

Epidemiological features of oral cancer – a world public health matter

Epidemiologia do câncer bucal – um problema mundial de saúde pública

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Abstract

The objective of this present paper is to evaluate the impact of oral cancer over the international public health status and to search for its predictor factors heading for early intervention attempting to reduce its incidence and mortality rates. This critical review takes into account several publications related to oral cancer epidemiology searching for international data. Annually, over 300.000 new cases of oral cancer are diagnosed all over the world where the majority is in the advanced stages III or IV. Such data make the oral cancer an important public health matter which is responsible for 3% to 10% of cancer mortality worldwide. Ethnology, socioeconomic factors, lifestyle like dietary and bad habits, leukoplakia and eritroplakia are considered, by several authors, as important predictor factors for the oral cancer incidence. It is possible to conclude that the incidence and mortality rates of oral cancer can be reduced by means of health promotion policies its early detection and the development of healthy lifestyle.

Key words: Oral cancer epidemiology. Predictors. Incidence and mortality rates.

Introduction

Cancer is a multifactorial disease brought on by a combination of causal and predisposing genetic factors, and which at a given moment and under favorable conditions may take effect in predisposed people¹. Mortality from malignant neoplasm figures among the principles cause of death worldwide, and it is therefore a highly serious public health matter.

There is a wide variation in the incidence and mortality rates of oral cancer in different regions around the world. The incidence of oral cancer is greater in men in the Lower Rhine area of France, in the south of India, in certain areas of Central and Eastern Europe and in some regions of Latin America².

Oral cancer is the eighth most common tumor in Brazilian's male with 9.985 estimated cases/year, and the ninth among women, 3.895 estimated cases/year, where its main primary site is the first one-third anterior portion of tongue, lower lip, mouth floor and hard palate³.

In Spain, approximately 3% of malignant tumors originate in oral cavity and the majority of them correspond to oral squamous cell carcinoma (OSCC), followed by malignant tumors of salivary glands, lymphoreticular disease, bone tumors, melanomas, sarcomas, malignant odontogenic tumors and oral metastasis of tumors from other primary sites¹.

Ilye et al.⁴ (2001) assert that tongue cancer is the most common oral cancer in India constituting

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about 36.5% of all oral malignancies, attributing its high prevalence due to tobacco chewing, smoke and alcohol use.

Oliveira et al.³ (2006) claim that 10% of malignant tumors have their primary site in oral cavity, where it is the sixth leading cause of human cancer worldwide. Oral cancer might be considered as the most common cancer in head-neck region affecting predominantly male with 75% of diagnosed cases around 60 year-old, to which 90% are oral squamous cell carcinoma.

Oral squamous cell carcinoma is the most frequent tumor of oral cavity, statistically responsible for 90% of oral cancer world data diagnosed every year⁵.

The American National Cancer Institute (NCI), the Center for Disease Control and Prevention (CDC) and the American Cancer Society (ACS) have found increases in the incidence of oral cancer among specific segments of the population, including minorities, although oral cancer incidence and mortality rates in USA has declined. This study showed that although incidence rates of oral cancer have steadily decreased among white males, incidence rates among older black males have increased. Currently in The USA, cancer remains the second leading cause of mortality whereas oral cancer is the eighth cause of cancer death among males⁶.

According to the World Health Organization⁷ (2005) cancer might kill 10.3 million people by the year of 2020, with an increase trend in developing and newly industrialized countries. Thus, the objective of this present paper is to spread out the current knowledge on oral cancer features in order to encourage its early detection, attempting to reduce its incidence and mortality rates all over the world.

Materials and methods

The present review has been engaged to select publications which are able to contribute to this matter by focusing on oral cancer epidemiology, oral cancer survival, incidence and mortality rates, oral cancer predictor factors including ethnology, dietary, lifestyle, HPV virus infection and heritance.

Five electronic databases, WHO, Medline, Lilacs, Scopus and Isiknowledge were used to gather publications on this subject setting the oral cancer keyword and others specific keywords correlated to this study described above. The papers selection was performed toward this thinking queue proposed, excluding publications which are not in accordance with this purpose.

