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EPIDEMIOLOGY AND POPULATION ATTRIBUTABLE FRACTION OF MELANOMA TO ULTRAVIOLET RADIATION IN ASIA: AN ECOLOGICAL STUDY

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Abstract – *Objective:* *Skin cancer was considered as the most common cancer worldwide and UV (Ultraviolet) as a major risk factor for this type of cancer. The aim of the current study was to investigate the association between UV-radiation and melanoma in Asia.*

Materials and Methods: *National estimates of new cases of cutaneous melanoma, herein referred to as melanoma, were obtained from GLOBOCAN 2012, with only those countries/territories with at least 10 melanoma cases (in both genders) included in the study (n = 153 countries/territories, accounting for 96% of the estimated global melanoma burden).*

Results: *A total of 168,000 cases of UV-related cancer were recorded in 2012, with 75.7% of all cases of melanoma and 1.2% of all cancer worldwide being exposed to UV. According to the Human Development Index (HDI) in 2012, the very high HDI with 2.63 (2.6, 2.66) of all UV-related cancers, as compared with other areas, has the most UV-related cancers. The largest number of cases of UV-related cancer was reported for Europe (78000 cases) as compared to the lowest incidence for Asia (2180 cases); the largest number of cases of UV-related cancer was reported in Israel (939 cases) in West Asia and the lowest in Malaysia (1 case) in South-East Asia. In Asia, the countries of Israel and Timor-Leste have 88.2% and 87% of the most UV-related melanomas, respectively. The highest incidence of UV-related cancers in all areas was in the age group of 50-69.*

Conclusions: *One of the biggest risk factors for developing skin melanoma is exposure to UV radiation. Melanoma is relatively rare in Asia than other continents. In countries where there are more cultural and occupational issues in contact with UV rays, there should be measures to reduce contact.*

KEYWORDS: *Cancer, Melanoma, UV, Asia continent.*

INTRODUCTION

Cancer is one of the leading causes of mortality worldwide, and cardiovascular disease was reported as the second most common cause in developed countries and the third most common cause of mortality in less developed countries afterwards[1-4]. Cancer is one of the most important factors in the world's disease burden in the coming decades and the number of new cases expected to increase to

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15 million in 2020[5-8]. According to the WHO, the cancer-related mortality in the Middle East will be increased by 80-100% in the next 15 years. Skin cancer is the most common cancer in the world and is ranked first in men and second in women[9]. Skin cancer accounts for 25% to 32.7% of all cancers[10]. There are three main types of skin cancer: squamous cell carcinoma (SCC), basal cell carcinoma (BCC), and melanoma[11]. Although melanoma accounts for less than 10% of all skin malignancies, it accounts for about three quarters of mortality from skin cancer[12]. The incidence of skin cancers has increased in recent decades. Ultraviolet radiation is a known carcinogen and is the first environmental cause of skin cancer. Climate change, including changes in the thickness of the protective layer of ozone combined with changes in personal and social habits, can justify this increase. Other factors may include: smoking, HPV, genetic syndromes, ionizing radiation, or use of immunosuppressive drugs[13]. It is estimated that ultraviolet radiation is a risk factor for approximately 65% of melanoma and 90% of non-melanoma skin cancers, and that the risk for a person with melanoma is doubled in case of multiple sunburns. Therefore, environmental changes results in increased UV light transmission imply direct consequences on human health. The history of sunburn and high-dose intermittent sunshine has a direct relation with the relative risk of melanoma in life spans[14,15]. The Academy of Skin in the United States has stated that melanoma is prevalent in Australia and New Zealand, but is also common in Asia, Africa and Latin America. In the United States, Europe and Australia, 25, 20 and 45% of cancers reported in one year are skin cancers, respectively[16]. Melanoma is more common in men than in women because it is three times more likely to be higher in men over 80 and over than women over the age of 80 years[11]. Protecting sunlight has a protective effect on SCCs and BCCs, however; more studies are needed to fully characterize the role of UV light as a carcinogen in the skin. The aim of this study was to investigate the epidemiology of UV-related melanoma in Asia.

MATERIALS AND METHODS

National estimates of new cases of cutaneous melanoma, herein referred to as melanoma, were obtained from GLOBOCAN 2012[17], with only those countries/territories with at least 10 melanoma cases (in both genders) included in the study (n = 153 countries/territories, accounting for 96% of the estimated global melanoma burden). One of the ways the results were grouped was by Human Development Index (HDI), a composite indicator of life expectancy, education, and gross domestic product per person. The 153 countries/territories included were grouped into four categories according to their UN-defined HDI groups as of 2012: very high, high, medium, and low HDI (UNDP 2013 Human Development Report)[18].

