Patterns of sunlight exposure and risk of basal cell carcinoma: A case-control study

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Abstract

Background: Basal cell carcinoma is the most common keratinocyte skin cancer worldwide in fair skin colored people and its incidence is rising annually. The main risk factor for developing the disease is natural or artificial ultraviolet radiation. Different studies suggest that for development of basal cell carcinoma more important is intermittent and intense sunburns, rather than cumulative and long-term exposure to UV. However, many studies investigated the association between chronic occupational solar exposure and basal cell carcinoma.

Aim: The aim of our study was to analyze the recent clinical trends and risk factors associated with basal cell carcinoma and reveal the possible correlation between sunburn occurrences, outdoor activities, and the risk of disease development.

Methods: A hospital-based case-control study was conducted, involving 47 histologically confirmed basal cell carcinoma patients. The control group, comprising 94 participants who visited the clinic for other non-cancerous skin dermatosis, was matched for age and gender with the cases. Data on various factors like gender, age, residence, Fitzpatrick skin type, experiencing sunburn, using sunscreens, outdoor activities, use of solariums and UV therapy, were collected using an adapted questionnaire and subjected to analysis. The gathered data underwent statistical analysis.

Results: The majority of cases (n=52; 71.2%) were situated in areas exposed to sunlight (p<0.001), with a female-to-male ratio of 1.35 to 1. The nodular subtype of basal cell carcinoma emerged as the predominant form (n=49; 67.2%). Furthermore, the proportion of patients in the study cohort with Fitzpatrick phototypes I and II (n=38; 80.9%) was notably higher compared to controls (n=50; 53.2%, p=0.002). The percentage of patients with having a job related to outdoor activities in the study group (n=29; 61.7%) was significantly higher than in controls (n=36; 38.3%) - OR=3.27 (95%CI - 1.58-6.78, p=0.001). The association between intermittent sun exposure and BCC development risk was not statistically significant in both study groups (OR 0.74, 95% CI 0.37-1.50, p=0.404).

Conclusions: The etiology of BCC often involves a complex interplay of various etiological factors, posing challenges in isolating each factor's specific contribution. Our study highlighted a strong association between Fitzpatrick skin types I and II and occupational exposure to sunlight, significantly increasing the likelihood of BCC development in cases compared to controls. However, we did not observe a statistically significant correlation between intermittent sun exposure and the risk of developing BCC. **(TCM-GMJ December 2024; 9 (2): P23-P28)**

Keywords: Basal cell carcinoma, BCC, Risk factors, Sun exposure, Outdoor activity, Sunburn .

Introduction

Skin cancer ranks as the most prevalent form of cancer globally among people categorized under Fitzpatrick skin types I–III(1). Both melanoma and keratinocyte skin cancers (also known as nonmelanoma skin cancers) have seen a steady rise in occurrence over recent years and are expected to continue this trend. The World Health Organization (WHO) predicts that by 2025, there will be over 1.7 million new cases of melanoma and keratinocyte skin cancers worldwide. Among keratinocyte skin cancers Basal cell carcinoma (BCC) accounts for approximately 75%, followed by squamous cell carcinoma (SCC) with 20%(2). While BCC is indeed a malignant form of cancer, its rate of metastasis (0.0028% to 0.5%) and morbidity (10-year MRR = 0.91) is extremely low, however this tumor can be associated with significant morbidity and cost(3–5). Typically, indi-

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viduals are diagnosed with BCC during their sixth or seventh decade of life, with men having double the likelihood of developing this type of cancer compared to women. Although in recent years, the incidence rate has increased significantly in younger patients and in females due to the increasing use of artificial solar beds(6–8).

Exposure to ultraviolet radiation (UVA and UVB wavebands) remains the primary risk-factor for BCC and other skin cancers. It triggers the progression of skin cancer through direct cellular damage, such as DNA mutations like pyrimidine substitutions, induction of oxidative stress, creating an "energy crisis" that impairs effective DNA repair, initiating local inflammatory responses, and suppression of cutaneous antitumor immunity(9). However, the exposure patterns associated with the risks of various skin cancer types appear to be different. Some research suggests that intermittent and intense sunlight exposure, like experiencing multiple sunburns, increases the likelihood risk of BCC development, whereas cumulative and long-term UV exposure over time does not appear to have the same effect, while SCC is linked to cumulative or occupational exposure(10,11).

Many epidemiological studies have been done to see whether occupational chronic exposure to sunlight raises the risk of developing BCC. A systematic review and meta-analysis conducted by Bauer et al. concluded that outdoor workers are at significantly increased risk for BCC(12). Although recently published review of epidemiologic literature with meta-analysis focusing on particular methodological aspects says, that the current epidemiologic evidence base does not permit the conclusion that regular outdoor workers have an increased risk of BCC(13). According to this study, research with minimal bias, especially regarding selection bias, indicates no significant link between occupational solar exposure and BCC.

