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Early-life or lifetime sun exposure, sun reaction, and the risk of squamous cell carcinoma in an Asian population

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Abstract

Background—It has been widely accepted that sun exposure is a risk factor of squamous cell carcinoma (SCC) among fair-skinned populations. However, sun exposure and sun reaction have not been explored in Asians and no gender-specific data were available.

Method—In a case–control study, 176 incident skin cancer cases were recruited from National Cheng-Kung University Medical Center from 1996 to 1999. Controls included 216 age-, gender-, and residency-matched subjects from the southwestern Taiwan. A questionnaire was administered to collect information on life style and other risk factors. Logistic regression analysis was

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performed to evaluate the association between sun exposure or sun reaction and the risk of SCC by gender.

Results—Early-age (age 15 to 24) and lifetime sun exposure were significantly associated with increased risk of SCC in a dose–response pattern [odds ratio (OR) = 1.49–3.08, trend $p = 0.009$ and 0.0007, respectively]. After stratified by gender, the third tertile of early-age sun exposure was significantly associated with the SCC risk among men (OR = 3.08). The second and third tertiles of lifetime sun exposure was significantly associated with SCC risk among women (OR = 3.78 and 4.53, respectively). Skin reaction after 2-h sun exposure during childhood and adolescence was not significantly associated with the risk of SCC.

Conclusions—Lifetime sun exposure was more related to SCC risk in women, while early-age sun exposure was more relevant to men's SCC risk. This may be attributable to different lifestyle between men and women.

Keywords

Squamous cell carcinoma (SCC); Early age; Lifetime; Sun exposure

Introduction

Squamous cell carcinoma (SCC) is more prevalent than basal cell carcinoma (BCC) in the Taiwanese population (45 vs. 28%) [1], which is different from the distributions in the US population [2] and other Asian populations, e.g., Singaporean (BCC is 1.9 times prevalent than SCC) [3, 4] and Japanese (BCC is 1.6 times prevalent than SCC) [5]. In addition, age-adjusted incidence rates of non-melanoma skin cancer in Taiwan (0.55 and 0.37 per 100,000 persons for men and women using 2000 world standard population, respectively) [1] are much lower than that in the US New Hampshire population (SCC: 519 and 260 per 100,000 persons per year for men and women; BCC: 1,697 and 1,200 for men and women for BCC; using the 1970 US population) [2]. These data suggested that SCC maybe a more important subtype of skin cancer among Taiwanese, although the incidence rate is relatively low in Taiwanese comparing to fair-skinned population.

Several environmental factors have been related to SCC including sun exposure [6–8], cigarette smoking [7, 9], arsenic exposure [10, 11], diet [12–14], industrial carcinogen (coal tars and oils) [15], ionizing radiation [16, 17], human papillomavirus infection [16, 18, 19], and betel quid chewing (in many Asian countries) [20, 21]. Among these factors, sun exposure is a confirmed risk factor of skin cancer in the fair-skinned populations [7, 8, 22–25] and the etiology of skin cancer varies by pathological types. For example, SCC reflects a pattern of chronic long-term exposure as well as short-term sunburn episodes; BCC is mainly related to either short-term burning episodes or long-term exposure at head or neck [26]; melanoma is associated with excess UV exposure [6, 27].

Only few studies explored the association between sun exposure or skin reaction and the risk of skin cancer in Asian American or Asian Canadian and their study populations were adolescents or college students [28–31]. These studies focused on the attitude and behavior toward sun exposure, which have been very different between Asians and Asian Americans/Caucasians. Therefore, previous studies were unable to reflect the true risk of skin cancer in Asians. SCC is more prevalent in Taiwanese than in Whites. Up to date, no studies have explored the association between sun exposure and the risk of skin cancer among Asians. Therefore, we hypothesized that early-age or lifetime sun exposure or sun reaction was associated with SCC risk in the Taiwanese population. We will also assess how gender affected these associations.

Materials and methods

Study population

From January 1996 to December 1999, a hospital-based case–control study was conducted in the southwestern Taiwan. One hundred and seventy six patients newly diagnosed as having skin cancer were recruited from National Cheng-Kung University (NCKU) Medical Center, which is the main medical referral center for cancer diagnosis and treatment for residents in Tainan City and the surrounding rural communities. Controls were 216 persons recruited from the same community of cases and were matched with cases on age and gender. All participants were over 30 years old. To prevent the effect of arsenic exposure on the risk of skin cancer, participants from Blackfoot disease endemic area were excluded. The research protocol was approved by the Institutional Review Boards of the Harvard School of Public Health and NCKU. Informed consent was obtained from each participant.

