Epidemiological and histopathological profile of cutaneous melanoma at a center in northeastern Brazil from 2000 to 2010*

Perfil epidemiológico e histopatológico do melanoma cutâneo em um centro do nordeste brasileiro de 2000 a 2010

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Abstract: BACKGROUND: While representing only 3-4% of malignant skin tumors, cutaneous melanoma is the most aggressive and lethal. Statistical knowledge about the biological behavior of this tumor is essential for guiding daily outpatient practice and aiding public health policies.
OBJECTIVES: To analyze the profile of patients with cutaneous melanoma attending a pathology department in Teresina (state of Piauí) between 2000 and 2010.
METHODS: Retrospective study of melanoma patients diagnosed between 2000 and 2010 in the São Marcos Hospital in the city of Teresina. The pathology laboratory reports were studied and all the statistical analyses performed using SPSS 19.0.
RESULTS: A total of 25 in situ, 199 invasive and 89 metastatic melanomas of unknown primary site were observed. Histological types found were nodular (52.8%), superficial spreading melanoma (18.6%), acral (10.6%) and lentigo maligna (9.5%). In 144 (73.4%) cases the Breslow thickness was >1 mm. Metastasis was found in 28.6% of invasive melanomas and nodular melanoma, Clark IV/ V, Breslow > 1 mm, mitotic index ≥ 6 and ulcerated lesions were more likely to metastasize.
CONCLUSION: Most melanomas presented Breslow> 1mm. The main factors associated with metastasis were nodular type, Clark IV / V, Breslow> 1mm, mitotic index ≥ 6 and ulcerated lesions.
Keywords: Epidemiology; Melanoma; Neoplasm metastasis; Neoplasms, unknown primary; Skin neoplasms

Resumo: FUNDAMENTOS: Apesar de representar apenas 3-4% dos tumores malignos de pele, o melanoma cutâneo é o mais agressivo e letal deles. O conhecimento estatístico do comportamento biológico deste tumor em nosso meio ambiente é fundamental para orientar a prática ambulatorial diária e para auxiliar políticas de saúde pública.
OBJETIVOS: Analisar o perfil de pacientes com melanoma cutâneo diagnosticados em serviço de referência em patologia em Teresina-Piauí no período de 2000 a 2010.
MÉTODOS: Estudo retrospectivo de pacientes com melanoma diagnosticados entre 2000 e 2010 no Hospital São Marcos, Teresina-Piauí-Brasil. Estudou-se laudos histopatológicos e realizou-se análises estatísticas com o programa SPSS 19,0.
RESULTADOS: Um total de 25 melanomas in situ, 199 invasivos e 89 metastáticos de sítio primário desconhecido foram observados. Tipos histológicos encontrados foram nodular (52,8%), melanoma extensivo superficial (18,6%), acral (10,6%) e lentigo maligno (9,5%). Em 144 (73,4%) casos o índice de Breslow foi >1 mm. Verificou-se metástases em 28,6% dos melanomas invasivos e melanoma nodular, Clark IV/V, Breslow >1 mm, índice mitótico ≥6 e lesões ulceradas estavam mais propensos a metástases.
CONCLUSÃO: Melanomas com Breslow >1mm foram os casos predominantes. Principais fatores associados a metástase foram tipo nodular, Clark IV/V, Breslow >1mm, índice mitótico ≥6 e lesões ulceradas.
Palavras-chave: Epidemiologia; Melanoma; Metástase neoplásica; Neoplasias cutâneas; Neoplasias primárias desconhecidas

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INTRODUCTION

Cutaneous melanoma (CM) is an uncommon but often aggressive form of skin cancer owing to its significant morbidity and high mortality rates. Although it accounts for less than 5% of all skin cancers, most deaths related to skin cancer are from melanoma.[1] The incidence of melanoma is increasing rapidly. Brazil´s National Cancer Institute (INCA), estimates that approximately 6,230 new cases of melanoma can be expected in 2012. Around 1392 people died of the disease in Brazil in 2009.[2]

