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Basal Cell Carcinoma Risk Factors: A Case-Control Study from Dr. Hasan Sadikin Hospital of Bandung, Indonesia

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ABSTRACT

Background: Basal Cell Carcinoma (BCC) is the most common non-melanoma skin cancer in humans (75%). BCC is a slow-growing, malignant tumor with a destructive nature, yet it rarely metastasizes. Prevention is better than curative medicine. The risk factors of BCC in Bandung area are still not known. Hence, a study regarding BCC risk factors in Bandung is needed. The objective in this paper is to determine basal cell carcinoma risk factors in Dr. Hasan Sadikin Hospital, Bandung, Indonesia.

Method: Analytical research with a case-control approach was carried out on patients with a diagnosis of BCC who came to Dr. Hasan Sadikin Hospital outpatient clinic in Bandung between July and December 2023. Data was collected and analyzed with SPSS version 29.0 using the chi-square method to determine the association between risk factors and BCC occurrence. Risk factors studied in this research were age, gender, occupation, family history, Fitzpatrick skin phototype, duration of sun exposure, time of sun exposure, smoking, alcohol, and chemical exposure.

Results: There were 41 subjects in the case group and 82 subjects in the control group. The results of bivariate analysis using chi-square showed that old age ($p < 0.001$; OR (95% CI = 6.35 (2.51–16.04)), duration of sun exposure 8–40 hours within a week ($p = 0.049$; OR (95% CI) = 2.09 (0.98–4.49)), and sun exposure time from 06.00 to 18.00 (morning to evening) ($p = 0.026$; OR (95% CI) = 7.25 (2.07–25.41) had significant association with the occurrence of breast cancer.

Conclusion: The study conducted at Dr. Hasan Sadikin Hospital, Bandung, found that significant risk factors associated with Basal Cell Carcinoma (BCC) are advanced age, sun exposure duration of 8 to 40 hours per week, and sun exposure during the hours of 06:00 to 18:00 (morning to evening). These findings emphasize the importance of preventive measures by limiting sun exposure, especially among the older population, to reduce the risk of BCC in the Bandung area.

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INTRODUCTION

Basal cell carcinoma (BCC) is the most common type of non-melanoma skin cancer (75% to 80%), arising from the basal layer cells of the epidermis [1]. BCC typically appears in areas that are exposed to the sun. As much as 70–80% of BCC occurs in the head and neck region, followed by the trunk (25%), penis, vulva, or perianal skin [2]. It is characterized by slow-growing, and rarely demonstrates aggressive invasion of deeper structures or significant metastatic tendencies, but it can cause significant local infiltration and destruction of surrounding tissue if not recognized and adequately treated [3].

The increasing incidence of BCC has been reported all over the world. The highest incidence had been reported in Australia, followed by the United States (US) and Europe [4]. BCC is fairly common in Caucasians and quite uncommon in dark-skinned populations. It contributes to 65–75% of cutaneous malignancies in whites and 20–30% in Asian Indians. The most important risk factors appear to be UV radiation exposure and genetic predisposition [5]. A family history of skin cancer

is closely related to an increased risk of developing BCC [6]. A higher incidence of BCC observed among Asians living close to the equator suggests that UV exposure is the major risk factor for BCC in Asian skin [7]. BCC is especially prevalent in the elderly population, given their association with cumulative sun exposure and other risk factors [8]. Several studies reported that BCC is more common in males than in females due to the lack of risk awareness, long shifts of outdoor work, and rarely seeking medical treatment. Thus, BCC had a higher development of BCC in men than in women [9]. However, a study revealed that the number of BCC in females is greater than in males because, in Asia, women are as likely to work outdoors as men [10]. Other risk factors, such as smoking, alcohol consumption, and exposure to chemical substances, correlated with BCC due to oxidative reactions that can produce ROS and affect gene transcription [11].

Currently, the analytical study report on risk factors for BCC patients, particularly at Dr. Hasan Sadikin General Hospital, as a referral hospital in West Java, does not yet exist. This condition encourages the writer to research the relationship between risk factors and BCC. The present study aimed to determine BCC risk factors in Dr. Hasan Sadikin General Hospital, Bandung, Indonesia.

METHODS

A case-control study was conducted with an analytical approach. The aim of using this research design was to assess the role of some suspected risk factors in the occurrence of BCC in Dr. Hasan Sadikin General Hospital. The sample was collected from July to December 2023. The case group (41 cases) was comprised of histologically confirmed cases of BCC, consecutively diagnosed at the surgical oncology outpatient clinic, Dr. Hasan Sadikin Hospital, Bandung, Indonesia. The control group (82 cases) consisted of healthy people with no history of BCC. This study used a consecutive sampling method, according to the inclusion and exclusion criteria, until the minimum sample size was fulfilled. Patients diagnosed with BCC, as proven by the results of anatomical pathology, and willing to fill out an informed consent sheet for the questionnaire, were included. The exclusion criteria in this study were genetic syndromes such as xeroderma pigmentosum, basal cell nevus syndrome, Bazex-Dupre-Christol syndrome, and Rombo syndrome.

