Squamous cell cancer – 31-year epidemiological study in a city of south Brazil*

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Abstract: BACKGROUND: The incidence and morbidity of squamous cell cancers are increasing worldwide. Epidemiological studies with morbidity coefficients about this type of cancer are scarce in Brazil.
OBJECTIVES: To determine morbidity coefficients, analyze and classify the squamous cell cancers diagnosed in the city of Blumenau - SC from 1980 to 2011, according to clinical and histological features.
METHODS: The authors revised 4000 histopathological exams with respect to sex, age, anatomic site and histological type. The morbidity coefficients were calculated using the number of squamous cell cancers found and the annual population estimated by the Brazilian Institute of Geography and Statistics between 1980 and 2011.
RESULTS: A total of 4000 tumors were identified, 2249 (56.2%) in male and 1751 (43.8%) in female patients. The standard incidence rates varied from 40 cases in 1980 to 120 cases/100,000 inhabitants in 2011. The morbidity above 70 years of age reached 1484 cases/100,000 inhabitants in male and 975 in female patients. As to primary anatomic site, we found more tumors on the lips and ears in male and on the face and legs in female patients. As to the degree of involvement, the more frequent were Well Differentiated Squamous cell carcinomas (70%) and Moderate Squamous cell carcinomas (19,1%). The Low Differentiated Squamous cell carcinomas, which represented those with the worst prognosis, were found in 4.5% of the tumors.
CONCLUSIONS: Squamous cell cancers in Blumenau - SC have similar patterns of distribution regarding age, primary anatomic site and histological types as found in the international literature. The morbidity increased by 300% in the last 31 years, which indicates that we need to dedicate special attention to the older population.
Keywords: Carcinoma, squamous cell; Epidemiology; Neoplasms

INTRODUCTION

Squamous Cell Cancers of the skin and vermilion border or lip semimucosa rank second in the incidence of malignant skin tumors, appearing in all statistics as reaching 20 % of total cases.[1,2]

In the United States, around 3.5 million nonmelanoma skin carcinomas are diagnosed every year, of which 700,000 are new cases of squamous cell carcinomas, resulting in 2500 deaths per year.[1,2,3]

In Australia, 138,000 new squamous cell carcinoma cases are expected per year, a number that is considered underestimated.[4]

In the United Kingdom, the nonmelanoma skin carcinomas are extremely common but with low mortality rate, reaching 99,000 cases in 2010.[5,6,7]

In 2012, it was estimated that, in Brazil, there would be 62,680 new cases of nonmelanoma skin carcinomas in men and 71,490 cases in women. These numbers correspond to an estimated risk of 65 new cases for every 100 thousand men and 71 for every 100 thousand women (according to Instituto Nacional do Câncer - INCA [National Cancer Institute]).[8]

The ultraviolet radiation from indoor tanning salons plays an important role and was considered a carcinogenic factor by the World Health Organization (WHO).[9]

The squamous cell carcinoma occurs in all body areas, including mucosas and genitals, but it is more common in areas exposed to ultraviolet radiation, such as the head, ears, neck and back of hands.[10]

Other causes include chronic exposure to chemical products like tar, arsenic-contaminated water, use of herbicides, insecticides and tobacco.

Severe burns, chronic ulcers and some types of HPV (papillomavirus) are also considered carcinogenic.[10,11]

Although basal cell and squamous cell carcinomas are the most common types of skin cancer, they are easily treated when promptly detected. The per-

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centage of cure is approximately 95% of cases, when early diagnosed and treated.[12,13]

Due to this high incidence, studies concerning their types, degree of involvement and epidemiology are important for prevention and early treatment of these tumors.

Vital statistics are focused on diseases that are almost always fatal and do not include much information about nonmelanoma skin cancers, such as basal cell and squamous cell carcinomas.

There are practically no records of basic measures of population morbidity concerning these cancers in global literature, since squamous cell skin and vermilion border cancers appear in statistics together with basal cell cancers and classified as nonmelanoma skin carcinomas.