Since all the therapies normally used in advanced cases, such as chemotherapy, radiotherapy, biochemical therapy and vaccines, seem to be incapable of providing cures or improving survival rates, early diagnosis and therapy remain the main key to managing melanoma.[3,4] A diagnosis of melanoma should be suspected in all melanocytic lesions presenting changes in color, size or shape. The presence of asymmetry of the lesion, irregular borders, colour variation and with a diameter over 6 mm are the ABCD diagnosis of melanoma and are indicative of biopsy for diagnostic confirmation.[5]

The exact process that leads to the malignant transformation of melanocytes remains uncertain, but among the possible etiological factors solar radiation, particularly ultraviolet light (UV), is one of the more likely factors. It is believed that UV radiation can cause direct damage to the DNA.[1] Since Teresina is a city located at latitude 5º south and 73% of its population refer sun exposure without protection, skin cancer is without any doubt a public health problem in our city.[6]

In south and southeast Brazil, with the highest estimated melanoma rates, epidemiological studies on this neoplasm are now more common.[1-5,7-19] Epidemiological data on the prevalence and clinical features of melanoma nevertheless are in short supply in the northeast of the country. Considering the size of our country and the ethnic characteristics of the Brazilian population, these types of studies are important for better understanding the characteristics and behavior of this disease. Such an approach could facilitate medical initiatives aimed at identifying cases, as well as boosting relevant campaigns to draw attention to the disease of the healthcare community and the population in general.[11,14]

The aim of present study was to analyze the epidemiological and histopathological data of patients with cutaneous melanoma attending a reference pathology department service in Teresina from 2000 to 2010 and to present statistical data that could be useful as a basis for epidemiological studies and disease prevention in northeast Brazil. A further aim was to identify the histopathological factors associated with melanoma metastasis.

METHODS

A retrospective study was conducted of all patients who had had a histopathologic diagnosis of melanoma in a pathology reference laboratory located in Teresina (Piauí), Brazil, between January 2000 and December 2010.

The sample was non-probabilistic (convenience sample), comprising all patients with a histopathologic diagnosis of melanoma during the period under study. Cutaneous melanoma located in the mucosa or eyes, slides review, residual melanomas and relapse melanomas were excluded. A total of 313 cases of metastatic or primary cutaneous melanoma were assessed.

Data collected in protocol by the authors included patient characteristics (age, sex, origin, tumor location) and melanoma morphology (histological type, stage of invasion using Clark level and Breslow thickness, radial growth phase, vertical growth phase, Mitotic index, tumor-infiltrating lymphocytes, regression, ulceration) and surgical outcomes (clear surgical margins, analysis of sentinel lymph node and metastasis). Each slide from the 11-year period was evaluated by one of four pathologists from our dermatology service. To classify the subtype of melanoma, we used by World Health Organization criteria.[20]

The statistical analyses were performed using SPSS for Windows, 19.0 (SPSS, Inc., Chicago, Illinois). Descriptive statistics were reported for all variables. The correlation between the categorical variables were studied with the Pearson chi-square test or Fisher's exact test. All statistical tests were 2-sided, and we considered a *P* value of less than 0.05 to be statistically significant. Differences between means for continuous variables were evaluated by one-way analysis of variance (ANOVA) test.

A logistic regression was also performed using as a dependent variable the presence of metastases, and as independent variables gender, age group, site, histological type, Breslow thickness, Clark level, tumor-infiltrating lymphocytes, mitotic index, ulceration and histopathological regression. As association measure we used Odds Ratio (OR), considering a confidence interval of 95% (95 CI).

This project was approved by the Research Ethics Committee of the São Marcos Hospital, in accordance with National Health Council Resolution Nº 196/96 guidelines.

RESULTS

A total of 313 patients were included in the analysis: 25 (7.9%) were *in situ* cutaneous melanoma (CM), 199 (63.6%) were invasive CM and 89 (28.4%) were metastatic CM. Concerning histological type in the invasive group, nodular melanoma was found in 105

cases (52.8%), superficial spreading melanoma in 37 cases (18.6%), acral-lentiginous melanoma in 21 cases (10.6%) and lentigo maligna melanoma in 19 cases (9.5%). Other types of CM were found in 5 cases (2.5%) (Table 1). Graph 1 shows the distribution of cases according to histological type per year.