Results

This critical review has found several subject papers of oral cancer, including epidemiological data, dietary and ethnology factors, incidence and

mortality rates, survival rates and stage, virus infection and cancer, and at last heritance. The content of these publications was properly analyzed and then chosen after filling the criteria adopted in this review, as described previously. The results were gathered into two sections: cancer predisposing factors responsible for its incidence and cancer survival factors responsible for its mortality.

Cancer predisposing factors

Oral cancer world epidemiology registers over 300.000 new cases of oral cancer annually. In general cancer begins with white patches, leukoplakia, or red patches, erythroplakia, associated with risk factors such as tobacco or/and alcohol⁸.

The main disorders that may lead to the development of oral cancer, pointed out by WHO experts working group recently defined are: leukoplakia, erythroplakia, palatal lesion of reverse cigar smoking, oral lichen planus, oral submucous fibrosis, discoid lupus erythematosus, hereditary disorders such as dyskeratosis congenital and epidermolysis bullosa⁹.

Tobacco users – smoked, chewing or both – developed most oral lesions with an annual incidence rate ranging from 5.2/1.000 to 30.2/1.000, whereas non-user develop the fewest oral lesions ranging from 0.6/1.000 to 5.8/1.000 per year. Thus, tobacco use is claimed the commonest pre-disposing factor for the development of intraoral white lesion. Furthermore, the white lesion distribution is associated to the type of tobacco use as previously described⁹.

Larond et al.¹⁰ (2008) claim that oral cancer has no single factor but results from a variety of factors including the person's lifestyle, especially regarding tobacco and alcohol consumption. Some others factors may also potentially contribute to it, such as human papilloma virus, since over 90% of oral cancer is HPV-16 positive. Yet, dietary factors like high consumption of vegetables, and particularly fruits seem to reduce the risk of oral cancer in premalignant lesions.

Petti¹¹ (2003) summarized the world prevalence of leukoplakia from 17 countries in a systematic review collecting data from 1986 to 2002. The possible bias, that is still a concern for this study, is the concept of oral leukoplakia, to adopt an international criteria of classification, since it can show a wide variety of clinical appearance. Actually, predictors of malignant transformation in oral leukoplakia have been into the spotlight.

Numerous studies have shown that certain characteristics are more often potentially considered malignant disorders (PMD), in which the OSCC arises, than in those which cancer does not occur. These observations suggest that these features may indicate what lesions have a greater tendency to malignant transformation or not. They are shown in Square 1.

Predictive factors	Potential for malignant disorders
Age and duration	The first five years of oral lesion is the most critical period for the malignance development. The older is the patient the worse is the prognosis.
Site	Lateral border of tongue and floor of mouth are the most critical sites for malignant transformation. Tongue carcinoma is more aggressive than any other oral site.
Size	Multiple lesions have four times more chances to become malignant than single anatomical lesion.
Gender and clinical appearance	Several studies point out a propensity of leukoplakias in female to become malignant when compared to male. Lesions containing nodular and red areas have been shown to be a greater risk of malignant transformation than the uniformly ones.

Liu et al.¹² (2008) have also addressed an epidemiological investigation about the oral cancer incidence by gender, race and anatomical site, with data collected from California Cancer Registry (CCR), the USA. The results have shown Hispanic and Asians ethnology to have the lowest cancer incidence rates when compared to others in the state of California. These findings claim the impact of varied cultural and behavioral factors in the development of oral cancer in different ethnic populations.

Iype et al.⁴ (2001), when analyzing the incidence of tongue cancer in young Indians, found that 12.2% of the patients had family history of cancer, whereas only 2.6% had history of oral cancer.

The occupational risk and the oropharyngeal cancer were studied by Andreotti et al.¹³ (2006) in an epidemiologic case-control study performed in Brazil. Only male gender was allocated to this study with 266 cases and 362 controls. The results were shown by odds ratio (OR) calculated by the unconditional logistic regression controlled for age, tobacco and alcohol consumption. Employees working in vehicle maintenance shops showed OR. 2.45, and those working with vehicle repair showed OR. 2.10. There was a tendency on increasing this rates among workers exposed to 10 or more years of occupation.

Survival related factors

Several prognostic factors may influence the survival of oral and pharyngeal carcinoma, including ethnic group, stage of diagnostic, gender, age, anatomic site, morphologic type and the sort of therapy adopted for treatment¹⁴.

