***Original Research Article***

**Squamous cell carcinoma of the skin among albinos: A case study in Southeastern Nigeria**

**Abstract**

I**ntroduction**: Squamous Cell Carcinoma (SCC) is a prevalent skin cancer, with a higher incidence among individuals with albinism due to their lack of melanin protection. **Aim:** This study investigates the association between SCC and different types of albinism, ocular-cutaneous, cutaneous, and ocular, by evaluating serum markers such as Squamous Cell Carcinoma Antigen (SCCag), Human Melanoma-Associated Antigen (HMAA), and Alpha-Tumour Necrosis Factor (Alpha-TNF) and was conducted in Southeastern Nigeria, where albinism prevalence is relatively high. **Method:** A total of 300 individuals with albinism, consisting of 100oculo-cutaneous (OCA), 100 cutaneous (CA), and 100 ocular albinism (OA), participated in this study. Age-matched controls (n=100) were included. In order to conduct the study, an 8 ml venous blood sample was collected from each participant. Serum SCCag, HMAA and alpha-TNF levels were determined using the ELISA technique. The data generated were subjected to statistical analysis using IBM SPSS version 23. **Results:** The results revealed significantly higher serum levels of SCCag, HMAA, and Alpha-TNF in individuals with ocular-cutaneous, cutaneous and ocular albinism compared to controls (p=0.000 in each case). Suggesting a heightened risk of SCC development. **Conclusion:** These findings underscore the need for targeted interventions, including regular skin screenings and preventive measures.

**Keywords:** Squamous Cell Carcinoma, Albinism, SCCag, HMAA, Alpha-TNF, Nigeria, Skin Cancer

**Introduction**

Non-melanoma skin cancers (NMSCs) are the most common human malignancies, with steadily rising incidence. The main types of NMSC, basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), account for about 99% of all NMSCs (Ciążyńska et al., 2021). Squamous Cell Carcinoma (SCC) is a common non-melanoma skin cancer arising from keratinocytes, often linked to excessive ultraviolet (UV) exposure [4]. Individuals with albinism, particularly those with ocular-cutaneous albinism, face a higher risk of developing SCC due to their lack of melanin, which provides natural UV protection [5]. In Nigeria, where sun exposure is high, SCC cases among albinos are frequently reported [1]. Studies in Nigeria have documented that malignant skin cancers constituted 7% to 20% of all malignancies. There is also a worldwide increase in the prevalence, morbidity, and mortality rate of skin cancer (Ozor et al., 2023). However, limited studies have assessed the biochemical markers associated with SCC risk in albinos [5]. This study evaluates the association of SCC with serum markers in different types of albinism, providing insight into their vulnerability and potential preventive strategies.

SCC is a prevalent form of non-melanoma skin cancer that arises from keratinocytes and is frequently associated with excessive ultraviolet (UV) radiation exposure. Chronic sun exposure is a well-established risk factor for SCC, particularly in individuals with reduced skin pigmentation, as melanin plays a crucial role in protecting the skin from UV-induced DNA damage [1,2]. SCC patients tend to undergo surgical treatment that involves excision of the tumour, lymph node dissection, and reconstruction (Shambharkar et al., 2021). Albinism, a genetic condition characterised by the partial or complete absence of melanin, increases the risk of developing SCC, particularly among individuals with oculo-cutaneous albinism (OCA), cutaneous albinism (CA), and ocular albinism (OA). OCA affects the skin, hair, and eyes, rendering individuals highly susceptible to UV damage [3]. CA primarily affects the skin and hair, while OA primarily impacts the eyes, with minimal or no skin involvement. Among these subtypes, individuals with OCA and CA face a significantly higher risk of SCC due to their extensive sun exposure and lack of protective melanin [4,5]. In tropical regions such as Nigeria, where sun exposure is intense, cases of SCC among albinos are frequently reported [6]. Despite this, research focusing on the biochemical markers associated with SCC in albinos remains limited. Understanding the molecular and biochemical changes that predispose individuals with albinism to SCC is essential for developing early diagnostic tools and effective preventive strategies [7].

