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An Epidemiology Study and Risk of Subsequent Basal Cell Carcinoma, A 5-year Retrospective Investigation

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Abstract

Background: This study aimed to investigate the epidemiology of basal cell carcinoma (BCC) and the probability of having another lesion in patients diagnosed with BCC.

Methods: This descriptive-analytical study was conducted from 2015 to 2017, based on the data from patients with definitive diagnoses of BCC in two university hospitals in Birjand. In this study, 85 patients with BCC were selected based on pre-defined inclusion criteria and then divided into two groups, including single and subsequent asynchronous lesions in another anatomic area. In this study, the information was collected by census method from diagnosed patients two years after surgery. The subsequent lesions in other anatomical areas were investigated, then tumor risk factors were compared in the two groups.

Results: The mean age of the patients was 67.83 ± 12.29, and the youngest and the oldest patients were 38 and 92 years old, respectively. Among the studied patients, 75.3% had a history of sun exposure. The most common occupations of the patients were farmer, rancher, and housekeeper. Head and neck regions were involved in 96.5%. The patients with subsequent asynchronous BCC in another facial skin region were 10.6% (CI95: 4.06 - 17.14). These patients have been subject to several simultaneous risk factors in their medical history; most of them were farmers older than 65 years. Two patients experienced three lesions in three different anatomical regions at different times. There was no statically significant difference between the two groups regarding mean age ($P = 0.47$), gender ($P = 0.73$), pathologic subtype ($P = 0.06$), and other risk factors ($P > 0.05$).

Conclusions: This study confirms the likelihood of having a subsequent lesion in other anatomical regions in patients diagnosed with BCC. Patients with a history of BCC require prolonged follow-up because of the probability of new BCC developing.

Keywords: Basal Cell Carcinoma, Skin Neoplasm, Non-melanoma Skin Cancer

1. Background

Basal cell carcinoma (BCC) is a slow-growing, non-progressive malignancy arising from basal cells of the epidermis or follicular structures (1). It was first described in 1824 by Jacob, who coined the term "ulcus rodents," and in 1951, Takarhad linked histopathological information about a specific tumor growth pattern to the clinical aspect (2, 3). BCC is characterized by a relatively low metastatic rate and slow growth (4), and it is most common after age 50 among males and females (5). An increased incidence has recently been noted in the population younger than 40 years. Compared to industrialized countries, increased exposure to UV light, ozone depletion, increased surveillance, and change in habits, such as smoking, dressing changes, and low mobility, are the reasons for the increase in the prevalence of BCC in developing countries (6). Over 80 percent of BCCs occur in the head and neck regions (7). The prevalence of non-melanoma skin cancers (NMSCs), including BCC and squamous cell carcinoma (SCC), is increasing globally and is subject to high government funding (8, 9).

Given the relatively hot and dry climate and many occupations that have constant and intense sun exposure, Iranian people, especially those living in South Khorasan province, have a high risk of contracting skin cancer. The patients diagnosed with BCC will likely experience subsequent lesions in other anatomical regions in the upcoming years. The geographical epidemiology of BCC helps ex-

plain the impact of the known factors and identify the environmental risk factors and unknown endogenous factors to the therapeutic system.

2. Objectives

In this study, considering the high probability of SCC in South Khorasan province in Iran due to its climate conditions, we investigated the epidemiological aspects of this disease in the region and evaluated the likelihood of subsequent lesions among the patients who have been diagnosed with BCC.

3. Methods

3.1. Study Design and Sampling

This paper is based on a cross-sectional (descriptive-analytical) study. The study population included all patients with BCC whose surgical resection and diagnosis were confirmed and registered in the pathology laboratories of Imam Reza hospital and Valiasr hospital in Birjand, in South Khorasan, Iran, from 2015 to 2017 by census method. Inclusion criteria were BCC's pathology sample that was the free margin and without metastatic evidence, residence in South Khorasan province, and between two and four years after surgical resection. Exclusion criteria were patients with positive margin or metastatic stage, lack of information, and no response from the patient.

3.2. Data Collection Methods

In this study, the information was collected via census method from the recorded information of patients admitted to the pathology sector of these hospitals. All patients were investigated two to four years after the operation, and complementary information was gathered via interview. The subsequent lesions were detected in other anatomical areas. Then, the patients with single lesions were allocated to the first group, and patients with subsequent lesions after the first surgical resection were assigned to the second group. Epidemiological information was analyzed, and tumor risk factors were compared between the two groups.

