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Prevalence of premalignant and malignant skin lesions in oculocutaneous albinism patients

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SUMMARY

OBJECTIVE: Oculocutaneous albinism describes a group of pigmentary disorders that lead to skin sensitivity and predisposition to skin malignances.

Aims: To analyze clinical and epidemiological data in oculocutaneous albinism patients and to determine the prevalence of malignant skin lesions, assessing possible risk factors for skin cancer.

METHODS: Cross-sectional study evaluating epidemiological data, habits of sun exposure and sun protection, and clinical examination of albino patients followed in a reference dermatology outpatient clinic in Brasil. Our primary outcome was the occurrence of malignant skin lesions in biopsied tissues.

RESULTS: Of 74 patients analyzed, 11 (15%) had one or more suspicious lesions and were biopsied, of which 8 (72.7%) patients presented with basal cell carcinomas, 7 (63.3%) presented with squamous cell carcinoma, and 1 (9%) presented with melanoma. Moreover, 32(43%) patients presented with actinic keratosis. Age, female gender, previous history of sunburn, history of malignant lesions and history of sun exposure without photoprotection were associated with the presence of malignant lesions.

Limitations: Unicentric, non-aleatory sample.

CONCLUSIONS: There was a high prevalence of malignant and pre-malignant lesions in this population. Some potentially modifiable risk factors were associated with the occurrence of malignant skin lesions.

KEYWORDS: Albinism. Epidemiology. Skin neoplasms. Albinism, oculocutaneous. Pigmentation disorders.

INTRODUCTION

Albinism is a generic term used to describe a heterogeneous group of inherited autosomal recessive disorders characterized by changes in melanin biosynthesis causing absence or reduction in the pigmentation of the skin, hair, and/or eyes[1-4]. Albinism is caused by mutations in different genes[1-4] and is classified as oculocutaneous albinism (OCA), when it affects the skin, hair and eyes, or ocular albinism (OA), when the phenotype is primarily restricted to the eyes and optical system[5]. Albinism affects all ethnic groups, with an estimated global prevalence of 1: 17,000 live births[6]. However, the prevalence varies widely in the world, with a major impact on the African continent[6,7].

Due to pigmentary alterations, OCA patients may be more prone to increased morbidity and mortality related to the development of premalignant and malignant skin lesions, even at young ages[8]. Despite the global distribution, data on the prevalence and risk factors for malignant lesions in this population are scarce in the literature, especially in the Brazilian population[6,9-12].

The aim of the present study was to analyze the clinical and epidemiological data and to determine the prevalence of malignant and pre-malignant skin lesions in OCA patients. Additionally, we sought to identify potential risk factors associated with skin cancer in this population.

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METHODS

This study was conducted in the outpatient clinic for OCA patients in the Dermatology department of an academic center, Hospital Professor Edgar Santos, of Universidade Federal da Bahia (HUPES-UFBA), in Salvador, Bahia, Brasil. Data were collected from March 2016 to June 2017. The outpatient clinic is a referral center for albinism patients in the state of Bahia since 2013 and agreements have been made with associations of albinism patients to increase referral and adherence to the clinic.

This is a cross-sectional, observational, and unicentric study. All OCA patients who were followed at the dermatology outpatient clinic in the study period and that gave informed consent were included, with no age restriction.

All patients were submitted to a questionnaire and total body skin examination. Demographic and epidemiological data and habits of sun exposure and adherence to photoprotection were recorded. In addition, previous history of sunburn and previous history of pre-malignant or malignant lesions were also collected. Total body skin examination also included dermoscopic examination and was performed by the same investigator (ANR). Additionally, patients with suspicious malignant skin lesions were submitted to cutaneous biopsy for histopathological study. Skin lesions with suspected actinic keratosis were diagnosed clinically and were not submitted to biopsy. Dermoscopy findings during the clinical exam have been reported elsewhere[12].

Categorical variables were described as proportions. Continuous variables were described as mean ± standard deviation or median (interquartile range), as appropriate. Proportions were compared using the χ^2 test. Continuous variables were compared with the Student's *t*-test or the Mann-Whitney U-test, as appropriate.