**Justification for the Study**

Studies have shown that individuals with albinism, particularly in sun-intense regions, experience disproportionately high rates of SCC [8]. Due to the lack of melanin, these individuals suffer from frequent sunburns, actinic keratosis, and subsequent malignant transformations leading to SCC. The limited availability of effective sunscreen and protective measures exacerbates their vulnerability [9].
While the link between albinism and SCC is well recognised, few studies have investigated the biochemical markers that could serve as indicators of SCC development in different types of albinos [10]. Most existing research focuses on clinical observations rather than molecular or biochemical assessments [11]. The importance of serum biomarkers in early detection is that identifying serum biomarkers associated with SCC in albinos could provide valuable insights into the disease's pathogenesis and aid in early diagnosis [12]. Biomarkers such as inflammatory cytokines, oxidative stress indicators, and genetic mutations linked to SCC could be explored to develop non-invasive diagnostic tools [13].

Understanding the molecular pathways involved in SCC progression among albinos could inform the development of targeted preventive and therapeutic strategies. These could include enhanced sun protection protocols, antioxidant-based interventions, and personalised treatments tailored to the specific needs of albino subpopulations [14]. This research has significant public health relevance, particularly in regions with a high albino population and intense UV exposure [15]. The findings could contribute to policy recommendations for improved healthcare access, education on sun protection, and early cancer screening programs for albinos [16].

**Inclusion criteria**: Subjects were male and female between the ages of 18-60 years and were characterised by those with skin, hair and eyes hypo pigmented, characteristic skin lesion distribution, reduced visual acuity, nystagmus and strabismus. The cutaneous were primarily characterised by hypopigmented skin without any direct involvement of the eyes, while Ocular were characterised only by those with ocular involvement, with characteristics like nystagmus, strabismus and poor visual acuity [5].

**Exclusion criteria**: Pigmented healthy subjects without any of the characteristics listed for albinism [5].

**Materials and Methods**

**Study Population and Design**

The sample size was calculated based on a 95% confidence interval and, desired accuracy of 0.05. This study was conducted in some South-eastern Nigerian Universities, namely, Anambra State University teaching hospital Awka, Imo State University teaching hospital Orlu and University of Nigeria teaching hospital Enugu. Focusing on individuals diagnosed with ocular-cutaneous, cutaneous, and ocular albinism. An approval was obtained from the albino foundation of Nigeria, and informed consent was obtained from all participants.

Participants were clinically examined and categorised based on standard diagnostic criteria for albinism. The study population included 100 OCA, 100 CA, 100 OA and 100 control group of non-albino individuals for comparison.

**Sample Collection and Storage**

In this study, 8 millilitres of venous blood samples were collected from participants under aseptic conditions. They were stored in plain tubes, centrifuged, and serum separated into aliquots, stored at -20oC for makers for determination of squamous carcinoma antigen, Human melanoma antigen and alpha-TNF.

**Laboratory Analysis Methods**

The Enzyme-linked Immunosorbent Assay (ELISA) method was used for the estimation of serum SCCag, Alpha-TNF and Human melanoma Associated antigen (HMAA) concentration, using reagent kits all supplied by Melsin Medical Company Limited. Catalogue numbers EKHU-0259 for SCCag, EKHU-2228 for HMAA, and EKHU-2141 for alpha-TNF.

Principle of ELISA technique: The Enzyme-linked Immunosorbent Assay (ELISA) is an analytical technique designed to detect and quantify soluble substances such as peptides, proteins, antibodies and hormones. The fundamental principle involves the specific interaction between an antigen and its corresponding antibody, utilising an enzyme-linked detection system to produce a measurable signal indicative of the presence and concentration of the target analyte [6].