EXPOSURE ASSESSMENT

The prevalence and intensity of ultraviolet (UV) radiation exposure are difficult to quantify at the population level. Because there are no populations completely unexposed to sunlight, the traditional approach to quantifying population attributable fractions (i.e. using population prevalence of exposure and corresponding relative risks of cancer) cannot be applied. Instead, observed melanoma incidence rates were compared with those in a minimally exposed reference population, with differences in the numbers of new cases attributed to corresponding differences in UV radiation exposure between the reference and study populations. PAF (population attributable fraction) was calculated as the proportional difference between the estimated number of new cases in 2012 – by country/territory, 5-year age group (ages ≥ 30 years), and gender – and the expected number of cases, using incidence rates from the reference population[19]. The following formula was used to calculate country/territory-, age-, and gender-specific

PAF: $PAF = (I_p - I_u)/ I_p$

Where I_p is the incidence of melanoma in 2012 in the study population and I_u is the incidence in the reference population. The number of cancer cases attributable to UV radiation exposure was also expressed as a percentage of the total number of all new cancer cases in 2012, excluding non-melanoma skin cancers. The variance estimate of the PAF obtained via the delta method was used to compute 95% uncertainty estimates.

RESULTS

The results showed that 168000 UV-related cancers were reported in 2012, with 75.7% of cases of all melanoma and 1.2% of all cancer worldwide being exposed to UV. In men some 95,100 cases (81.3%), and in women 72900 cases (69.4%) were reported for UV-related melanoma. New Zealand and Australia had the highest percentage of UV-related cancer associated with 11.1% and 9.44% of total cancers and 96.3% and 96.1% of UV-related melanomas, respectively (Figure 1 and Figure 2).

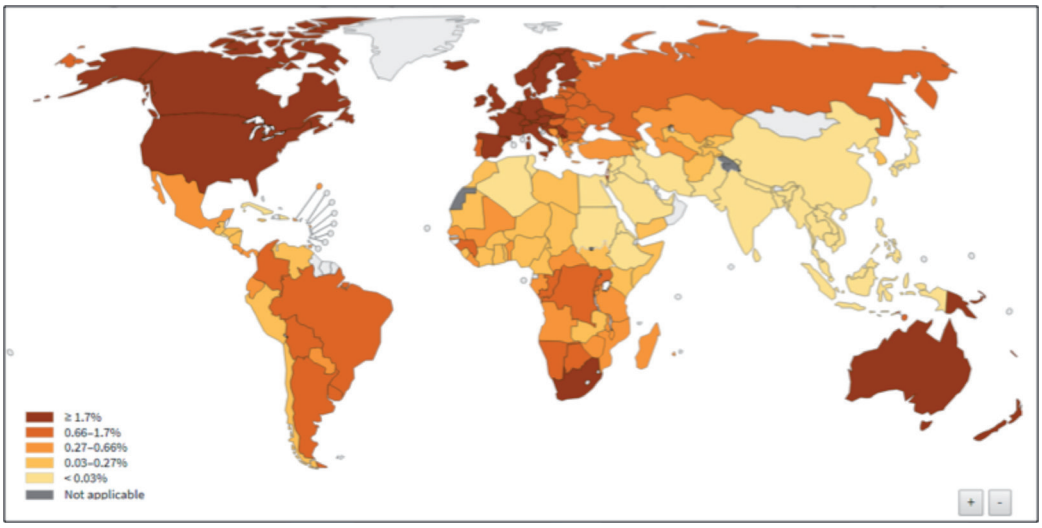

Fig. 1. Population attributable fraction (PAF) of all cancer cases worldwide in 2012, among men and women of all ages (30+ years), attributable to ultraviolet (UV) radiation exposure, by country.