All participants were interviewed using a targeted and detailed questionnaire. Data analysis includes a sample of demographic characteristics such as age and gender, occupation (student, housewife, retired, employee, self-employed, laborer, farmer), family history, Fitzpatrick skin phototype, duration of sun exposure, time of sun exposure, smoking, alcohol, and chemical exposure mete including arsenic, coal, paraffin, and petroleum. Six skin types were defined according to the Fitzpatrick skin phototype as shown in **Figure 1**; type 1- pale white skin, type 2- white skin, type 3- light brown skin, type 4- moderate brown skin, type 5- dark brown skin, and type 6- deeply pigmented dark brown.

The statistical analysis was performed using Microsoft® Excel 2016 and IBM® SPSS® Statistics Data Editor version 29.0. The association between risk factors and BCC occurrence was analyzed using a chi-square test with odds ratios (ORs), 95% CI, and p-value. Therefore, p-value < 0.05 is considered statistically significant.

RESULTS

This study obtained 123 data through medical records and direct interviews using a targeted and detailed questionnaire. There were 41 BCC patients included in the case group, and 82 healthy participants were included in the control group. Patients' characteristics are presented in **Table 1.**

Most BCC patients were female, with a female-male ratio of 5:3, and were mostly over 40 years old. Most BCC patients worked as housewives without a family history of BCC. Fitzpatrick Skin Phototype result showed that the population had a range of skin types II-V, mostly having type III and IV. Most BCC patients had 8-40 hours of sun exposure within a week. Sun exposure is commonly experienced from 6 AM until 4 PM. The majority of BCC patients had no exposure to smoking, alcohol consumption, or chemical substances.

Figure 1. Fitzpatrick skin phototype [12]

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Table 1. Characteristics of basal cell carcinoma patients and the controls

Variable	Cases	Controls
	n (%)	n (%)
Gender		
Female	25 (60.98)	38 (46.34)
Male	16 (39.02)	44 (53.66)
Age groups		
Children (≤ 19 years old)	1 (2.44)	2 (2.44)
Young adult (20–39 years old)	3 (7.32)	47 (57.32)
Middle age (40–59 years old)	19 (46.34)	24 (29.27)
Elderly (≥ 60 years old)	18 (43.9)	9 (10.97)
Occupation		
Students	1 (2.44)	9 (10.97)
Housewife	16 (39.02)	19 (23.17)
Retired	6 (14.63)	3 (3.66)
Employee	1 (2.44)	21 (25.61)
Laborer	3 (7.32)	4 (4.88)
Self-employed	8 (19.51)	18 (21.95)
Farmer	6 (14.63)	8 (9.76)
Family history		
Yes	3 (7.32)	23 (28.05)
No	38 (92.68)	59 (71.95)
Fitzpatrick skin phototype		
1: pale white skin	0	1 (1.22)
2: white skin	5 (12.19)	8 (9.76)
3: light brown skin	23 (56.1)	37 (45.12)
4: moderate brown skin	10 (24.39)	32 (39.02)
5: dark brown skin	3 (7.32)	4 (4.88)
6: deeply pigmented dark brown	0	0
Duration of sun exposure		
< 8 hours a week	8 (19.51)	34 (41.46)
8–40 hours a week	24 (58.54)	33 (40.24)
> 40 hours a week	9 (21.95)	15 (18.29)
Time of sun exposure		
06.00–10.00	6 (14.63)	29 (35.36)
10.00–16.00	3 (7.32)	7 (8.54)
16.00–18.00	0	0
06.00–16.00	13 (31.71)	21 (25.61)
10.00–18.00	3 (7.32)	3 (3.66)
06.00–10.00 and 16.00–18.00	4 (9.76)	14 (17.07)
06.00–18.00	12 (29.27)	8 (9.76)
Smoking		
Yes	14 (34.15)	26 (31.7)
No	27 (65.85)	56 (68.29)
Alcohol		
Yes	1 (2.44)	2 (2.44)
No	40 (97.56)	80 (97.56)
Chemical exposure		
Arsenic	7 (17.07)	5 (6.1)
Coal	0	0
Paraffin	3 (7.32)	2 (2.44)
Petroleum	0	0
No exposure	31 (75.61)	75 (91.46)

Table 2 shows bivariate analysis with odds ratios (ORs). There was a significant relationship between age, occupation, family history, duration of sun exposure, time of sun exposure, and BCC. That means the elderly, people who work indoors (housewives, retired), a negative family history of skin cancer, and long duration and time of sun exposure increase the risk of occurrence of BCC. The relationship between family history and BCC is statistically significant as a protective factor against BCC.