The invasive CM group comprised 101 (50.8%) women and 97 (48.7%) men, a ratio of 1.04 women to men. Mean age was 70.1 ± 16.3 years. The majority of the patients were aged over 50 (n = 167, 83.9%) and lived in rural areas of Piauí (n = 79, 39.7%) (Table 1).

With regard to the topography of lesions, these were located on the upper limbs (n = 22, 11.1%), lower limbs (n = 67, 33.7%), trunk (n = 62, 31.2%) and head and neck (n = 40, 20.1%) (Table 1). The women predominantly presented tumors on the trunk (28.7%), lower limbs (27.7%) and head/neck (25.7%) while the men had tumors mainly on their lower limbs (40.2%) and trunk (34.0%). These differences were statistically significant (p = 0.038) (Table 1).

A total of 72.4% had a Breslow thickness of over 1 mm. The men presented more cases with a higher Breslow thickness (78.4% versus 67.3% of women) and this difference was statistically significant (p = 0.045) (Table 1). The mean thickness of the primary tumors was 8.8 mm (95 CI = 7.3-10.5). Nodular melanoma had the highest mean Breslow thickness (12.2 mm; 95 CI = 9.7-14.8), followed by acral-lentiginous (8.9 mm; 95 CI = 6.2-11.8)), lentigo maligna (2.7 mm; 95 CI = 0.4-6.9) and superficial spreading (1.4 mm; 95 CI = 1.0-1.8). This difference of the average Breslow thickness was statistically significant with p <0.0001 (one-way ANOVA) (Graph 2).

Among the patients identified with nodular melanoma, the mean age was 71.3 years and the majority was Clark IV (46.3%) or Clark V (33.7%). Regarding acral lentiginous melanoma, the mean age was 76.1 years and the Clark V was predominant (52.4%). Of those who had lentigo maligna melanoma, the mean age was 65.1 years and the Clark level predominant was II (76.5%). The superficial spreading melanoma group had a mean age of 65.3 years and 48.6% were Clark III.

Of the total sample of invasive CM, there was a predominance of cases with Clark IV (n = 65, 32.7%) and V (n = 52, 26.1%) levels (Table 1). Tumor-infiltrating lymphocytes, ulceration and histopathological regression were found in 76.9%, 54.8% and 17.1% of the invasive tumors respectively. The mitotic index was ≥ 6 mitoses/HPF (high-power field) in 37.2%. This value was statistically significantly higher (p = 0.011) in men (n = 45, 46.4%) than in women (n = 29, 28.7%) (Table 1).

Sentinel lymph node biopsy was performed in 19 cases (9.5% of invasive melanomas). In 9 of these (47.4%), frozen section examination was undertaken, showing compromised lymph nodes by neoplasia in 4 cases (44.4%). The result of the histopathological study revealed 13 cases (68.4%) free of cancer. There was no discrepancy between the results of the frozen section procedures and histopathology.

Metastasis was observed in 28.6% (n = 57) of the patients with invasive CM (Table 2). Considering these 57 cases and 89 cases of metastatic melanoma (a total of 146), the main sites of regional and distant metastases were lymph nodes (78.1%), skin and subcutaneous areas (22.6%), lung (6.8%) and liver (4.8%) (Table 3).

As shown in table 2, nodular melanoma (OR = 4.88; 95 CI =1.61-14.8), Clark IV (OR = 4.12, 95 CI = 1.29-13.15), Clark V (OR = 5.79, 95 CI = 1.77-18.89), Breslow > 1 mm (OR = 11.1, 95 CI = 2.57-47.91), mitotic index ≥ 6 (OR = 2.57, 95 CI = 1.33-4.98) and ulcerated lesions (OR = 2.41, 95 CI = 1.21-4.79) were more likely to metastasize.

