

Basal cell Carcinoma - Analysis of 300 cases observed in Uberlândia - MG, Brazil*

*Carcinoma basocelular - Análise de 300 casos observados em Uberlândia - MG**

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Abstract: BACKGROUND - Basal cell Carcinoma is the most common type of skin cancer and represents 75% of malignant epithelial tumors. It usually occurs on the face of white individuals aged over 40 years, with history of repetitive exposure to sunlight.

OBJECTIVE - To describe the epidemiological data, clinical presentation and histopathological findings of 300 patients with basal cell carcinoma.

CASUISTIC - A cross-sectional study of 300 patients with Basal cell Carcinoma seen at the outpatient Dermatology clinic from 1999 to 2003. Information was obtained on identification, exposure to sunlight and characterization of Basal cell Carcinoma.

RESULTS - The pathological examinations confirmed the clinical diagnoses of 447 tumor lesions of 300 patients. Most patients were female (59.3%), white (93%), had exposure to sunlight (90.3%), with a single lesion (74%), involving predominantly the face (77% of the lesions). The most frequent pathological type was nodular carcinoma (46.3% of the lesions) and the superficial type predominated on the trunk.

CONCLUSION - There was a predominance of female patients showing the current tendency of Basal cell Carcinoma. The presence of several successive or simultaneous tumors in the same patient emphasizes the importance of periodical exams in these patients. No exact correlation between exact clinical and pathological findings was established. The superficial type was confirmed as more frequent on the trunk.

Keywords: Basal cell Carcinoma; Epidemiology; Skin neoplasms

Resumo: FUNDAMENTO – O carcinoma basocelular é o câncer da pele mais comum, compreendendo 75% dos tumores epiteliais malignos. Localiza-se na face e acomete indivíduos brancos, acima de 40 anos de idade, com história de exposição repetitiva à luz solar.

OBJETIVO – Descrever o carcinoma basocelular em suas variáveis epidemiológica, clínica e histopatológica.

CASUÍSTICA – Realizou-se estudo transversal de 300 pacientes com carcinoma basocelular atendidos no Serviço de Dermatologia do Hospital de Clínicas, no período de 1999 a 2003. Foram preenchidos protocolos com identificação do paciente, história de exposição solar e caracterização do carcinoma basocelular.

RESULTADOS – Foram identificadas 447 lesões de carcinoma basocelular nos 300 pacientes estudados, cuja maioria era do sexo feminino (59,3%) e da raça branca (93%), com história de exposição solar (90,3%), apresentando lesão única (74%), predominantemente facial (77% das lesões). O tipo histopatológico mais frequente foi o nodular (46,3% das lesões), com predomínio do superficial no tronco.

CONCLUSÕES – Observou-se predomínio do carcinoma basocelular no sexo feminino, demonstrando a tendência atual desse tumor. A presença de vários tumores sucessivos ou simultâneos em um mesmo paciente salienta a importância de exames periódicos nesses doentes. Não se estabeleceu correlação entre os tipos clínicos e histopatológicos. Confirmou-se que o tipo superficial é mais frequente no tronco.

Palavras-chave: Carcinoma basocelular; Epidemiologia; Neoplasias cutâneas

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Conflict of interest: None

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INTRODUCTION

Skin neoplasms have become more relevant in the last decades due to its increasing incidence. Basal cell carcinoma (BCC) stands out among them because it accounts for about 75% of total malignant skin tumors.¹ BCC usually affects the face.²⁻⁸ of male patients, mainly fair-skinned and aged over 40 years, with history of chronic sun exposure. In addition to its increased incidence,^{2,9-11} BCC has changed over the last years affecting sun-protected sites¹² and greater likelihood to affect women.¹¹

BCC originates from the basal cells of the epidermis and the follicular gland. It is considered a low malignancy-grade tumor, able to present local invasion, tissue destruction and recurrences, and has limited power to metastasize. The mortality rate is low due to early diagnosis of lesions on exposed areas and slow growth of lesions.

The role played by sun exposure as a risk factor for BCC is extremely clear.^{2,4,7,9,13-15} The action of ultraviolet B light results in several mutagenic photoproducts in the DNA, which need to be repaired before cell division;⁷ otherwise, it can lead to the mutation of the PTC gene, which induces the development of BCC.¹⁶⁻¹⁷

This study contributes to the BCC research since it is extremely important and there are scarce studies published with statistical analysis. Its goal is to present a prospective study of patients with BCC, with the statistical analyses of the epidemiological, clinical and pathological variables.

