

Epidemiology of basal cell carcinomas in Tubarão, Santa Catarina (SC), between 1999 and 2008

Epidemiologia dos carcinomas basocelulares em Tubarão, Santa Catarina (SC), entre 1999 e 2008

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Abstract: BACKGROUND: Skin cancer is the most frequent type of neoplasm in Brazil. There are no data on the incidence of basal cell carcinoma in the Southern region of Santa Catarina.

OBJECTIVE: To establish epidemiological data on basal cell carcinoma in Tubarão, Santa Catarina, between 1999 and 2008.

METHODS: A cross-sectional study was conducted in which anatomopathological reports of basal cell carcinoma from the laboratories of Tubarão, Santa Catarina, were analyzed. We considered the following variables: year of diagnosis, age, gender, city of origin, tumor site, histological subtype, lesion diameter, margin involvement, and relapse.

RESULTS: Reports of 3,253 subjects most frequently between the ages of 61 and 80 years diagnosed with basal cell carcinoma were obtained. The incidence of basal cell carcinoma was 164.5 cases per 100,000 inhabitants in 1999 and 295.2 per 100,000 in 2008, showing an increase of 80%. Most lesions occurred in the cephalic region and nodular was the most common histological subtype. There was an association between males and basal cell carcinoma of the torso and ear, and between females and basal cell carcinoma of the nose. The sclerodermiform subtype was the most aggressive in relation to margin involvement.

CONCLUSION: There was a prevalence of involved margins following resection in 27% of lesions. Based on multivariate analysis, lesions ≥ 2 cm in diameter were 5.5 times more likely to present margin involvement, and basal cell carcinoma of the face was 1.8 times more likely to occur ($p < 0.0001$).

Keywords: Carcinoma, basal cell; Epidemiology; Skin neoplasms

Resumo: FUNDAMENTOS: O câncer da pele é frequente no Brasil, com incidência crescente. Na Região Sul de Santa Catarina não existem dados da incidência de carcinoma basocelular.

OBJETIVO: Estabelecer dados do carcinoma basocelular em Tubarão (SC) entre 1999 e 2008.

MÉTODOS: Estudo transversal com revisão dos laudos anatomopatológicos de carcinoma basocelular dos laboratórios de Tubarão (SC), com coleta das variáveis de interesse: ano do diagnóstico, idade, gênero, cidade de origem, local da lesão, subtipo histológico, diâmetro da lesão, comprometimento de margem e ocorrência de recidiva.

RESULTADOS: Identificaram-se 3.253 laudos de carcinoma basocelular, com maior frequência na faixa etária entre 61 e 80 anos. Calculou-se o coeficiente de incidência para carcinoma basocelular de 164,5 em 1999 e 295,2 em 2008 para cada 100 mil habitantes, acarretando aumento de 80%. A região cefálica foi a mais acometida e o subtipo histológico mais comum foi o nodular. Houve associação entre gênero masculino e a localização em tronco e orelha, e entre gênero feminino e ocorrência de carcinoma basocelular no nariz. O subtipo esclerodermiforme foi o mais agressivo em relação ao comprometimento de margens.

CONCLUSÃO: Do total de casos de carcinoma basocelular, houve prevalência de margens comprometidas após ressecção em 27% das lesões. Após análise multivariada, as lesões de 2cm ou mais apresentaram probabilidade 5,5 vezes maior de comprometimento de margens, ao passo que a localização em face indicou probabilidade 1,8 vez maior ($p < 0,0001$).