**Statistical Analysis**

Data were analysed using SPSS version 25.0. The mean ± standard deviation (SD) of SCCag, HMAA, and Alpha-TNF levels were compared between albino individuals groups and controls using independent t-tests. A p-value < 0.05 was considered statistically significant.

**Results**

**TABLE 1**

**Mean±SD values of serum markers of squamous cell carcinoma of skin; SCCag, HMAA, and alpha-TNF in Ocular-Cutaneous albino and Control**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| VARIABLESMEAN± SD | OCULAR-CUTANEOUS, N=100 | CONTROLN= 100 | t-Value | p-Value0.05 |
| SCCag mg/dlLower 95% C.IUpper 95% C.I | **288.72±98.97****265.07****312.00**  | **217.51±30.45****211.50****223.52** | **4.421** | **0.000** |
| HMAA(mg/dl)Lower 95% C.IUpper 95% C.I | **2.31±1.90****1.94****2.70** | **1.07±0.57****0.90****1.23** | **4.433** | **0.000** |
| TNF(mg/dl)Lower 95% C.IUpper 95% C.I | **99.73±83.10****85.78****125.71** | **74.59±7.68****72.40****76.77** | **2.137** | **0.038** |

**OCA: Ocular-Cutaneous Albino**

**SCC: Squamous Cell Carcinoma**

**HMAA: Human Melanoma Associated Antigen**

**TNF: Cellular Damage Marker**

**Presents Mean±SD values of serum markers of squamous cell carcinoma of skin; SCCag, HMAA, and alpha-TNF in Ocular-Cutaneous albino and Control groups.**

There were statistically significantly higher serum levels of SCCag (288.7296 ±89.9769 vs 217.5150 ± 30.4535, P=0.000), HMAA (2.3168 ± 1.9005 vs 1.0726± 0.5756, P=0.000) and alpha-TNF (99.7359 ± 83.1010 vs (74.5924 ± 7.6895, p=0.000) in Cutaneous albino compared to the control (Table 1).

 **TABLE 2**

**Mean±SD values of Serum markers of Squamous Cell Carcinoma of skin; SCCag, HMAA, and alpha-TNF in Cutaneous albino and Control**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| VARIABLESMEAN± SD | CUTANEOUS N=100 | CONTROLN= 100 | t-Value | p-Value0.05 |
| SCCAg mg/dlLower 95% C.IUpper 95% C.I | **298.62±120.65****274.91****322.53** | **217.51±30.45****211.50****223.52** | **4.513** | **0.000** |
| HMAA(mg/dl)Lower 95% C.IUpper 95% C.I | **1.81±0.14****1.79****1.85** | **1.07±0.57****0.95****1.18** | **8.497** | **0.000** |
| TNF(mg/dl)Lower 95% C.IUpper 95% C.I | **120.9475±111.46****99.30****143.29** | **74.59±7.68****73.07****76.11** | **2.928** | **0.005** |

**OCA: Ocular-Cutaneous Albino**

**SCC: Squamous Cell Carcinoma**

**HMAA: Human Melanoma Associated Antigen**

**TNF: Cellular Damage Marker**

**Presents Mean±SD values of serum markers of squamous cell carcinoma of skin; SCCag, HMAA, and alpha-TNF in Cutaneous albino and Control groups.**

There were significantly higher serum levels of SCCag (298.6292±120.6539 vs. 217.5150±30.4535, p=0-000), HMAA (1.8154±0.14897 vs. 1.0726±0.5756, p=0.000) and Alpha-TNF (120.9475±111.4628 vs. 74.5924±7.6895, P=0.005) in Cutaneous Albino compared to the control (Table 2).

