Epidemiology of squamous cell carcinomas among the population attended in the city of Tubarão, Brazil, between 1999 and 2009*

Epidemiologia dos carcinomas espinocelulares na população atendida em Tubarão (SC), entre 1999 e 2009

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Abstract: BACKGROUND - Skin cancer is the most common neoplasm in Brazil, with increasing incidence in recent decades. Data on the incidence of squamous cell carcinoma are scarce in southern Santa Catarina.
OBJECTIVE: To establish epidemiological data on squamous cell carcinoma in Tubarão, State of Santa Catarina.
METHODS: A cross-sectional review was conducted on anatomical pathology reports, positive for squamous cell carcinoma of the skin, found in the local laboratories. A convenience sampling method was used for data collection, since all the pathology reports from the local laboratories between 1999 and 2009 were included. The collected variables included year of diagnosis, age, gender, city of origin, tumor site, histological type and subtype, lesion size, margin involvement and relapse.
RESULTS: In total, 1,437 case reports were identified, most frequently in individuals between 70 and 79 years old. Patient morbidity was 69.5 per 100,000 population for the year 1999, and 136.7 per 100,000 population for the year 2009, which represents a 50 percent increase. The face was the most affected area and the most common histological subtype was the well-differentiated tumor.
CONCLUSION: There were 1,437 reports of squamous cell carcinoma of the skin between 1999 and 2009, with a significant increase in patient morbidity. There was an association between male gender and location on the lip and ear, and between females and the occurrence of squamous cell carcinoma of the skin on the nose, and upper and lower limbs. There was a prevalence of margin involvement after resection in 18% of lesions.
Keywords: Carcinoma, squamous cell; Epidemiology; Morbidity; Neoplasms

Resumo: FUNDAMENTOS: O câncer da pele é a neoplasia mais frequente no Brasil, com incidência crescente nas últimas décadas. Na Região Sul de Santa Catarina os dados sobre a incidência de carcinoma espinocelular são escassos.
OBJETIVO: Estabelecer dados epidemiológicos do carcinoma espinocelular em Tubarão (SC).
MÉTODOS: Foi realizado estudo transversal com revisão dos laudos anatomopatológicos positivos para o carcinoma espinocelular dos laboratórios de Tubarão, SC amostragem por conveniência, e as variáveis coletadas foram: ano do diagnóstico, idade, sexo, cidade de origem, local da lesão, grau de diferenciação, diâmetro da lesão, comprometimento de margem e ocorrência de recidiva.
RESULTADOS: Identificaram-se 1.437 laudos com diagnóstico de carcinoma espinocelular, com maior frequência na faixa etária entre 70 e 79 anos. Foi calculado o coeficiente de morbidade para carcinoma espinocelular de 69,5 em 1999 e 136,7/100.000 habitantes para 2009, acarretando aumento de 50%. A região de face foi a mais acometida e o subtipo histológico mais comum foi o bem diferenciado.
CONCLUSÃO: Ocorreram 1.437 laudos de carcinoma espinocelular entre 1999 e 2009, com aumento significativo da morbidade. Houve associação entre sexo masculino e a localização em lábio e orelha, e entre sexo feminino e ocorrência de carcinoma espinocelular no nariz, membros superiores e inferiores. Houve prevalência de margens comprometidas após ressecção em 18% das lesões.
Palavras-chave: Carcinoma de células escamosas; Epidemiologia; Morbidade; Neoplasias

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INTRODUCTION

Squamous cell carcinoma (SCC) is a malignant epithelial neoplasm derived from the keratinocytes. Sun-exposed skin, such as on the head and neck, followed by the hands, arms and legs are the most affected areas. [1-3]

When detected early, the SCC is highly curable. However, the occurrence of metastases worsens the prognosis. [1,3] Patients with a history of SCC should be screened for the presence of new lesions due to a 30 percent risk of recurrence within five years. [1]

The incidence of skin cancer has been increasing over recent decades in the United States, Europe and Australia. [4] The non-melanoma skin cancer (NMSC), which includes basal cell carcinoma (BCC) and SCC, is the most common incident cancer for both men and women, in most Brazilian regions. [5] Eighty percent of NMSC are BCC and 20 percent are SCC. In the United States, NMSC is the most common neoplasm, with 1.3 million cases estimated to occur in 2001. [1]

In Brazil, 115,010 new cases of non-melanoma skin cancer were estimated to occur in 2010, with an estimated incidence of 86 cases per 100,000 people in Southern Brazil, 58 cases per 100,000 people in the Northeast, 55 per 100,000 people in the Midwest, 54 per 100,000 people in the Southeast, and 27 per 100,000 people in the North. [5,6] Mortality attributed to SCC is estimated at 1,000 to 2,000 deaths per year in the United States, and these deaths often are caused by the occurrence of metastases. [2]