The aim of our study was to analyze the recent clinical trends and risk factors associated with basal cell carcinoma and reveal the possible correlation between sunburn occurrences, outdoor activities, and the risk of developing BCC.

Methods

A hospital-based case-control study was conducted at the Dermatology Department of Scientific/Research National Center of Dermatology and Venereology. Study protocol was approved by the Ethics Committee of the same Center (Approval N 18/6, date 20.09.2018).

The inclusion criteria of the study were only those patients diagnosed with histologically confirmed BCC who provided consent. An exclusion criterion involved patients with genetic disorders like Basal cell nevus syndrome (Gorlin-Goltz syndrome), Xeroderma pigmentosum, Nevus sebaceous, Epidermodysplasia verruciformis, Rombo syndrome, Bazex syndrome, and Albinism. Additionally, exclusion criteria were patients who were unable to independently complete the questionnaire (disability of writing, reading, and understanding the questions), individuals who underwent photo and radiotherapy, and those with chronic immunosuppression.

Based on these inclusion and exclusion criteria, 47 patients met the selection criteria as cases. The control group, comprising 94 participants, included the patients who visited our clinic for other non-cancerous skin problems. Patients in control group were matched for age and gender with the cases. Consequently, the ratio between cases and controls stood at 1:2.

The diagnosis of BCC in all patients was made by clinical manifestation, followed by dermoscopy and histological confirmation. After obtaining informed consent, the patients were requested to fill out an anonymous questionnaire. The study instrument was an adapted version of a self-administered questionnaire designed to quantify the risk for skin cancer, validated by Mexican dermatologists, along with a questionnaire used in Euromelanoma Campaign(14,15). The questionnaire obtained information regarding gender, age, residence, Fitzpatrick skin type, experiencing sunburn, using sunscreens, outdoor activities, use of solariums and UV therapy. Separate questionnaires were filled out for each patient, documenting the medical history of the disease, clinical and morphological forms, and distribution of BCC lesions. The clinical subtypes of BCC were classified as nodular, superficial, morphoeic, pigmented and fibroepithelial.

Statistical analysis of the obtained data was performed using the software SPSS22.0 (IBM, Chicago, Illinois, USA). Continuous variables are presented as Mean ± Standard Deviation (SD). The difference between these parameters of the study and control groups was assessed by 2-sided t-test and Fisher's exact test. Categorical variables are presented as percentages. The difference between these parameters of the study and control groups was evaluated by Chi2-test and Fisher's exact test. The odds ratio (OR) and its 95% confidence intervals were used to evaluate the risk factors of the disease. The results were considered significant at $p < 0.05$.

Results

Among the 47 patients with BCC 27 (57.4%) were female and 20 (42.6%) were male, with a mean age of 67.2±12.5 and a median of 71 years, ranging from 32 to 88 years old. The female-to-male ratio was 1.35:1. Eight patients (17.02%) had a personal and/or family history of BCC. Seven patients (14.9%) were presented with multiple BCC lesions with the number of tumors ranging from 2 to 18.

Of the 73 tumors observed, the nodular subtype of BCC was the most prevalent, accounting for 49 cases (67.2%), followed by pigmented BCC with 16 cases (21.9%), superficial BCC with 5 cases (6.8%), and morphoeic BCC with 3 cases (4.1%). No individuals diagnosed with fibroepithelial BCC were found among the patients.

Regarding tumor location, the majority of lesions were situated on the head, with the face being the area most commonly affected. The most prevalent area was the nose (n=18; 24.6%) followed by the waist (n=9; 12.3%), periorbital area (n=7; 9.6%), and forehead (n=6; 12.8%). Most of the BCCs (n=52; 71.2%) were in the sun-exposed areas revealing a statistically significant association (Chi2=3.16, df=1, p<0.001). Of non-sun-exposed skin areas, a high percentage of cases were found on the waist (n=9; 12.3%)

and on the abdomen (n=4; 5.5%). Of non-sun-exposed skin areas, a high percentage of cases were found on the waist (n=9; 12.3%) and on the abdomen (n=4; 5.5%). The data presented is shown in Table 1.

Based on the Fitzpatrick skin type the participants from both case and controls groups were presented with Fitzpatrick phototype I to IV. The difference between the distribution of phototypes in the groups was significant (Chi2=11.03, df=3, p=0.012). The obtained results showed that the percentage of patients in the study group with Fitzpatrick phototype I and II (n=40; 80.9%) was significantly higher than in controls (n=50; 53.2%) – OR=3.71 (95%CI – 1.62-8.54, p=0.002). Mentioned data is presented in Table 2.