Ide et al.¹⁵ (2008) performed a nation-wide large-scale cohort study in Japan, including 34.136 men and 43.711 women, aging from 40 to 79 years old, utilizing the cox proportional hazard model to esti-

mate the relative risk (RR) of death from oral and pharyngeal cancer for smoking and drinking adjusted by age, gender and dietary. Men smokers were found to have a 2.6 (RR) death when compared to non-smokers, and for women the relative risk was 8.2. The risk for current drinkers was not significant when compared to non-drinkers. However, simultaneous exposure to both smoking and drinking was associated to a high elevate risk of oral and pharyngeal cancer (RR = 3.3).

By reviewing the literature it has been observed how many different factors have been evaluated as prognostic markers in oral cancer. A study performed by Leite and Koifman¹⁶ (1998) observed parameters like high-lighting clinical stage, gender, early diagnosis, treatment modality and the time elapsed between initial symptoms and treatment as prior prognostic factors on oral cancer survival. Notwithstanding, Beltrani et al.¹⁷ (1992) considered tumor site, size, microscopic gradation and DNA content as prognostic factors on cancer survival. González Moles et al.¹⁸ (1998) evaluated clinical and histological parameters in relation to survival, pointing out as the most influential factors the primary site, presence of lymph node metastasis, clinical stage and degree of cellular differentiation and pleomorphism.

Capilla et al.¹ (2007) accomplished a study in Spain and concluded that the risk of death from oral cancer is 1.7 higher in tobacco users when compared to non-users. Concerning the location of tumor, squamous cell carcinoma in gingiva (1.72 times) and trigone (2.14 times) represented the greatest risk of mortality when compared to other sites. Chen et al.¹⁹ (2007) have also found poor survival rates in groups of different socioeconomic status as previously described by Kingsley. Moreover, this study has also concluded that ethnology play an important role in molecular modification associated with oral carcinoma mutations such as p53 or RAS. This

genetic polymorphism reflects the variation of oral carcinoma survival in ethnicity. In addition, diet seems to be another prior factor which influences steadily ethnic survival rates due to lifestyle habits and customs.

Discussion

Oral cancer is undoubtedly considered by several authors as an important global health disease totalizing over 275.000 cases and 128.000 deaths per year¹². Due to its multifactorial aspect, malignant oral lesions comprised of exogenous factors like tobacco, alcohol and toxin exposure as well as endogenous factors like genetic heritance, malnutrition, hormones, virus exposure, glutathione S-transferase (GTS), N-acetyl transferase (NTS), molecular modifications such as p53 or RAS mutation, among others^{18,19}.

A cohort study achieved by Rusthoven et al.²⁰ (2008) involving 6.791 patients, in a sample of stage I and II OSCC of the oral cavity taking the long-rank test to compare the overall survival between

tongue versus other site in the mouth, had 1.26 CHR (cox proportional hazard ratio). These findings are in agreement with Larond et al.¹⁰ (2008) showing the tongue and the floor of mouth cancer as the lower 5 year survival rate. Nevertheless, Capilla et al.¹ (2007) claims that the mandibular trigone is the worst site for survival prognosis when compared to lip, tongue and floor of mouth.

According to González Moles et al.¹⁸ (1998) in the Mary Curie Oncology Hospital files, Cuba, the most common symptom described by patients which motivate them to search for the health service, is ache, then representing 44.30% of the total clinical symptoms. At this phase, the majority of lesions, 53.16%, were at stage III. These findings concerning the stage of disease at the diagnostic are in agreement with Rusthoven et al.²⁰ (2008) and Larond et al.¹⁰ (2008). All of them show the need for early intervention on the OSCC, since most of the patients had oral cancer diagnostic in the advanced stage III and IV. This is a matter of concern regarding oral cancer mortality rates, since the earlier the intervention is the better the prognosis for 5-year survival rate, as it is shown in Figure 1.

