Dermatology Reports
https://www.pagepress.org/journals/index.php/dr/index

eISSN 2036-7406

Please cite this article as:

Makhakhe L, Oliver BJ, Motloung M, et al. The prevalence of epidermal skin malignancies in people living with oculocutaneous albinism attending the Universitas Academic Hospital, Bloemfontein, South Africa. *Dermatol Rep 2025 [Epub Ahead of Print] doi: 10.4081/dr.2025.10038*

Submitted 06/05/24 - Accepted 11/05/25

The prevalence of epidermal skin malignancies in people living with oculocutaneous albinism attending the Universitas Academic Hospital, Bloemfontein, South Africa

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Key words: oculocutaneous albinism; African; sun exposure; solar keratoses; epidermal malignancy; squamous cell carcinoma; basal cell carcinoma.

Conflict of interest: the authors have no conflict of interest to declare.

Ethics approval and consent to participate: the study obtained approval from the Ethics Committee at the University of the Free State and from the head of the Free State Health Department. All patients gave their consent to participate in this study.

Consent for publication: all participants provided informed consent for the publication of this article and any accompanying images.

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Acknowledgments: the South African Institute of Dermatology generously provided all the technical support and further assisted with the high-quality photos used.

Abstract

Oculocutaneous albinism (OCA) is a group of heterogeneous genetic disorders caused by the absence or reduced biosynthesis of melanin pigment within the melanocytes in the epidermis. Patients with OCA are prone to certain types of epidermal skin cancers, premalignant skin lesions, and eye-related symptoms and signs. The study aimed to evaluate the prevalence of common epidermal skin cancers and premalignant skin lesions in patients living with OCA attending an academic hospital in Bloemfontein, Free State province (South Africa). This research focused on individuals referred within the public health sector. We evaluated all patients with this specific condition across the entire Free State province of South Africa and in Lesotho. The study was conducted as a cross-sectional, retrospective review of the medical records of all patients known to the clinic, as well as those referred with OCA, from January 2017 to January 2019. A total of 36 patients were included in this study, with 11 (30.6%) males and 25 (69.4%) females. Thirty-two (88.9%) had a history of active or past epidermal skin cancers or pre-malignant skin lesions, while the remaining 4 (11.1%) had no history of secondary skin pathology. The distribution of the pathology was notable in relation to sun exposure, with the face being mostly affected in 31 (96.9%) of cases assessed. OCA has been identified as a risk factor for solar keratosis, squamous cell carcinoma (SCC), and basal cell carcinoma (BCC).

Introduction

The term albinism stems from the Latin word "*albus*", meaning "white". The global prevalence of oculocutaneous albinism (OCA) is approximately 1 in 20,000, with different rates across geographic regions and ethnic groups.[1]

OCA is an autosomal recessive genetic disorder characterized by the absence or defect in the tyrosinase enzyme, which converts tyrosine to dihydroxyphenylalanine, the precursor of melanin pigment, leading to varying levels of deficit in melanin pigment synthesis within the epidermal layer of the skin, hair, and the iris of the eyes.[2] It can be classified as either ocular or oculocutaneous. Unlike the ocular variant, which only affects the eyes, OCA affects the optical system, the skin, and the hair.[3]

Ocular abnormalities, such as lack of pigmentation of the iris and retina, foveal hypoplasia, and atypical decussation at the optic chiasm, also characterize the disorder, resulting in a wide spectrum of visual signs and symptoms, such as reduced visual acuity, impaired stereopsis, strabismus, nystagmus, iris translucency, and photophobia.[4,5]

Within the current updated literature, OCA has been concisely classified into eight genetic subtypes. Due to clinical overlap because of near-similar genetic phenotypes, clinical variants range from type I to VII (Table 1).[6] The main reason is that the type II variant is clinically similar to type IV. Several

alterations in genes encoding proteins involved in the melanin biosynthesis pathway have been identified. Specifically, the *TYR gene* (OCA1), OCA2 or *P gene* (OCA2), *TYRP1* (OCA3), *SLC45A2* (OCA4), *SLC24A5* (OCA6), *LRMDA* (OCA7), and *DCT* (OCA8); the genetic mutation for the OCA5 subtype has not yet been identified but is mapped to chromosome 4q24. OCA can also occur in several rare syndromic disorders, such as the Hermansky-Pudlak syndrome and the Chediak-Higashi syndrome.[7-13]

Affected people present with a normal number of melanocytes in the epidermis and hair follicles; however, they lack melanin pigment to a varying degree. People living with OCA are more susceptible to developing common epidermal skin cancers and pre-malignant lesions due to a lack of skin pigment protection and the long-term effects of UV rays from chronic sun exposure.[14]

Although distinctly a melanocyte-originating malignancy, malignant melanoma remains exceedingly rare in patients living with OCA.[15]

Materials and Methods

The primary focus of this research was the public sector. All patients included in the study were from the Free State province of South Africa and Lesotho. The study was conducted as a cross-sectional, retrospective review, examining the files of all patients known to the clinic, as well as new referrals with oculocutaneous albinism (OCA), from January 2017 to January 2019. Data were collected electronically using the Research Electronic Data Capture (REDCap) system. Compliance with South African legislative policy under the Protection of Personal Information Act (POPIA) was ensured by using pseudonyms, and all participants were de-identified. Two files were excluded due to insufficient data, and duplicate files were also removed.