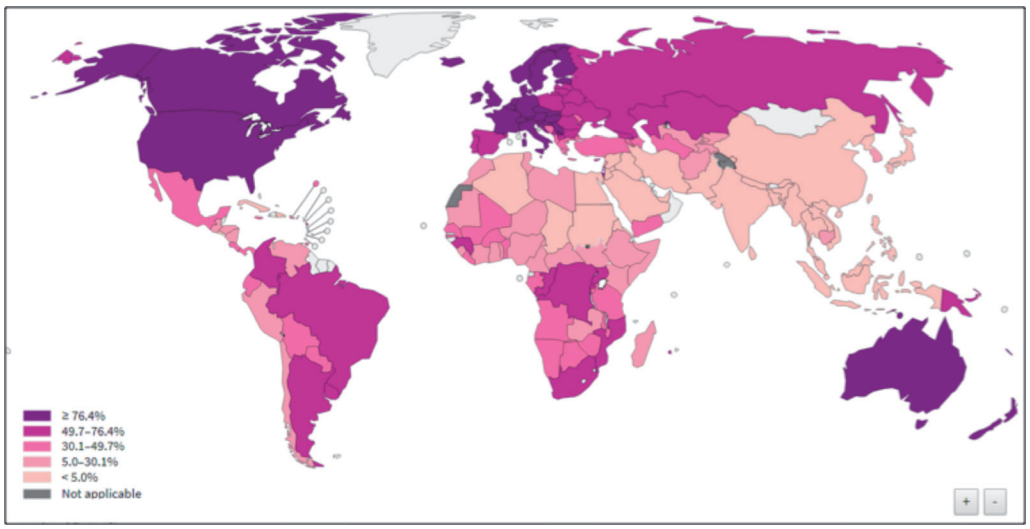

Fig. 2. Population attributable fraction (PAF) of melanoma cases worldwide in 2012, among men and women of all ages (30+ years), attributable to ultraviolet (UV) radiation exposure, by country.

The highest incidence of UV-related cancer (78000 cases) was reported for Europe. In Europe, 2.31% (2.27, 2.34) of all cancers and 81.7% (80.4, 82.9) of the melanomas were exposed to UV radiation. The lowest incidence of UV-related cancer (2180 cases) was observed in Asia. In Asia, 0.033% (0.031, 0.036) of all cancers and 10.5% (9.7, 11.4) of melanomas were exposed to UV radiation (Table 1).

According to the results of the Asia-Pacific survey, the highest incidence of UV-related cancer (1920 cases) was in West Asia and the lowest (64 cases) related to South-East Asia. The largest number of cases of UV-related cancer was reported in Israel (939 cases) in West Asia, and the lowest in Malaysia (1 case) in South-East Asia (Table 2, Figure 3).

According to the obtained results in Asia, Israel, Timor-Leste, and West Bank and Gaza Strip, have the most UV-related melanomas with the rates of 88.2%, 87.0% and 77.9%, respectively (Figure 4).

According to the Human Development Index (HDI) of 2012, the results showed that very high HDI with 2.63 (2.6, 2.66) of all UV-related cancers had the most UV-related cancers than other areas. In the study of UV-related melanomas, the results also showed that very high HDI with 86.6 cases (85.7, 87.4) had the highest incidence of UV-related melanomas. This incidence in men was 91 (90.3, 91.7) and in women 81.4 (80.3, 82.4). The lowest incidence of cancer and low-HDI-related UV-related melanomas was 0.033 (0.031, 0.035) and 10.2 (9.6, 10.8), respectively (Table 3).

In the study of incidence rates based on age groups, the results showed that the highest incidence of UV-related cancers in all areas was in the age group of 50-69 years (Figure 5).

TABLE 1. Number and percentage of all cancer and melanoma in 2012, among men and women of all ages (30+ years) attributable to Ultraviolet (UV) radiation exposure, by continent.

Continent	*Number of attributable cases to UV*	*Population attributable fraction (all cancers)*	*Population attributable fraction (Melanoma)*
Europe	78000 (76800, 79200)	2.31% (2.27, 2.34)	81.7% (80.4, 82.9)
North America	64900 (64300, 65300)	3.71% (3.68, 3.74)	90.1% (89.4, 90.8)
Oceania	13900 (13800, 13900)	9.34% (9.31, 9.37)	95.8% (95.5, 96.1)
South America	6280 (5850, 6700)	0.61% (0.57, 0.65)	48.3% (45.1, 51.6)
Africa	2790 (2630, 2940)	0.37% (0.35, 0.39)	44.7% (42.2, 47.2)
Asia	2180 (2020, 27370)	0.033% (0.031, 0.036)	10.5% (9.7, 11.4)
World	168000	1.24%	75.7%

TABLE 2. Number of cancer cases in 2012 among men and women of all ages (30+ years) attributable to ultraviolet (UV) radiation exposure, shown by Country in Asia.

