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REVIEW

Epidemiological characterization of oral cancer.

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Abstract: Oral cancer is a disease of high impact globally. It ranks as the sixth more frequent one among all types of cancer. In spite of being a widely known pathology and easy access to the diagnosis, the lack of epidemiological data reported in the last 10 years in Chile called attention to. At the global level, the World Health Organization (WHO) has developed a project called "GLOBOCAN" in order to collect epidemiological data of the global cancer, between its data, highlights the high incidence and high rate of mortality in the male sex, parameter that shows tendency to replicate in both America and Chile. In consequence to these data, a narrative review of the literature concerning the epidemiological profile of the different forms of oral cancer in the past 15 years was done. The diagnosis of oral cancer crosses transversely the Dental Science, forcing us to establish triads of work between oral and maxillofacial surgeons, pathologists and dentists of the various specialties, so as to allow a timely research, appropriate biopsies and histopathological studies finishes with the purpose of, on the one hand, obtain timely and accurate diagnostics, in addition, maintaining the epidemiological indicators.

Keywords: *Head and neck neoplasms, oral cavity, neoplasms by histologic type, cancer epidemiology, public health.*

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INTRODUCTION.

Cancer is one of the leading causes of death in the world. In 2012, it is estimated that 36.2 million people were living with cancer and 8.2 million of them died from this cause[1].

The World Health Organization (WHO) is carrying out a project named GLOBOCAN, with the goal of establishing data on incidence, mortality and prevalence of almost all types of cancer, in people over 15 years in 184 countries of the world. The estimation methods and measurement quality are different and specific in each country, making difficult to establish a global quality score. Nevertheless, there is a qualification system that describes independently the availability of incidence and mortality data which has allowed the creation of the published data in GLOBOCAN[2].

Among all types of cancer, the oral cavity cancer is located in the 6th place in the world[3] and it comprises a heterogeneous group of tumors which vary in their origin tissue, histopathology, anatomical sites where they are developed and clinical presentations[4]. According to the origin of the tissue and histopathology, there are several forms of malignant neoplasms (Table I and II); each chart with certain prevalence, incidents, and survival prognosis. Regarding the involved parts: the lips, mouth , gums, alveolar ridge, two-thirds in front of the tongue, floor of mouth, hard palate and retromolar trigone were observe to be compromised.

In regard to the clinical presentations, it is usual to observe the presence of ulcers which are not repaired, white and red spots, lumps associated or not with pain, tooth mobility, difficulty to move the tongue, chew and swallow. However, the clinical characteristics on theirselves are not sufficient to confirm or establish an accurate diagnosis , so it is always necessary to take also an histopathologic diagnosis[5].

The objective of this review is to typify epidemiologically the several forms of presentation of oral cancer as of the reported data in recent literature and databases of national and international health agencies.

EPIDEMIOLOGY OF ORAL CANCER AT A GLOBAL LEVEL

In 2012, the results of GLOBOCAN regarding oral cancer pointed out an incidence of 300,373 people worldwide, with an estimated rate of 5.5 in men and 2.5 in women each 100,000 people. The estimated prevalence was 702,373 during the last 5 years, with a rate of 1.8 in men and 1.2 in women each 100,000 people. On the other hand, the mortality for malignant neoplasia of the oral cavity was 145,326 with an estimated rate of 2.7 in men and 1.2 in women[2].

A high level of incidence and mortality from oral cancer were observed in South Asian countries such as Sri Lanka and India; east Asian countries such as China and Taiwan; part of France and eastern Europe as Hungary, Slovakia and Slovenia; as well as in South American countries such as Brazil and Uruguay; and in Central America as Puerto Rico and Cuba, among others[6].

In the Americas, the incidence of oral cancer is higher than worldwide incidence, being greater in men: 5.9 per 100,000 inhabitants. In women incidence does not appear among the 10 most common types of cancer.

EPIDEMIOLOGY OF ORAL CANCER IN CHILE

In Chile, the oral and pharyngeal cancer is located in 17th place with an incidence of 3.2 per 100,000 inhabitants[7].

The Ministry of Health obtains cancer data from a program called "Population Records of Cancer"[8] (Registros Poblacionales de Cáncer), where the information of all new cases of cancer, which occured in a population and in a defined geographic area, are validated. The objective is to establish the incidence and risk of the population to develop this pathology, but unfortunately this record is not in force at the national level, it is only implemented in the regions of Antofagasta (1998), Los Rios (1998), Arica and Parinacota (2009), the Provinces of Biobio (2004) and Concepción (2006), emphasizing the National Record of Child Cancer (2006). These records began in Chile thanks to the initiative of clinical specialists of the Health Services. The first to start this task were professionals of Antofagasta and Los Rios (former Valdivia Province), to which were added in 2000, the team of the Department of Epidemiology, Ministry of Health, which took over the responsibility to coordinate the National Population Records of Cancer[8].