Identification of cases of skin cancer

Newly diagnosed skin cancer patients (n = 176) were recruited and confirmed in the following proportions: 49% (=87/176) SCC, 36% (=64/176) BCC, and 14% (25/176) Bowen's disease (BD). The pathologic diagnosis was performed at the Pathology Department, NCKU, using the International Classification of Diseases, version 9 (ICD-9), code 173. Details on sites of SCC, BCC, or BD were not available because this is a secondary analysis of previous studies [10, 32, 33].

Ascertainment of exposure variables

Trained interviewers, who were blinded to exposure status and study hypotheses, administered a questionnaire to each subject. Information collected from the questionnaire included demographic information (gender, age, ethnicity, height, body weight, and education); personal habits (sun exposure at different time period of lifetime, skin reaction after 2-h sun exposure); disease history; and other relevant questions (history and duration of each residence and occupations). Information on sun exposure was collected combining the hours per week spent outdoors at work, sports, recreation, or yard work in direct sunlight. Participants who failed to complete or refused to answer the questionnaire were excluded. Completed questionnaires were obtained on 95 and 94% of cases and controls, respectively.

Statistical analysis

We used multiple logistic regression models to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for the association between sun exposure or sun reaction and the risk of SCC. Early-age and lifetime sun exposure (h/weeks) were tertiled using the exposure data from the control group, respectively. Three groups of each sun variable were also coded as ordinal variables for trend test to assess the dose– response relationship between sun exposure and skin cancer risk. Education was collinear with sun exposure; age and gender were matching factors and were no longer adjusted in the models. To control for other potential confounders, we adjusted for body-mass index (BMI, kg/m^2) and smoking status in the multivariate models. All statistical tests were two-sided. All analyses were performed using SAS version 9.1 (SAS Institute Inc, Cary, NC).

Results

A total of 176 skin cancer cases (87 SCC, 64 BCC, 25 BD) were recruited at NCKU Medical Center from 1996 to 1999 (Table 1). Controls were 216 age-, gender-, and residency-matched subjects from the southwestern Taiwan. There was more BCC patients in the younger age group (>30 to 50 years old) than SCC patients (14 vs. 6%). Except BCC (64% for men and 36% for women), gender distribution was similar between SCC or BD

and controls. Besides BCC, over 70% of SCC, BD, and controls were never smokers. Skin cancer cases showed a consistently higher proportion of high-dose sun exposure (34–40%) at an early age as compared to that of controls (26%). In contrast, high-dose lifetime sun exposure was observed among patients with SCC (41%) and BD (52%) only. Except BD, the distributions of skin reaction or sun tan after 2-h sun exposure during childhood and adolescence were similar across cancer subtypes and controls. Relatively fewer BCC patients (19%) developed a deep sun tan after 2-h sun exposure during childhood and adolescence as compared to that for patients with SCC (29%), BD (28%), and controls (33%).

Early-age sun exposure showed an exposure–response relationship with SCC (second vs. first tertile: OR = 1.49, 95% CI = 0.72–3.09; third vs. first tertile: OR = 2.43, 95% CI = 1.25–4.75; trend $p = 0.009$, Table 2). After stratified by gender, the third tertile of sun exposure at early age was associated with 3.08-fold increased risk of SCC in men (95% CI = 1.09–8.67) as compared to the first tertile. However, results did not reach statistical significance in women.

The associations between lifetime sun exposure and the risk of skin cancer were tabulated in Table 3. Lifetime sun exposure were associated with an elevated risk of SCC in a dose–response pattern (second vs. first tertile: OR = 2.98, 95% CI = 1.36–6.53; third vs. first tertile: OR = 3.95, 95% CI = 1.81–8.59; trend $p = 0.0007$). Lifetime sun exposure significantly increased the risk of SCC in women (second vs. first tertile: OR = 3.78, 95% CI = 1.32–10.84; third vs. first tertile: OR = 4.53, 95% CI = 1.62–12.68; trend $p = 0.004$). Similarly, results were not reach statistical significance in men.

Skin reactions (none, some redness, and burn) and sun tan (none or light brown, median brow, and deep brown) after 2-h sun exposure during childhood and adolescence were not associated with SCC (Table 4). Results remained non-significant after stratified by gender.

Discussion

This is the first study explored the association of early-age or lifetime sun exposure and skin reaction with the risk of SCC in Asians. Sun exposure at early age was related to men's SCC, and life time sun exposure was related to women's SCC. Both relationships were in a dose–response pattern.