Region	*Number of attributable cases*	*Relative proportion of the total number of attributable cases*	*Country*	*Number of attributable cases*	*Relative proportion of the total number of attributable cases*
West Asia	1920	88.1%	Israel	939	48.8%
			Turkey	588	30.6%
			Kazakhstan	246	12.8%
			Georgia	45	2.4%
			Armenia	41	2.1%
			Azerbaijan	25	1.3%
			West Bank and Gaza Strip	18	1%
			Lebanon	9	0.5%
			Yemen	9	0.5%
East Asia	103	4.8%	Republic of Korea	66	63.7%
			China	28	27.2%
			Japan	9	9%
South-Central Asia	85	4.8%	Turkmenistan	15	17.9%
			Uzbekistan	15	17.4%
			Iran (Islamic Republic of)	13	15.4%
			Afghanistan	13	15.2%
			Pakistan	12	14.1%
			Tajikistan	11	12.9%
			Kyrgyzstan	6	7.1%
South-East Asia	64	3.1%	Timor-Leste	10	15.5%
			Cambodia	2	3.7%
			Malaysia	1	1.6%
Total	2178	100%	—	2178	—

DISCUSSION

Studies performed to survey the skin cancer in the world show that the cancer accounts for about 20-40% of all types of cancers. Various studies showed that exposure to radiation is an important risk factor for skin cancer, and that the cause of 65 to 90 percent of skin cancers is exposure to UV rays. So protecting the skin is very important and this is an important and complex work[20]. The incidence of melanoma is different throughout the world. In western countries, skin melanoma is relatively common, especially in populations with brighter skin colors[21]. The results showed that 168000 new cases of UV-related cancer were reported in 2012, accounting for 75.7% of all melanoma cases and 1.2% of all cancer worldwide. New Zealand and Australia have the highest percentage of UV-related cancer, with 11.1% and 9.44% of all cancers and 96.3% and 96.1% of UV-related melanomas, respectively. More developed regions are more affected by UV radiation than less developed regions. The highest incidence of UV-related cancer

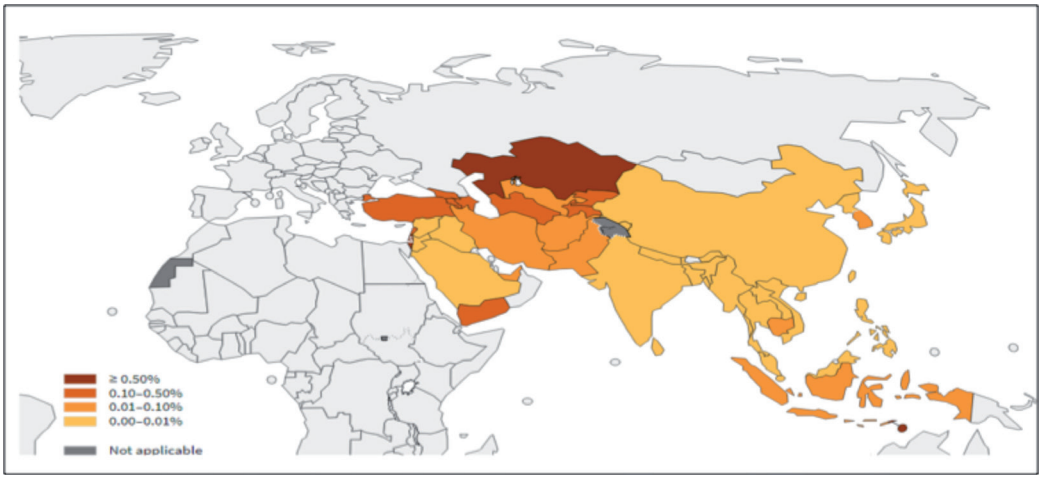

Fig. 3. Population attributable fraction (PAF) of all cancer cases in Asia in 2012, among men and women of all ages (30+ years), attributable to ultraviolet (UV) radiation exposure, by country.