**TABLE 3**

**Mean ±SD values of Serum markers of Squamous Cell Carcinoma of skin; SCCag, HMAA, and alpha-TNF in Ocular Albino and Control**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| VARIABLESMEAN± SD | OCULARN=100 | CONTROLN= 100 | t-Value | p-Value0.05 |
| SCCag mg/dlLower 95% C.IUpper 95% C.I | **260.49±11.72****258.60****263.24** | **217.51±30.45****211.50****223.52** | **9.277** | **0.000** |
| HMAA(mg/dl)Lower 95% C.IUpper 95% C.I | **1.98±0.08****1.96****1.99** | **1.07±0.57****0.95****1.18** | **10.823** | **0.000** |
| TNF(mg/dl)Lower 95% C.IUpper 95% C.I | **86.05±1.59****85.71****86.33** | **74.59±7.68****73.07****76.11** | **10.383** | **0.000** |

OCA: Ocular-Cutaneous Albino

SCC: Squamous Cell Carcinoma

HMAA: Human Melanoma Associated Antigen

TNF: Cellular Damage Marker

**Presents Mean±SD values of serum markers of squamous cell carcinoma of skin; SCCag, HMAA, and alpha-TNF in Ocular albino and Control groups.**

There were significantly higher serum levels of SCCag (260.4962±11.772553 vs. 217.5150±30.4535, p=0-000), HMMA (1.9825±0.08336 vs. 1.0726±0.5756, p=0.000) and Alpha-TNF (86.0535±1.5975 vs. 74.5924±7.6895) in Ocular Albino compared to the control (Table 3).

**Discussion**

In tables 1, 2 and 3 show significantly higher serum levels of SCCag, in ocular-cutaneous (282.75±98.97 mg/dl), cutaneous (298.62±120.65 mg/dl) and ocular albino (260.49±11.72 mg/dl) compared to controls (217.51±30.45 mg/dl), with p-values of 0.000. This suggests a higher risk or presence of SCC in albino individuals, likely due to increased UV radiation susceptibility in individuals with reduced melanin protection levels [6].These findings reaffirm that albinos are at a higher risk of SCC due to their inherent lack of melanin, leading to increased UV-induced DNA damage [6]. The cutaneous albino group had the highest SCCag levels, which may be attributed to greater cumulative UV exposure compared to ocular and ocular-cutaneous albinos [7].

HMAA levels were also significantly increased in ocular-cutaneous albino (2.31±1.90 mg/dl) and cutaneous albino (1.81±0.14 mg/dl) and ocular (1.98±0.08 mg/dl) compared to controls (1.07±0.57 mg/dl), with p-values of 0.000. HMAA is associated with melanoma and other skin-related malignancies, and its elevation in albino populations suggests increased cellular stress or premalignant transformation [1]. This suggests a possible predisposition to melanoma-like changes or increased skin cell turnover in albino populations [1].

The higher HMAA levels in ocular-cutaneous albinos could indicate a more widespread systemic response to UV damage compared to purely cutaneous or ocular albinos [3].

Alpha-TNF, a pro-inflammatory cytokine involved in tumour progression, was significantly higher in cutaneous albino (120.947±111.46 mg/dl, p=0.005), Ocular-cutaneous albino (99.73±83.10 mg/dl, p=0.038) and Ocular albino 86.05±1.59 mg/dl, p=0.000) compared to controls (74.59±7.68 mg/dl). This suggests a heightened inflammatory response in albinos, likely due to chronic UV exposure and oxidative stress leading to SCC development [8]. The higher Alpha-TNF in cutaneous albino compared to ocular-cutaneous albino supports the idea that inflammation-driven carcinogenesis is more pronounced in individuals with extensive skin exposure [1].

The findings of this study support existing evidence that albino individuals, particularly those with ocular-cutaneous and cutaneous forms, have a significantly higher risk of developing SCC [9]. The elevated SCCag and Alpha-TNF levels indicate increased inflammation and tumour activity, aligning with SCC pathogenesis [10].

Comparisonwithprevious studies has demonstrated that SCC is more prevalent among albinos in sun-intensive regions [11]. The high SCCag levels found in this study reinforce the role of SCCag as a reliable biomarker for early SCC detection in albinos [5]. The increase in Alpha-TNF further suggests a strong inflammatory response, which may contribute to tumour progression [12].