In this study we analyzed squamous cell skin and vermilion border cancers diagnosed in Blumenau - SC in the period from 1980 to 2011, according to the main clinical and histological characteristics, taking into consideration sex, age, primary location and histological types.

The morbidity coefficients of skin squamous cell carcinoma were calculated for the period between 1980 and 2011, using only data from anatomopathological exams from the three existing laboratories in the city, excluding clinical cases not verified by means of laboratory tests and should, therefore, be regarded as underestimated.

Blumenau, a city in the south of Brazil located in the northeast of the state of Santa Catarina, 26º 55' 10" South latitude, 49º 03' 58" longitude, 21 meters above sea level altitude. In 2000 the studied population in Blumenau represented 4.89% of the population of Santa Catarina and 0.15% of the population of Brazil.[14]

The results found allow us to show new data for Brazil and referentials for almost the entire southern region of the country, since we have a population predominantly white exposed to great intensity of ultraviolet radiation.

MATERIAL AND METHODS

This is an epidemiological cross-sectional study based on secondary data. The morbidity coefficients of skin and vermilion border squamous cell carcinoma for the city of Blumenau were calculated based on the annual population from 1980 to 2011, estimated by the Brazilian Institute of Geography and Statistics - IBGE (*Instituto Brasileiro de Geografia e Estatística* and review of cases histopathologicaly diagnosed in the pathological anatomy laboratories of the city, the Laboratório de Citologia, Imunopatologia e Anatomia Patológica - CIPAC *(Citology, Immunopathology and Pathological Anatomy Laboratory),* Pathology Diagnósticos em Medicina *(Pathology Medical Diagnoses)* and Laboratório Beatriz Moreira Leite (*Beatriz Moreira Leite Laboratory - BML Pathology*), between 1980 and 2011, in a total of 4000 cases of skin and vermilion border squamous cell cancers.[14]

Descriptive epidemiology was used to present the characteristics of the studied population. Case selection considered only those from the city of Blumenau, for greater fidelity in calculation of the morbidity coefficient.

This study was approved by the Research Ethics Committee of the Regional University of Blumenau (Universidade Regional de Blumenau – FURB), according to protocol 019/2012.

Statistical Methodology

Data were organized in tables containing absolute and relative frequencies, as well as incidence rates. Rates were compared by means of the Chi-square Test. In all of the tests $P < 0.05$ was considered as statistically significant. The data were analyzed through the software EpiInfo version 7 from 2013.

RESULTS

In the period between 1980 and 2011 4000 primary cases of squamous cell carcinomas of the skin and lip semimucosa were reviewed in the 3 (three) laboratories of pathological anatomy in the city of Blumenau**,** without taking into account the clinical diagnoses; therefore the data found were considered as underestimated, although with an incidence epidemiological value not smaller than the actual one.

The distribution of cases according to gender was 2249 cases (56.2%) in male patients and 1751 cases (43.8%) in female patients.

Table 1 shows squamous cell carcinoma general incidence rates per 100,000 inhabitants, gross and adjusted, and standardized for the world population and by gender in the city of Blumenau, between 1980 and 2011.

We point out the gross general incidence rates of 82.6 and 108.7 cases of squamous cell carcinoma per 100,000 inhabitants/year in the years 1989 and 2011, respectively and the adjusted general incidence rates for the global population of 125.6 in 1989 and 110 in 2011. (Table 1)

As to incidence rates adjusted for the male sex, they reached 152 cases/100,000 inhabitants in 1989 and 123 in 2011. The incidence rates adjusted for the female sex were 104.5 in 1989 and 99 in 2011. (Table 1)

Regarding age groups, incidence rates were calculated per decade and we point out the greater incidence above 70 years of age, with 1484 cases/100,000 inhabitants in male patients in the 1980 decade and 718 cases/100,000 inhabitants in female patients in the period between 2000 and 2011(Table 2).