Statistical analysis was performed with SPSS version 21.0 (SPSS Inc., USA). A p-value of less than 0.05 was considered as statistically significant.

This study was approved by the research ethics committee of the HUPES-UFBA. Participants in the study agreed to participate in the study and signed the informed consent form.

RESULTS

During the study period, 74 patients with OCA were evaluated. Mean age was 22±18 years, ranging from 1 to 67 years. There were 39 women (53%) (Table 1). Although 42 (57%) of the patients reported having other relatives with albinism, only 3 (4%) reported having albino parents.

Most patients reported previous history of sunburn (61 patients, 82%) or previous sun exposure without photoprotection (57 patients, 77%). Moreover, 28 (41%) patients reported previous history of skin malignancies or premalignant lesions. In contrast, 50 patients (68%) reported current

Table 1. Characteristics of the patients (n=74).

Characteristics	
Female gender, N (%)	39 (52.7)
Age, mean ± SD	22±18
Family income inferior to 2 minimum wages, N (%)	68 (95.8)
Alcohol consumption, N (%)	15 (20.3)
Smoking, N (%)	0 (0)
Parents with OCA, N (%)	3 (4.2)
Other relatives with OCA, N (%)	42 (56.8)
Current sun exposure, N (%)	16 (21.6)
History of sunburn, N (%)	61 (82.4)
Previous sun exposure without photoprotection, N (%)	57 (77.0)
Frequency of use of sunscreen, N (%)	
Do not use	14 (18.9)
Rarely use	4 (5.4)
1–3 days per week	2 (2.7)
4–6 days per week	4 (5.4)
Daily use	50 (67.6)
Use of mechanical photoprotection, N (%)	
Long sleeve clothes	48 (64.9)
Sun umbrella	50 (67.6)
Hat	47 (63.5)
Reasons for non-utilization of photoprotection measures, N (%)	
Cost	54 (73.0)
Cosmetics	18 (24.3)
Heat	32 (43.2)
Aesthetics	11 (14.9)
First consultation with dermatologist, N (%)	11 (15.3)
Previous history of malignant or premalignant skin lesions, N (%)	28 (40.6)
Actinic keratosis, N (%)	27 (36.5)
BCC, N (%)	10 (13.5)
SCC, N (%)	2 (2.7)
Melanoma, N (%)	1 (1.4)
Previous lesion with unknown histology, N (%)	4 (5.4)

OCA: oculocutaneous albinism. BCC: basal cell carcinoma. SCC: squamous cell carcinoma.

use of sunscreen cream daily and about 60% reported current mechanical photoprotection (Table 1). The main related reason of non-use of photoprotection was the high cost of sunscreens, as reported by 54 (73%) patients. On clinical examination, 69 (93%) patients presented with one or more benign lesions, as described in Table 2A.

Premalignant or malignant skin lesions were found in 32/74 (43%) patients (Table 2B). Nineteen (59%) patients presented only with lesions with suspicion for actinic keratoses, which were diagnosed on clinical examination and were not submitted to biopsy. Thirteen (40.6%) patients had one or more suspicious malignant lesions on physical examination and 11/13 (84.6%) of these had a biopsy done. As each of the 11 patients could have had more than one lesion biopsied, a total of 29 lesions were biopsied. Of the biopsied lesions, 15 (51%) resulted in basal cell carcinomas (BCC), 9 (31%) resulted in squamous cell carcinomas (SCC), 1 (3%) resulted in a melanoma *in situ*, 1 (3%) was an undifferentiated epithelioid neoplasia, and 3 (10%) resulted in actinic keratoses. The distribution of the 29 biopsied lesions according to their site in the body is depicted in Table 3. Most lesions were in the trunk (62%), followed by limbs (20%), and head or neck (17%).

Table 2. Patients with skin lesions on clinical examination. Each patient may have presented with more than one lesion. A= Patients with benign skin lesions on clinical examination (n=69). B= Patients with pre-malignant and malignant lesions (n=32). Diagnoses were made with biopsy of suspected lesions (basal cell carcinoma, squamous cell carcinoma, melanoma and others) or clinical exam (actinic keratoses).