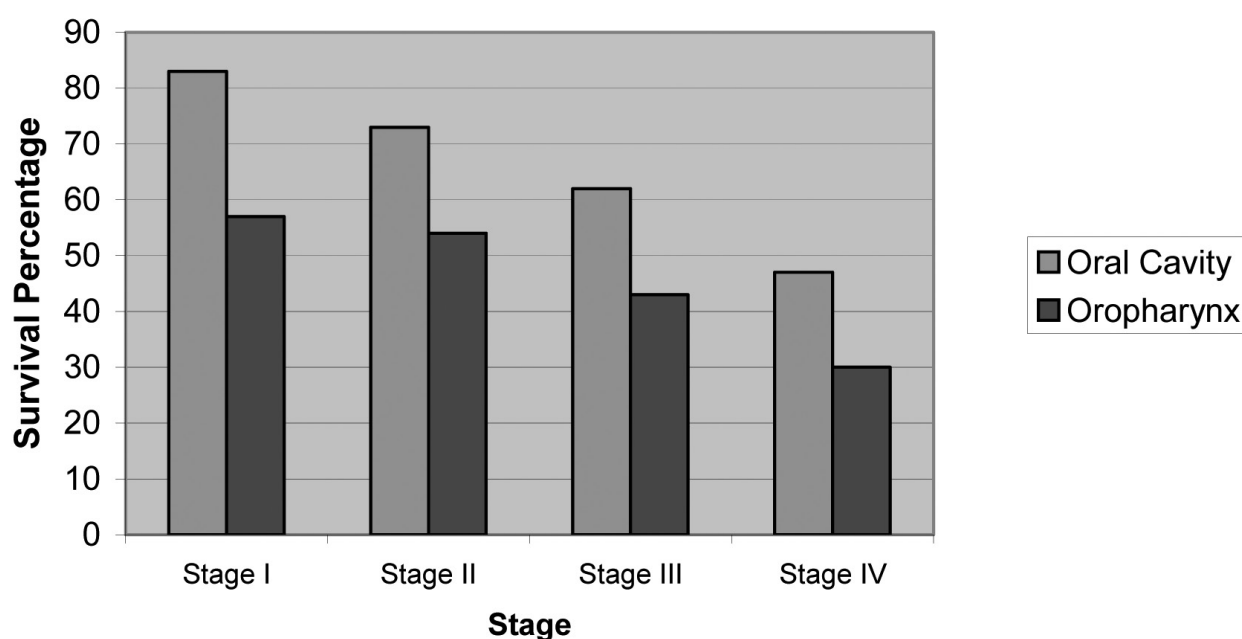


Figure 1 - Relative 5-year survival rate by stage. The following survival statistics come from the AJCC Cancer Staging Manual²¹

The American Cancer Society²² (2007) recommends that primary care doctors and dentists examine the mouth and throat as part of a routine cancer-related checkup. They have the opportunity to see abnormal tissue changes and to detect cancer early at curable stage. Doctors and dentists should also encourage their patients, especially those exposed to higher risk, to take an active role in the early detection of these cancers by doing monthly self-examination. Likewise, in 2007, in the cancer statistics from Canada, 3200 people were diagnosed

with oral cancer where 2700 (84%) could be potentially detected by health providers, thus reducing the statistic of 1100 deaths¹⁰.

Oral cancer also affects patient quality of life factors such as social, psychological, physical and spiritual. The concerns that patients and survivors most often express are fear of recurrence; chronic and acute pain, sexual problems, changes in physical appearance, depression, insomnia, social stigma, self-confidence loss, and the burden over finances and beloved ones.

In agreement with Sapkota et al.²³ (2008), dietary factors are considered to play an important role in the development of cancer, as well as the tobacco and alcohol intake. Few cohort studies have attributed the incidence cancer decrease to the consumption of yellow/orange fruits and vegetables, but pumpkin, tomato, cabbage and carrots consumption, especially, has been inversely associated with oral pharyngeal cancer. Some prospective studies have also pointed to red meat consumption associated with cancer incidence, especially processed ones. No significant difference was established between red and white meat.

Chen et al.¹⁹ (2007) also agree that ethnologic habit food related to a study developed in Taiwan,

showed a diet based in fish, rice and fresh vegetables and fruits, particularly carotene and vitamin C and E have a protective effect against oral carcinoma. On the other hand, it has been said that ethnology has contributed to cancer development, not due to genetic factors, but due to lifestyle and sociocultural habits such as: chewing betel-quid, areca nut and paan in Taiwan, Pakistan, India and other cultures as well as alcohol wine consumption in France are meant the main factors to lead higher incidence in tongue oral cancer when compared to lip cancer incidence as demonstrated in Figure 2, when the same ethnology is compared in different countries taking into account different lifestyles.