Table 1: General and gender-specific squamous cell carcinoma incidence rates, gross and standardized for the global population in Blumenau – SC – Brazil from 1980 to 2011

YEAR	CB [1]			ASF(W)[2]		
	M	F	T	M	F	T
1980	44.1	18.6	31.1	77.5	27.3	50.3
1981	51.8	26.6	39.0	90.3	41.6	64.1
1982	67.3	35.2	51.0	120.7	55.1	84.6
1983	77.2	20.5	48.3	142.4	34.4	81.5
1984	86.4	33.2	59.3	151.7	49.3	94.4
1985	95.2	46.3	70.2	163.0	68.6	110.2
1986	82.7	56.5	69.4	140.5	81.8	108.2
1987	90.1	53.0	71.2	152.7	75.0	109.1
1988	95.1	62.7	78.6	163.4	89.4	121.6
1989	90.8	74.8	82.6	152.8	104.5	125.6
1990	91.7	66.5	78.8	152.9	91.7	118.6
1991	66.3	50.0	58.0	110.6	67.5	87.1
1992	53.8	47.3	50.5	82.7	61.0	70.4
1993	75.5	41.6	58.2	125.0	55.9	85.4
1994	56.2	32.3	44.0	98.3	45.1	68.3
1995	42.0	38.7	40.3	69.1	52.6	60.2
1996	40.4	31.4	35.8	61.4	38.7	48.4
1997	32.7	28.3	30.4	48.9	36.0	41.6
1998	55.8	28.6	42.0	87.1	36.8	58.6
1999	56.5	31.4	43.7	88.2	41.3	61.3
2000	35.0	24.7	29.7	51.4	27.3	37.7
2001	35.8	38.1	36.9	55.4	42.5	52.5
2002	33.7	30.2	31.9	52.1	33.3	40.9
2003	28.7	15.5	22.0	45.5	18.0	28.6
2004	47.7	25.7	36.5	76.0	28.9	47.6
2005	43.8	29.4	36.5	63.5	32.1	46.4
2006	53.3	66.9	60.2	80.0	76.4	77.9
2007	35.6	56.6	46.3	46.7	53.8	50.5
2008	51.8	41.6	46.5	65.2	36.3	49.7
2009	75.1	86.2	80.8	92.2	79.8	85.8
2010	93.7	64.7	78.9	110.2	55.3	78.7
2011	104.3	112.9	108.7	123.4	99.0	110.0

Source: *Brazilian Institute of Geography and Statistics (Instituto Brasileiro de Geografia e Estatística - IBGE), Citology, Immunopathology and Pathological Anatomy Laboratory (Laboratório de Citologia, Imunopatologia e Anatomia Patológica - CIPAC), Pathology Medical Diagnoses (Pathology Diagnósticos em Medicina) and Laboratório Beatriz Moreira Leite (Beatriz Moreira Leite Laboratory - BML Pathology).*
**per 100,000/inhabitants. M=male F=female T=total1 CB – gross incidence rate 2 ASR(W)2 standardized incidence rate for the global population*

Table 2: Morbidity incidence rates* per age group and per decade of squamous cell carcinoma in the city of Blumenau – SC - Brazil from 1980 to 2011

Years	1980- 1989		1990-1999		2000-2011	
Age Group	M	F	M	F	M	F
0 - 4	0	0	0	0	0	0
5 - 9	0	0	0	0	0	0
10 - 14	0	1	0	0	0	0
15 - 19	5.3	1.01	5.7	0	0	0.64
20 - 24	6.2	1.02	6.3	1.8	0	0
25 - 29	8.8	4.2	13.3	8.6	0.63	1.2
30 - 34	30.8	14.46	20.9	13.8	2.3	4.7
35 - 39	46.5	16.4	31.3	16.	6.7	8.5
40 - 44	72.7	30.2	41.9	25.2	22.3	18.1
45 - 49	135.6	66.3	82.8	43.8	49.5	28.
50 - 54	196	79	123.4	77.4	86.	32.6
55 - 59	299.3	137.3	180.8	123.6	145.6	74.3
60 - 64	471.1	185.4	327.9	188.1	223.7	176.4
65 - 69	630.6	437.3	480.8	296.	381.1	226.18
70 or +	1484.8	679.2	929.5	487.6	975.7	718.1