Results

A total of 36 patients were included in this study, with 11 (30.6%) males and 25 (69.4%) females. Thirty-two (88.9%) had a history of active or past epidermal skin cancers or pre-malignant skin lesions, while the remaining 4 (11.1%) had no history of secondary (neoplastic) skin pathology. Among the affected group, 15 (46.9%) had a history of squamous cell carcinoma (SCC), all concurrent with solar keratoses, and 13 (40.6%) had basal cell carcinoma (BCC), with 6 of those also having a history of solar keratoses concurrently. None of the patients had active or past melanoma. Premalignant lesions in the form of solar keratoses were present in 25 (78.1%) patients, including those with concurrent BCCs and SCCs, as well as 4 (12.5%) patients who had solar keratoses alone without any epidermal malignancies (Figure 1).

It was notable that some patients had a history of BCC, SCC, and premalignant skin lesions that could be concurrent, recurrent, or serial over the period reviewed. However, the clinical notes were at times not adequate for us to reliably extract conclusive data in that regard. We also struggled to conclusively extract reliable data for a select group of patients presenting with both types of prevalent skin cancers, even though this is clinically common. Our study did not aim to link genotyping or phenotyping with the types of skin cancers.

From our findings, males tend to present late with advanced malignancies in numbers and sizes, and have a high rate of not attending their follow-up appointments. In contrast, the female group was more than twice the size of their male counterparts, more compliant with clinic visits, more concerned with preventative measures, and had fewer overall complications. The hypothesized reasons for males with OCA to present with more advanced malignancies are twofold: firstly, their tendency to work outdoors, resulting in substantial solar exposure; secondly, their reluctance to seek medical attention at an early stage, a phenomenon observed anecdotally across the medical spectrum.

Patients without any history of secondary or malignant involvement were noted to have attended dermatology clinics earlier, were actively involved in preventative measures, and presented frequently for routine skin check-ups. However, the number of individuals without neoplastic manifestations was too small to draw conclusive associations with higher socio-economic status.

Erythema from chronic sunburn was noted in all 32 individuals with skin neoplastic involvement and served as an independent risk factor for future malignant transformation.

Our study reiterated the poor link between malignant melanoma and OCA, despite the lack of protection from melanin amidst chronic sun exposure in those with repeated incidences of non-melanoma skin cancers. We further confirmed a close association between solar keratosis and SCC.

The distribution of neoplasms was closely associated with sun exposure. The face, including the ears, was the most commonly affected site (31 cases, 96.9%), followed by the upper limbs (21 cases, 65.6%), lower limbs – both anterior and posterior aspects (17 cases, 53.1%) – and the neck (12 cases, 37.5%). Less frequently affected areas included the upper back (3 cases, 9.4%), upper chest (2 cases, 6.3%), trunk (3 cases, 9.4%), and scalp (1 case, 3.1%). Most individuals exhibited involvement of multiple sites, as confirmed by tumor sampling and histopathological examination.

Discussion

OCA is a congenital skin condition, affecting melanin-containing structures derived from the ectoderm during embryogenesis, namely, the skin, the eyes, and the hair. This results in a generalized depigmentation of the skin, light yellow to white hair, and pale or often light blue iris of the eyes.[16]

Melanin has been found to protect the skin from the harmful effects of radiation from the sun. The absence of this protective pigment in individuals living with OCA predisposes them to sunburns and subsequent dysplastic changes in their skin, which may later progress to malignant transformation.[17] Consistent with our findings, current literature also indicates that the most common skin cancers are squamous cell carcinoma (SCC) and basal cell carcinoma (BCC), with a slight predominance of SCC. Pre-malignant lesions, such as solar keratoses – which can progress to SCC – are also frequently observed in individuals with significant and chronic sun exposure.[18]

Due to eye-related complications, many affected individuals do not advance to higher levels of education, as reduced visual acuity often limits their performance in mainstream schools.[19]

Low socio-economic status is linked to manual labor in productive years as the only viable option in developing countries, like South Africa, consequently leading to higher chances of prolonged and repeated sun exposure, sunburn, pre-malignant and malignant transformation of sun-exposed skin sites.[20]

