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COVID-19 Pandemic Impacted the Histopathological Staging of Patients Newly Diagnosed with Melanoma: Single-Center Study

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Background

Cutaneous melanoma is a skin malignant tumor, considered to be aggressive and potentially lethal in advance stages [1]. Its incidence has been increasing in recent decades, especially in countries with an increased incidence of Ultraviolet rays (UVs), such as Brazil [2]. It is more common in Caucasian men over the age of 60, but is not rare in other age groups, especially in young women [3]. The south and southeast regions of our country have the highest number of identified cases [2,3]. It is currently considered multifactorial, presenting risk factors resulting from genetic susceptibility and environmental exposure [1,2]. Early diagnosis of this neoplasm is fundamental for a better prognosis, since the metastatic potential is directly related to the invasion of the tumor in relation to the basal membrane and its thickness, verified by the distance in millimeters between the epidermal granulosa layer and the deeper portion of neoplastic cells in the dermis. This thickness is called Breslow index [4].

In 2020, a pandemic began, and many health efforts returned to combating it, thus, chronic diseases and new diagnoses were overcome. Therefore, this study aims to evaluate the impact that the COVID-19 pandemic had on the diagnosis of Melanoma, in relation to its pathological staging.

Methods

Observational study with a cross-sectional design, carried out by reviewing the medical records of patients undergoing their first consultation at the Dermatology outpatient clinic of Hospital Santa Teresa, between January 1st, 2019, and December 31st, 2019 (pre-pandemia), and January 1st, 2021, until January 31st, 2021 (during pandemia), with a confirmed diagnosis of Melanoma at the institution.

Convenience non-probabilistic sample. We chose to include only first consultation since patients already being monitored at our hospital had some type of access to the dermatologist, albeit remotely, during the pandemic period. What might have been impacted was the first referral for evaluation in the face of suspicion, as this service depended on a screening evaluation in basic health units.

To analyze the prognostic impact, in relation to anatomopathological staging, we checked the number of "*in situ*" melanomas compared with the number of invasive ones. Among the invasive ones, we differentiate the frequency between the thin (<1 mm) and thick ones, in the studied years. Also, que compared the average Breslow indices. Secondarily, we evaluated patients who were referred due to suspected melanoma and those for whom melanoma was identified on examination, without it being the reason for referral for consultation.

Data were collected only after approval without pending approval from the Research Ethics Committee (CEP) of SES/SC (number for consultation - 71300123.0.0000.0115; Plataforma Brazil). For collection, an Excel 2011 software spreadsheet (Microsoft® Excel® for Mac 2011/Version: 14.2.0) was used where data from the included patients were categorized. Statistical analysis was carried out using SPSS 20.0 software. The initial data analysis was processed descriptively and presented in the form of tables, expressed by the mean, standard deviation, median (Q2) for numerical data, and frequency (n) and percentage (%) for categorical data. The association studies between the dependent and independent variables were accessed through the student's *t*-test for independent

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Table 1: General overview of our selected cases of Melanoma in both periods.

Clinical-Epidemiological- Histopathological Profile	Sample N=95	Pre-Pandemic: 2019 N = 28	Pandemic: 2021 N=67	p=
Mean age at diagnosis (years):	56.88 ± 14.5	56.89 ± 14.43	56.88 ± 14.68	0.997
Gender (females)	52 (54.7%)	16 (57.2%)	36 (53.7%)	0.824
Skin color - self-declared (Caucasian):	95 (100%)	28	67	
Referral: suspected Melanoma	78 (82.1%)	23 (82.1%)	55 (82.1%)	
Cutaneous location:				
- Neck	5 (5.3%)	(7.1%)	3 (4.5%)	
- Scalp	1 (1.1%)	(3.6%)	0	
- Back	37 (38.9%)	9 (32.1%)	28 (41.8%)	
- Face	12 (12.9%)	4 (14.3%)	8 (11.9%)	
- Buttocks	1 (1.1%)	1 (3.6%)	0	
- Lower limbs	7 (7.4%)	3 (10.7%)	4 (6%)	
- Upper limbs	12 (12.6%)	3 (10.7%)	9 (13.4%)	
- Shoulder	4 (4.2%)	0	4 (6%)	
- Ear	(5.3%)	4 (14.3%)	1 (1.5%)	
- Foot	(5.3%)	0	5 (7.5%)	
- Chest	(6.3%)	1 (3.6%)	5 (7.5%)	
Melanoma *in-situ:*	28 (29.5%)	13 (46.4%)	15 (22.4%)	
Thin Melanomas (≤ 1 mm):	75 (78.9%)	25 (89.2%)	50 (74.6%)	
Thick Melanomas (>1 mm):	20 (21.1%)	3 (10.8%)	17 (25.4%)	
Mean Breslow (mm):	0.95 ± 1.59	0.52 ± 0.72	1.14 ± 1.81	
Clark:				
- I:	4 (4.2%)	0	4 (6%)	
- II:	4 (4.2%)	2 (7.1%)	2 (3%)	
- III:	30 (31.6%)	7 (25%)	23 (34.3%)	
- IV:	25 (26.3%)	6 (21.4%)	19 (28.4%)	
- V:	4 (4.2%)	0	4 (6%)	
ND*	28 (29.5%)	13 (46.4%)	15 (22.4%)	
Ulceration (yes):	3 (4.4%)	2 (13.3%)	1 (1.9%)	
Mitoses by field (yes):	23 (34.3%)	6 (40%)	17 (32.6%)	
Nevus Subtype:				
- Congenital:	1 (10%)			
- Melanocytic, junctional and compound nevus:	5 (50%)			
- Intradermal Nevus:	4 (40%)			
Staging (pT):				
- pTis:	28 (29.5%)			
- pT1a:	31 (32.6%)			
- pT1b:	16 (16.8%)			
- pT2a:	7 (7.4%)			
- pT3a:	7 (7.4%)			
- pT3b:	2 (2.1%)			
- pT4a:	3 (3.2%)			
- pT4b:	1 (1.1%)			

*ND: Not Described

samples or Mann Whitney (nonparametric), and for categorical data the Chi-square test (X^2) or Fisher's exact test was applied. As measures of association, prevalence ratios and their respective Confidence Intervals (CI: 95%) were calculated. The significance criterion adopted was the 5% level.