DISCUSSION

This study included 41 histologically confirmed BCC cases and 82 healthy adults as controls with case: control ratio of 1:2. Various studies have reported that BCC is more common in males than in females [12]. This may be explained by a lesser general risk awareness among males. Some studies showed that males had less tendency to perform sun protective behaviors such as wearing sunglasses, wearing covering clothing, staying in the shade, and applying sunscreen than females [13]. The majority of men worked outdoors with longer shifts, so they had greater occupational and recreational hazards. However, they rarely seek medical treatment. Therefore, BCC in males had larger developmental rates than females [9]. However, this study revealed that the number of BCC in females is greater than in males. These differences may be related to cultural patterns of sun exposure (outdoor work, recreation, etc). In the United States, men traditionally work outdoors, whereas women traditionally have indoor jobs. Meanwhile, in Asia, women are as likely to work outdoors as men [10].

The study by Kuklinski et al. [14] about contraception on female patients diagnosed with BCC in America found an association between oral contraceptives and newly diagnosed BCC. Estrogen receptors are present on the surface of keratinocytes and, when activated, induce proliferation. That study explained that the use of hormonal contraception has a risk of 1.4 times increased risk of BCC. A study from Gayatri et al also explained that most women in Indonesia use hormonal contraception (pills or injections) [15]. Other lifestyle factors are also associated with the risk of skin cancer in women, such as the use of deodorants, creams, and

Table 2. Risk factors for basal cell carcinoma: bivariate analysis with odds ratios (ORs)

Variable	OR (95% CI)	p
Gender		
Female	1.81 (0.84–3.88)	0.13
Male	1.00	
Age groups		
Children (≤ 19 years old)	1.00 (0.8–11.36)	
Young adult (20–39 years old)	0.06 (0.02–0.21)	< 0.001
Middle age (40–59 years old)	2.09 (0.96–4.54)	
Elderly (≥ 60 years old)	6.35 (2.51–16.04)	
Occupation		
Students	0.20 (0.03–1.66)	
Housewife	2.12 (0.94–4.77)	
Retired	4.51 (1.07–19.09)	
Employee	0.07 (0.01–0.56)	0.005
Laborer	1.54 (0.33–7.23)	
Self-employed	0.86 (0.34–2.19)	
Farmer	1.59 (0.51–4.92)	
Family history		
Yes	0.2 (0.06-0.72)	0.008
No	1	
Fitzpatrick skin phototype		
1: pale white skin	0	
2: white skin	1.28 (0.39–4.21)	
3: light brown skin	1.55 (0.73–3.31)	
4: moderate brown skin	0.50 (0.22–1.17)	0.5
5: dark brown skin	1.54 (0.33–7.23)	
6: deeply pigmented dark brown	0	
Duration of sun exposure		
< 8 hours a week	0.34 (0.14–0.83)	
8–40 hours a week	2.09 (0.98–4.49)	0.049
> 40 hours a week	1.26 (0.49–3.18)	
Time of sun exposure		
06:00–10:00	1	
10:00–16:00	2.07 (0.41–10.39)	
16:00–18:00		
06:00–16:00	2.99 (0.98–9.16)	0.026
10:00–18:00	4.83 (0.78–30.0)	
06:00–10:00 and 16:00–18:00	1.38 (0.34–5.69)	
06:00–18:00	7.25 (2,07–25,41)	
Smoking		
Yes	1.12 (0.5–2.47)	0.78
No	1	
Alcohol		
Yes	1 (0.08–11.36)	1.0
No	1	
Chemical exposure		
Arsenic	3.39 (1.0–11.49)	
Coal	0	
Paraffin	3.63 (1.57–22.79)	0.46
Petroleum	0	
No exposure	1	

make-up that contain certain chemicals that come in contact with a woman's skin, which can pose a potential risk in the development of skin cancer[14]. There is a significant relationship between age and BCC. This study reveals that the majority of BCC cases are over 40 years old. This finding was similar to a study by Slavenka et al. [16].

This research explained that the majority of BCC patients worked as housewives (39.02%). This result is different from the theory, which explains that the risk of BCC is associated with sun exposure, meanwhile, housewives usually spend more time indoors. However, an unusual female preponderance was noticed in the study conducted by Kumar et al. [9] in the Indian population. Indian housewives, especially rural women, work in open kitchens during their household chores and work in the fields during sowing and harvesting seasons, exposing them to intermittent, high-intensity UV exposure [9]. If we look for more details at the results of the data, BCC patients who are women and work as housewives are mostly exposed to the sun between 6 AM and 4 PM, with a duration of 8-40 hours within a week.