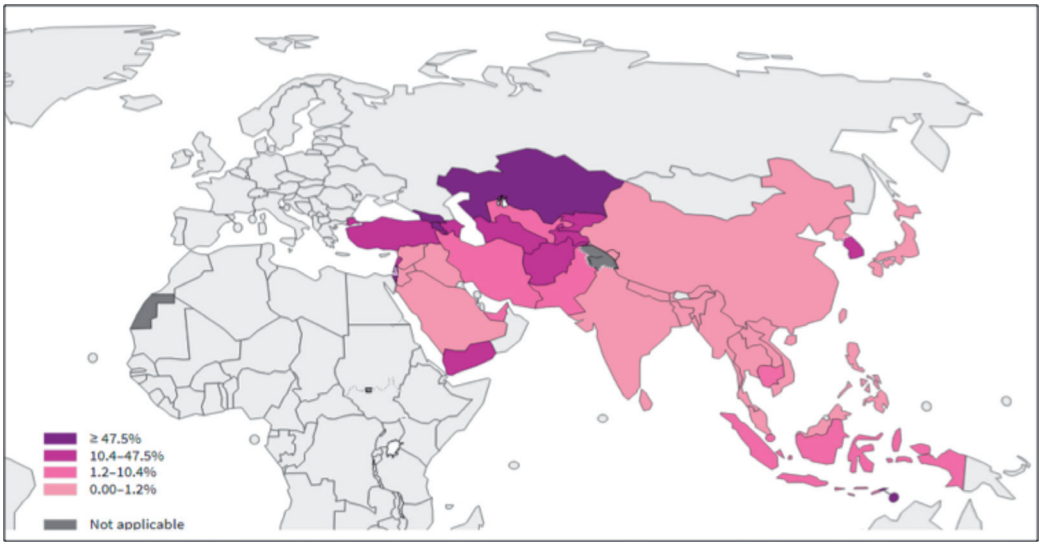

Fig. 4. Population attributable fraction (PAF) of melanoma cases in Asia in 2012, among men and women of all ages (30+ years), attributable to ultraviolet (UV) radiation exposure, by country.

TABLE 3. Level of development.

Human Development Index (HDI)	*Population attributable fraction (PFA)(%)(all cancers)*			*Population attributable fraction (PFA)(%)(all cancers)*		
	Male	*Female*	*Total*	*Male*	*Female*	*Total*
Very high HDI	2.76 (2.74,2.78)	2.47 (2.4, 2.5)	2.63 (2.6,2.66)	91 (90.3,91.7)	81.4 (80.3,82.4)	86.6 (85.7, 87.4)
High HDI	0.86 (0.83,0.9)	0.65 (0.6, 0.7)	0.76 (0.72, 0.8)	66.8 (64.1,69.4)	43.9 (40.9,47)	54.5 (51.6, 57.3)
Medium HDI	0.2 (0.18, 0.21)	0.18 (0.17, 0.2)	0.19 (0.17, 0.2)	34.9 (31.6,38)	33 (31,35.1)	33.8 (31.2, 36.3)
Low HDI	0.035 (0.034, 0.037)	0.03 (0.02, 0.032)	0.033 (0.031, 0.035)	11.1 (10.5,11.7)	9.1 (8.5, 9.6)	10.2 (9.6, 10.8)
World	1.33	1.14	1.24	81.3	69.4	75.7

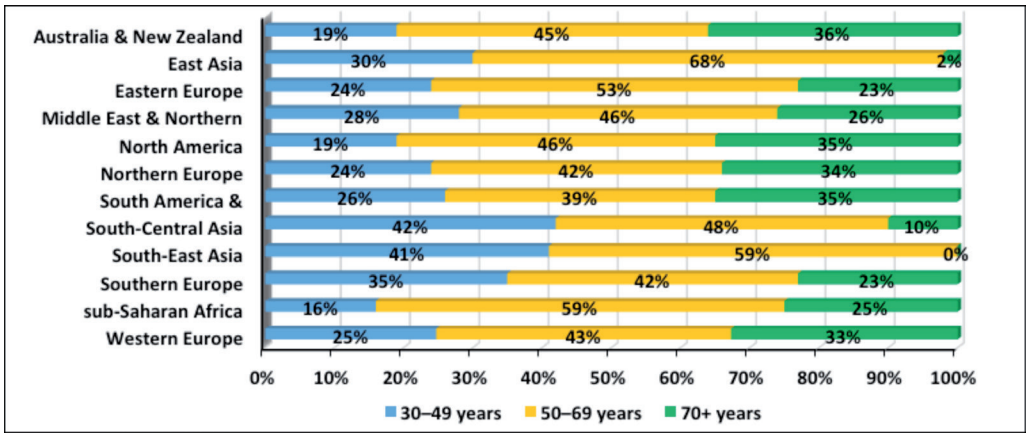

Fig. 5. Relative proportion (by age group) of cancer cases in 2012 attributable to ultraviolet (UV) exposure, among men and women of all ages (30+years), by region.