Palavras-chave: Carcinoma basocelular; Epidemiologia; Neoplasias cutâneas

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INTRODUCTION

Skin cancer is the neoplasm of greatest incidence in various regions of the world, including Brazil.^{1,2} About a million cases of basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), both non-melanomas, are estimated to have been diagnosed in 2008 in the United States.³ Australia is the country with the highest incidence of skin cancer worldwide, with an incidence rate of BCC in the order of 884/100,000 inhabitants/year.⁴

The number of new cases of non-melanoma skin cancer estimated for Brazil in 2008 was 115,000. This value corresponds to an estimated risk of 120 new cases/100,000 inhabitants per year. Non-melanoma skin cancer is the most prevalent in most regions of Brazil, with an estimated risk of 82/100,000 in the South, 66/100,000 in the Southeast, 50/100,000 in the Northeast, 27/100,000 in the North, and 54/100,000 in the Central West.²

The incidence of skin cancer in the Southern region is higher than the national average. Santa Catarina is the state with the highest concentration of skin cancer in Brazil, with 133.22 cases/100,000 inhabitants for non-melanoma cancer and 8.61/100,000 inhabitants for melanoma.² However, there are not enough data for us to understand the causality or whether this incidence is growing as in the rest of the country. The combination of two factors probably explains this. First, the population of Santa Catarina is mainly constituted by individuals of European descent with phenotypic characteristics that predispose them to the development of this neoplasm, such as blue eyes, blond hair, and skin phototypes I and II (based on Fitzpatrick classification scale).^{1,5,6} Second, they are exposed to a great amount of ultraviolet radiation (UV) due to the ozone layer destruction found in the state's topography.^{1,2,7}

Basal cell carcinomas are the most common type of skin cancer, being responsible for about 70 to 75% of the cases based on statistical data.^{8,9} Since the first histogenic studies, researchers have attempted to associate the origin of basal cell carcinomas with epidermal basal cells and skin annexes. It is considered a low-malignancy grade tumor, with capacity for local invasion, tissue destruction, recurrences, and with limited power to metastasize.¹⁰

Basal cell carcinoma often appears as an isolated lesion, although the occurrence of various simultaneous or subsequent lesions is not unusual.¹⁰ They occur predominantly in sun-exposed areas, especially in the head and neck (80% of the cases), followed by trunk (15%), hands and legs.⁹

The prognosis of BCC depends on the type of tumor and the treatment established. The risk factors associated with the recurrence of metastases include a

tumor > 2 cm in diameter, localized in the central part of the face or ears, longer duration of the lesion, incomplete excision, aggressive histological type and perineural or perivascular involvement.⁹ The development of metastases is rare in BCC. It is estimated that their incidence ranges between 0.0028% and 0.5%.¹¹ Metastatic lesions are usually large, ulcerated, highly infiltrating and recurrent.¹⁰ The rate of cure for a BCC adequately treated is around 90% or higher. The latency period between surgery and recurrence may vary from two months to two years, frequently occurring in the first six months. The later a recurrent tumor is treated, the worst the prognosis is.¹¹

There are few scientific studies published in the Brazilian literature about epidemiological data involving BCCs separately. This is due to the fact that BCCs, together with SCCs, are classified as non-melanoma cancers and are published as such.⁶ It is known, however, that the incidence of BCC has progressively increased throughout the years.⁴ This increase may be due to the higher demand for histopathological exams of suspicious lesions, greater awareness and uneasiness in relation to these tumors, and a larger number of Dermatologist physicians and educational and preventive campaigns.

The high frequency of skin BCC in the country, especially in Santa Catarina, makes it a serious public health issue.^{1,2} This study aimed at establishing epidemiological data about BCC in patients seen in the city of Tubarão. This is a pioneer work since data about the prevalence of BCC in this municipality is not found in the literature.

METHODS

A cross-sectional epidemiological study that investigated a secondary databank was conducted. The anatomopathological findings of patients diagnosed with BCC seen at the two pathological anatomy laboratories in the municipality of Tubarão, from 1999 to 2008, were included in the study. Tubarão is located in the South of Santa Catarina, in the coastal region. All positive findings for histopathological types other than BCCs were excluded.

The information obtained was transferred to a protocol data record, created by the authors, with the following variables: year of diagnosis, age, gender, city of origin, site of lesion, histological subtype, diameter of lesion, margin involvement, and recurrence.