A. Benign lesions (N=69)	N (%)
Elastosis	48 (64.9)
Melanocytic nevi	38 (51.4)
Solar melanosis (solar lentigo)	22 (29.7)
Actinic cheilitis	19 (25.7)
Glandular cheilitis	15 (20.3)
Seborrheic keratosis	5 (6.8)
Lentigo simplex	2 (2.7)
Ephelides	1 (1.4)
B. Pre-malignant or malignant lesions (N=32)	**N (%)**
Basal cell carcinomas (BCC)	8 (10.8)
Squamous cell carcinomas (SCC)	7 (9.5)
Melanoma	1 (1.4)
Undifferentiated epithelioid neoplasia	1 (1.4)
Actinic keratosis	32 (43.2)

Some characteristics were associated with an increased prevalence of pre-malignant or malignant skin lesions on clinical examination. Female gender [OR (95%CI)= 4.1 (1.5–11.2), p=0.004], no previous use of regular photoprotection [OR (95%CI)= 8.3(1.7–39.9), p=0.003], and prior history of pre-malignant lesions or skin cancer [OR (95%CI)= 52.5 (11.9–230.6), p<0.001] were associated with an increased prevalence of pre-malignant or malignant lesions. Additionally, among patients with and without prior history of sunburn, 32 (52%) and 0 (0%) had pre-malignant or malignant lesions, respectively, p=0.001. Moreover, patients with pre-malignant or malignant lesions were older, with a mean age of 38±15 years, while patients without pre-malignant or malignant lesions were younger, with a mean age of 10±9 years, p=0.001.

DISCUSSION

In this study, we observed a high prevalence of malignant and pre-malignant lesions in OCA patients. In addition, some sun exposure and photoprotection habits were associated with a higher prevalence of malignant or pre-malignant skin lesions. Furthermore, some potentially modifiable barriers to adherence to the use of photoprotection measures were found, which could possibly be addressed by healthcare policies.

Actinic keratosis was the most frequent lesion among malignant and pre-malignant lesions, with a prevalence of 43%. This high prevalence is demonstrated in other studies. For instance, in a population of 164 OCA patients in Tanzania, a prevalence of 42% of actinic keratosis was found, reaching 100% in those with more than 30 years of age[13]. However, even

Table 3. Distribution of the 29 biopsied skin lesions.

Distribution of skin lesions	N (%)
Lesions in the trunk	18 (62)
BCC	13 (72)
SCC	3 (16.6)
Melanoma	1 (5)
Actinic keratosis	1 (5)
Lesions in the limbs	6 (20)
SCC	3 (50)
Actinic keratosis	2 (33.3)
Undifferentiated epithelioid neoplasia	1 (16.6)
Lesions in the head or neck	5 (17)
BCC	2 (40)
SCC	3 (60)

BCC: basal cell carcinoma. SCC: squamous cell carcinoma.

in the population without OCA, the prevalence of actinic keratosis can be high, ranging from 15–23% in the United Kingdom, reaching 40–60% in the population over 40 years of age in Australia, the country with the highest number of cases of skin cancer in the world and where the ultraviolet radiation rates are also high[14,15]. As such, the study design, which lacks a control group, prevents conclusions on the role of albinism as a risk factor for such skin lesions.

In our data, the prevalence of BCC was higher than that of SCC. This finding goes against previous data showing SCC as the most common subtype of skin cancer in OCA patients[3,5,8,13,16,17]. Only one previous study, also conducted in Brasil and evaluating biopsy results, showed a higher prevalence of BCC compared to SCC, however the difference between the prevalence of the subtypes of skin cancer was of only 3%, with a prevalence of 37% for BCC and of 34% for SCC[10]. In our study, the difference was greater, as the prevalence of BCC was 51% compared with 31% for SCC. This discrepancy could be explained by the fact that our patients are accompanied regularly and 85% of the patients had more than one consultation, so the lesions may be diagnosed and treated in early phases. For example, the actinic keratoses could have been treated before transformation to SCC. Moreover, most of those studies were based in histological reviews of excised biopsies, which could lead to an overestimation of SCC in relation to BCC of slow growth[5,17], as previous discussed by Kiprono et al.[8]. An alternative hypothesis is that those differences may be due to chance, as most OCA studies have small sample sizes.