Actinic keratosis (AK) is the primary precursor of SCC, a more felt than seen disease, because it has the same skin color: pink or brown, and which may be distinguished from SCC by the skin thickening and tenderness. [1,7] From a therapeutic standpoint, treating each keratotic lesion can be a preventive measure. In addition to the existing AK, there are other diseases that may develop into invasive SCC, such as warts, Bowen's disease (SCC in situ), and erythroplasia of Queyrat. [1,7-8]

SCC ranks second in the incidence of malignant skin tumors, accounting for approximately 20 percent of its total incidence. [9] In addition to local recurrence, the biological behavior of SCC enables the occurrence of distant metastases. According to Rowe et al., metastasis rates are at 8 percent at five years, while local recurrence is 5 percent; therefore, it has a higher metastatic probability when compared to BCC. [1-3,10] Despite the low mortality rate, this type of tumor has a high morbidity because it causes patient disfigurement, resulting in physical and psychological disability. [2]

Therefore, NMSC is a major public health problem due to its high prevalence, the highest among all cancers, and can be refrained with simple measures such as avoiding excessive sun exposure and using sun protection. [11] In Brazil, despite the high incidence of these tumors, epidemiological data on NMSC, i.e., SCC and BCC combined are currently published. [12] Quality publications with statistical data solely on SCC are scarce, both in Brazil and in other countries. Because of the high morbidity and mortality when discovered late, we intended to increase knowledge about this tumor by providing data from the city of Tubarão and region, so that preventive measures can be taken based on data found in this study. Tubarão is located in the southern coastal region of Santa Catarina, and its population has a predominance of Whites, due to European colonization in the region. According to data from IBGE, Santa Catarina has 86.6 percent of Whites. [13] The city is geographically located at 28º28'00''S latitude and 49º00'25''W longitude, and is a regional health center for 14 surrounding municipalities.

METHODS

We conducted a cross-sectional epidemiological research based on secondary data. This study included a convenience sample of the reports of patients with a pathological diagnosis of SCC from the two existing pathology laboratories in Tubarão, in the period between 1999 and 2009. All reports of patients with positive results for histological types of tumor other than SCC were excluded.

The information from the reports was transferred to a data registration protocol, developed by the authors of this study, with the following variables: year of diagnosis, age, gender, place of origin (residence), site of lesion, histological type and subtype, lesion diameter and ellipse, margin involvement and occurrence of relapse.

The data collected were entered into EpiData 3.1 software (EpiData Denmark), and statistical analysis was performed using SPSS 16.0 (SPSS Inc., Chicago, IL). Descriptive epidemiology was used to present the surveyed population characteristics. Nominal variables were presented as absolute and relative frequency. Numerical variables were presented according to their central tendency measures and dispersion. Chi-square test was used to compare categorical variables, with a confidence interval set at 95%. Morbidity rates for the city of Tubarão were calculated based on the estimated population in the years between 1999 and 2009 by using DATASUS. [14] Only cases from the city of Tubarão were included in this analysis.

This study was approved by the Ethics Committee (CEP-UNISUL) under registration nr. 09.418.4.01.III.

RESULTS

In total, 1,437 reports positive for SCC were identified between 1999 and 2009 in the pathology laboratories surveyed. Of these, 720 (50.1%) occurred in men. The mean age was 67±13.7 years, ranging from 13 to 98 years. Table 1 shows the age group of patients categorized according to the SCC incidence rate.

With regards to the place of origin, 947 (65.9%) were reports of individuals from Tubarão and the remaining were from neighboring towns. Table 2 shows the morbidity coefficient of SCC only for the city of Tubarão, between 1999 and 2009.

Prevalence rates of SCC diagnosed in patients regarding tumor location were: 32.6 percent in the face, 6.0 percent in the trunk, 12.6 percent in the upper limbs, 6.1 percent in the lower limbs and 1.2 percent elsewhere in the body. However, 597 (41.5%) reports did not disclose this information. There was a predominance of SCC on the head, especially on the nose. Table 3 shows the location of the SCC categorized by gender

The most frequent histological type was well-differentiated SCC, with 1,107 (77%) cases, followed by moderately differentiated SCC, with 199 (13.8%) cases, and poorly differentiated, with 46 (3.2%) cases. The SCC in situ was found in 79 (5.5%) cases. There were no cases of undifferentiated SCC.

With respect to surgical margins, 259 (18%) had compromised margins, but only 10 lesions (0.7%) were forwarded to laboratories for analysis; five of them still had compromised margins.

The largest lesion was 13.0 cm in diameter, while the smallest was 0.2 cm, resulting in a mean diameter of 3.6±3.7cm.