The data collected were entered into Epidata version 3.1, and the statistical analysis was done with the SPSS 16.0 software. Descriptive epidemiology was used for presenting the characteristics of the study population. Nominal variables were presented as absolute and relative frequencies. Numerical variables

were presented as measures of central tendency and dispersion. The Chi-square test was used to compare categorical variables, with a preestablished confidence interval of 95% ($p < 0.05$). A multivariate logistic regression analysis to control confusion factors in relation to surgical margin involvement was performed. The incidence coefficients for the city of Tubarão were calculated based on population estimates between 1999 and 2008 by DATASUS.¹² Only cases from the municipality of Tubarão were considered in this analysis.

This work was approved by the Research Ethics Committee of Santa Catarina South University (CEP-UNISUL), registration number 08.382.4.01.III.

RESULTS

Between 1999 and 2008, 3,253 medical reports with diagnosis of BCC were found in the two laboratories of pathology in the municipality of Tubarão (SC). Of this total, 1,667 (51.2%) were women. They were aged between 15 and 99 years, with a mean of 62 ± 14.7 years. Table 1 shows the categorized age range of patients based on the frequency of BCC cases. The age range with the greatest prevalence of BCC was between 61 and 80 years.

Regarding the city of origin, 1,892 medical reports (58.2%) were of individuals who lived in Tubarão and the remaining were patients who lived in neighboring cities. Table 2 shows the incidence coefficients of BCCs for cases diagnosed in Tubarão between 1999 and 2008.

The frequency of BCCs in relation to site of the lesion is shown in figure 1. However, 1,146 (35.2%) reports did not present this information. BCC predominated in the cephalic region, especially the nose. There was an association between males and BCC in the trunk and pinna ($p < 0.001$) and females and BCC in the nose ($p < 0.001$). Table 3 shows the site of BCCs in relation to gender.

The most frequent histological type, based on the classification suggested by the World Health Organization,¹⁰ was nodular (81.7%) – with or without ulceration, followed by superficial (14.1%), sclerodermiform (1.4%) and basal squamous (1.4%). The sclerodermiform histological subtype was the most aggressive on margin involvement, 70% greater than other histological subtypes ($RP = 1.73$; $IC95\% 1.23-2.44$, $p < 0.006$).

With regard to the 3,253 resected BCCs, occurrence of margin involvement in the histopathological examination was observed in 884 lesions, corresponding to 27.2% of the cases. Nonetheless, only 32 reports were resent to laboratories for resection due to margin enlargement. Of these, 17 still showed margin involvement.

TABLE 1: Percentage distribution of BCC according to age range

Age in years	Percentage %
0-20	0,4
21-40	7,8
41-60	36,5
61-80	43,4
81-99	8,3
Uninformed	3,6

SOURCE: São Lucas and DiPrever Laboratory of Pathology, Tubarão (SC), 2009

In relation to size of the lesions, 51 (1.6%) had a diameter ≥ 2 cm and 1,108 (34,1%) reports had lesions < 2 cm. The remaining reports, 2,094 (64.3%), did not inform the size of the lesion or included irregular skin surface lesions, making it difficult to establish their size. BCCs with a diameter ≥ 2 cm showed a gross risk of margin involvement nearly 80% higher as compared with lesions < 2 cm ($RP = 1.783$ ($IC95\%: 1.62-1.97$; $p < 0.0001$)).

Table 4 shows the results of the multivariate analysis of some variables in relation to surgical margin involvement after resection of BCCs.

DISCUSSION

A total of 3,253 medical records with anatomopathological diagnosis of BCC obtained in the two laboratories of pathology of Tubarão were analyzed. Tubarão is a regional health pole and reference center for about 20 cities in the South of Santa Catarina. Therefore, the sample is a good representation of the

TABLE 2: Incidence coefficients of BCC for the municipality of Tubarão from 1999 to 2008

Year	Coefficient*
1999	164,5
2000	166,2
2001	200,9
2002	172,5
2003	166,4
2004	235,2
2005	229,0
2006	205,5
2007	208,5
2008	295,2

*Number of BCC cases for every 100,000 inhabitants.