**Conclusion**

The significant differences in serum markers among albinos highlight the urgent need for early screening programs in Nigeria. Sunscreen use, protective clothing, and community awareness campaigns should be prioritised to mitigate SCC risk. This study demonstrates that albino individuals, especially those with ocular-cutaneous and cutaneous albinism, have significantly higher SCCag, HMAA, and Alpha-TNF levels, indicating a higher risk of SCC. The findings emphasise the need for proactive skin cancer surveillance and protective measures among albinos in Southeastern Nigeria.

**Recommendations**

Early screening programs and regular dermatological screenings for all albinos’ individuals with albinism are necessary. These findings reinforce that albino populations, particularly cutaneous albinos, are at greater risk of SCC due to increased biomarker expression linked to skin malignancies. Regular dermatological screening and protective measures such as sunscreen application and reduced UV exposure are strongly recommended.

Disclaimer (Artificial intelligence)

Option 1:

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

Option 2:

Author(s) hereby declare that generative AI technologies such as Large Language Models, etc. have been used during the writing or editing of manuscripts. This explanation will include the name, version, model, and source of the generative AI technology and as well as all input prompts provided to the generative AI technology

Details of the AI usage are given below:

1.

2.

3.

**References**

1. Awe O., O. and Azeke T., A. (2018). Cutaneous Cancers in Nigerian Albinos: A Review of 22 Cases. Nigerian Journal Surgery. 24(1):34-38.
2. Enechukwu Nkechi Anne, Ogun Gabriel Olabiyi, Ezejiofor Ogochukwu Ifeanyi, Chukwuanukwu Titus Osita, Yaria Joseph, George Adekunle Olufemi, Ogunbiyi Adebola Olufunmilayo (2020). **Histopathologic patterns of cutaneous malignancies in individuals with oculocutaneous albinism in Anambra state, Nigeria: a paradigm swing?**ecancer **14** 1013.
3. Thomas MG, Zippin J, Brooks BP. Oculocutaneous Albinism and Ocular Albinism Overview. 2023 Apr 13. In: Adam MP, Feldman J, Mirzaa GM, (2023).. *Gene Reviews* [https://www.ncbi.nlm.nih.gov/books/NBK590568
4. Fania L, Didona D, Di Pietro FR, Verkhovskaia S, Morese R, Paolino G, Donati M, Ricci F, Coco V, Ricci F, Candi E, Abeni D, Dellambra E.(2021). Cutaneous Squamous Cell Carcinoma: From Pathophysiology to Novel Therapeutic Approaches. *Biomedicines.* 9;9 (2):171.
5. Lekalakala PT, Khammissa RA, Kramer B, Ayo-Yusuf OA, Lemmer J, Feller L. (2015). Oculocutaneous Albinism and Squamous Cell Carcinoma of the Skin of the Head and Neck in Sub-Saharan Africa. *Journal of Skin Cancer.* :167847. doi: 10.1155/2015/167847
6. Mabula JB, Chalya PL, Mchembe MD, Jaka H, Giiti G, Rambau P, Masalu N, Kamugisha E, Robert S, Gilyoma JM. Skin cancers among Albinos at a University teaching hospital in Northwestern Tanzania: a retrospective review of 64 cases. *BioMedical Central Dermatol*. 8;12:5.
7. Osama, A., Neringa J., Saif A., Saleh A., Andrew G., Lee Francisco J., James R., Donny, W., Mounir, B., Gerhard, W., Iqbal Ike, K., A., and Khalid H.(2024).Albinisim; Bckground, Pathophysiology, Epidemiology *Mediscape*. 23 6**(8**)
8. Brenner M, Hearing VJ. The protective role of melanin against UV damage in human skin. *Photochem Photobiol. ;*84(3):539-49.
9. Onyishi N., and, Ohayi S., R. (2022). Prevalence of Squamous and Basal Cell Carcinomas in African Albino Skin Cancer Lesions: A Systematic Review and Meta-Analysis of Proportion. *Journal of Skin Cancer*. 30: 5014610. doi: 10.1155/2022/5014610.