Unlike BCC, which is mainly related to short-term burning episodes or part of long-term exposure at head or neck [26], long-term sun exposure is more relevant to the risk of SCC [6]. Some epidemiologic and experimental studies showed that total cumulative lifetime sun exposure is related to the risk of SCC [6, 24], and this association was confirmed in our study but not in a Canadian study [22]. This may be a result of different attitude and behavior toward sun exposure between Asians and Asian Americans/Caucasians. For example, Asian Americans tend to promote sun exposure as a result of adaptation of Western culture [34]. In contrast, chronic ''occupational'' sun exposure 10 years before diagnosis was significantly associated with SCC [22]. Early-age sun exposure has been related to a higher risk of skin cancer [35]. An Australia study found that the risk of SCC was significantly lower for immigrants arrived in Australia age 20 and above than those who were born in Australia (OR = 0.36, 95% CI = 0.16–0.72) [8]. This implies that less sun exposure at early age, sun exposure started later in life, or different attitude toward sun exposure may explain a lower risk of SCC. Our study found that sun exposure at early age was associated with an increased risk of SCC, which supported their finding. However, the risk of SCC resulting from early-age sun exposure was in a lower magnitude as compared to

that of lifetime sun exposure. This indicated that the lifetime sun exposure have a larger contribution to the risk of SCC.

The association between sun exposure and the risk of SCC by gender has not been explored previously. Our study found that sun exposure at early age was only related to men's SCC probably due to more outdoor activities in men at early age as compared to that of women. In addition, Taiwanese women tend to use umbrella, wear long sleeves or hats to protect themselves from UV exposure while performing outdoor activities. This may explain the lower risk of SCC among women in early age. In contrary, lifetime sun exposure was only associated with women's SCC risk in a dose–response pattern. This may be due to higher incidence of osteoporosis in postmenopausal women, who were encouraged to have more sun exposure in their later life and thus lifetime sun exposure was related to increased SCC risk.

The history of sunburn [35] and the ability to tan [24] have been associated with an elevated risk of skin cancer among fair-skinned populations. In Nurses' Health Study, women who tended to burn after two or more hours of sun exposure as children had a slightly higher risk of SCC than those who never burned (RR = 1.5, 95% CI = 1.1–2.1) [7]. Freckling on arms as a child was significantly associated with the risk of SCC in an Australian population, who are not southern European [8]. Our study observed similar associations, but results did not reach statistical significance, probably due to darker skin color in this Asian population, who were relatively protective to sun exposure.

We acknowledge some limitations to this study. Selection bias is not a concern in this case–control study because the NCKU Medical Center is a comprehensive referral center, which captures approximately 80% of all disease requiring specialists in the region. Therefore, cases in this study are likely to be representative of skin cancer in the general community. Because of the case–control design, recall bias is a potential confounder in this study. We got the lists of names and addresses of residents in the study area from the household registry, of which socio-demographic characteristics (e.g., gender, age, educational level, marital status, and occupation) of all residents were registered and updated annually. Questionnaire data were thus verified through the cross-validation with the information obtained from the registry.

In conclusion, our study provides some first findings. In this Asian population, early-age and lifetime sun exposures were significantly associated with men's and women's risk of SCC in a dose–response pattern, respectively, which can be a result of different lifestyle and attitude toward sun exposure. Importantly, this study highlights the significantly different SCC risk patterns between Asians and Asian Americans/Canadians as well as Caucasians. More studies in Asian population will help researchers to clarify the different risk of skin cancer across ethnic groups.

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Table 1

Characteristics of skin cancer cases and community controls

Variable	Squamous cell carcinoma (*n* = 87)		Basal cell carcinoma (*n* = 64)		Bowen's disease (*n* = 25)		Control subjects (*n* = 216)	
	n	%	*n*	%	*n*	%	*n*	%
Age								
>30–50	5	6	9	14	2	8	21	10
>50–70	43	49	27	42	14	56	100	48
>70	39	45	28	44	9	36	86	42
Gender								
Men	41	47	41	64	13	52	122	56
Women	46	53	23	36	12	48	94	44
BMI								
<18.5	10	14	5	9	3	13	12	6
18.5–23	35	49	28	49	8	35	107	55
>23	26	37	24	42	12	52	74	38
Smoking (pack-years)								
Never	67	79	38	59	18	72	143	72
>0–30	10	12	15	23	7	28	34	17
>30	8	14	11	17	0	0	23	12
Sun exposure at early age (15–24 years old, h/week)								
First tertile (≦18)	32	37	21	33	8	32	102	47
Second tertile (>18–40)	20	23	21	33	7	28	58	27
Third tertile (>40)	35	40	22	34	10	40	56	26
Lifetime sun exposure (h/week)								
First tertile (≦13.5)	16	18	16	25	5	20	77	36
Second tertile (>13.5–37.8)	30	34	25	39	7	28	73	34
Third tertile (>37.8)	41	41	23	36	13	52	66	31
Skin reaction[a]								
None	38	45	23	37	10	40	86	41
Some redness	34	41	31	49	8	32	91	43