O presente estudo tem como objetivo a realização de uma análise prospectiva dos casos de CBC com resultados estatísticos de suas variáveis epidemiológica, clínica e histopatológica.

METHODS

A prospective cross-sectional observational study of 300 patients with BCC seen at the Dermatology Clinic of the *Hospital de Clínicas – HC* [Teaching Hospital] of the *Universidade Federal de Uberlândia*, from March 1999 to July 2003.

The protocol included the following data: patient's identification (name, age, gender, skin color according to Fitzpatrick skin type classification,¹⁸ place of birth, origin, occupation, marital status), sun exposure habits and characterization of the BCC (onset, size, localization, clinical and pathological types).

Clinically, BCC was classified¹⁹ as papular-nodular, nodular-ulcerative, superficial, ulcer terebrans, vegetative, pigmented, sclerodermiform, scar-like and cystic. In order to make comparative analysis easier, the several clinical types were classified in four main types: nodular-ulcerative (papular-

nodular, nodular-ulcerative, vegetative, ulcer terebrans and cystic), pigmented, fibrosing (scar-like and sclerodermiform) and superficial.²⁰ The presumptive diagnosis of BCC was confirmed via biopsy or tumor exeresis, with later description of the pathological types observed in the specimens, which was performed by the Pathological Anatomy Service of the *Hospital de Clínicas*, in accordance with Kirkham²⁰ and Rippey,²¹ classifications. The presence of 447 BCC was confirmed in the 300 patients studied.

Since the objective of this study was to analyze epidemiological data and the clinical and pathological presentations of primary BCC in patients seen at the *Hospital de Clínicas*, lesions of recurrent BCC, tumors related to other diseases (basal cell nevus syndrome, xeroderma pigmentosum and albinism) and certain risk factors for skin cancer (chronic radiodermatitis, chronic ulcers, immunosuppression, and chronic arsenicism) were excluded.

Statistics

Tables, percentages, chi-square test (χ^2), sign test (Z), Mann-Whitney U test (U) and Pearson correlation (r) were used for statistical studies. $P \geq 0.05$ was considered significant.

RESULTS

Patient's age ranged from 30 to 88 years, mean age of 64.2 years (64.8 for men and 63.7 for women). The age group mostly affected ranged from 70-79 years (86 patients; 28.7%), followed by groups of 50-59 years (64 patients; 21.3%), 60-69 years (63 patients; 21%), 40-49 years (39 patients; 13%), 80-89 years (37 patients; 12.3%) and 30-39 years (11 patients; 3.7%).

Out of the 300 patients, 178 (59.3%) were women, and 122 (40.7%) were men attaining a statistically significant ratio of 1.4:1 ($\chi^2 = 10.453$; $p < 0.01$).

Correlation between gender and age group was not statistically significant ($\chi^2 = 3.87$; $p = 0.5682$), that these variables are independent.

Most patients, that is, 279 (93%) had fair-skin (phototypes I, II and III), followed by 18 (6%) with brown skin (phototypes IV and V) and 3 (1%) with black skin (phototype VI).

It was observed that 225 (75%) patients came from the city where the study took place, whereas 75 (25%) came from other cities.

Urban origin was mentioned by 88% of the sample, and only 12% came from rural areas. However, it was observed that 63.7% of them had lived or worked in rural areas at some point of their lives.

Their occupations were quite diverse, and the most common were: housewife (29.6%), agricultural worker (16.9%), housewife/female agricultural worker (13.3%), salesperson (5%), merchant (3.6%), bricklayer (3.3%), driver (2.6%) and seamstress (2.3%).

Out of the 300 patients with BCC, 271 (90.3%) declared high level of sun exposure throughout their lives, mainly related to daily working activities.

Mean duration of lesions, from the time they emerged to diagnosis was 37.1 months – 36.3 months for men, with standard deviation (SD) of 54.6 and 37.7 months for women, with SD of 52.6 months. The differences between these mean periods of duration of lesions in both genders were not statistically significant ($U = 10182.5$; $p = 0.4203$).