One of the survey questions addressed whether participants had ever suffered from severe sunburn, characterized by intense pain, redness, and blisters. The responses are detailed in Table 3. Despite a higher percentage of individuals reporting no history of sunburn in both the case (N=23, 48.9%) and control (N=53, 56.4%) groups, no significant difference was observed between the two groups' responses (OR 0.74, 95% CI 0.37-1.50, p=0.404).

One of the questions asked if the study subjects had jobs that involved working outdoors in the sun. Table 4 shows the distribution of "Yes" and "No" responses in each group. In the study group, 29 patients (61.7%) had these jobs, which is significantly higher than the 31 patients (38.3%) in the control group. The odds ratio was 3.27 (95% CI – 1.58-6.78, p=0.001).

The study subjects were asked how often they use sunscreens when they are exposed to the sun for > 1 hour for sunbathing and for other than sunbathing. The findings are outlined in Table 5 and Table 6. Across both groups, the majority indicated never using sunscreen during sunbathing (cases N=39, 83.0% and controls N=77, 81.9%) or for purposes other than sunbathing (cases N=43, 91.5% and controls N=85, 90.4%). However, the odds ratio of responses in both case and control groups did not yield statistical significance.

One question inquired whether the individuals under study typically spent their vacations in sunny resorts. Among the 47 cases, 22 (46.8%) indicated regular summer holidaying in such destinations, while among the 94 controls, 47 participants (50%) reported the same vacationing pattern in sunny resorts. The findings are outlined in Table 7. The distribution of responses within each group did not yield statistical significance. Similarly, comparing responses between the case and control groups using odds ratios did not yield statistical significance either.

Neither the study participants nor the control group had undergone UVA and UVB therapy, or ever used artificial tanning beds.

Discussion

Basal cell carcinoma ranks as the most common type of skin cancer in humans. Contrary to global trends that often highlight higher incidence rates in men compared to women (2,16), our study revealed a distinct pattern: it was 1.35 times more prevalent in women than in men. This may be explained by the fact, that women in our country are more likely to seek the sun during their leisure time.

BCC has the potential to develop anywhere on the face and body, but it tends to appear more prominently on areas that are regularly exposed to the sun, particularly on the face (17). Our study revealed that the face was the most frequently affected area, with frequent occurrences observed on central facial sites such as the nose, forehead, periorbital, and perioral regions. Once more, this underscores the significance of solar radiation as a primary contributing factor to the development of basal cell carcinoma.

One of the major phenotypic risk factors of the occurrence of basal cell carcinoma is influenced by individual skin type. This suggests that individuals with lower melanin levels in their skin, who are prone to easily burning rather than tanning, face a higher risk(18). The Fitzpatrick skin type serves as a dependable gauge of BCC risk among individuals with fair skin. In the case group, participants classified as Fitzpatrick phototypes I to IV were examined, revealing a higher prevalence of the disease among those with lighter skin tones (types I and II). These findings align with existing literature, indicating a greater incidence among individuals of Caucasian descent. This contrast may be attributed to the protective properties of darker skin against the harmful effects of UV radiation, primarily due to higher melanin levels(19). Although we still see the development of BCC lesions in the darker skin colored people, however there are very few cases described in the literature(20).

The primary risk factor for BCC and other skin cancers continues to be exposure to ultraviolet radiation. UVR exposure includes factors such as indoor or outdoor occupation, geographic location, sunny vacations, and sunburn. The degree of risk for BCC is likely influenced by various aspects of sun exposure, including its pattern, timing, and quantity. Contradictory findings exist in the literature regarding the relationship between sun exposure aspects and the risk of developing BCC. The findings of a population-based, case-control study suggest that recreational sun exposure during childhood and adolescence increases the risk of developing BCC(21). Previous researches has shown that compared to prolonged, cumulative UV exposure, intermittent intense exposure is more strongly linked to BCC risk(22–24). However, Iannacone et al. examined the significance of sun exposure patterns (intermittent or continuous) and timing in BCC development(25). Their findings indicated that sun exposure correlated with the incidence of BCC regardless of the exposure pattern. A meta-analysis of sunburn and basal cell carcinoma risk conducted by Lashway et al. clearly highlights, that sunburn at any stage of life increases the risk of developing BCC, childhood sunburn doesn't increase basal cell carcinoma risk more than adult sunburn and the risk of basal cell carcinoma rises with an increase in the number of sunburns(24). Our study revealed a substantial correlation between prolonged sun exposure and the risk of developing BCC. Individuals in the case group, in contrast to the controls, exhibited a significantly elevated risk of BCC development (OR=3.27, 95% CI: 1.58-6.78, p=0.001),

particularly due to occupational engagement in outdoor activities. However, we did not observe any statistically significant correlation between sunburn and the risk of BCC development. The presence of this factor might stem from the limited sample size in our study, which can be viewed as a limitation of our research.