In this study, smoking was defined as a history of daily utilization of a minimum of ten cigarettes during a minimum of five years, sun exposure was described as being exposed to sunlight for more than three hours per day during a minimum of three years, contact with organophosphorus materials was defined as exposure to the materials or plant pesticides for minimum one year, and long-term immunocompromised history included organ transplant, leukemia, chemotherapy, and AIDS. Prepared questionnaires were approved by Research Council and Ethics Committee (approval number: Ir.bums.REC.1397.125). The data were analyzed using SPSS software version 16 by performing descriptive and analytical statistics using chi-square or Fisher's exact tests at a statistical significance level of $P \leq 0.05$.

4. Results

In this study, 85 patients with BCC were examined for demographic characteristics and risk factors. The mean age of the patients was 67.83 ± 12.29. The youngest and the oldest patients were 38 and 92 years old, respectively. Over half of the participants were farmers, 68 (80%) of the patients were occupied with outdoor professions, and 64 (75.3%) reported a history of sun exposure (Table 1).

Eighty-two patients (96.5%) had tumors in their heads and necks. In three patients (3.5%), tumors were located in the rest of their bodies. The most common tumor location was the nose, with a frequency of 22 patients (25.9%), and then periorbital, with a frequency of 20 patients (23.5%), followed by ten patients in the cheek (11.8%). There was no significant difference between BCC location and the patients' gender (P-value = 0.1). The most common location of the tumor was the face in both females and males (Table 2).

In this analysis, eight patients with subsequent asynchronous lesions were withdrawn to reduce the analysis. Moreover, 10.6% of the patients experienced asynchronous facial lesions, that their confidence interval 95 out of 10.6 was 4.06 - 17.24, and two patients experienced three asynchronous facial lesions. These patients were people with high-risk factors, aged over 65 years old (Seven patients), residency in rural areas (Seven patients), sun exposure (Seven patients), family history of cancer (Three patients), and exposure to organophosphates (Three patients). However, there was no statically significant difference between the two groups regarding age (P = 0.47), gender (0.73), and other risk factors ($P > 0.05$) (Table 3).

The highest frequency was in patients with macronodular, diagnosed in 54 patients (63.5%), and the least was related to sclerosis and micronodular, each of which was diagnosed in three patients. There was no significant relationship between tumor type and age groups (P-value = 0.90, between tumor type and gender (P-value = 0.1), and between tumor and skin distribution (P-value = 0.46).

According to Table 4, there was no statically significant difference between the two groups regarding pathologic subtype.

Table 1. Relative Occurrence of Evaluated Risk Factors in Patients with BCC

Variant	Subgroup	Occurrence (%)
Gender	Female	42 (49.4)
	Male	43 (50.6)
Age group, y	40 - 20	4 (4.7)
	60 - 40	17 (20)
	60 - 80	50 (58.8)
	100 - 80	14 (16.5)
Residency area	City	25 (29.4)
	Village	60 (70.6)
Skin and eye color	Light	47 (55.3)
	Dark	38 (44.7)
Job environment	Outdoor	68 (80)
	Indoor	17 (20)
Sun exposure	Yes	64 (75.3)
Family history of cancer	Yes	11 (12.9)
Smoking	Yes	9 (10.6)
Contact with organophosphorus materials	Yes	24 (28.2)
Immunocompromised history	Yes	1 (1.2)
Radiotherapy	Yes	2 (2.4)

Table 2. Comparison of BCC Location According to Patients' Gender [a]

Location	Head and Neck, No. (%)	Face, No. (%)	P-Value	OR (CI)
Male	10 (24.4)	31 (75.6)	0.10	2.74 (0.78 - 9.64)
Female	4 (10.5)	34 (89.5)		

[a] Head and neck = scalp, auricle, and neck

5. Discussion

The global prevalence of BCC is increasingly growing. Recently, its increased prevalence has taken special attention among young populations, especially females. In a few studies, the risk of subsequent BCC has been explained, and we tried to study this issue in this epidemiologic study. In our study, 10.6% of the patients experienced subsequent BCC between two and four years after the First presentation.

In this study, 85 patients with BCC were examined concerning tumor type, living area, occupation, and other factors. The average age of the patients in our study was lower than that of similar studies. One of the influential factors is the geographical conditions and lifestyle of the province residents where this study was conducted. The evaluation of other risk factors is necessary. In a study by Szewczyk et al. in 2016 conducted to evaluate BCC in farmers, the average age of patients was 73 years in the range of 32 to 96 years. In our study, the most commonly affected age group was 60 to 80 years old, with (58.8%) which is in line with other studies (10). It is worth mentioning that age is not a factor in diagnosing this disease. Most studies have reported a higher prevalence of BCC in males, and the ratio of males to females in our series is 1.02:1 (11-14). Similar disease prevalence in both sexes reflects the importance of the region's occupational and social issues in which people, especially females, have an active role in various activities, including farming, ranching, and sun exposure conditions. The next section of the survey concerned sun ex-