The Department of Epidemiology in the division of Rectory and Sanitary Regulation of the Ministry of Health (Rectoría y Regulación Sanitaria del Ministerio de Salud), together with a group of national experts, developed a manual of technical regulations for population-based records of cancer, with the purpose to homogenize and standardize the functioning of the records which are currently operating and those which will be developed in the future in the country[9].

The first report of population based cancer record in Chile is about the five-year period 2003-2007, published in 2012 by the Ministry of Health. The methodology used for the analysis of results of the records are based on the existing national regulations based on international criteria[8].

The results of population-based records of cancer in the Regions of Antofagasta and Los Rios; and in the province of Bio Bio, between the years 2003-2007 (Table 1)[8] are shown below.

CHARACTERISATION OF ORAL CANCER: TISSUE OF ORIGIN, LOCATIONS AND EPIDEMIOLOGICAL INDICATORS

Table 1. Incidence of Cancer in the oral cavity and lips, according gender. (Rate per 100.000)

Region	Incidence in men	Incidence in women
Antofagasta Region	N° 43	N° 30
	% 1.4	% 1.1
	GIR 3.1	GIR 2.5
	AIR 4.1	AIR 2.8
Los Rios Region	N° 30	N° 11
	% 1.3	% 0,5
	GIR 3.2	GIR 1.2
	AIR 3.4	AIR 1.1
Bio Bio Region	N° 13	N° 13
	% 0,6	% 0,7
	GIR 1.4	GIR 1.4
	AIR 1.4	AIR 1.3

GIR: Gross Incidence Rate. AIR: Adjusted Incidence Rate.

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Oral cancer can affect different areas of the oral cavity, generally they can be grouped if they affect soft or hard tissues; where soft tissues are the most affected, emphasizing the commitment of the lateral border of the tongue. In Tables II and III a general classification of the different types of oral cancer more frequent, according to tissues of origin are observed[10].

The epidemiological profile of the most frequent histopathological forms of cancer, affecting the oral cavity, is exposed below[10, 11].

Malignant neoplasms of soft tissue:

In the oral cavity, the most frequent group of tumors are of epithelial origin, specially the squamous cell carcinoma (SCC), which are observed in 9 out of 10 neoplasias[11]. The prevalence of SCC is about 95% of all types of oral cancer and during the past decade its incidence increased by 50%. The probability of occurrence increases even more after the years, and the highest incidence is observed after 40 years old[12]. Ryan reported that there is a positive association between the age of diagnosis of oral SCC and survival. In fact, studies show that after 65 years of age the prognosis aggravates and its survival varies among 42- 46 months once detected, declining in 10 months of life, when it is detected over the 75 years old. The reason is based on the effects of aging itself, which make the older patients more susceptible to the pathogenesis of SCC[13]. In a comprehensive manner, the survival rate has not changed with regard to the last decade, being this 53-56% at 5 years.

Its pathogenesis is multifactorial, associations such as tobacco, alcohol, viral infections (HPV), bacterial and fungal infections, radiation, genetics, immunosuppression, expression of oncogenes and also deactivation of tumor and malnutriton supresion genes have been described[14]. The presence of SCC in different geographic regions is associated to the habits in those regions. For example, in North America, Latin America and Europe the high consumption of tobacco and its association is approximately 33% of the cases. If the amount of alcohol consumption is added to this interaction, the association is multiplied, affecting even three quarters of them[4]. Additional to this it is the fact that 11% - 67% of the oral SCC may be developed from potentially malignant lesions[15].

Another malignant neoplasia of epithelial origin is the Verrucous Carcinoma, which represents less than 5% of all neoplasms in this zona[11], but it covers 75% of all verrucous carcinomas[16], its incidence rate is estimated at 1 every 1,000,000 people each year[9]. It is characterized by slow growth, high tendency to local invasion and low capacity to disseminate from afar11. Its etiology is associated to the consumption of tobacco, alcohol, betel nut and Human Papilloma Virus. It is usually developed from the fourth decade but, it is more common between the sixth and seventh decade. The oral mucosa and gingiva are the most affected areas. Its favorable prognosis is reflected by a high survival rate of 93-94% at 5 years. After the surgical treatment, the recurrence rate varies between 0 to 67% at 5 years[5].

