits (Johnson *et al.*, 2011, Udeabor *et al.*, 2012). However, it should be noted that in Malaysia, with different ethnicity, the betel quid chewing habit is common among women. This present results showed that majority of the female patients are from Indian ethnic. Study by Razak et al, (2010) showed that betel quid, a traditional stimulant was common in Malaysia associated in these ethnic groups (Razak *et al.*, 2010). Betel-quid is a masticatory mixture combining the areca nut, betel leaf, slaked lime and locally varied flavorings. It is a the fourth most frequently consumed psychoactive substance worldwide. Moreover, our results were also supported as in study by Lee et al, (2012) which reported that in Malaysia, habits of chewing betel leaf are higher among female rather than male (Lee *et al.*, 2012).

According to Surveillance, Epidemiology, and End Results (SEER) database, the mean diagnosis age of oral cancer is 62 years while it is 52.07 years old in another study from Eastern India (Shenoi *et al.*, 2012, Chi *et al.*, 2015). Predictably in our study, the most affected age group was 51-60 years, youngest of all patients affected was 20-years old and the oldest was 90 years old. The mean age of patients of oral cancer was found to be 58 years old. Like most

cancer, oral cancer is disease of older age. It is diagnosed mostly in people above 40 years old (Silverman and Society, 2003). On the other hand, there are also trends nowadays where oral cancer was diagnosed in younger generation especially in developing countries (Llewellyn *et al.*, 2004). In this study 14% of OSCC patients were at age \leq 40 years old. Our results are quite high showing significant value (p<0.005) compare to other reports (Komolmalai *et al.*, 2015, Udeabor *et al.*, 2012). The high cases in younger population in this country might due to the ease of getting alcohol, tobacco and its related products at very affordable prices at the grocery stores. Even though there are strict warning from the Health Ministry not to sell the tobacco product for teenagers <18 years old, yet many smuggled cigarettes are accessible to them (Hizlinda *et al.*, 2012).

By looking at site of infection, our results are in agreement with de Camargo *et al.*, (2010) which reported that the common site affected is on buccal region (de Camargo Cancela *et al.*, 2010). Epidemiological studies have shown that the sites of occurrence for oral cancer differ widely (Kerawala *et al.*, 2016). It is stated that tumor site is related to specific risk factors (Warnakulasuriya, 2009, Johnson *et al.*, 2011). Tumors of the tongue and the floor of the mouth may be associated with excessive alcohol consumption and cigarette-smoking habits, whereas lesions on the buccal mucosa and gingiva may be related to tobacco/betel quid chewing habits (Johnson *et al.*, 2011), de Camargo Cancela *et al.*, 2010, Oo *et al.*, 2011, de Camargo Cancela *et al.*, 2012). Taken together, these factors could explain the high percentages of tumors on the buccal mucosa since OSCC population in this study have betel quid chewing habits. Second affected site were on tongue followed by gingiva. The least was on lip site.

Majority of patients, 25 (45.5%) were in stage IV. Fourteen patients (25.5%) presented in stage III. Seven (12.7%) in stage II and nine patients (16.4%) were in stage I. There was delay in reporting and diagnosis of the cancer. The delay in diagnosis could be correlated to patient delay (in looking for professional care), professional delay (in reading a diagnosis), or both. Moreover, the time interval between the onset of symptoms and the start of treatment depends on various factors such as patient behavior, clinical course of the illness and the quality of the health services (Kerdpon and Sriplung, 2001, Esmaelbeigi *et al.*, 2014, Naseer *et al.*, 2016). In our study however, these factors were not analyzed yet no conclusion can be made.

Along with other factor, genetic also contribute to OSCC. In this study, 20% have family history of cancer and 7.3% previously diagnosed with other head and neck cancer. It is now established that up to 10% of all cancers have a strong hereditary component. There were study showing that, a clustering of oral cancer has been seen in certain ethnic groups, like Askenazi group in Israel which the incidence being double as compared to other Jewish population in that country. However, the basis of this genetic susceptibility is not well understood, as yet (Ram *et al.*, 2011).