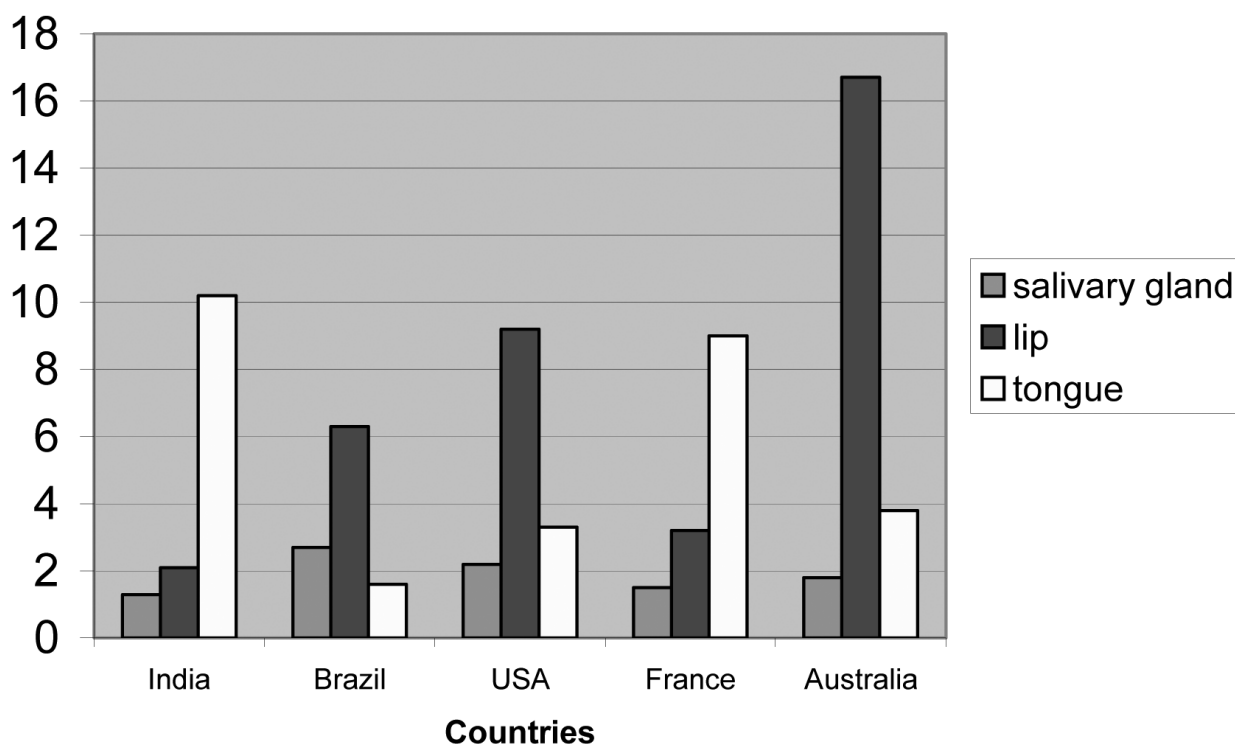


Figure 2 - WHO - Oral cancer standardized incidence rate (1/100.000) per primary site from 1988 to 1993. Oral cancer incidence rates in four countries. WHO Oral Health Country / Area Profile programme²⁴

By the year of 2020, WHO estimative of cancer incidence rates will be nearly 16 million people, as shown below in Figure 3. In order to save these lives and protect them from any sort of permanent impairments, health provider and public health services must turn their eyes toward to continue pro-

fessional health education in order to improve early diagnostic and set up programs to promote quality of life by establishing healthy diet and banishing harmful habits to reduce cancer incidence and mortality rates and prevent suffering as well.