Among the malignant neoplasms of glandular origin, mucoepidermoid carcinoma and adenoid cystic are the most frequent[17]. At the major salivary glands level, the parotid glands are the most affected. In spite of the fact that this group is relatively unusual, they are outlined due to its heterogeneity with numerous histopathological varieties. They represent between 3% to 6% of all malignant neoplasms of head and neck, covering a 21.7% - 53.5% of all neoplasms in salivary glands, and its incidence rate is between 0.2-9.7% per 100,000 personas18. The survival rate is 65% at 5 years and it is greater in women than in men, 72% and 58% respectively[2°]. At any age it can be developed, but it is most commonly diagnosed between the fourth and seventh decade, presenting a slight predilection in men[17,18]. Its cause is uncertain, though some reports as the Lawal report associates the cause to factors such as ultraviolet radiation dose, tobacco and alcohol consumption and the presence of virus Epstein Barr[17].

Among the neoplasms of mesenchymal origin, the ones that affects the soft tissue comprise a heterogeneous group of tumors which are originated from different mesenchymal cells[18]. They are relatively rare and they present a variation in their clinical behavior[19]. In the head and neck

Table 2. Clasification of Oral Cancer in soft tissue.

NEOPLASM	MALIGNAN				
			GLOBAL PREVALENCE	AGE OF INCIDENCE	SURVIVAL RATE AT AGE OF 5
Epitelial Origin	Epithelial Origin Of Lining	Spinocellular Carcinoma	95% ≈	>40 years	53-56%
		Warty Carcinoma	<5%	60-70 years	93-94%
	Glandular	Mucoepidermoid Carcinoma			
		Adenoid Cystic Carcinoma	3-6% ≈	40-70 years	65%
		Unspecified Adenoid Carcinoma			
Mesenchymal Origin	Fibroblastic	Fibrosarcoma			
	Fibrohistiocitary	Malignan	<2% ≈	>40 years	55-68%
		Fibrohistiocitoma			
	Adipose Cells	Liposarcom			
	Muscular:				
	Smooth Musle	Leiomyosarcoma			
		Angioleiomiosarcoma			
	Skeletal Musle	Rhabdomyosarcoma			
		Alveolar			
		Rhabdomyosarcoma			
	Vascular:				
	Blood Endothelial Cells	Angiosarcoma			
		Kaposi's Sarcoma			
	Lymph Capillary Endothelial Cells	Lymphangiosarcoma			
	Perycites	Malignant			
		Hemangiopericytoma			
	Neuropathic Nervous	Neurofibrosarcoma			
		Schwanoma malignan			
Melanocyte Cells origin		Melanoma	2% ≈	40-70 years	4.5-29 %
Linfoid origin		Hodgkin Linfoid	5% ≈		
		Non Hodgkin Linfoid			
Metastasis			1-1.5 % ≈	40-70 años	10%

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Table 3. Clasification of Oral Cancer in hard tissue.

MALIGNANT NEOPLASM					
			GLOBAL PREVALECENCE	INCIDENCE AGE	SURVIVAL AT THE AGE OF 5
Mesenchymal Origin	Osteogenic	Osteosarcoma	1% ≈	15–40 years	27-84%
	Chondrogenic	Chondrosarcoma			
		Fibrosarcoma			
		Malignant Fibrous			
		Liposarcoma			
		Leiomiosarcoma			
		Angiosarcoma			
Of the medulla	Linfoyds	Lynphoma			
	Plasmocytoids	Mieloma	3.5% ≈	67-71 years	55%
		Ewing Sarcoma			
Odontogenic origin	Epithelial Origin	Ameloblastic Carcinoma	1.17% ≈	30 years ≈	-
		Odontogenic Carcinoma			
	Mesenchimal Origin	Ameoblastic Fibrosarcoma			
Intraosseous Carcinoma	Invasion Origin		12-56% ≈	-	25.80%
	Glandular Origin				
	Odontogenic				
	Metaplasia Origin				
	Sinus				
Metastasis			2-3% ≈	>40 years	10%

region they have a prevalence between 4% to 10% of all soft tissue sarcomas and less than 2% of all malignant neoplasms of the oral cavity[20]. The estimated survival rate for the group is between 55.5% - 68% at 5 years[20,21] and the recurrence rate is between 10% to 30%[20]. The malignant fibrous histiocytoma, fibrosarcoma, and leimoiosarcoma liposarcoma are the most common among them[20,21]. The malignant fibrous histiocytoma corresponds to the soft tissue sarcoma and it is more common among adults. It affects, in order of frequency, to the extremities, trunk, head and neck[22]. In the latter area it represents 3% to 7% of all the neoplasms[23]. It has a bigger impact over the 40 years, with a peak in the seventh decade and a tendency to be developed by men. It behaves as an aggressive tumor, of poor prognosis with a high probability to develop a metastasis via bloodstream and linfatic[23]. The survival rate is 48% at 5 years[22] and the majority of patients die within two years of its diagnosis[23]. The recurrence rate after surgical treatment varies between 23% and 86%[22].