Source: *Brazilian Institute of Geography and Statistics (Instituto Brasileiro de Geografia e Estatística - IBGE), Citology, Immunopathology and Pathological Anatomy Laboratory (Laboratório de Citologia, Imunopatologia e Anatomia Patológica - CIPAC), Pathology Medical Diagnoses (Pathology Diagnósticos em Medicina) and Laboratório Beatriz Moreira Leite (Beatriz Moreira Leite Laboratory - BML Pathology).*

**per100,000/inhabitants.*

Table 3 shows numerical and percentage distribution of squamous cell carcinoma of the skin and vermilion border, according to primary location on the skin where 43% (n= 1369) of cases were found on the face, reaching a total of 70% (n= 2232) on the head and 29.7% (n=949) on the trunk and limbs.

It should be observed that the incidence of squamous cell carcinomas found on the ear reached 6.7% (n= 107) in men and 2.6% (n= 42) in women.

Squamous cell cancers on the lips appear with a frequency much higher in men, with 5.2% (n= 82) of the cases compared with the lower lip of women, with 3% (n= 48).

Table 3: Numerical and percentage distribution of squamous cell carcinoma according to primary skin location site and sex in Blumenau – SC – Brazil from 1980 to 2011

LOCATION	MALE	FEMALE	TOTAL	P
FACE	668 (42%)	701 (44,1%)	1369 (43%)	0.2312
LIPS	82 (5.2%)	48 (3%)	130 (4.1%)	0.0023
NOSE	108 (6.8%)	159 (10%)	267 (8.4%)	0.0011
EAR	107 (6.7%)	42 (2.6%)	149 (4.7%)	0.0001
SCALP + NECK	187 (11.8%)	130 (8.2%)	317 (10%)	0.0007
TRUNK	161 (10.1%)	133 (8.4%)	294 (9.2%)	0.0875
UPPER LIMBS	199 (12.5%)	272 (17.1%)	471 (14.8%)	0.0002
LOWER LIMBS	79 (5%)	105 (6.6%)	184 (5.8%)	0.0478
TOTAL	**1591 (100%)**	**1590 (100%)**	**3181 (100%)**	

Source: *Brazilian Institute of Geography and Statistics (Instituto Brasileiro de Geografia e Estatística - IBGE), Citology, Immunopathology and Pathological Anatomy Laboratory (Laboratório de Citologia, Imunopatologia e Anatomia Patológica - CIPAC), Pathology Medical Diagnoses (Pathology Diagnósticos em Medicina) and Laboratório Beatriz Moreira Leite (Beatriz Moreira Leite Laboratory - BML Pathology).*
P Value: Chi-square significance test.

Table 4 shows the percentage of squamous cell carcinomas of skin and vermilion border according to the degree of involvement and histological type. The most frequently found histological type among primary skin and vermilion border squamous cell cancers was the well-differentiated, with 70% (n=1610) of cases, while the moderately differentiated reached 19.2% (n=443). The little differentiated histological type appeared in 4.5%(n= 105) of the studied cases and the "*in situ*" in 1% (n=141).

DISCUSSION

Frequency and Incidence rates

This study considered only histopathological exams with definitive diagnosis of skin and vermilion border squamous cell carcinomas, in a total of 4000 cases; therefore, the data are underestimated, resulting in rates lower than they actually are (review of populational data), although high when compared with the incidence rates found in Brazil.