Interestingly, none of the patients reported using tanning beds in case and control groups. Additionally, it's worth noting that more than 80% of all participants in our study had never used sunscreen in their lifetime.

Conclusion

BCC frequently arises from the interplay of multiple etiological factors, making it challenging to determine each factor's individual contribution. Our study showed that Fitzpatrick skin type I and II and a job involving work outside in the sun was strongly associated with the development of BCC in cases compared to controls. We didn't find a statistically significant association between intermittent sun exposure and BCC development risk.

As a result, the link between sun exposure patterns and BCC risk remains uncertain, necessitating additional research. It is imperative to comprehensively understand and delineate the particular risk factors associated with individuals who develop skin cancer. This understanding can help identify high-risk individuals, enabling early detection and treatment.

Table 1. Distribution of tumors (n=73) by sites.

Localization	n=	%
Nose	18	24.6%
Waist	9	12.3%
Periorbital area (eyelids)	7	9.6%
Forehead	6	8.2%
Cheek	5	6.8%
Perioral area	5	6.8%
Scalp (Parietal part)	4	5.5%
Ear	4	5.5%
Abdomen	4	5.5%
Shoulder	3	4.1%
Eyebrow	2	2.7%
Clavicle area	2	2.7%
Chest	2	2.7%
Hip	1	1.4%
Upper arm	1	1.4%
Chi2 = 36.22, df=14, p=0.001		

Table 2. Distribution of participants according to Fitzpatrick skin phototype.

Answer	Cases (n=47)		Controls (n=94)		Chi2 -test	p
	n=	%	n=	%		
Phototype VI	0	0%	0	0%	N/A	N/A
Phototype V	0	0%	0	0%	N/A	N/A
Phototype IV	1	2.1%	11	11.7%	3.66	0.056
Phototype III	8	17.0%	33	35.1%	4.93	0.026
Phototype II	32	68.1%	44	46.8%	5.66	0.017
Phototype I	6	12.8%	6	6.4%	1.63	0.202

Table 3. Distribution of the answers on the question „Have you ever suffered from severe sunburn (with intense pain, redness and blisters?)" in the study groups.

Answer	Cases (n=47)		Controls (n=94)		OR (95%CI, p)
	n=	%	n=	%	
No	23	48.9%	53	56.4%	0.74 (0.37-1.50, p=0.404)
I don't remember	3	6.4%	5	5.3%	1.21 (0.28-5.31, p=0.797)
Yes, before the age of 20	7	14.9%	15	16.0%	0.92 (0.35-2.44, p=0.870)
Yes, after the age of 20	14	29.8%	21	22.3%	1.47 (0.67-3.25, p=0.336)
Chi2, p	19.63; <0.001		54.94; <0.001		

Table 4. The distribution of the answers to the question about having a job that involved working outside in the sun.

Answer	Cases (n=47)		Controls (n=94)		OR (95%CI, p)
	n=	%	n=	%	
No	18	38.3%	63	67.0%	**0.31 (0.15-0.63, p=0.001)**
Yes	29	61.7%	31	33.0%	**3.27 (1.58-6.78, p=0.001)**
Chi2, p	2.57; 0.108		10.89; 0.001		

Table 5. Distribution of the answers to the question „How often do you use sunscreen when you are outdoors for >1 hour for sunbathing?" in the study groups.

Answer	Cases (n=47)		Controls (n=94)		OR (95%CI, p)
	n=	%	n=	%	
Never	39	83.0%	77	81.9%	1.08 (0.43-2.71, p=0.876)
Sometimes	7	14.9%	8	8.5%	1.88 (0.64-5.55, p=0.252)
Always	1	2.1%	9	9.6%	0.21 (0.03-1.67, p=0.139)
Chi2, p	53.28; <0.001		99.85; <0.001		

Table 6. Distribution of the answers to the question „How often do you use sunscreen when you are outdoors for >1 hour for other than sunbathing?" in the study groups.

Answer	Cases (n=47)		Controls (n=94)		OR (95%CI, p)
	n=	%	n=	%	
Never	43	91.5%	85	90.4%	1.13 (0.33-3.91, p=0.837)
Sometimes	4	8.5%	4	4.3%	2.09 (0.50-8.77, p=0.321)
Always	0	0.0%	5	5.3%	0.17 (0.01-3.16, p=0.236)
Chi2, p	72.04; <0.001		137.89; <0.001		

Table 7. Distribution of the answers to the question „Did you spend your holidays in sunny resorts?" in the study groups.

Answer	Cases (n=47)		Controls (n=94)		OR (95%CI, p)
	n=	%	n=	%	
No	25	53.2%	47	50.0%	1.14 (0.56-2.29, p=0.721)
Yes	22	46.8%	47	50.0%	0.88 (0.44-1.77, p=0.721)
Chi2, p	0.19; 0.662		0.00; 1.000		

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