Analysis of the relationship between family history and BCC shows that there is a significant relationship with the occurrence of BCC. However, family history is a protective factor against the incidence of BCC. This finding is different from the Nicholas et al. [18] study, which reported that a family history of skin was associated with an increased risk of early-onset BCC. Individuals with a first-degree relative diagnosed with skin cancer before age 50 and those with a family history of both melanoma and non-melanoma skin cancer are at the highest risk for early-onset BCC. Importantly, family history is thought to be not only a marker of genetic susceptibility but also to reflect shared lifestyle in environmental, and behavioral factors. This finding needed further investigation and larger research.

A study from Kasumagic-Halilovic et al. [19] explained that all BCC patients in their study were Fitzpatrick phototypes II and I, similar to the literature, which shows a greater incidence in the white race. The incidence of non-melanoma skin cancer depends on individual susceptibility related to the amount of melanin in the skin and the capacity of the skin to tan when exposed to UV radiation. Darker skin is more protected against the damaging effects of UV radiation from solar light, mostly due to the protective effect of melanin.

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Meanwhile, in this study, most subjects were Fitzpatrick phototype III. It happened because the research was conducted in Bandung, Indonesia. Most Asians have Fitzpatrick phototypes III and IV [20].

Analysis of the relationship between light exposure and BCC explained that the highest risk occurred in the group with light exposure of 8-40 hours a week. This result is different from a study by Bauer et al. [21], which explains that participants with a high (≥90th percentile) total UV exposure showed a more than 2-fold significantly increased risk of developing BCC in sun-exposed body sites compared to participants with low total UV exposure. Best to know more about the area where the patient lives, as this is related to the intensity of sunlight. UV intensity and transmission can be influenced by weather conditions and air quality. UV intensity on a sunny day is significantly higher than on a cloudy day [22]. In this study, there was a relationship between the time of UV exposure and the incidence of BCC. The highest UV exposure risk occurred between 6 AM and 6 PM (7.25 times more susceptible to BCC). UV rays are divided into UVA and UVB, where UVB is thought to be the main cause of BCC. UVB usually appears from 10 AM to 4 PM [23]. This study found that UV exposure from 10 AM until 4 PM (strongest UVB exposure) had a 2.07 times greater risk of causing BCC compared with UV exposure from 6 until 10 AM.

The relationship between tobacco smoking and BCC is still unclear. The study from Uotila et al. [24] at Kuopio University Hospital, Finland, revealed that smoking was associated, though not dose-dependently, with an increased likelihood of SCC; it was not associated with BCC or malignant melanoma. In this study, patients with a past or current history of smoking had 1,12 times to have BCC than non-smokers, but not statistically significant. This finding is different from a study by Boyd et al. [25], which explained that young women with a BCC are more likely to have a past or current history of cigarette smoking and blistering sunburns. The relationship between alcohol consumption and BCC in this study was not significant. This finding was different from several studies. Wu et al. [26] explained that alcohol consumption is associated with an increased risk of cutaneous BCC in both women and men. The study from Husein-Elahmed et al. [27] had the same result that alcohol intake may be linked with a higher incidence of aggressive subtypes of BCC.

This research is a case-control study with primary data obtained using a direct interview technique. An important limitation of our study is recall bias, which may affect the reported history. Most of the sample consists of middle-aged and elderly, so detailed information about daily activities related to sun exposure, smoking history, including amount and duration, alcohol consumption, including amount and duration, and exposure to chemical substances is difficult to obtain.

CONCLUSION

There is a significant relationship between old age, duration of sun exposure, and time of sun exposure with the occurrence of BCC in the polyclinic of surgery, Dr Hasan Sadikin Hospital, Bandung. The relationship between occupational and BCC is statistically significant, but the risk increases in patients who are expected to spend more time indoors, such as housewives and the retired. This anomaly needed further investigation, as to how long they spend time their time outdoors. The relationship between family history and BCC is also statistically significant as a protective factor against the incidence of BCC. There is no significant relationship between gender, Fitzpatrick skin phototype, smoking, alcohol consumption, and chemical exposure with the occurrence of BCC.

Further multicentre research could be carried out to enlarge the study population and enrich the subject characteristics. Research regarding the clinical manifestation of each BCC type and BCC risk factors in females is needed.

DECLARATIONS

Competing interest

The author(s) declare no competing interest in this study.

Ethics approval and consent to participate

This study was permitted by the Medical Research Ethics Committee of Dr. Hasan Sadikin General Hospital with a letter Number LB.02.01/X.6.5/252/2023. This study was also acknowledged and approved by the Oncological Surgery Division of Oncology Surgery, Department of Surgery, and Department of Pathology Anatomy of Dr. Hasan Sadikin General Hospital and Hospital Information System (SIRS).

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