We found only one patient with malignant melanoma and another patient reporting previous melanoma, despite the presence of nevi in 51.4% of the patients. Those findings may be due to the overall young age of our population, but are also corroborated by the literature, since melanoma in OCA is rarely described in albino patients[18,19].

In our study, we found the trunk to be the commonest site of cancer, followed by the limbs and head/neck. In contrast, in the literature, the most usual site for skin cancers in OCA patients was head and neck followed by trunk and limbs[5,8,17]. One possible explanation is that, as Brasil is a tropical country, with median temperatures near 30°C, even in the winter, OCA patients may be exposed to sunlight with the trunk uncovered. This is supported by the fact that 57 (77%) of the participants referred previous sun exposure without protection. Another hypothesis is that the use of sunscreen may be more usual on the face, which can lead to the neglect of the trunk and members[20].

Age, previous sun exposure without photoprotection, previous history of malignant or premalignant lesions and previous sunburn were associated with a higher prevalence of current pre-malignant or malignant lesions. These characteristics are well-described risk factors for the appearance of malignant or pre-malignant skin lesions in the general population[5,16,21]. In addition, in the present study, female gender was associated with a higher prevalence of pre-malignant and malignant lesions. Although it cannot be completely ruled out that these findings are due to chance, it is possible that women are more concerned about skin lesions and seek health services earlier, a fact already described in other healthcare situations[22].

We observed a great variation in photoprotection habits, with 50 (67.8%) participants using daily photoprotection measures, although almost 20% did not use any measures. Among the reasons to non-adhesion to photoprotection measures, lack of money to buy sunscreens was the most frequently described, being cited by 73% of the participants, which can be explained by the low socioeconomic status of the studied population. This information suggests that socioeconomic status may influence the process of preventing the development of skin lesions in this more susceptible population. This lower adherence to photoprotection habits, when compared to what has been shown in the literature, in which adherence may reach 95%, can be explained by the fact that, during the study period, sunscreens were not being freely distributed to the patients, which may have limited the access to this photoprotection measure[23].

This study has several strengths. This is one of the few studies evaluating skin cancer in albinism patients and one of the few carried out in Brasil. In addition, we were able to cover many albinism patients, with high data completeness and it was possible to describe in detail the lesions found in those patients. Moreover, despite the cross-sectional nature of the study, it was possible to describe some putative risk factors for skin cancer in albinos and to elaborate hypotheses that can be tested in the future.

However, the study has limitations. This is a convenience sample study, which may limit the interpretation of the findings, although our results may be generalizable to sites with similar contexts. Specifically, the prevalence presented in this study may be interpreted in the context of the relatively young age of the population studied, considering such prevalence may increase with older age. However, despite the young age of our sample, we have found a high prevalence of malignant or premalignant skin lesions, which harbors the hypothesis that albino patients may benefit from increased surveillance of skin lesions, even in younger ages. Due to the observational design, we only biopsied suspected lesions (and not all lesions found

in the clinical examination), which may have influenced the final diagnosis. Moreover, because of the cross-sectional design of the study, it is not possible to make causal statements about the associations found, nor to rule out the presence of confounding factors, although it was possible to evaluate some relevant information about the characteristics and habits of this specific population.

CONCLUSIONS

In our study, we found a high prevalence of malignant and pre-malignant lesions in OCA patients. Moreover, some potentially modifiable risk factors have been associated with the occurrence of malignant skin lesions in this population.

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AUTHORS' CONTRIBUTIONS

ANR: Conceptualization, Data Curation, Formal Analysis, Writing – Original Draft, Writing – Review & Editing. **JGRR**: Methodology, Formal Analysis, Writing – Original Draft, Writing – Review & Editing. **JDF**: Methodology, Formal Analysis, Writing – Original Draft, Writing – Review & Editing.

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