Mean tumor area was 4.3 mm², 5.7 mm² in men, SD:12.8 and 2.9 mm² in women, SD: 5.6. The difference between the mean areas of both genders was significant (Mann-Whitney U test; $p < 0.05$).

When the size of the lesions was related to time of diagnosis via Pearson's test, no association trend between these variables was found, which can be confirmed by the small correlation between these figures ($r = 0.23$; $p > 0.05$).

The diagnosis of the total number of tumor lesions was made in the first visit of the patient or within the four years of this study. Four hundred, forty-seven BCC lesions were found in the 300 patients studied; the number of tumors per patient ranged from one (74% of patients) to eight. There was no statistically significant difference between genders regarding the number of patients and lesions ($\chi^2 = 1.026$; $p = 0.311$ and $\chi^2 = 3.19$; $p = 0.074$, respectively). Mean number of lesions per patient was 1.5; the difference between the mean number of tumors in both genders was not statistically significant ($Z = 1.102$; $p = 0.2585$).

The tumor lesions were found in the head (344 lesions; 77%), trunk (53 lesions; 11.8%), limbs

(34 lesions; 7.6%) and cervical area (16 lesions; 3.6%). Most lesions were found in the head ($\chi^2 = 649.7$; $p < 0.01$) and site of the lesion and sex were correlated ($p < 0.05$) – in women, the most affected site was the head; in men, the trunk and cervical areas.

The frequency of tumor lesions in the head was distributed as follows: nasal (26%); malar/zygomatic (18.1%), frontal (10.1%), auricular (8.5%), buccinator muscle (5.8%), orbit (4.7%), scalp (2.5%) and mandibular areas (1.3%). The chi-square test demonstrated significant dependence ($\chi^2 = 16.39$; $p < 0.05$) between variables localization of the lesion in the head and gender.

The most common type of BCC was the nodular-ulcerative, 297 lesions (66.5%; $\chi^2=406.55$; $p < 0.01$), followed by pigmented, 61 lesions (13.6%); fibrosing, 56 lesions (12.5%) and superficial, 33 lesions (7.4%).

The clinical types of BCC were distributed according to the body region affected (Table 1); this distribution was not related to the tumor site ($\chi^2 = 9.55$; $p = 0.374$).

The pathological types of BCC were initially distributed based on Kirkham²¹ classification, and the rates found were: solid (39.8%), mixed (37.1%), fibrosing (8.7%), superficial (7.8%), adenoid (5.1%), cystic (0.7%), keratotic (0.2%), basal-squamous (0.2%) and clear cells (0.2%). The mixed type presents, in the same case, two or more histological patterns (for example, solid and adenoid), with no predominance of one type over the other. The statistical analysis of pathological type and gender showed no significant correlation ($\chi^2 = 4.52$; $p = 0.2104$).

Ripley's short proposal,²⁰ was used to compare our data to that found in the literature and the pathological types were classified in nodular (46.3%); mixed (37.1%), infiltrating including sclerodermiform (8.7%) and superficial (7.8%). Differences between the pathological types were statistically significant χ^2

TABLE 1: Distribution of clinical type of tumors by affected region

Region	CLINICAL TYPE							
	Nodular-ulcerative		Pigmented		Fibrosing		Superficial	
	N	% (447)	N	% (447)	N	% (447)	N	% (447)
Head	227	50.8	50	11.2	45	10	22	4.9
Trunk	36	8.1	5	1.1	4	0.9	8	1.8
Limbs	24	5.4	5	1.1	4	0.9	1	0.2
Cervical	10	2.2	1	0.2	3	0.7	2	0.4
Total	297	66.5	61	13.6	56	12.5	33	7.4

Independence result: ($\chi^2 = 9.55$; $p = 0.374$)

TABLE 2: Distribution of clinical type of tumors by pathological types (Rippey, 1998)

Pathological type	CLINICAL TYPE							
	Nodular-ulcerative		Pigmented		Fibrosing		Superficial	
	N	% (447)	N	% (447)	N	% (447)	N	% (447)
Nodular	146	32.7	28	6.3	19	4.3	14	3.2
Mixed	111	24.8	20	4.5	25	5.6	10	2.2
Infiltrative	26	5.8	3	0.7	7	1.6	3	0.7
Superficial	14	3.2	10	2.2	5	1.1	6	1.3
Total	297	66.5	61	13.6	56	12.5	33	7.4

Independence result: ($\chi^2 = 19.93$; $p < 0.05$)

= 206.88; $p < 0.01$).