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Variable	Squamous cell carcinoma (*n* = 87)		Basal cell carcinoma (*n* = 64)		Bowen's disease (*n* = 25)		Control subjects (*n* = 216)	
	n	**%**	***n***	**%**	***n***	**%**	***n***	**%**
Burn	12	14	9	14	7	28	34	15
Sun tan[a]								
None or Light brown	28	33	23	36	7	28	80	38
Median brown	31	37	28	44	11	44	62	29
Deep brown	24	29	12	19	7	28	69	33

[a]Skin reaction/sun tan after 2-h sun exposure during childhood and adolescence

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Table 2

Association between sun exposure at early age (age 15–24) and the risk of squamous cell carcinoma

Sun exposure[a] (h/week)	Case (*n*)	Control (*n*)	OR (95% CI)	Trend *p*
All				
First tertile(≦18)	32	102	1.00	0.009 *
Second tertile(>18–40)	20	58	1.49 (0.72–3.09)	
Third tertile (>40)	35	56	2.43 (1.25–4.75) *	
Men				
First tertile(≦18)	12	50	1.00	0.03 *
Second tertile(>18–40)	10	39	1.64 (0.55–4.92)	
Third tertile (>40)	19	33	3.08 (1.09–8.67) *	
Women				
First tertile(≦18)	20	52	1.00	0.11
Second tertile(>18–40)	10	19	1.43 (0.52–3.89)	
Third tertile (>40)	16	23	2.06 (0.84–5.05)	

[a] Variables adjusted in the model included early-age sun exposure at early age, cigarette smoking, and body-mass index

* OR does not include 1 or *p*-value < 0.05

Table 3

Association between lifetime sun exposure and the risk of squamous cell carcinoma

Sun exposure[a] (h/week)	Case (*n*)	Control (*n*)	OR (95% CI)	Trend *p*
All				0.0007*
First tertile(≦18)	16	77	1.00	
Second tertile(>18–40)	30	73	2.98 (1.36–6.53)*	
Third tertile (>40)	41	66	3.95 (1.81–8.59)*	
Men				
First tertile(≦18)	7	34	1.00	0.07
Second tertile(>18–40)	13	47	2.25 (0.68–7.37)	
Third tertile (>40)	21	41	3.09 (0.94–10.12)	
Women				
First tertile(≦18)	9	43	1.00	0.004*
Second tertile(>18–40)	17	26	3.78 (1.32–10.84)*	
Third tertile (>40)	20	25	4.53 (1.62–12.68)*	

[a] Variables adjusted in the model included lifetime sun exposure, cigarette smoking, and body-mass index

* OR does not include 1 or *p*-value < 0.05

Table 4

Skin reaction after 2-h sun exposure during childhood and adolescence and the risk of squamous cell carcinoma

	Case (*n*)	Control (*n*)	OR (95% CI)	Trend *p*
Skin reaction				
All				
None	38	86	1.00	0.89
Some redness	34	91	0.98 (0.53–1.80)	
Burn	12	34	0.95 (0.42–2.15)	
Men				
None	19	47	1.00	0.55
Some redness	16	47	1.04 (0.42–2.60)	
Burn	6	24	0.66 (0.21–2.11)	
Women				
None	19	39	1.00	0.72
Some redness	18	44	0.91 (0.39–2.12)	
Burn	6	10	1.43 (0.42–4.84)	
Sun tan				
All				
Deep brown	24	70	1.00	0.34
Median brown	38	72	2.04 (0.98–4.23)	
None or light brown	24	69	1.47 (0.70–3.10)	
Men				
Deep brown	10	35	1.00	0.85
Median brown	20	44	1.70 (0.60–4.78)	
None or light brown	10	39	1.15 (0.38–3.54)	
Women				
Deep brown	35	11	1.00	0.31
Median brown	28	18	2.29 (0.85–6.11)	
None or light brown	30	14	1.71 (0.63–4.69)	