The estimate number of cancer new cases per region for 2020

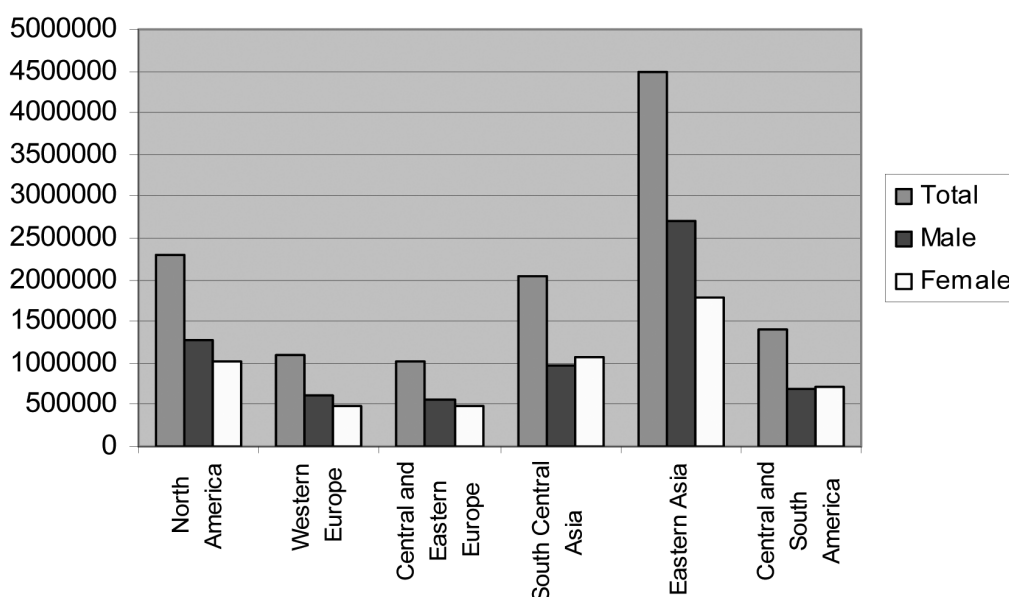


Figure 3 - Due to a steadily increase of elderly people and maintenance of unhealthy lifestyle, the estimative of cancer new cases in 2020 will be nearly 16 million people as shown below the cancer global feature incidence per region by WHO⁷ (2005)

Final considerations

Based on the data presented in this paper, it is possible to conclude that health education and health promotion must be encouraged by public health policies worldwide in order to reduce the incidence of 16 million cases by the year of 2020 and therefore, cancer mortality rates. Health providers should also encourage self-examination in risk patients to perform early intervention, in early stages.

Resumo

Este trabalho busca analisar o impacto do câncer bucal sobre a saúde pública mundial, atentando para seus principais fatores preditores, de modo que a intervenção precoce reduza sua taxa de incidência e óbito. Esta revisão crítica leva em consideração várias publicações cujo tema principal é a epidemiologia do câncer bucal, coletando dados de âmbito internacional que descrevem as taxas de incidência e mortalidade mundiais, bem como seus principais preditores. Anualmente, mais de trezentos mil casos de câncer bucal são diagnosticados em todo mundo, sendo a maior parte deles em estágios avançados (III e IV). Tais dados fazem do câncer bucal um sério problema de saúde pública, responsável por 3 a 10% da taxa de mortalidade mundial. Etnia, fatores socioeconômicos, estilos de vida, tais como dieta, hábitos nocivos e a presença de leucoplasia ou eritroplasia, são considerados por alguns autores importantes preditores na incidência do câncer bucal. Com base neste estudo é possível concluir que as taxas de incidência e mortalidade do câncer bucal no mundo

podem ser reduzidas com a implantação de políticas públicas de promoção e educação em saúde, por meio do desenvolvimento de hábitos saudáveis, diagnóstico e tratamento precoce.

Palavras-chave: Epidemiologia do câncer bucal. Preditores. Taxa de incidência e mortalidade.

Referências

1. Capilla MV, Olid MNR, Gaya MVO, Botella CR, Ruiz VB. Factors related to survival from oral cancer in an Andalusian population sample. *Med Oral Pathol Oral Cir Bucal* 2007; 12(7):518-23.
2. Moore SR, Johnson NW, Pierce AM, Wilson DF. The epidemiology of mouth cancer: a review of global incidence. *Oral Dis* 2000; 6(2):65-74.
3. Oliveira LR, Silva AR, Zucoloto S. Perfil da incidência e da sobrevida de pacientes com carcinoma epidermóide oral em uma população brasileira. *J Bras Patol Médica e Laboratorial* 2006; 42(5):385-92.
4. Iype EM, Pandey M, Mathew A, Thomas G, Sebastian P, Nair MK. Squamous cell carcinoma of the tongue among young Indian adults. *Neoplasia* 2001; 3(4):273-7.
5. González AP, López MA, Martínez LV. Comportamiento clínico y epidemiológico del cáncer de cavidad oral. Hospital Oncológico Provincial Docente María Curie. Instituto Superior de Ciencias Médicas Dr. Carlos Juan Finlay; 2005.
6. Kingsley K, O'Malley S, Ditmyer M, Chino M. Analysis of oral cancer epidemiology in the US reveals state-specific trends: implication for oral cancer prevention. *BCM Public Health* 2008; 8:87.