5. CONCLUSION

OSCC was predominantly found in elderly female with habits of betel quid chewing. It was commonly found within buccal region and the majority of the cases presented were at advanced stage IV.

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REFERENCES

Antunes, J. L. F., Toporcov, T. N., Biazevic, M. G. H., Boing, A. F. & Bastos, J. L. (2013). Gender and racial inequalities in trends of oral cancer mortality in Sao Paulo, Brazil. *Revista de Saúde Pública*, **47**470-478.

Chi, A. C., Day, T. A. & Neville, B. W. (2015). Oral cavity and oropharyngeal squamous cell carcinoma—an update. *CA: A Cancer Journal for Clinicians*, **65**(5), 401-421.

de Camargo Cancela, M., de Souza, D. L. & Curado, M. P. (2012). International incidence of oropharyngeal cancer: a population-based study. *Oral Oncol*, **48**(6), 484-90.

de Camargo Cancela, M., Voti, L., Guerra-Yi, M., Chapuis, F., Mazuir, M. & Curado, M. P. (2010). Oral cavity cancer in developed and in developing countries: population-based incidence. *Head Neck*, **32**(3), 357-67.

Department of Statistics Malaysia (2014). Statistics Malaysia [Online]. [Assessed Available from World Wide Web: *e*cancer, o. (2010). ecancer news, the latest oncology headlines [Online]. [Assessed 3 July 2017 2017]. Available from World Wide Web: <u>http://ecancer.org/news/3080-oral-cancer-in-malaysia.php</u>

Esmaelbeigi, F., Hadji, M., Harirchi, I., Omranipour, R., vand Rajabpour, M. & Zendehdel, K. (2014). Factors affecting professional delay in diagnosis and treatment of oral cancer in Iran. *Arch Iran Med*, **17**(4), 253-7.

Hizlinda, T., Noriah, M. I., Noor Azimah, M., Farah Naaz, M. A., Anis Ezdiana, A. A. & Khairani, O. (2012). Perceived Effects of the Malaysian National Tobacco Control Programme on Adolescent Smoking Cessation: A Qualitative Study. *The Malaysian Journal of Medical Sciences : MJMS*, **19**(2), 35-47.

Johnson, N. W., Jayasekara, P. & Amarasinghe, A. A. (2011). Squamous cell carcinoma and precursor lesions of the oral cavity: epidemiology and aetiology. *Periodontol 2000*, **57**(1), 19-37.

Kaminagakura, E., Villa, L. L., Andreoli, M. A., Sobrinho, J. S., Vartanian, J. G., Soares, F. A., Nishimoto, I. N., Rocha, R. & Kowalski, L. P. (2012). High-risk human papillomavirus in oral squamous cell carcinoma of young patients. *International Journal of Cancer*, **130**(8), 1726-1732.

Kerawala, C., Roques, T., Jeannon, J. P. & Bisase, B. (2016). Oral cavity and lip cancer: United Kingdom National Multidisciplinary Guidelines. *The Journal of Laryngology and Otology*, **130**(Suppl 2), S83-S89.

Kerdpon, D. & Sriplung, H. (2001). Factors related to delay in diagnosis of oral squamous cell carcinoma in southern Thailand. *Oral Oncol*, **37**(2), 127-31.

Komolmalai, N., Chuachamsai, S., Tantiwipawin, S., Dejsuvan, S., Buhngamongkol, P., Wongvised, C., Chitapanarux, I. & Iamaroon, A. (2015). Ten-year analysis of oral cancer focusing on young people in northern Thailand. *J Oral Sci*, **57**(4), 327-34.

Lee, C.-H., Ko, A. M.-S., Yen, C.-F., Chu, K.-S., Gao, Y.-J., Warnakulasuriya, S., Sunarjo, Ibrahim, S. O., Zain, R. B., Patrick, W. K. & Ko, Y.-C. (2012). Betel-quid dependence and oral potentially malignant disorders in six Asian countries. *The British Journal of Psychiatry*, **201**(5), 383-391.