Clinical and pathological types were correlated (Table 2). The distribution of a certain pathological type was not the same for all clinical types ($\chi^2 = 19.93$; $p < 0.05$).

Pathological findings and site affected were correlated (Table 3), which revealed close dependence ($\chi^2 = 24.1397$; $p < 0.01$). Nodular type was mostly found in the cervical region (62.5%), affecting the head in 47.3%, the trunk in 39.6%, and the limbs in 35.3% of patients. The superficial type was highly common in the trunk (20.7%).

DISCUSSION

Patient's age ranged from 30 to 88 years, mean age of 64.2 years, in accordance to data found by other authors.^{1,3-6,11,14-17,19,21,22} The age group mostly affected by BCC was 70-79 years, similar to the findings of Bastiaens et al.³ The increasing incidence of BCC in young individuals has been emphasized;^{8,11} however, the mean age is still high, probably because of the cumulative action of ultraviolet light throughout life and of reduction of the ozone layer.^{4,7,8}

In this study, BCC affected mostly women. This finding could be at least partially explained by the fact

that the female population represents the target audience for several educational campaigns against cancer, making women more aware and careful about their own bodies.

According to the literature, most authors observed higher incidence of BCC in men.^{2,3,5,9,22,23} Prado,¹⁴ Machado Filho et al.¹³ and Maffs et al.⁵ it prevalent in women whereas Dahl et al. (1992)²⁴ and Betti et al. (1995)¹² reported similar frequency in both genders. Recent studies have demonstrated discreet trend toward women.¹¹

In this study, BCC was more common in patients with skin types I, II and III,¹⁸ in accordance with other authors, due to the proved susceptibility of these phototypes to UV radiation.^{10,13,15,23}

Most patients were from urban areas, although most of them have history of having lived or worked in rural areas for a certain period of their lives. Prado¹⁴ reported higher incidence of BCC in patients in the rural area. Machado Filho et al.¹³ mentioned the urban origin of all patients.

Out of the total number of patients studied, 90.3% reported sun exposure throughout their lives, mainly related to daily work activities. One hundred, thirty-one women (43.7%) mentioned frequent sun exposure without adequate protection

TABLE 3: Distribuição dos tipos histopatológicos (Rippey, 1998) de acordo com a localização

Site	PATHOLOGICAL TYPE							
	Nodular		Mixed		Infiltrative		Superficial	
	N	% (447)	N	% (447)	N	% (447)	N	% (447)
Head	164	36.7	131	29.4	27	6.3	22	4.9
Trunk	21	4.7	17	3.8	4	0.9	11	2.5
Limbs	12	2.7	16	3.6	5	1.1	0	-
Cervical	10	2.2	2	0.4	2	0.4	2	0.4
Total	207	46.3	166	37.2	39	8.7	35	7.8

Independence result: ($\chi^2 = 24.1397$; $p < 0.01$)

while they performed household tasks. Analysis of their occupations showed that 68.1% were subject to repeated and/or prolonged exposure to UV light. Some authors also consider prolonged and continuous sun exposure, related or not to occupational activities, responsible for the high incidence of BCC.^{3,8,10,11,23} Contrary to this theory, English et al.¹⁵ did not observe any correlation between BCC and daily sun exposure for working-related activities, differently from what happens with squamous cell carcinoma. According to these authors, rural workers subject to sustained sun exposure protected themselves wearing clothes and hats whereas those under intermittent sun exposure, for instance, on weekends, spent more time under the sun and did not wear adequate clothing, running the risk of presenting sunburns.

Mean duration of lesions, from its onset to diagnosis was 37.1 months for both genders, in accordance to the general idea that BCC is a slow-growing tumor.

The area of tumor lesions ranged from one to 240 mm². The mean general area was 4.3 mm², significantly higher in men than in women, probably because women seek medical advice faster.

The literature shows mean tumor area ranging from 1.7 to 3.9 m².^{5,9} As mentioned by Holme et al.,²⁵ the reduced size of the tumor is due to the early sought of medical advice and appropriate education of healthcare professionals to identify the initial lesions.