Table 1: Distribution of SCC cases by gender and age groups

Age (yrs.)	Total n (%)	Men	Women
0-19	2 (0.1)	-	2
20-29	6 (0.4)	2	4
30-39	35 (2.4)	17	18
40-49	99 (6.9)	57	42
50-59	234 (16.3)	148	86
60-69	351 (24.4)	194	157
70-79	382 (26.6)	155	227
>80	276 (19.2)	114	162
Not informed	52 (3.6)	33	19
Total	**1,437**	**720**	**717**

Source: Pathology Laboratory, São Lucas and DiPrever, Tubarão (SC), 2010.

DISCUSSION

Prevalence studies with large intervals, performed exclusively on SCC are rare in southern Santa Catarina. The most common studies are on NMSC, i.e. on SCC and BCC combined. The resident population of this region is predominantly white, of European descent (skin type I and II, according to Fitzpatrick's Color Atlas & Synopsis of Clinical Dermatology) and has a major risk factor for the development of SCC, demonstrating the importance of epidemiological studies related to skin diseases among this population. [2,15,16]

A total of 1,437 SCC-positive patients were reported by the accredited pathology laboratories in the study period. The estimated morbidity rate allowed us to assess the incidence of skin cancer in the past 10 years in the city of Tubarão. There was a considerable increase in morbidity, which increased from 69.5 per 100,000 people in 1999 to 136.7 per 100,000 people in 2009, resulting in around a 50 percent increase. The same fact can be observed when the morbidity rate by gender is examined. Women had a higher rate of SCC compared to men, though women comprise the majority of the population in that municipality. A study conducted in Blumenau, Santa Catarina, also found a significant increase in morbidity, since there were 31.1 cases per 100,000 population in 1980, and it reached 43.8 cases per 100, 000 population in 1999. This increased incidence was also found in another study in the city of Tubarão, confirming the data of that study. [9,17] The increase can be explained by greater public awareness about skin care, improved access to health services, prevention campaigns undertaken by the government, and increase in ultraviolet rays. Thus, with a larger number of cases diagnosed, the incidence and prevalence increased considerably. The increase in ultraviolet radiation has occurred due to ozone layer depletion, which may explain the increased incidence and prevalence of SCC in the population. Two percent reduction in the ozone layer results in a 6 to 12 percent increase in the prevalence of NMSC. [1,2,5,15,16,18]

Regarding the prevalence difference between men and women, a 2:1 prevalence ratio was estimated, men being more affected than women[15]. However, this study revealed that 50.1 percent of SCC occurred in men and 49.9 percent in women, showing no gender-related differences, which is in accordance with some other studies conducted in this area. [6,17,19]

With regards to age, an increase in cases occurred in the age group of 70 to 79 years (27.6%), which indicates the harmful effect of cumulative exposure to ultraviolet radiation, and is similar to the results from several studies. [6,8,9,17,19,20] Approximately 90 percent of NMSC and 65 percent of melanomas can be attributed to sun exposure, especially to ultraviolet B rays. This

Table 2: Distribution of SCC cases by gender and morbidity rates for the city of Tubarão, between 1999 and 2009

	Mortality rate (MR)*					
	Total		Men		Women	
Year	n	MR	n	MR	n	MR
1999	60	69.5	43	102.4	17	38.3
2000	53	59.9	23	53.5	30	65.9
2001	60	66.2	33	75.0	27	58.0
2002	82	90.7	38	86.5	44	94.6
2003	68	74.5	32	72.1	36	76.7
2004	80	86.7	44	98.2	36	75.9
2005	83	88.0	35	76.4	48	99.0
2006	81	85.0	37	79.9	44	89.7
2007	110	114.1	52	111.3	58	116.8
2008	138	144.0	64	137.9	74	149.7
2009	132	136.7	58	124.1	74	148.6

*Number of SCC reports per 100,000 population.
Source: Pathology Laboratory, São Lucas and DiPrever, Tubarão (SC), 2009.The estimated population of the municipality for each year of the considered period was used to calculate the morbidity rate. Data available at DATASUS14.

assumption is supported by the findings of increasing sun exposure caused by a longer life expectancy and higher number of people working outdoors compared to indoor workers. In addition, there are other factors such as phenotype and personal or family history of skin cancer, arsenic intake, potential causes of immunosuppression, chronic skin ulcers and chronic radiodermatitis. [1,2,7,15,16]

This increased prevalence in older age groups can also be explained by the impaired immunity of elderly people, which would reduce the capacity for DNA regeneration. [1,6,12]

Most injuries occurred in chronically sun-exposed areas, once again proving the importance of using physical (clothing) and chemical barriers (sunscreens) to ultraviolet rays. Squamous cell carcinoma of the head was the most frequently observed tumor (32.1%), which is in accordance with the national and world literature. [9,11,17,19-21]

Table 3: SCCs of the skin location categorized by gender

Location	Male	Female	PR*	P value
Face	271	197	1.03	0.54
Nose	19	33	0.63	0.0023
Ear	47	3	1.71	<0.0001
Lips	66	17	1.45	<0.0001
Eyelid	7	3	1.23	0.52
Trunk	50	36	1.02	0.80
Lower limbs	34	54	0.66	0.003
Upper limbs	85	96	0.80	0.0029

Source: Pathology Laboratory, São Lucas and DiPrever, Tubarão (SC), 2010.
*PR = prevalence ratio, Chi-square test.