SOURCE: São Lucas and DiPrever Laboratory of Pathology, Tubarão (SC), 2009. To calculate the incidence coefficient, the estimated population of the municipality of Tubarão in the years of interest was considered. Data available at DATASUS.

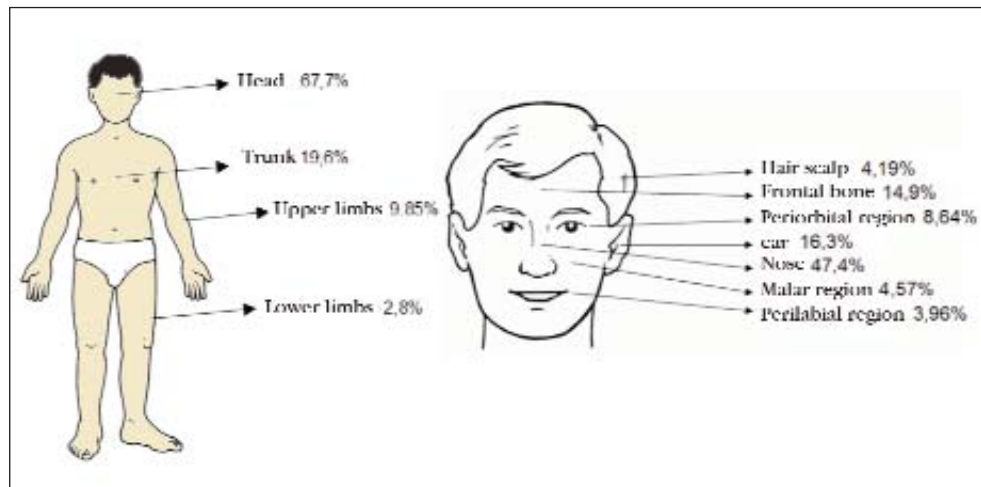


FIGURE 1: Frequency of BCC in relation to anatomical site

Fonte: São Lucas and DiPrever Laboratory of Pathology, Tubarão (SC), 2009

region studied. Data analysis showed a significant increase in the occurrence of these tumors in the period of the study, corroborating similar studies in the literature.^{3,4,6,8}

The incidence coefficient allowed us to estimate the increase in the number of skin cancer cases over the last 10 years among those found in city of Tubarão. There has been a significant increase in the incidence of the disease: in 1999 there were 164.5 cases/100,000 inhabitants and in 2008 it reached 295.2/100,000 inhabitants, resulting in an increase of about 80%. Other studies also revealed an increase in incidence, such as the study conducted in Australia. In this country, a survey carried out in 1985 estimated the incidence of BCC to be of 657/100,000 and in 2002, 884/100,000 inhabitants.⁴ Another study conducted in Blumenau (SC) showed a significant increase in the incidence of BCC; in 1980 there were 51.5 cases/100,000 inhabitants and in 1999, 225 cases/100,000 inhabitants.⁶ This increase could be explained by the higher number of diagnoses established in the municipality due to greater knowledge and awareness about the lesion by doctors and

patients, increase of sun radiation intensity and the habit of sunbathing.