Challenges such as limited health-related awareness, restricted access to health services, stigmatization, poverty, social discrimination, and lack of knowledge among affected individuals, their families, the broader society, and even healthcare practitioners have all been identified as plausible factors contributing to late referrals. This leads to late presentation at appropriate centres of treatment with multiple or deep skin malignancies (>4 cm in diameter), often warranting advanced treatment that is associated with disfigurements, repeated medical visits, and significantly high costs. SCC is the most common among all epidermal skin cancers and tends to be recurrent and aggressive in individuals with chronic skin damage from prolonged UV exposure.[21,22]

Financial constraints, lack of community support, and superstitious beliefs remain major concerns. Furthermore, threats, attacks, abductions, mutilations, killings, and even the exhumation of graves of individuals with OCA in certain African countries continue to pose significant challenges for affected individuals and their families.[19,23]

The above factors collectively lead to a heightened relation between certain types of skin cancers and OCA.

Conclusions

OCA is one of the most common causes of cutaneous malignancies in Africans. A significant number of affected people present with locally advanced malignant disease, often needing excision and/or radiation therapy, resulting in permanent disfigurements. In addition, many of them require multiple visits to specialized medical centers for cryotherapy and regular follow-up appointments.

There is a notable association between certain types of skin malignancies and cutaneous premalignant conditions in patients with OCA. The high prevalence of epidermal malignancies in this group of individuals can be reduced through many interventions, such as access to free and quality health care, enhanced community education, better structured support systems, and intentional education drives for communities and health care workers about OCA.[24]

Equipping medical personnel with essential knowledge will enable early detection of skin pathology through targeted screening and prompt referral to appropriate medical centers. An education drive can play a significant role in reducing ignorance and encourage more community involvement in preventing crimes against affected individuals.

Universal precautions against sunlight exposure should be introduced early in childhood, continue throughout life, and include minimizing outdoor activities during peak sunlight hours, wearing protective clothing to cover as much of the skin as possible, and applying sunscreen to exposed skin during the day.

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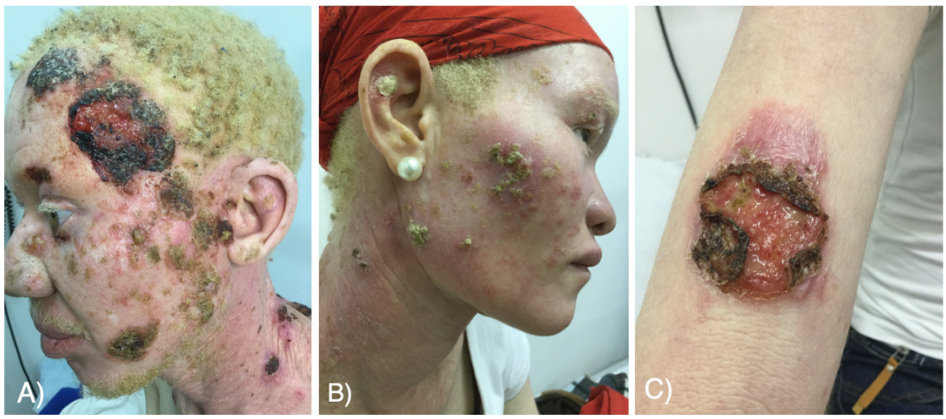
Table 1. Clinical subtypes of OCA.

OCA type I	Classical tyrosinase-negative albinism, pale skin and yellow to white hair, and eyes are blue-grey (often with decrease in visual acuity). This is the sub-type of OCA that present with highest of cutaneous complications.
OCA type II	Phenotypes with pigmentary dilution that ranges from minimal to moderate. Pigmented nevi "normal skin sites" may develop and darken when the skin is exposed to the sun. Eye color varies greatly.
OCA type III	Skin is light brown, hair is reddish-brown, and eye color can be blue or brown. Also called Rufous type.
OCA type IV	The phenotype is similar to that of OCA type II.
OCA type V	Skin is pale and hair is golden-colored.
OCA type VI	Skin can be pale, and hair can be light at birth and may darken with age.
OCA type VII	Skin pigment is decreased, and hair can range from whitish to brown.

Figure 1. A) 32-year-old male patient, presenting for the first time at the dermatology outpatient department with marked erythema, multiple solar keratoses, squamous cell carcinoma, and a large basal cell carcinoma in sun-exposed areas; **B**) 32-year-old male patient, presenting for the first time at dermatology outpatient department with marked erythema, multiple solar keratosis, squamous cell carcinoma and a large basal cell carcinoma in sun exposed areas; **C**) A large poorly differentiated squamous cell carcinoma on the anterior aspect of the right arm, with marked ulceration and necrotic, raised edges in a male patient with OCA.



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