DISCUSSION

Cutaneous melanoma (CM) is a serious threat to public health, and early diagnosis currently remains the "best therapy" for this type of skin cancer. Unlike in the United States where, according to the Surveillance, Epidemiology and End Results (SEER) Program, the incidence of *in situ* CM has increased over the past 30 years due to increased attention paid by physicians and the general population to the early diagnosis of CM, we observed a low rate of *in situ* CM (7.9%) in our study.[21] This rate was also lower than that found in other surveys performed in south and southeast Brazil, in which *in situ* diagnosis is as high as 39% (Table 4).[1,3-5,7-19]

Brazilian studies tend to disagree regarding the predominant histological CM type. Although superficial spreading melanoma is the main diagnosed histological CM type in the majority of studies,[1,3-5,7,8,13,16,19] we found that majority of cases involved nodular melanoma (52.8%), as shown in Porto Alegre (RS)[10] and São Paulo (SP)[9] in the 1980s (36.6% and 19.8% respectively) and Londrina (PR)[11] and Brasília (DF)[14] in the 1990s (41.1% and 45.0% respectively).

The predominance of nodular melanoma is alarming, since the nodular and acral lentiginous histological types are generally associated with a worse prognosis - and consequently a greater Breslow thickness.[22] We were able to identify nodular melanoma (12.18 mm) and acral-lentiginous (8.95 mm) with a higher Breslow thickness mean than lentigo maligna (2.74 mm) and superficial spreading (1.37 mm) (Graphic 2). In their evaluation of 496 cases Weber et al. also observed a statistically significant difference between histological types lentigo maligna melanoma and superficial spreading melanoma (mean 1.829 mm) and nodular and acral types (mean 5.035 mm).[1]

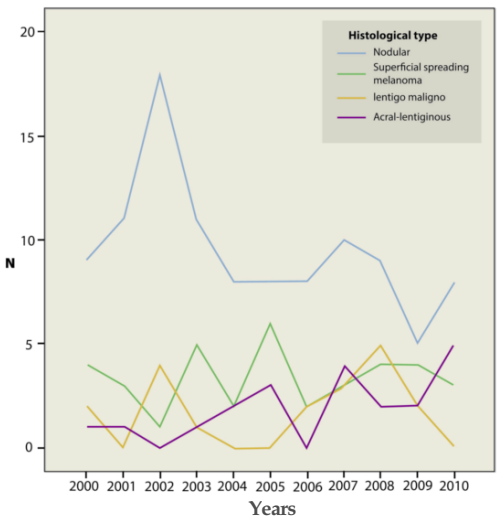
In the analysis of these results it is important to keep in mind that these data refer to a pathology reference laboratory in a tertiary care hospital, where cases

Table 1: Distribution and features of 199 invasive cutaneous melanomas, according to gender, diagnosed in a Pathology reference service in Teresina (Piauí), 2000-2010