Results

Nighty five patients were diagnosed on their first consultation in

Table 2: Double entry table, correlating invasion stage and year of diagnosis.

Year of Diagnosis	*in-Situ*	Invasive	Mean Breslow (mm)
2019	13/28 (46.4%)	17/28 (60.7%)	0.52
2021	15/67 (22.4%)	52/67 (77.6%)	1.14
	PR 2.04 / *p*=0.027 / 95% CI: 1.1-3.7		*p*=0.027

Legend: PR: Prevalence Ratio; CI: Confidence Interval

the studied years: being 28 in 2019 and 67 in 2021. Table 1 presents the main data regarding the general overview of all cutaneous melanomas included in this study.

All 95 patients were Caucasian. There was a slight predominance of women (54.7%), with a mean age of 56.88 years. The most common site of melanoma was the back. Most patients, in both years, had already been referred for consultation with suspected melanoma.

Table 2 presents the outcome variables, divided into two groups: 2019 and 2021.

In 2019, 46.4% of patients were diagnosed in-situ, compared to only 22.4% in 2021, with a twice as high chance (PR 2.04, p=0.027, 95% CI: 1.1-3.7) of being diagnosed in the in-situ phase in 2019, when compared to 2021. In 2019, the average BI was 0.52 millimeters. In 2021, it was 1.14 millimeters, therefore almost twice as high as in 2019 (1.14 *vs.* 0.52, p=0.027).

Discussion

An observational, cross-sectional study was conducted based on a review of medical records of patients undergoing their first consultation at our Dermatology outpatient clinic, between January 1st, 2019, and December 31st, 2019, before the COVID-19 pandemic, and January 1st, 2021, and January 31st, 2021, during the pandemic, but with health services already reestablished, with a confirmed diagnosis of Melanoma at our institution. In 2020, health efforts were almost exclusively dedicated to combating the pandemic, which resulted in delays in referring patients from primary health care units to tertiary care [5]. This also impacted the diagnosis of melanoma and worsened the disease prognosis.

The study conducted by Tejera-Vaquerizo and Nagore investigated the impact of diagnostic delays for melanomas during the COVID-19 lockdown. The results showed that a three-month delay in diagnosis could negatively change the melanoma's stage classification by up to 49%, highlighting the adverse effect of such delays on patient prognosis [6].

In a European meta-analysis published in 2024, Díaz-Calvillo et al. reviewed 27 studies and analyzed the short- and long-term effects of delayed melanoma diagnosis and non-melanoma skin cancers. In the short term, the decrease in melanoma prevalence and surgeries was directly related to long-term effects such as an increased risk of ulceration and poorer prognosis for these melanomas. This initial decrease in prevalence is also evidenced in the present study, showing a global trend of diagnostic delays [7].

Compared to 2019, which had a significantly higher prevalence of in situ melanomas and thinner melanomas, the data from 2021 show an increase in the average Breslow index. During the pandemic, the average Breslow index increased significantly, being up to twice as high as before the pandemic, with a mean of 1.14 millimeters in 2021 compared to 0.52 millimeters in 2019. This phenomenon is supported by other studies, such as the review by James Fanning et al., and the meta-analysis by Konstantinos Seretis et al., on the impact of the COVID-19 pandemic on the diagnosis of cutaneous melanoma [8,9]. These studies showed statistically significant increases in Breslow thickness [0.29 mm (0.03-0.55 mm)], ulceration rates [OR=1.66 (1.29-2.13)], and tumor staging [8,9].

Consistent with the present study, despite the small sample size regarding absolute mitotic index numbers, the systematic review by Ana-Olivia Toma et al. indicates that most of the studies analyzed also found an increase in the number of mitoses in melanomas diagnosed after the COVID-19 pandemic [10].

The impact of the COVID-19 pandemic on melanoma diagnosis was observed not only locally but also globally. Diagnostic delays led to an increase in prevalence and, notably, a statistically significant increase in the average Breslow index of melanomas diagnosed in 2019 and 2021, as exemplified by the studies mentioned. Therefore, the number of melanomas diagnosed at more favorable stages occurred pre-pandemic, with post-pandemic data showing a worse prognosis in terms of staging.

Among the limitations of the study, it is noted that medical records often contain incomplete information, which affects the accuracy of the epidemiological profile of patients and the extrapolation of these data to the state of Santa Catarina, which still lacks statistical data on this neoplasm. Additionally, due to the observational nature and cross-sectional design of the study, it was not possible to track the clinical outcomes of patients to the present date. These limitations highlight the need for further studies, preferably with longitudinal designs, to more clearly define the epidemiology of the neoplasm in the state and to explore other potential reasons for delays in the diagnosis of cutaneous melanomas.

Conclusion

It can be concluded that the COVID-19 pandemic, both in Brazil and worldwide, has impacted public health in various ways. Beyond the disease itself, the repercussions also included creating obstacles for the follow-up of chronic conditions that were sidelined during this period, such as melanoma skin cancer discussed in this study.

Finally, regarding the disease discussed here and in the presented study, in addition to significantly altering the stage of melanoma, as analyzed through average Breslow data, mitotic index, and risk of ulceration, the delay in diagnosis has resulted in prognostic consequences with a substantial impact on public health.

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