Behavioral factors associated with the development of skin cancer in patients of arsenicosis

Towhida Noor, Md. Shahidullah Sikder, Lubna Khondker, Mohammed Saiful Islam Bhuiyan and Tanvir Rahman

Article Info

Department of Dermatology and Venereology, Faculty of Medicine, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh

For Correspondence:
Lubna Khondker
lubnaderma@gmail.com

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Abstract

The study was conducted to evaluate the behavioral factors associated with the development of skin cancer in arsenicosis patients. Arsenicosis patients without skin cancer were taken as control. In the sun-exposed area of the body, 57.2% of skin carcinoma was Bowen's disease. In the covered area of the body, 56.0% was Bowen's disease, 36% was squamous cell carcinoma and 8% was basal cell carcinoma. Again, 53.1% of case and 59.4% of control never used fertilizer and pesticide. The majorities were non-smoker (case 53.1%, control 59.3%). Mean cumulative sun exposure was more in the case group (5853.9 ± 2219.7 hours) than in the control group (2219 ± 392.4 hours) and the rate of sun exposure was also higher in the case group. In conclusion, sun exposure was significantly higher in carcinoma patients and since most of the lesions were in the covered areas of the body, it can be said that these carcinomas were due to arsenicosis and not due to sun exposure and smoking status, use of fertilizer and pesticides were not associated with the development of skin carcinoma.

Introduction

Arsenic is a naturally occurring metalloid. More than 30 countries in the world have arsenic contamination in their water.[1-5] Skin cancer in arsenicosis patients has been well documented over the past several decades. Most common forms of skin cancer found in these patients are Bowen's disease, squamous cell carcinoma and basal cell carcinoma.[6, 7] The body response to arsenic exposure varies among individuals. Other factors such as sun exposure, smoking, fertilizer use etc. might also contribute to the development of skin lesion in arsenicosis.[8-14] So, the identification of environmental factors that enhance the development of skin cancer and by modifying them might lessen the carcinoma burden.

Materials and Methods

This study was conducted from April 2015 to August 2016. Consecutive type of sampling technique was applied to collect the sample from the study population. Arsenicosis patients who fulfilled the inclusion and exclusion criteria were selected as case and without skin cancer were taken as control. Inclusion criteria were age >20 years and both sexes, patients with skin lesions fulfilling WHO diagnostic criteria of a clinically confirmed case of arsenicosis were taken as control. Arsenicosis patient with skin cancer histopathologically confirmed was taken as case and participants who had willingly given written consent were included. Exclusion criteria were skin conditions mimicking arsenicosis, subjects having carcinoma other than skin carcinoma and skin carcinoma secondary to other skin diseases.

Study procedure

An informed consent was taken from each patient who met the inclusion criteria. For data collection, structured questionnaire and consent form were used when interviewing each respondent. At the baseline visit, the questionnaire was used to collect data on the background of the respondents, socio-demographic factors, family history, community status, personal history, occupational history, disease type and its duration. Arsenicosis patients were diagnosed by the history and clinical examination with the help of an arsenic expert. Cutaneous manifestations of arsenicosis include melanosis, raindrop pigmentation, leucomelanosis of the trunk and extremities; and focal or diffuse thickening of the palms and soles. Skin cancer diagnosed clinically by the presence of erythematous scaling or crusted patches and plaques; non-healing

Table I

Skin cancers and its distribution in the body

Histopathology	Site of skin cancer		p value
	Sun-exposed area (n=7)	Covered area (n=25)	
Bowen's disease	57.2%	56.0%	0.852
Squamous cell carcinoma	28.6%	36.0%	
Basal cell carcinoma	14.3%	8.0%	

Table II

Smoking habit and user of fertializer, pesticide

	Case (n=32)	Control (n=32)	p value
Smoking status			
Smoker	25.0%	31.3%	0.380[ns]
Past smoker	21.9%	9.4%	
Non-smoker	53.1%	59.3%	
Use of fertilizer and pesticide			
Never user	53.1%	59.4%	0.614[ns]
User	46.9%	40.6%	

Table III

Rate of sun exposure in different age group

Age (year)	Rate of sun exposure (hours)			
	Case (n=32)		Control (n=32)	
	n	Mean ± SD	n	Mean ± SD
20-29	0	-	6	1071.7 ± 581.6
30-39	7	1413.1 ± 293.8	7	1301.7 ± 633.8
40-49	11	2075.7 ± 1152.2	11	1583.3 ± 531.8
50-59	9	1728.7 ± 472.8	6	1299.2 ± 720.2
> 60	5	1747.0 ± 314.2	2	1729.0 ± 643.5

ulcers and confirmed by lesional skin biopsy for histopathology. Patients with skin cancer were taken as case and without skin cancer were taken as control. Then each group of patients was evaluated using body mass index, the severity of arsenical skin lesions, smoking status, exposure to fertilizer and pesticides, sun exposure, protection from sun, duration of cessation of drinking arsenic water and family history of arsenical skin lesions.