In Brazil, INCA (National Cancer Institute) estimated around 62,680 cases of nonmelanoma cancers for 2012, that corresponds to an estimated risk of 65 cases/100,000 inhabitants/year for men and 71 for women, and 80 for men and 68 for women in the southern region.[8]

Our study shows that the gross incidence rate of squamous cell carcinomas in Blumenau increased from 31 to 108 cases per 100,000 inhabitants (300%) and the rate adjusted to the global standard increased from 50 to 110, much higher data than those predicted by INCA (Table 1).

In Tubarão, Santa Catarina, a study of 1437 histopathological reports found an incidence rate of squamous cell carcinoma that reached 136.7 cases per 100,000 inhabitants in 2009.[15]

In Australia, 138,000 cases of squamous cell carcinoma were found in 2008.[4]

In the United States, the squamous cell carcinoma ranked second as the most common skin cancer, with around 700,000 new cases diagnosed per year.[1,2]

The incidence of squamous cell carcinoma increased about 200% in the last 3 decades in the United States and approximately 2% of those affected die from this disease.[3]

Actinic keratosis is the most common precancerous dermatosis; it currently affects 58 million Americans and 65% of squamous cell carcinomas were previously diagnosed as actinic keratoses.[16,17]

Early diagnoses and treatment, mainly of precancerous skin lesions such as actinic keratoses, prevent their progression to squamous cell carcinoma, causing the incidence to decrease.

The treatment of actinic keratoses in dermatological outpatient clinics has decreased and/or maintained the incidence of skin and vermilion border squamous cell carcinomas in the city of Blumenau.

Sex

National and international literature shows that squamous cell cancer is more frequent in men than in women; in fact, it can even affect twice as many men as women.[1,2,18,19]

In the United Kingdom, in a study with 99,549 non-melanoma carcinomas cases, 56 % were found in male and 44% in female patients.[19,20]

In this study there were 2249 cases (56.2%) in male and 1751 cases (43.8%) in female patients, which is compatible with global and national literature.

In Germany we found, in a study covering the period between 1998 and 2001, the incidence of 1184 cases in men and 978 cases in women.[21]

Age group

The incidence of non-melanoma cancers increases significantly with age, especially skin and vermilion border squamous cell carcinomas.[1,2,3,4,12,22]

Squamous cell carcinomas of the skin and of the vermilion border reached alarming incidence rates for decades in the age group older than 60 years of age (Table 2).

The incidence by age group and by sex has been very high for decades in the age groups between 60

Table 4: Numerical and percentage distribution of squamous cell carcinoma, according to histological type and sex, from 1980 to 2011 om Blumenau – SC - Brazil

HISTOLOGICAL TYPE	M	F	TOTAL	P
WELL DIFFERENTIATED	844 (70%)	766 (70%)	1610 (70%)	0.9903
MODERATELY DIFFERENTIATED	255 (21.2%)	188 (17.2%)	443 (19.3%)	0.0157
LITTLE DIFFERENTIATED	68 (5.6%)	37 (3.4%)	105 (4.6%)	0.0095
IN SITU	38 (3.2%)	103 (9.4%)	141 (6.1%)	0.0001
TOTAL	**1205 (100%)**	**1094 (100%)**	**2299 (100%)**	

Source: *Brazilian Institute of Geography and Statistics (Instituto Brasileiro de Geografia e Estatística - IBGE), Citology, Immunopathology and Pathological Anatomy Laboratory (Laboratório de Citologia, Imunopatologia e Anatomia Patológica - CIPAC), Pathology Medical Diagnoses (Pathology Diagnósticos em Medicina) and Laboratório Beatriz Moreira Leite (Beatriz Moreira Leite Laboratory - BML Pathology).*
P Value: Chi-square significance test.

and 65 years of age and 70 and plus, reaching 1484 cases per 100,000 inhabitants in men older than 70 years of age and 975 in women of the same age group.

These numbers indicate the need for special attention to these age groups in the city of Blumenau.