Destruction of the ozone layer increases ultraviolet radiation and this explains the higher incidence and prevalence of BCC in the population.¹⁴⁻¹⁶ It is estimated that for every 10% of ozone layer loss there is a 40% increase in the incidence of skin cancer.¹⁷ According to meteorological data, there has been a 7 to 8% decrease in the ozone layer in the state of Santa Catarina per decade, from 1979 to 2000¹⁴, which inevitably influences the incidence rate found in this study. Moreover, most individuals living in this state are white with light-colored eyes, due to European colonization,^{1,6} being thus more susceptible to the damage caused by ultraviolet radiation.^{6,9,18}

There was no difference in the incidence of BCC in relation to gender; 51.2% of the cases involved females, which corroborates with data from the scientific literature.^{6,8,19} Cases predominated in individuals between 61 and 80 years old (43.4%), similar to works developed by Bariani and Silveira, which showed 59% and 50% of the BCC cases in this age range.^{8,19} This could be explained by the fact that older individuals

TABLE 3: Specific skin localization of BCCs categorized by gender

Localization	Masculine	Feminine	PR*(IC 95%)	p
Face	697	727	0.99(0.93-1.06)	0.8
Nose	155	229	1.05(1.02-1.07)	<0.0001
Ear	99	33	3.15(2.14-4.65)	<0.0001
Lips	13	19	1.00(0.99-1.01)	0.4
Eyelid	33	37	1.00(0.99-1.01)	0.8
Trunk	249	164	1.60(1.33-1.92)	<0.0001
Limbs	128	138	0.97(0.77-1.23)	0.8
Others/ignored	512	638	0.84(0.77-0.93)	<0.0001

*Prevalence ratio, Chi-square test

Source: São Lucas and DiPrever Laboratory of Pathology, Tubarão (SC), 2009

TABLE 4: Multivariate analysis of risk factors for surgical margin involvement after resection of BCCs

Variable	Gross RR*	Adjusted OR**	CI 95%	P
Gender	1.07	1.05	0.84-130	0.7
Diameter \geq 2 cm	2.92	5.48	4.37-6.86	<0.0001
Age > 60 years	1.16	1.09	0.67-1.36	0.5
Sclerodermiform	1.88	1.35	0.41-4.46	0.6
Localization face	1.57	1.82	1.31-2.52	<0.0001

* Risk ratio;

** Odds ratio

have a less efficient immune system, with lower capacity of DNA regeneration,^{9,16,20} and are more exposed to BCC risk factors, especially due to the cumulative effect of intense and continuous sun exposure.^{9,15}

Most skin cancers occur in areas of the body frequently exposed to the sun.^{6,8,9,15,21,22} In this study, 67.7% of the BCCs were localized in the cephalic region, similar to the percentage found in the literature, which varied from 52.1 to 86%.^{6,19,21,23,24} This finding strengthens the relevance of chronic sun exposure as a risk factor, with the face being highly exposed to the sun. Incidence in the trunk was 19.6% and was more frequent in men ($p < 0.001$). This incidence was similar to the one found in the study conducted in Blumenau (SC), but different from those of studies conducted in other Brazilian regions.^{6,19} Perhaps this difference occurred due to the characteristics of Tubarão and Blumenau, since agriculture is a very important economic activity in these regions and is mostly practiced by men who expose themselves to the sun without protection. In addition, it is common for men to be outdoors on very hot days without a physical (shirt) and chemical (sunscreen) barrier due to cultural characteristics. Predominance of Caucasians and intense ultraviolet radiation also aggravate the problem.^{1,19,25}

More cases of BCC involved the nose (47.4%), which is in agreement with other studies.^{6,8,21,25} There was greater incidence in women, with a significant statistical association ($p < 0.001$). This suggests that, perhaps, men protect their heads and consequently noses more often by wearing hats. The incidence of BCC in the pinna was higher in men, with a significant statistical difference between gender and BCC in the ear ($p < 0.001$). This may be explained by women's longer hair, which covers their ears, with consequent natural physical protection against ultraviolet radiation.⁶

The most typical histological type was nodular, with or without ulceration (81.7%), which is also the most prevalent type based on other studies; however, the incidence was above the averages found.^{8,9,19} A

study by Mantenese showed an incidence rate of 46.3% for nodular BCC.²⁵ In the present study, the sclerodermiform histological type, the most aggressive basal cell carcinoma, occurred in only 1.4%, which is a low incidence when compared with the results of other studies, such as the one by Nasser (10%), but similar to that conducted by Bariani (0.9%).^{6,19}