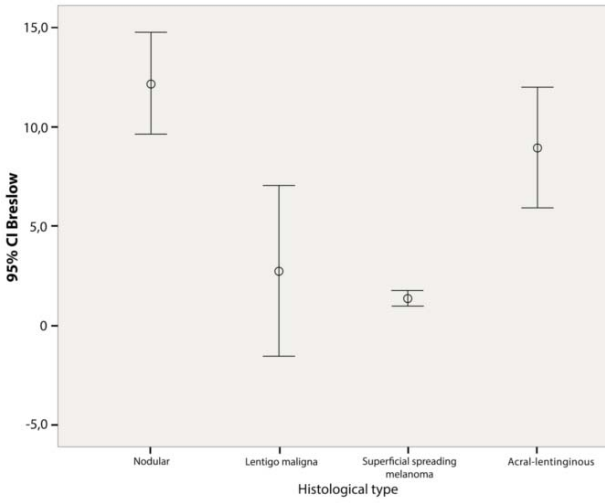
Category	Gender						p**
	Male		Female		Total		
	n	%	n	%	n	%	
Total	**97**	**48.7**	**101**	**50.8**	**199***	**100.0**	
Age Group (years)							0.400
≤ 50	12	12.4	10	9.9	22	11.1	
> 50	82	84.5	85	84.2	167	83.9	
Missing	3	3.1	6	5.9	10	5.0	
Origin							0.381
Teresina	28	28.9	31	30.7	59	29.6	
Rural area of Piauí	42	43.3	37	36.6	79	39.7	
Other state	23	23.7	33	32.7	56	28.1	
Missing	4	4.1	0	0.0	5	2.5	
Site							0.038
Head and neck	14	14.4	26	25.7	40	20.1	
Trunk	33	34.0	29	28.7	62	31.2	
Upper Limbs	7	7.2	15	14.9	22	11.1	
Lower Limbs	39	40.2	28	27.7	67	33.7	
Missing	4	4.1	3	2.9	8	4.0	
Histological Type							0.678
Nodular	55	56.7	50	49.5	105	52.8	
Lentigo maligna	10	10.3	9	8.9	19	9.5	
Superficial spreading	15	15.5	22	21.8	37	18.6	
Acral lentiginous	10	10.3	11	10.9	21	10.6	
Other	3	3.1	2	2.0	5	2.5	
Missing	4	4.1	7	6.9	12	6.0	
Breslow							0.045
≤ 1 mm	14	14.4	25	24.8	39	19.6	
> 1 mm	76	78.4	68	67.3	144	72.4	
Missing	7	7.2	8	7.9	16	8.0	
Clark Level							0.461
II	11	11.3	20	19.8	31	15.6	
III	18	18.6	16	15.8	34	17.1	
IV	35	36.1	30	29.7	65	32.7	
V	26	26.8	26	25.7	52	26.1	
Missing	7	7.2	9	8.9	17	8.5	
Tumor-infiltrating lymphocytes							0.299
Absence	17	17.5	14	13.9	31	15.6	
Presence	73	75.3	80	79.2	153	76.9	
Missing	7	7.2	7	6.9	15	7.5	
Mitotic index							0.011
< 6 mitoses/HPF	44	45.4	60	59.4	104	52.3	
≥ 6 mitoses/HPF	45	46.4	29	28.7	74	37.2	
Missing	8	8.2	12	11.9	21	10.6	
Ulceration							0.147
Absence	32	33.0	42	41.6	74	37.2	
Presence	57	58.8	52	51.5	109	54.8	
Missing	8	8.2	7	6.9	16	8.0	
Histopathological regression							0.060
Absence	66	68.0	80	79.2	146	73.4	
Presence	21	21.6	13	12.9	34	17.1	
Missing	10	10.3	8	7.9	19	9.5	

* One patient with missing gender data

** Pearson chi-square test or Fisher's exact test



Graph 1: Distribution of invasive cutaneous melanomas diagnosed per year in a pathology reference service in Teresina (Piauí), according to histological type, 2000-2010



*** 95% CI = 95% Confidence interval ** p < 0,001 (one-way Anova)**

Graph 2: Error bar representing Breslow thickness mean of nodular, superfical spreading, acral-lentiginous and lentigo maligna melanoma diagnosed in a pathology reference service in Teresina (Piauí), 2000-2010

are likely to have been diagnosed later rather than sooner and involving lesions already growing vertically, thereby masking possible histopathological findings of other types of melanoma.[4]

Late diagnosis was in fact the rule in our study: only 19.6% showed Breslow thickness <1 mm, the lower nationwide rate (Table 4),[1,3-5,7-19] and the average Breslow thickness was 8.57 mm. This is of major concern given that approximately 20% of tumor patients presenting Breslow 1-4 mm have sentinel lymph node metastases, with this value increasing to 34% among patients with an index of over 4mm.[23]

The identification of the early stages of cancer can reduce morbidity and mortality. Three levels of prevention exist: primary, which prevents the occurrence of the disease; secondary, which consists of early diagnosis through screening; and tertiary, which prevents deformities, recurrence and death.[6]