This study did not show any correlation between to progression time and area of tumor lesions. Bandeira et al.¹¹ reported slow growth of BCC in the first two years, with no relationship between size and progression time.

As to number of tumors diagnosed per patient, 26% of sample presented multiple lesions, mean of 1.5 lesions per individual. The presence of more than one lesion showed no correlation with gender; however, it suggests that it is related to environmental factors and or genetic predisposition. The literature studied showed general mean of 1.3 to 1.7 tumors per patient, and the percentage of patients with more than one lesion ranged from 6.6 to 32%.^{2,5,9} The accumulated likelihood that a patient with previous diagnosis of BCC presents with another type of BCC is 44%, that is, 10-fold higher than in the general population.²⁶

In this study, most BCC lesions affected the head ($p < 0.01$), being the face responsible for 66% of lesions; the nasal area was affected in 39.3% of the face lesions and in 26% of total body lesions. These results probably reflect the areas receiving greater intensity of sun radiations. The literature reveals that

the BCC frequency is higher in the face (27.5% to 91.1%),^{6,14,23} in the face and in the neck (30.9% to 80%)^{2,7,24} and in the nasal region (30.1% to 35.9%).^{14,23}

Men and women of this study had more lesions in the face, but when the segment affected and the gender were compared, it was observed that BCC affected mostly the trunk, the cervical region and the pinna in men. These findings are probably related to the fact that working men usually have those areas exposed.^{9,27}

The most common type of BCC found in this study was the nodular-ulcerative (66.5%), in accordance to the findings of other authors (53.4% to 70.6%).^{2,27}

A correlation study between the clinical type and the site of the tumors was conducted and it revealed that the head was the most affected area for all clinical types, and the nodular-ulcerative type was the most common. However, statistical analyses demonstrated that the distribution of clinical type is independent of tumor site.

The pathological examinations of this study showed that, based on the general Kirkham,²¹ classification, there was a predominance of the solid type (39.6%) and on Rippey,²⁰ resumed classification, the nodular type (46.1%), in agreement with other studies published in the literature, which show higher incidence of the solid (27.4 to 69.1%) and nodular (40 to 63.8%) types.^{9,11,12,20,27}

No difference between genders was observed for a specific pathological type. Scrivener et al.²⁸ showed that the superficial and fibrosing types were most common in women than in men.

In this study, the correlation between clinical and pathological types of tumor showed partial correlation between clinical and pathological data. Clinical hypothesis was correct in 49.1% for nodular-ulcerative cases and in 18.1% for superficial cases. Rassner et al.²⁹ found no close correlation between clinical morphology and pathological findings of BCC. On the other hand, Kopke & Schmidt³⁰ considered important to characterize the tumor lesion as circumscribed or diffuse, both clinically and pathologically, in order to establish a clinical-surgical prognosis.

The mixed type, in which two or more pathological patterns are found in the same lesion, without prevalence of one over the other, was the second most common type found in this study. Kopke & Schmidt³⁰ emphasized that distinct pathological patterns are commonly observed in the same BCC lesion.

High frequency of the superficial type in the trunk (20.7%), as mentioned in other studies,^{3,27,28} was found when pathological types were related to the sites affected.

CONCLUSIONS

This study confirmed that BCC affects more fair-skinned patients in the age group of 70-79 years, probably due to cumulative effect of sun radiation throughout a long period of sun exposure since the their occupations exposed them to sunlight.

The highest number of BCC cases and the smallest mean tumoral area were found in females. These facts have not been explained yet, but they can be partially explained by the higher level of awareness among women, who seek early medical advice.

The presence of more than one tumor lesion in the same patient was a common finding, justifying the periodic evaluation of individuals with history of BCC.

The head was commonly affected, mainly the nasal dorsum, probably because of higher exposure to sunlight. Male patients were mostly affected in the trunk, cervical region and pinna, probably because these areas are usually exposed when men are working or during their leisure time and because they have short hair.

Clinical and pathological types varied, but the nodular-ulcerative and the nodular types were the most common. There was no correlation between the clinical type and site affected, and with the pathological type. The superficial pathological type affects mainly the trunk.

Further studies with larger samples, should be carried out in order to provide better epidemiological and pathological evaluation of basal cell carcinoma. □

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