Body mass index was evaluated by measuring weight in kg divided by height in meter square and the patients were divided into the following categories: Underweight (<18.5 kg/m^2), normal weight (18.5-23.0 kg/m^2), overweight (23.0-25.0 kg/m^2) and obese (>25.0 kg/m^2). Sun exposure was measured by cumulative sun exposure and rate of sun exposure. The climate of our country is mostly hot and summer season mostly extends from March to October. During winter season people intentionally expose to sunlight for warming body. The lifetime cumulative sun exposure was measured according to time-based questionnaire as described by Yu et al. (2009).[14] Here participants were asked about how much time they usually spent outdoor, according to the period during the week (weekday and weekend) and different age intervals. Participants response categorized for estimating the average number of hours spent in the outdoor each day between 9:00 am to 3:00 pm in the summer and winter as: 0, <1, 1 to 2, 3 to 4 and 5 to 6 hours per day. To recall the summer outdoor exposures during the age intervals 0-12 and 13-19, the only categories included are the distance from home to school and time required to reach there, outdoor activities e.g. running or playing outside, swimming, time spent outdoors in a job.

Cumulative lifetime sun exposure in both summer and winter during 9:00 am to 3:00 pm was calculated by summing weekday and weekend day exposures across different age intervals. The rate of sun exposure i.e. the average number of hours spent outdoors per year was estimated to observe the effect of current age, e.g., total hours spent in outdoor for older than for the younger participants.

Severity of arsenical skin lesions

Arsenic-induced skin lesion served as a biological marker of exposure. Melanosis is the early and common manifestation of arsenicosis. Keratosis appears in more advanced stages of arsenicosis. A sudden increase in the size of keratotic lesion or crack or bleeding of lesion suggests malignant transformation.

Results

Table I shows that in sun-exposed area, 57.2% of skin carcinoma was Bowen's disease, 28.6% was squamous cell carcinoma and 14.3% was basal cell carcinoma. In the covered area, 56% was Bowen's disease, 36% was squamous cell carcinoma and 8% was basal cell carcinoma. Chi-square test (χ^2) was performed and found not significant (p=0.852). Table II shows the distribution of study subjects by use of fertilizer and pesticide. About 53.1% of case and 59.4% of control had never used fertilizer and pesticide. About 46.9% of case and 40.6% of control were fertilizer and pesticide user. Chi-square test (χ^2) was not significant (p=0.614).

Table II shows the majority of patients in case (53.1%) and control (59.3%) groups were non-

smoker, 21.9% of case and 9.4% of control were past smokers and the rests were the smoker. Chi-square test (χ^2) was performed and found not significant (p=0.380).

Table III shows that the rate of sun exposure was more in cases in different age groups than in the control. The range of the rate of sun exposure in case group was 938-5469 hours and in control group was 242-2184 hours. Data were analyzed by unpaired t-test and was significant (p=0.022).

Discussion

Arsenic-associated squamous cell carcinoma is distinguished from the ultraviolet-induced squamous cell carcinomas by their tendency to occur on the palms, soles and trunk rather than solely on sun-exposed areas such as the head and neck.[2] In this study, most of skin cancers were found both in the exposed and covered areas and the lesions in the covered areas outnumbered the sun-exposed areas. Arsenical basal cell carcinomas most often arise from the normal tissue, frequently occur on the trunk.[2] In this study, among the 3 basal cell carcinoma, 2 were found on the trunk and one in the palm.

As there is negligible amount of arsenic absorbed through the skin, the mechanisms through which exposure to fertilizers and pesticides lead to increased risk of arsenic-induced skin lesions remain unknown. Fertilizers and pesticides usually cause irritant contact dermatitis which may aggravate or modify the arsenic-induced skin lesions. Studies conducted by Melkonian et al. (2010) and Chen et al. (2003) found that users of fertilizers and pesti-cides were more prone to arsenic-induced skin lesions.[8, 15] In this study, no association was found regarding exposure to fertilizer and pesticide with severity of arsenical skin lesions and the effect of these agents were comparable in both groups.

A cross-sectional study in Chile found that methylation capacity of arsenic was poor among the smokers, as indicated by a higher ratio of urinary monomethylarsonate to dimethylarsinate in smokers.[16] In two different studies conducted in Araihazar, Bangladesh by Melkonian et al. (2010) and Chen et al. (2006) have found increased skin lesions among the smokers.[8, 15] In this study, the smoking status was observed between the two groups and no association was found in the development of skin cancer with the smoking status.

In an experimental study conducted by Burns et al. (2004) showed that skin tumors occurring in mice given ultraviolet radiation along with arsenite appeared earlier and more invasive than in mice given ultraviolet radiation alone.[17] Chen et al. (2006) suggest that the risk of skin lesions associated with any given level of arsenic exposure was greater with excessive sun exposure.[15] This finding co-relates with the current study as greater cumulative sun exposure and the rate of sun exposure were observed in carcinoma group than in non-carcinoma group and found statistically significant.

Conclusion

Smoking status, use of fertilizer and pesticides were not associated with the progression of arsenical skin lesions to skin carcinomas. Sun exposure was significantly higher in carcinoma patients but as most of the lesions were in covered areas of the body, it can be said that these carcinomas were due to arsenicosis and not due to sun exposure.

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