Primary prevention of skin cancer focuses especially on sun protection, since the relationship between elevated levels of exposure to ultraviolet light (UV) and a higher incidence of skin cancer is well established in the literature. Studies have shown that the damage caused by UV radiation, particularly on DNA, has a major role in the development of melanoma, related to 65-90% of cases of tumor. The main target is usually children, since they are exposed to up to three times more sunlight than adults and the risk of cancer development is often related to cumulative exposure in childhood and adolescence.[14,24] Secondary prevention is based on mass detection campaigns to detect skin tumors at an earlier stage. In Brazil, the *Sociedade Brasileira de Dermatologia* (SBD) has since 1999 run the National Campaign to Prevent Skin Cancer, involving dermatologists examining and informing the population of the risks. Skin cancer screening programs can provide early diagnosis of melanoma in 90% of cases, with a significant reduction of mortality.[6,24] Knowledge of CM epidemiology is a vital component for both primary and secondary public health strategies.[3]

We observed a gender balance (48.7% male vs. 50.8% female) and prevalence in people over 50 years (83.9%). Lasithiotakis et al linked men and older people with a worse prognosis for melanoma.[25] Scoggins et al indicated that the male gender not only had worse prognosis but also greater incidence.[26]

Men presented a higher proportion of thicker Breslow (> 1 mm): 78.4% compared to 67.3% of women, which was statistically significant. At the Santa Casa Hospital in São Paulo, women presented a greater proportion (60%) of thinner CM (up to 2.0 mm) and men presented a greater proportion (74%) of thicker CM (> 2.0 mm).[3] Karakousis and Driscoll, in a study of 695 patients with primary melanoma, found 5-year survival rates of 75% for men versus 89% for women, and also higher age and thicker lesions among male patients.[27]

In women melanomas are generally located in women on the extremities, especially the lower limbs.[4,19] In our report, we identified a balanced distribution for this gender: trunk (28.7%), lower limbs (27.7%) and head/neck (25.7%). Meanwhile men usually have higher incidence of CM on the trunk (34.0%). According to our data, the most affected site in men was the lower limbs (40.2%).[23,28]

Anatomical distribution of CM changes according to sun exposure of the population. Distribution

Table 2: Distribution and features of 199 invasive cutaneous melanomas, according to gender, diagnosed in a pathology reference service in Teresina (Piauí), 2000-2010

Category	Metastasis				OR*	95 CI**
	Presence		Absence			
	n	%	n	%		
Total	**57**	**28.6**	**142**	**71.4**		
Gender						
Female	27	26.7	74	73.3	1.00	
Male	30	30.9	67	69.1	1.23	0.66-2.27
Age Group (years)						
≤ 50	5	22.7	17	77.3	1.00	
> 50	50	29.9	117	70.1	1.45	0.51-4.16
Site						
Head and neck	12	30.0	28	70.0	1.99	0.78-5.08
Trunk	11	17.7	51	82.3	1.00	
Upper Limbs	7	31.8	15	68.2	2.16	0.71-6.56
Lower Limbs	26	38.8	41	61.2	2.94	1.30-6.65
Histological Type						
Nodular	39	37.1	66	62.9	4.88	1.61-14.8
Lentigo maligna	2	10.5	17	89.5	0.97	0.16-5.85
Superficial spreading	4	10.8	33	89.2	1.00	
Acral lentiginous	6	28.6	15	71.4	3.30	0.81-13.45
Breslow						
≤ 1 mm	2	5.1	37	94.9	1.00	
> 1 mm	54	37.5	90	62.5	11.1	2.57-47.91
Clark Level						
II		4	12.9	27	87.1	1.00
III	3	8.8	31	91.2	0.65	0.13-3.18
IV	25	37.9	41	62.1	4.12	1.29-13.15
V	24	46.2	28	53.8	5.79	1.77-18.89
Tumor-infiltrating lymphocytes						
Absence	13	41.9	18	58.1	1.00	
Presence	43	27.9	111	72.1	0.54	0.24-1.19
Mitotic index						
< 6 mitoses/HPF	22	20.9	83	79.1	1.00	
≥ 6 mitoses/HPF	30	40.5	44	59.5	2.57	1.33-4.98
Ulceration						
Absence	15	20.0	60	80.0	1.00	
Presence	41	37.6	68	62.4	2.41	1.21-4.79
Histopathological regression						
Absence	45	30.6	102	69.4	1.06	0.47-2.39
Presence	10	29.4	24	70.6	1.00	