The number of squamous cell carcinoma cases has also increased significantly in the population younger than 40 years of age.[12,22]

Primary location

Most of the squamous cell carcinomas of the skin and vermilion border were found in exposed areas: head, face and neck, confirming what was found in the global literature (Table 3).[1,2,3,,21,22]

Exposed areas in men show a much higher incidence than covered areas in women; for example, the incidence in men's ears is much higher than in women, due to an important epidemiological factor: hair length covering women's ears, that is, natural protection against ultraviolet radiation, the main causal factor in the origin of these tumors (Table 3).[12,22]

It is noteworthy that the squamous cell cancer is much more common in lips of men that in lips of women, probably connected with the smoking habit, which increases the risk for this type of skin cancer (Table 4).[21]

In the study carried out in Tubarão – SC, higher incidences were found of squamous cell carcinoma in ears and lips of men compared with women.[15]

Race

In the census of 2000, the ethnic composition of the city was 247,527 (94.55%) white, 9171 (3.5%) mixed, 3042 (1.16%) afro-descendants, 340 (0.13%) indians and 252 (0.10%) yellow.[14]

The studied population is therefore 94.5 % white, most of them German and Italian descendants with skin phototypes I and II, according to the classification of Fitzpatrick (Fitzpatrick's Color Atlas & Synopsis of Clinical Dermatology). The incidence of squamous cell carcinomas is much higher in the white race with skin phototypes I and II, or most of the inhabitants of the city of Blumenau .

Solar radiation

It is well known that ultraviolet radiation is a most important risk factor for the onset of squamous cell carcinoma, and chronic exposure to the sun since early childhood has great relevance in the etiology of this skin cancer.[2,4,6,10,11,12.]

The risk for development of squamous cell cancer is higher in whites, who never get tanned, have a tendency to get sunburned, have light hair and blue eyes.[2,4,6,10,11,12.]

The greater the UVB radiation, the higher the incidence of skin cancers; this radiation also depends on the ozone layer, which filters ultraviolet radiation.[23,24,25]

The white population of Blumenau, who are mainly German and Italian descendants with skin phototypes I and II, according to the classification of Fitzpatrick, is subject to intense radiation in the summer, when the UVB-Index is between 11.5 and 13.0, as per the National Institute of Space Research (Brazil) and very high according to the Environmental Protection Agency/Operational Satellites (EPA/NOOA) – United States, which makes this population subject to the main risk factors of non-melanoma carcinomas.[1,24]

Exposure to ultraviolet radiation-A, found in tanning salons, has been associated by epidemiological studies with the onset of skin cancers in its users and is therefore forbidden in Brazil.[8]

The high incidence of squamous-cell carcinomas found in Blumenau has as important risk factors the high degree of ultraviolet radiation in that region (UVB-Index between 11.5 and 13 in summer) and the white population (94.5%), descendants of Germans and Italians from the north of Italy.

CONCLUSIONS

In a sample with 4000 cases of primary squamous-cell cancers of the skin and vermilion border diagnosed in a period of 31 years and with morbidity coefficients determined every year, we may verify:

Increase of morbidity coefficients by 300% between 1980 and 2011.

Relevant prevalence of the male sex.

The greater incidence was among those older than 60 years of age and absence among those under 18 years of age.

High incidence rates above 70 years of age, reaching 1484 cases/100,000 inhabitants – the highest rate ever registered in epidemiological studies in Brazil.

Predominant primary location on exposed areas.

The skin and vermilion border squamous-cell cancers with well-differentiated degree of involvement were the most often found.

According to the data found in this study, we conclude that the population of Blumenau, mostly white, with skin phototypes I and II, exposed to intense solar radiation is at a great risk of developing squamous-cell cancer.

These tumors constitute a public health hazard in the city of Blumenau. We suggest several actions in the Sanitary Education field for prevention, early diagnosis and treatment of the disease, increasing resolution and preventing more advanced cases that may metastasize.

Increased early diagnosis and treatment of actinic keratosis as well as education and prevention campaigns are the objectives of the dermatologists in the city of Blumenau to obtain control of this neoplasm. ❑

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