(78000 cases) was reported for Europe, and the lowest incidence (2180 cases) was for Asia. The largest number of cases of UV-related cancer was reported in Israel (939 cases) in West Asia and the lowest in Malaysia (1 case) in South-East Asia. In Asia, Israel, Timor-Leste, and West Bank and Gaza Strip, have the most UV-related melanomas with the rates of 88.2%, 87.0% and 77.9%, respectively. The highest incidence of UV-related cancers in all areas was in the age group of 50-69. The sun is the main source of UV radiation, and the amount of radiation received at any point in the earth depends on latitude and elevation, day and time, cloud cover, air pollution, and thickness of the protective layer of the ozone in the stratosphere[22]. Therefore, outdoor activities and exposure to sunlight over the past 50 years are the most important factors in increasing the incidence of melanoma[23]. According to the obtained findings, 168000 UV-related cancers were reported worldwide in 2012. Studies showed that about 230000 cases are reported annually and 55000 deaths from melanoma are estimated worldwide. New Zealand has the highest levels of UV-related cancer in the world. In New Zealand, the incidence, age, and mortality rate of melanoma are slightly higher than in Australia and twice in the UK. Estimates in New Zealand show that during 2007-2008, $ 57 million was spent on public health care and at least $ 26 million in the private sector for all skin cancers[24, 25]. The highest rate of melanoma was reported for New Zealand, Australia and Europe in the elderly people in which ultraviolet radiation (UV) was considered as most commonly cause of this disease in the aforementioned countries[26, 27]. Other reasons include genetics, lifestyles, living more in open environments and the tanning of the skin against sunlight. Epidemiological studies show that UV increases the risk of developing additional melanoma in vulnerable genetic populations as a risk factor. The presence of cancer markers is associated with a significant increase in the risk of melanoma. New Zealand's population is more prone to disease due to these cancer markers. In recent decades, the distribution of New Zealand population has dramatically changed, which may lead to a lower incidence of this disease in the future[28]. The risk of UVR-related melanoma in very high HDI countries is much higher than that of less developed countries, Therefore, in very high HDI countries, including Australia and New Zealand, public health measures are being taken to prevent further increases in cancer cases. Key interventions should include training and awareness of the melanoma and related risk factors that can mitigate the risk of infection. In the United States, melanoma is ranked as the fifth cancer. The prevalence of malignant melanoma in Europe and the United States was estimated to triple over the past 30 years[29, 30]. The incidence of melanoma in Asian populations is low[31] as compared to a rising trend in the Korean population[32]. Avoiding UVR, especially in childhood and adolescence, which is a critical period for UV carcinogenesis, and the protection of UVR with appropriate clothing and coverage can reduce the risk of cancer at an older age[33, 34]. The incidence of skin cancer increases significantly with age, which probably reflects long-term contact with carcinogenic factors and cancer formation[12]. Studies showed that protecting people while working outdoors to protect the harmful effects of UVR can result in a significant reduction in the amount of melanoma[35]. In the more developed countries, melanoma in men is 91 (90.3, 91.7) percent and in women 81.4 (80.3, 82.4) percent is UV-related and focuses more on the age group of 69-50 years. Because older and middle-aged men tend to be more exposed to sunlight than young men and women during their lives, they are more prone to develop skin cancer. In a study in Colombia, 62% of all melanomas were among men and 19% of women were exposed to UVR [36]. Melanoma is relati-

vely rare in Asian populations than other populations. There is evidence that there is a delay in diagnosis and treatment in the Asian population; therefore, educational efforts should be made to reduce delays in diagnosis. With the general increase in melanoma and the predicted increase in the population of Asia, physicians and patients alike should be aware of the risk of skin cancer. Currently, information on skin cancer in Asia, including melanoma, is limited[32]. For other reasons, the difference in UV-related cancer cases in continents and countries can be attributed to the difference in the registration system in different countries, which can be reduced by recognizing and recording correctly.

CONCLUSIONS

One of the biggest risk factors for developing skin melanoma is exposure to UV radiation. Melanoma is relatively rare in Asia than other continents. The lower incidence may be due to delay in the diagnosis of the disease. So increasing the awareness of physicians and patients can help diagnose and treat early illness. In countries that are more exposed to UV in terms of geographical location and cultural and occupational issues, protective measures need to be taken to reduce exposure to UV.

Conflict of Interest:

The authors declare no conflicts of interest.

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