Melanomas are rare neoplasms, they are very aggressive and, in the oral cavity, they have an impredictable behavior[24]. Its incidence is unknown but it is estimated that of all melanomas, 2% are presented in the oral cavity[25] and this group represent a 1.3 % of all neoplasms. They are developed preferably between the fourth and seventh decade, with a peak in the fifth[24] and on average will be developed 2 decades later that the skin melanomas[26]. It affects 3.5 times more women than men, and also people of fair complexion. Mund points out that it is more frequent in India and Japon[24]. Among the Japanese, the oral melanoma represents a 11% to 14% of all cases of melanomas[25]. Its etiology is unknown, but the consumption of tobacco

and alcohol are considered as high risk factors of chronic irritation but their association is not yet demonstrated. It is generally located in the gingival mucosa of the upper jaw and in the palatal mucosa. From fifty to seventy percent of the times emerges from normal mucosa and 30% -50% of previous pigmentations[24]. The clinical manifestations vary, but the most common presentation is the black or dark blue asymptomatic and sometimes ulcerated spot. They are the group that have a worse prognosis and 85% of the times are diagnosed in stage of invasion[25]. The rate of survival between a 4.5% to 29% in 5 years, with a prognosis of 18.5 months after diagnosis due to the large capacity to produce metastasis[24].

In the malignant lymphoproliferative neoplasms, lymphomas are the more heterogeneous group, representing approximately 5% of the tumors of head and neck. They are classically divided into two groups: Hodgkin lymphoma and non-Hodgkin lymphoma; within these, WHO describes more than 50 different histopathological subtypes. In the oral cavity, the most frequent group is non-Hodgkin type, which is usually located at the base of the tongue[27]. They present a less predictable evolution and a higher tendency to spread than the extranodal lymphoma type. Its etiology is unknown, but they are associated to genetic alterations, Epstein-Barr virus and autoimmune diseases such as the Syndrome of Sjögren[28].

A smaller but not less important group, where oral metastasis are located which correspond to the 1 to 1.5% of all the oral malignant neoplasms. They are more common among the 40-70 years and have a 2:1 ratio between men and women to be found respectively[29]. The importance of diagnosing metastasis at the oral level is based on that may be the first evidence of spread from a primary tumor (26.8%)[30], and at the level of soft tissue they usually came from the lung (31%). The most affected site is the gum (54%), followed by the tongue. Its presentation is unspecified, because in the initial gingival metastases are exophytic lesions, highly vascularised and hemorrhagic, and they are often confused with oral lesions such as granuloma pyogenic. In other locations of soft tissue and particularly in the tongue, manifested as submucosal mass that can be ulcerated[29,30]. The prognosis is poor and most patients die within one year after their diagnosis. The survival rate estimated at 4 years is 10%[31].

Malignant neoplasms of hard tissue:

Malignant tumors of the maxillae are scarce, the most frequent is osteosarcoma, which represents about 1% of all tumors of the oral cavity[32]. Its incidence is 1/10 million people per year[33], their survival rate at 5 years varies between 27% and 84%[34]. There is controversial information regarding the predilection for sex, on the one hand it is considered that there is not[31] and on the other hand that men are more affected[35]. In spite of the fact that in the long bones are diagnosed in the second decade, in the jaw present a wider range which goes between the 15 and 40 years. A specific trigger factor is unknown, although it has been associated with previous history of radiation therapy and in others to genetic susceptibility caused by a mutation in the chromosome 13q14. In the oral cavity the most affected area is the body of the jaw, followed by the angle, symphysis and ramus. It is possible to observe clinically an increase in the volume of hard consistency, or may not be associated with pain, paresthesia, mobility, displacement or tooth loss. The survival rate estimated at 5 years is 50%[36].

At the level of the head and neck, lymphomas are the second group of neoplasms more prevalents[37]. The most frequent type at the extranodal level is the Non-Hodgkin type and it shows a prevalence between 24%-48 %. At the level of the jaws, the prevalence is 3.5% in relation to malignant neoplasms of hard tissue in the oral cavity . The rate of survival in the jaw to the 5 years is approximately 55%, varying at the level of the maxillary sinus in a 30% at 5 years[38]. The average age is between 67-71 years without predilection of gender[37]. As well as lymphomas of soft tissue, its pathogenesis is unknown and it is associated with the same factors[38].