* Odds Ratio ** 95% Confidence Interval

Table 3: Metastatic sites of 146 melanomas presenting regional and distant metastases diagnosed in a reference pathology service in Teresina (Piauí), 2000-2010

Metastatic site	n	%
Lymph node	114	78.1
Skin and subcutaneous	33	22.6
Lung	10	6.8
Liver	7	4.8
Brain	4	2.7
Bowel	2	1.4
Bone	2	1.4
Adrenal	1	0.7
Parotid	1	0.7
Salivary gland	1	0.7
Cerebellum	1	0.7

Table 4: Comparison of various Brazilian studies on melanoma

City	Author	n	Years	Histological type		Clark level		Breslow ≤ 1mm	In situ
				SS	NO	IV	V		
São Paulo-SP	Criado et al.[7]	222	1963-1997	-	-	39.8%	10.2%	28.4%*	9.7%
Blumenau-SC	Naser[8]	1002	1980-2009	51.6%	37.0%	23.2%	22.8%	58.7%	10.5%
São Paulo-SP	Lapa et al.[9]	115	1985-1987	-	19.8%	-	-	9.6%*	-
Porto Alegre-RS	Venegas et al.[10]	101	1985-1989	-	36.6%	-	35.6%	-	-
Londrina-PR	Gon et al.[11]	303	1990-1999	37.1%	41.1%	23.1%	34.8%	13.4%*	12.9%
Porto Alegre-RS	Bakos[12]	153	-	51.6%	-	-	-	-	-
Rio de Janeiro-RJ	Fernandes et al.[13]	65	1993-2003	63.0%	12.3%	-	-	-	-
São Paulo-SP	Ferrari Júnior et al.[3]	364	1993-2006	33.8%	26.1%	25.4%	20.4%	23.9%	15.7%
Brasília-DF	Pinheiro et al.[14]	32	1994-1999	10.0%	45.0%	19.4%	32.3%	42.3%*	12.9%
Porto Alegre-RS	Bakos et al.[15]	103	1995-1998	61.2%	23.3%	-	-	-	-
Passo Fundo-RS	Borges et al.[16]	229	1995-2001	61.6%	25.3%	24.4%	7.9%	47.2%	7.9%
Porto Alegre-RS	Ponzio et al.[17]	167	-	35.3%	-	-	-	-	-
Florianópolis-SC	Weber et al.[1]	496	1999-2004	60.0%	30.0%	-	-	45.7%	37.5%
Porto Alegre-RS	Bonfá et al.[4]	328	2000-2005	62.8%	14.6%	27.4%	7.0%	36.9%	26.2%
São Paulo-SP	Maia et al.[18]	190	-	41.1%	-	-	-	-	-
Florianópolis-SC	Dimatos et al.[5]	105	2003-2007	68.7%	18.2%	19.0%	5.7%	30.4%	39.0%
Criciúma-SC	Konrad el al.[19]	72	2005-2007	50.0%	23.4%	26.1%	0.0%	25.0%*	29.6%
Teresina-PI	This study	313	2000-2010	18.6%	52.8%	32.7%	26.1%	19.6%	7.9%

SS: Superfical Spreading Melanoma **NO:** Nodular Melanoma *≤ 0.75mm

also changes with age. For example, melanomas in the chronically sun-exposed areas (face, scalp and neck) are more common in the elderly than the young.[29] Anatomic location of the primary melanoma is an important independent predictor of sentinel lymph node status and prognosis. Patients with primary melanomas of the head/neck and trunk usually have a worse prognosis than primary melanomas in other anatomic locations.[30]

In 109 cases (54.8%) the presence of ulceration was revealed. This is one of the independent factors associated with prognosis that is more consolidated in the literature. It is believed that ulceration develops due to ischemia secondary to a rapidly growing tumor, which suggests that it is associated with a worse prognosis.[22] Balch et al., in a study of 17,600 patients, demonstrated that tumor thickness and presence of ulceration were the most significant predictors of survival, with a relative risk of 1.558 (1.473-1.647) and 1.901 (1.735-2.083), respectively.[31]