There were statistically significant gender-related differences with regards to specific locations: nose, ears, lips, and upper and lower limbs. SCC on the nose was 37 percent less common in men than in women. Similarly, SCC occurred 34 percent less often on the lower limbs and 20 percent less often on the upper limbs in men than in women. On the other hand, men were 71 percent more affected on the ears and 45 percent more on the lips compared to women. Men were more likely to develop SCC on the ears and lips than women, which was statistically significant ($p < 0.001$). The gender-related difference may be due to the protective effect of long hair covering women's ears, as well as the use of lip-protecting lipstick among them. On the other hand, there is a greater number of male than female smokers. These findings were similar to those found in a study on BCC in Tubarão, and on SCC in Blumenau, Santa Catarina. [9,12] Concerning the head area, the incidence of SCC on the nose was higher in women than in men, having a statistically significant association ($p < 0.001$). This gender-related difference can be explained because men are more likely to wear caps or hats, providing them a protective effect. [12] The upper and lower limbs were more affected in women than in men, which was statistically significant ($p < 0.001$). The difference may be assigned to a phenotypic factor, since men tend to have more body hair in these areas than women; in addition, women wear shorter clothes than men.

Well-differentiated SCC was the most common

histological type (77%), followed by moderately differentiated (13.8%), in situ (5.5%), and poorly differentiated (3.2%). No cases of undifferentiated SCC were found, corroborating the findings by Scanavino Jr. [2]

There are reports that poorly differentiated SCC has a metastasis rate three times higher than that of well-differentiated SCC. Studies revealed that thick tumors have a worse prognosis compared to shallow tumors, and perineural and angiolymphatic invasions are also associated with a higher probability of metastasis. [2,3] Perineural invasion caused by SCC has a reported incidence of 2.4 to 7.4 percent, causing clinical signs and symptoms such as pain, burning, tingling, anesthesia, paresthesia, paralysis, diplopia and decreased corneal reflexes. The presence of these symptoms worsens the prognosis. [3]

Margin involvement was found in 18 percent of the lesions. In two experimental studies, a 97.3 percent cure rate was obtained with cryotherapy in 563 patients with primary SCC, whose lesion size was 0.5 to 1.2 cm in diameter. [1,2] Nonetheless, there was aesthetic concern in the resection of these lesions, because most of them were located on the face (32.1%), and scarring due to negligence or medical malpractice.

Limitations to this study include the research design, since causality cannot be established in cross-sectional studies, and the collection of data from secondary sources, impeding a comprehensive evaluation of all variables (skin type, sun exposure frequency, use of physical and chemical protection, among other things). In addition, several reports contained missing or incomplete data, and medical referral not always described the lesions anatomically. However, studies of such magnitude and sample size are too extensive to be performed by other designs in short time due to the high cost.

This study demonstrates the importance of this type of skin lesion that is one of the most prevalent in the world population. It emphasizes that precaution should be taken with exposure to ultraviolet radiation, especially at inappropriate hours without protection, especially in individuals of skin types I and II. [4,9,12] As shown in this study and other published literature, SCC incidence is increasing gradually, which may be due to the decrease in the ozone layer, making public awareness campaigns increasingly important, since this is a preventable and curable cancer. [15]

Further population-based studies with primary data collection are needed to determine the magnitude of this problem. This study shows the situation in the city of Tubarão, which is not different from the national and international panorama, revealing a high prevalence of skin cancer and a small number of studies on the subject.

CONCLUSION

In total, 1,437 anatomic pathology reports positive for SCC were found in patients treated in two laboratories in the city of Tubarão, between 1999 and 2009. During the study period, there was a 50 percent increase in morbidity. The incidence by gender was similar between males and females, and the most affected age group was between 70 and 79 years. SCC of the head was the most frequent. The incidence on the lips and ears was higher in men than women, while the incidence on the nose, upper and lower limbs was higher in women than men.

Due to the increased number of cases of skin cancer in the population, educational measures should be taken to inform people about the dangers of sun exposure and protective measures that should be adopted since childhood. Greater access to health services is also needed for the early diagnosis and treatment, besides the distribution of sun protection products by the Unified Health System to ensure adherence to daily sunscreen usage. ❑

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