The group of malignant odontogenic tumors are mentioned due to be a revision linked to the oral cavity, because in reality they represent a group of extremely rare appearance

at a global level. Its prevalence is not well established, but in Latin America it corresponds to 1.17%. The most frequent forms are of epithelial origin (between 76% to 95%), affecting more males and young adults (third decade). They are usually located in the posterior area of the lower jaw, where they invade and destroy adjacent structures, even have the capacity to produce metastasis. In addition, cause tooth mobility, pain and paresthesia among others[39].

Another rare group of this review is the intraosseous carcinoma, they are formed by different types of histopathological odontogenic and non-odontogenic origin. The most common type is the SCC by invasion, which usually comes from the gingival and alveolar mucosae[40], that invades the bone by direct extension or by perineural invasion. The incidence of invasion varies between 12 to 56%[41]. They show a high rate of recurrence (61.9%) and a low survival rate at 5 years (25.8%)[42].

On the other hand, oral metastasis are more frequent in bone tissue than in soft tissue, in a ratio of 2:1. The most affected are the patients older than 40 years and the gender distribution is equal in men and women[29]. The most frequent primary tumors that affect the jaw bones in men are lung (22%), and prostate (11%), and in women are breast (41%), followed by the genital organs and adrenal gland (7.7%)[31,43]. The jaw (specifically the area of the molars) is more affected than the maxilla, in 80% to 90% of cases. They are clinically presented with signs and symptoms such as tumors associated to the areas of infection , ulcers, fractures, bleeding, pain, trismus, tooth mobility and parestesia[29].

FINAL COMMENTS

The concern on the oral cancer is increasing, despite of knowing their ethiological factors and clinical presentations, the epidemiological figures have augmented. An evident need to collect the current maximum of epidemiological information more individulizada of oral cancer is been observed. While at a global level there are stage of preceedings and agencies seeking to gather more background and generating epidemiological indicators of oral cancer, in a diligent keen manner, in Chile these efforts do not show the same magnitude.This is why it is necessary to generate national epidemiological records, where various institutions, both in public and private health and also in educational centers collaborate with updated data in front of this pathology.

This study allows to identify those most frequent groups with oral cancer, the main caracteristicias and differences among them; as well as the epidemiological indicators existing so far. At the oral level, the compromise of soft tissues over the hard tissues is underlined, this tendency has been constant in time.

The high prevalence rate, an increase in its incidence and doubtful prognosis of the SCC is alarming, because it is known that within its carcinogenesis exists preventable factors and behaviors, for example, alcohol and tobacco consumption. Because of this, it must be increased the population educational initiatives of selfcare at the oral level, emphasizing on prevention and early diagnosis.

The diagnosis of oral cancer crosses on a transversal way the Dental Science, forcing us to establish work triads between general dentists and the different specialties of oral and maxillofacial surgeons and pathologists, in order to allow a timely research, obtaining adequate sample histopathological studies finished, to obtain timely and accurate diagnoses, and, on the other hand to generate greater awareness of the epidemiological indicators.

Caracterización epidemiológica del cáncer oral. Revisión de la literatura.

Resumen: El cáncer oral es una patología de alto impacto a nivel mundial, ocupando el sexto lugar más frecuente entre todos los tipos de cáncer. A pesar de una patología ampliamente conocida y de fácil acceso al diagnóstico, llama la atención la falta de datos epidemiológicos reportados en los últimos 10 años en Chile. A nivel mundial, la Organización Mundial de Salud (OMS) ha desarrollado un proyecto denominado "GLOBOCAN" con el fin de recolectar datos epidemiológicos mundiales del cáncer, entre sus datos, destaca la gran incidencia y

elevada tasa de mortalidad en el sexo masculino, parámetro que muestra tendencia a replicarse en tanto América como en Chile. En consecuencia a estos datos, se realizó una revisión narrativa de la literatura, referente al perfil epidemiológico de las diferentes formas de cáncer oral en los últimos 15 años. El diagnóstico del cáncer oral cruza de manera transversal a la Odontología, obligándonos a establecer triadas de trabajo entre cirujanos orales y maxilofaciales, patólogos y odontólogos de las diversas especialidades, para permitir así una oportuna pesquisa, biopsias adecuadas y estudios histopatológicos acabados con la finalidad de, por una parte, obtener diagnósticos oportunos y certeros, además, mantener actualizados los indicadores epidemiológicos.

Palabras clave: *Neoplasia cabeza y cuello, cavidad oral, neoplasias por tipo histológico, epidemiología del cáncer, salud pública.*

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