In our series, the high rate of ulceration was consistent with late diagnosis. In São Paulo (SP), Florianópolis (SC) and Porto Alegre (RS), the ulceration rate was 35.1, 23.3 and 24.4% respectively.[1,3,4] As observed at other studies, women presented fewer ulcerated lesions (51.5% in comparison to 58.8% of men, but no significant difference). It is possible that women devote more attention to their own health and are more likely to seek dermatological advice.[3]

In 74 cases (37.2%), the mitotic index was greater than or equal to 6 mitoses / HPF (high-power field). This proportion was significant higher among men (46.4% as against 28.7% women). It is suggested that high mitotic index is also an important prognostic factor. Azzola et al. investigated 3661 patients with cutaneous melanoma, finding that patients with a mitotic index of 0 mitoses/mm^2 presented a 10-year survival rate of 95%, as compared with 80% in patients with a mitotic index between 1 and 4 mitoses/mm^2, 70% in those withan index of 5-10 mitoses/mm^2 and 60% in those with 11 or more mitoses.[32]

Melanoma has the potential to metastasize through the lymph nodes to visceral organs. Metastases most commonly first present at regional lymph nodes, but around one third of them present directly at distant sites, with the lungs the main site.[1] Considering the 57 cases of invasive CM which presented metastasis and the 89 cases of metastatic melanoma (a total of 146), the main sites of regional and distant metastases were the lymph nodes (78.1%), skin and subcutaneous areas (22.6%), lung (6.8%) and liver (4.8%) (Table 3). Lymph nodes, skin and subcutaneous lesions were also found to be the most common sites by a Brazilian survey carried out in the city of Florianópolis (state of Santa Catarina).[1]

Nodular melanoma (OR = 4.88; 95 CI =1.61-14.8), Clark IV (OR = 4.12, 95 CI = 1.29-13.15), Clark V (OR = 5.79, 95 CI = 1.77-18.89), Breslow > 1 mm (OR = 11.1, 95 CI = 2.57-47.91), mitotic index ≥ 6 (OR = 2.57, 95 CI = 1.33-4.98) and ulcerated lesions (OR = 2.41, 95 CI = 1.21-4.79) were more likely to metastasize, representing factors of worst prognosis (Table 2). These were sadly the predominant features in our sample, revealing a history of late diagnosis and poor prognosis in Teresina. (Table 1).

Melanoma may present clinically as a metastatic disease, without evidence of primary cutaneous involvement. We observed 89 (28.4%) cases of melanoma of unknown primary site in our series, marginally higher than the rate observed in Florianópolis (SC) (20.2%).[1] Some theories have set out to explain this phenomenon: the primary lesion removed surgically without histopathological study of the material, the primary site cutaneous melanoma with clinical appearance of benign lesion, the primary lesion located in the scalp, gastrointestinal tract, adrenals, meninges, retina, palate, vulva, vagina, anorectal area; primary lesion with spontaneous regression (hypochromic macula) due to immunological phenomena.[33] In our study, we had to consider that this rate could well be an overestimate since all the histopathological examinations were included, and in some cases the patient only took the resected lesion for study and was not followed up in our dermatology department.

Over the past few years, with the use of PET-CT (Positron Emission Tomography-Computed Tomography), the incidence of melanoma of unknown primary site has tended to decrease. PET-CT is widely used in oncology for lesion detection and characterization, as well as for accurate lesion localization. Melanoma cells usually demonstrate a high uptake of the glucose analog F-fluorodeoxyglucose (FDG) - the finding that established the rationale for the use of FDG in melanoma, allowing whole-body tumor detection and which proved to be useful for detecting primary tumors.[18,34,35] Unfortunately the high cost of this test is a limiting factor in Brazil.

CONCLUSION

The histopathological profile of melanoma in our study was the nodular histological type, Breslow thickness> 1 mm, Clark level IV and V, with the presence of ulceration and lymphocytic infiltrate in the tumor and high rates of metastasis. The main factors associated with metastasis were of the nodular type, Clark IV / V, Breslow> 1mm, mitotic index ≥ 6 and ulcerated lesions. ❑

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