Table 3. Relative Occurrence of Evaluated Risk Factors in Patients with BCC

Specifications	Mono Lesion, No. (%)	Subsequent Lesions, No. (%)	Fisher's Exact Test P-Value	OR (CI)
Gender			0.73	1.28 (0.36 - 4.44)
Male	39 (90.7)	4 (9.3)		
Female	37 (88.1)	5 (11.9)		
Age group, y			0.47	2.41 (0.46 - 12.38)
< 65	31 (93.9)	2 (6.1)		
≥ 65	45 (86.5)	7 (13.5)		
Residency area			0.61	1.51 (0.29 - 7.87)
City	23 (92)	2 (8)		
Village	53 (88.3)	7 (11.8)		
Job			0.15	0.20 (0.02 - 1.70)
Farmer and rancher	47 (85.5)	8 (14.5)		
Other	29 (96.7)	1 (11.1)		
Sun exposure			≥ 0.99	0.85 (0.16 - 4.48)
Yes	57 (89.1)	7 (10.9)		
No	19 (90.5)	2 (9.5)		
Skin and eye color			0.28	2.75 (0.63 - 11.82)
Light	44 (93.6)	3 (6.4)		
Dark	32 (84.2)	6 (15.8)		
Family history of cancer			0.05	0.23 (0.04 - 1.12)
Positive	8 (72.8)	3 (8.1)		
Negative	68 (91.9)	6 (66.7)		
Smoking			0.58	1.13 (1.04 - 1.23)
Yes	9 (100)	0 (00)		
No	67 (88.2)	9 (11.8)		
Contact with organophosphorus materials			0.70	0.76 (0.17 - 3.33)
Yes	21 (87.5)	3 (12.5)		
No	55 (90.2)	6 (9.8)		
Long-term immunocompromised history			0.72	1.12 (1.04 - 1.20)
Yes	1 (100)	0 (0)		
No	75 (89.3)	9 (10.7)		
Job environment			0.19	0.86 (0.79 - 0.95)
Outdoor	59 (86.8)	9 (13.2)		
Indoor	17100)	0 (00)		
Exposure to other chemical materials			0.73	1.50 (0.17 - 13.11)
Yes	12 (92.3)	1 (7.7)		
No	64 (88.9)	8 (11.1)		

Table 4. Comparison of Subsequent Lesions According to BCC Subtype

BCC Subtype	No.	Mono Lesion, No. (%)	Subsequent Lesion, No. (%)	P-Value
Superficial	8	5 (62.5)	3 (37.5)	0.06
Sclerosis	3	2 (66.7)	1 (33.3)	
Adenoid	12	12 (100)	0 (0)	
Macronodular	54	49 (90.7)	5 (9.3)	
Pigmented	5	5 (100)	0 (0)	
Micronodular	3	3 (100)	0 (0)	

posure, where 64 patients (75.3%) reported sun exposure. According to the present study, the study by Gaspari et al. (15) demonstrated that there was a significant relationship between the onset of either recurrence or new BCC with sun exposure (P-value < 0.01). The study of Belbasis et al. in 2016 presented a similar pattern of results in which a correlation was confirmed between sunburns and BCC (16).

Other results have also reported sun exposure as the most critical BCC risk factor (12). Our study supports this theory. In the present study, 60% of lesions located on the center of the face, including nose skin, periorbital, and cheek, are mostly exposed to sunlight. The spread of lesions in different anatomical areas of the skin in different sexes showed that females were less likely than males to have scalp, auricle, and neck lesions compared to the face, which is important clinically, but statistical analysis of this comparison was not significant. A reason for this different distribution is the social behavior of females, which includes covering the scalp, neck, and auricle with a Hijab, which has a protective effect of reducing the exposure of these areas' skin to the sun ray. Our study was in line with the study by Kumar et al. about BCC risk factors and clinical and pathological characteristics (1). These results agree with Szewczyk et al.'s findings that females were less likely than males to have scalp and auricle lesions (10). It can be explained that the prevalence of long hair in females has a protective effect on their scalp and auricle. Another finding was that most patients were occupied as farmers, followed by ranchers, and next by housekeepers. Most patients had light skin and light eye color, which was in line with the study of Serna-Higuita et al., where they investigated the BCC modifiable risk factors in Australia and found that 58.1% of patients had blue or green eye color and light skin (11).

Regarding radiotherapy, in our study, only 2.4% of the patients had a history of radiotherapy. Concerning the family history of cancer, we found that breast cancer was the most frequent. However, these findings do not support the results demonstrated by the study by Kumar et al. where none of the patients had a family history of cancer (1). Six patients (7.1%) in our study had previous skin cancer. In contrast, in Kumar et al.'s study, a patient (2.8%) had a history of breast cancer and endometrial carcinoma (1).