7. World Health Organization. Global Action Against Cancer (2005). WHO library cataloguing in publication data. Available at: www.who.org
8. Sudbo J. Novel Management of Oral Cancer: A Paradigm of Predictive Oncology. *Clin Med Res* 2004; 2(4):233-42.
9. Napier SS, Speight PM. Natural history of potentially malignant oral lesions and conditions: an overview of the literature. *J Oral Pathol Med* 2008; 37:1-10.
10. Larond DM, Hislop TG, Elwood JM, Rosin MP. Oral Cancer: Just the Facts. *Clin pract* 2008; 74(3):269-72.
11. Petti S. Pooled estimate of world leukoplakia prevalence: a systematic review. *Oral Oncol* 2003; 39:770-80.
12. Liu L, Kumar SKS, Sedghizadeh PP, Jayakar AN, Shuler CF. Oral squamous cell carcinoma incidence by subsite among diverse racial and ethnic populations in California. *Oral Surg Oral Med Oral Pathol Radiol & Endon* 2008; 105:470-80.
13. Andreotti M, Rodrigues AN, Cardoso LMN, Figueiredo RAO, Eluf-Neto J, Wunsch-Filho V. Occupational status and cancer of the oral cavity and oropharynx. *Cad Saúde Pública* 2006; 22(3):543-52.
14. Chen PH, Ko YC, Yang YH, Lin YC, Shieh TY, Chen CH, et al. Important prognostic factor of long-term oropharyngeal carcinoma survivor in Taiwan. *Oral Oncol* 2004; 40(8):847-55.
15. Ide R, Mizoue T, Fujino Y, Hoshiyama Y, Sakata K, Tamakoshi A, et al. Cigarette smoking, alcohol drinking, and oral and pharyngeal cancer mortality in Japan. *Oral Diseases* 2008; 14:314-9.
16. Leite IC, Koifman S. Survival analysis in a sample of oral cancer patients at a reference hospital in Rio de Janeiro, Brasil. *Oral Oncol* 1998; 34(5):347-52.
17. Beltrani CA, Desinan L, Rubini C. Prognostic factor in squamous cell carcinoma of oral cavity. A retrospective study of 80 cases. *Pathol Res Pract* 1992; 188(4-5):510-6.
18. González Moles M, Rodríguez Archilla A, Caballero R, Avila I, García Anillo M, Bravo I. Estudio de los parámetros clínicos e histopatológicos del carcinoma epidermoide del cavidad oral. Implicaciones pronósticas. *Avances Odontoestomatol* 1998; 14:589-610.
19. Chen PH, Shieh TY, Ho PS, Tsai CC, Yang YH, Lin YC, et al. Prognostic factor associated with the survival of oral and pharyngeal carcinoma in Taiwan. *BMC Cancer* 2007; 7:101.
20. Rusthoven K, Ballonoff A, Raben D, Chen C. Poor prognosis in patient with stage I and II oral tongue squamous cell carcinoma. *Cancer* 2008; 112:345-51.
21. American Joint Committee on Cancer. Cancer Staging Manual. Available at http://www.who.int/oral_health/databases/malmo/en/index.html
22. American Cancer Society 2007: Oral Cancer brochure. Available at www.cancer.org
23. Sapkota A, Hsu CC, Zaridze D, Shangina O, Szeszenia-Dabrowska N, Mates D, et al. Dietary risk factor for squamous cell carcinoma of the upper aerodigestive tract in central and eastern Europe. *Cancer Causes Control* 2008; 19(10):1161-70.
24. WHO Oral Health Country / Area profile programme. <http://www.whocollab.od.mah.se/expl/oraldis.html>, Acesso em: 05/05/2009.

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Recebido: 29.05.2009 Aceito: 02.09.2009