 10.Brierly G, Celentano A, Breik O, Moslemivayeghan E, Patini R, McCullough M, Yap T. (2023). Tumour Necrosis Factor Alpha (TNF-α) and Oral Squamous Cell Carcinoma. Cancers. *Basel*.19;15 (**6):**1841.

 11.Kiprono SK, Chaula BM, Beltraminelli H.( 2014). Histological review of skin cancers in African Albinos: a 10-year retrospective review. *BioMedical Central Cancer*. 6(**14)** 157. doi: 10.1186/1471-2407-14-157.

 12 Jang D., I., Lee, A., H., Shin H., Y., Song H., R., Park, J., H., Kang, T.,B., Lee S., R., Yang S.,H.( 2021). The Role of Tumor Necrosis Factor Alpha (TNF-α) in Autoimmune Disease and Current TNF-α Inhibitors in Therapeutics. *International Journal Molecular Science*. 8; 22 **(5):**2719. doi: 10.3390/ijms22052719.

1. Lerche C., M., Togsverd-Bo K., Philipsen P., A., Wulf H., C.(2017) . Impact of UVR Exposure Pattern on Squamous Cell Carcinoma-A Dose-Delivery and Dose-Response Study in Pigmented Hairless Mice. *International Journal of Molecular Science.* ; 18(**12):**2738. doi: 10.3390/ijms18122738.
2. Huang, R., X., Zhou, P., K.(2020). DNA damage response signaling pathways and targets for radiotherapy sensitization in cancer. *Signal Transduction Targeted Ther*apy. (**5)**, 60 . <https://doi.org/10.1038/s41392-020-0150->

 15. Saka B., Teclessou J., N., Akakpo S., A., Gnossike P., Doh K., Adam S., Mouhari-Toure A., Mahamadou G., Kassang P., Elegbede Moise Y., Darre T., Kombate K., Pitché P. (2020). A Histopathological Study of Skin Lesions in Individuals with Oculocutaneous Albinism in Togo in 2019. *Journal of Skin Cancer*. 29:2361957. doi: 10.1155/2020/2361957.

17 Hong, E.S., Zeeb, H. & Repacholi, M.H. Albinism in Africa as a public health issue. *British medical Public Health* **6**, 212 (2006). https://doi.org/10.1186/1471-2458-6-212

 17. Asuquo1, M., E., Otei, O., O., Omotoso, J., and BasseyE., E.
(2010). Letter: Skin cancer in albinos at the University of Calabar Teaching Hospital, Calabar, Nigeria.Dermatology Online Journal 16 (4): 14*.*
<https://doi.org/10.5070/D37xj545jx>

18. Ciążyńska, M., Kamińska-Winciorek, G., Lange, D., Lewandowski, B., Reich, A., Sławińska, M., ... & Lesiak, A. (2021). The incidence and clinical analysis of non-melanoma skin cancer. *Scientific reports*, *11*(1), 4337.

19. Ozor, N. S., Ezejiofor, I. F., Ezejiofor, O. I., Menkiti, F. E., Madubuike, K. C., Ndukwe, C. O., ... & Osonwa, E. (2023). Malignant Skin Tumors seen in Nigeria Nnamdi Azikiwe University Teaching Hospital Nnewi: A 10-year Review (January 2008 to December 2017). *Clinical Dermatology Review*, *7*(4), 352-357.

20. Shambharkar, M., Udan, R., Swarkar, A., Khandar, J., Sakharkar, S., & Tembhare, V. (2021). Case Report on Squamous Cell Carcinoma of the Lip. *Journal of Pharmaceutical Research International*, *33*(53B), 182–188.