In this study, asynchronous facial skin lesion was detected in nine patients (10.6%) diagnosed and underwent surgical treatment for one to three years. They were over 60 years old, villagers, and the majority of them were farmers. A more significant percentage of BCC in this group had a family history of cancer than the percentage of the patients with a single lesion (33.3% versus 10.5%; P = 0.08), and a greater percentage were occupied in outdoor activities (100% versus 77.6%; P = 0.19). Although this difference was not statistically significant, it may be clinically significant. According to other studies, among all BCC patients, 40% of them experienced subsequent lesions in five years (12, 13, 15). There is a discrepancy in the rates in our study and the previous reports. This difference may result from a limited follow-up or change in the habit of sun exposure of the patients. It is important to note that skin examination and identifying possible cases of BCC should be considered in the family follow-up of patients with cancer, especially those with breast cancer and patients with previous skin cancer and immunocompromised history.

In our study, 10.6% were smokers, and in the study by Serna-Higuita et al., 54.7% were non-smokers (11). Also, 28.2% experienced exposure to organophosphorus. Other studies have reported the association of various chemical substances with an increased risk of BCC. Gallagher demonstrated that exposure to fiberglass material and dry cleaners could increase the risk of BCC (OR = 4.6), and contact with arsenic could predispose people to multiple BCC (16). Also, using organophosphorus material is considered a risk factor for BCC. Occupational exposure to chemical substances is a risk factor for BCC. A patient had an immunocompromised condition and was under treatment with oral prednisolone for rheumatoid arthritis for five years. This finding was in line with the results of a study by Serna-Higuita et al., where 12.6% of patients suffered from

immunocompromised conditions (11). Nine patients were exposed to a chemical substance from which one patient was exposed to battery acid, one experienced occupational exposure to transmission oil, one to refractory cotton, and five patients experienced exposure to fertilizer. There was no significant relationship between tumor type and skin distribution (P-value = 0.46). The most frequent tumor type in the head and neck was macronodular. A study by Puizina-Ivic et al. in 1999 showed a relationship between tumor location and tumor type; macronodular was less in the body than other tumor types (P-value = 0.022). In addition, the superficial type was in the body more than other tumor types (P-value = 0.003), which was in agreement with our study (17).

BCC, the most common skin cancer, is easily treatable through surgery. Its incidence could be reduced by avoiding exposure to risk factors. Given the high prevalence of its infliction in the head and neck, especially the nose and periorbital, a regular, periodic skin examination of any suspicious lesion is recommended, and immediate diagnostic action should be taken by performing a biopsy and pathological examination. The standard surgical method is resectioning the malignant lesion with a 4-to-5-millimeter margin. Surgery on the face, especially the skin of the nose and periorbital, is much easier to perform in the early stages of the disease if performed quickly, which would contribute to repairers of the remaining defect with less deformity and morbidity.

There are some limits to this study. Due to the retrospective nature of this study, we do not have detailed data on the patient's lifestyle. The studied people are not representative of the entire population with this disorder and in a cross-sectional study, the relationship between the risk factor and the disorder is weak, and it is necessary to conduct cohort and case-control studies.

5.1. Conclusions

This study confirms the likelihood of having a subsequent lesion in other anatomical regions in patients diagnosed with BCC and indicates the need for this to be considered during medical treatment. In particular, this study recommends that patients subject to several risk factors, such as being old, having prolonged exposure to ultraviolet radiation, and having a family history of malignancy, have to be more careful regarding the damaged skin and have a regular follow-up. These observations may support the recommendation of regular and long-term follow-up of patients diagnosed with BCC. After the initial treatment, proper care and action are required due to the likelihood of the appearance of lesions in other parts of the facial skin.

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Footnotes

Authors' Contribution: B.S conceived and designed the evaluation and drafted the manuscript. S.H.G. participated in designing the evaluation, performed parts of the statistical analysis and helped to draft the manuscript. N.A re-evaluated the clinical data, revised the manuscript, and performed the statistical analysis. M.CH. collected the clinical data, interpreted them and revised the manuscript. A.F re-analyzed the clinical and statistical data and revised the manuscript. All authors read and approved the final manuscript.

Conflict of Interests: The authors declare that there is no conflict of interest.

Data Reproducibility: The data presented in this study are openly available in one of the repositories or will be available on request from the corresponding author by this journal representative at any time during submission or after publication. Otherwise, all the consequences of possible withdrawal or future retraction will be with the corresponding author.

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