Llewellyn, C. D., Johnson, N. W. & Warnakulasuriya, K. A. A. S. (2004). Risk factors for oral cancer in newly diagnosed patients aged 45 years and younger: a case–control study in Southern England. *Journal of Oral Pathology & Medicine*, **33**(9), 525-532.

Naseer, R., Naz, I. & Mahmood, M. K. (2016). Frequency of Delayed Diagnosis of Oral Squamous Cell Carcinoma in Pakistan. *Asian Pac J Cancer Prev*, **17**(11), 5037-5040.

Noguti, J., De Moura, C. F. G., De Jesus, G. P. P., Da Silva, V. H. P., Hossaka, T. A., Oshima, C. T. F. & Ribeiro, D. A. (2012). Metastasis from Oral Cancer: An Overview. *Cancer Genomics - Proteomics*, **9**(5), 329-335.

Oo, H. N., Myint, Y. Y., Maung, C. N., Oo, P. S., Cheng, J., Maruyama, S., Yamazaki, M., Yagi, M., Sawair, F. A. & Saku, T. (2011). Oral cancer in Myanmar: a preliminary survey based on hospital-based cancer registries. *J Oral Pathol Med*, **40**(1), 20-6.

Paul, D. L. (2012), Vol. PhD University of Medicine and Pharmacy Craiova, University of Medicine and Pharmacy Craiova.

Ram, H., Sarkar, J., Kumar, H., Konwar, R., Bhatt, M. L. B. & Mohammad, S. (2011). Oral Cancer: Risk Factors and Molecular Pathogenesis. *Journal of Maxillofacial & Oral Surgery*, **10**(2), 132-137.

Razak, A. A., Saddki, N., Naing, N. & Abdullah, N. (2010). Oral Cancer Survival among Malay Patients in Hospital Universiti Sains Malaysia, Kelantan. *Asian Pacific J Cancer Prev*, **11**(1), 187-191.

Shenoi, R., Devrukhkar, V., Chaudhuri, Sharma, B., Sapre, S. & Chikhale, A. (2012). Demographic and clinical profile of oral squamous cell carcinoma patients: A retrospective study. *Indian Journal of Cancer*, **49**(1), 21-26.

Silverman, S. & Society, A. C. (2003) Oral Cancer. B.C. Decker.

Sousa, F. B., Silva, M. R. d. F., Fernandes, C. P., Silva, P. G. n. d. B. & Alves, A. P. N. N. (2014). Oral cancer from a health promotion perspective: experience of a diagnosis network in Ceará. *Brazilian Oral Research*, **28**1-8.

Udeabor, S. E., Rana, M., Wegener, G., Gellrich, N. C. & Eckardt, A. M. (2012). Squamous cell carcinoma of the oral cavity and the oropharynx in patients less than 40 years of age: a 20-year analysis. *Head Neck Oncol*, **4**28.

Vargas-Ferreira, F., Nedel, F., Etges, A., Gomes, A. P., Furuse, C. & Tarquinio, S. B. (2012). Etiologic factors associated with oral squamous cell carcinoma in non-smokers and non-alcoholic drinkers: a brief approach. *Braz Dent J*, **23**(5), 586-90.

Warnakulasuriya, S. (2009). Global epidemiology of oral and oropharyngeal cancer. *Oral Oncology*, **45**(4–5), 309-316.

World Health Organization (2014). World health statistics 2014 [Online]. [Assessed Available from World Wide Web: World Health Organization (2016). World Health Statistics 2016 [Online]. [Assessed Available from World Wide Web: Yardimci, G., Kutlubay, Z., Engin, B. & Tuzun, Y. (2014). Precancerous lesions of oral mucosa. *World Journal of Clinical Cases : WJCC*, **2**(12), 866-872.