The total prevalence of surgical margin involvement after resection of BCC often ranges from 5.5 and 12.5%.^{19,26-28} In this study the rate of margin involvement was 27.2%. This may be due to negligent surgical technique, aesthetic concerns in the removal of lesions, favorable prognosis and the performance of pre-surgical incisional biopsy by some doctors. The biopsy specimens of BCCs of the face showed nearly 50% more margin involvement when compared with other regions of the body (RP=1.44; IC95% 1.30-1.59; $p < 0.001$); the areas with greater involvement were the nose (45.8%), ear (17.3%), and periorbital region (11.5%). These data are similar to those obtained in studies by Farhi and Schirley on incomplete BCC excisions.^{23,28} This may illustrate aesthetic concerns in the resection of facial tumors and the proximity to vital structures, making excision difficult.^{26,28,29}

The ability to excise all margins is also correlated with the histological lesion type. In this study we could observe that sclerodermiform was the most aggressive on margin involvement, 70% higher as compared with other histological subtypes ($p < 0.006$), despite its low incidence.^{19,21,26,28} This is observed due to the poor definition of its margins, which makes the delimitation of the resection area difficult.²⁶

Indeed, in the present study, after adjusting for confusion factors, only localization in the face and diameter \geq 2 cm showed a significant statistical association with surgical margin involvement. Studies that evaluate risk factors for surgical margin involvement of BCCs revealed that localization in the face is the main associated factor, due to the abovementioned reasons.^{23,26,28} With regard to lesions \geq 2cm in diame-

ter, they were 5.5 times more likely to show margin involvement ($p < 0.0001$), which is in agreement with data from other studies.^{21,26,30} This may be explained by the fact that larger tumors have more complex resection and more aggressive biological behavior.²⁶

In relation to cases sent for margin enlargement, of the 32 diagnosed with margin involvement, 17 showed BCC in the specimen analyzed and the remaining no longer present BCC. The explanation for the absence of residual tumor in the subsequent surgery may be attributed to the false information of residual tumor in the surgical margin, due to retraction caused by fixation of the peritumoral tissue in paraffin sections. The hypothesis that the postsurgical inflammatory process may be the cause of the disappearance of tumor remains has also been recently disputed.¹¹

Among the limitations of the study we emphasize its design, since in cross-sectional studies it is impossible to establish causality. In addition, the data are from a secondary databank and some variables cannot be evaluated (skin phototype, frequency of sun exposure, use of physical and chemical protection, among other aspects). Moreover, some medical reports were incomplete, which jeopardizes data analysis and may lead to confusing information. Medical referral not always anatomically described the lesions, and it was difficult to know whether lesions belonged to the same individual or whether they were recurrent. However, studies of this magnitude and with this sample size are not viable with other designs within a short period of time and due to high cost.

It is important to emphasize the importance of skin cancer prevention, identifying the population at risk to define adequate control policies. Efforts should be made to divulge the issue so that these tumors can be diagnosed and treated early. Health

education, which makes the recognition of early alterations suggestive of malignancy possible, is an internationally accepted strategy.¹

Further population-based studies are needed to assess the real magnitude of the problem and its repercussion in public health. Through this work it was possible to understand more about the behavior of this neoplasm in the region of Tubarão. The creation of programs that effectively cause a change in behavior by unveiling the health damage caused by sun exposure is suggested. This, in turn, may reduce the incidence of BCC and other skin neoplasms in future generations.

CONCLUSION

This study allows us to conclude that there has been a significant increase in the incidence of BCC, similar for both genders. Those aged between 61 and 80 years are often more affected.

The cephalic region was the most affected and the most frequently found histological type was nodular.

This study showed prevalence of margin involvement after resection of BCC of 27%, having as main risk factors lesions > 2cm in diameter and localization in the face. □

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