

Most Common Skin Tumours in Correlation with Solar Ultraviolet Radiation in the Area of West Herzegovina

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ABSTRACT

Incidence rate of skin tumours, both, non-melanoma and melanoma, is increasing nowadays. Various etiological factors are of relevance for the occurrence of the diseases. The solar radiation, as well, long term exposure to ultraviolet (UV) radiation, have the greatest impact on development of these skin tumours. Non-melanoma skin tumours, Basal Cell Carcinoma (BCC) and Squamous Cell Carcinoma (SCC), are the most common skin tumours in humans, and usually develop on the chronically photo-exposed areas. As for the Malignant Melanoma (MM), one of the most aggressive skin tumours, the exposure to solar radiation also plays an important role. This study investigates the correlation between the skin tumours and UV radiation in the area of West Herzegovina, on the sample of 1676 patients. It presents the occurrence of skin tumours in the period from 1997 to 2003. The study investigates the incidence and the risk factors separately for every skin tumour which can be etiologically related to the occurrence of skin tumours and UV radiation: occupation, exposure to UV radiation, skin type, and family history on malignant tumours within the patient's family. The exact incidence rate of non-melanoma and melanoma skin tumours in Bosnia and Herzegovina is still unknown, for the reason that the united National Cancer Register does not exist yet.

Key words: skin tumours, UV radiation, risk factors

Introduction

Basal Cell Carcinoma (BCC) is a fairly benign tumour, which usually develops on chronically photo-exposed areas of the skin, hardly ever metastasizes and usually grows slowly¹. Squamous cell carcinoma (SCC) is clearly more aggressive, may grow rapidly and metastasizes at an early stage. Malignant melanoma (MM) is the most serious form of skin tumour that originates in melanocytes, the pigment producing cells of the skin². Incidence rates of skin tumour, both non-melanoma and melanoma, do increase today³. Various etiological factors are involved in the occurrence of the disease. The sunlight, as one of the first agents recognized to be carcinogenic for humans, is electromagnetic energy, which is propagated by electromagnetic waves⁴. Health wise, the most

important parts of the sunlight, electromagnetic spectrum, are ultraviolet (UV) radiation, invisible to the eye; visible light that allows us to see; and infrared radiation, which is our main source of heat, but is also invisible. Excessive exposures to them pose particular risks to health. The studies do indicate that the exposure to solar radiation is an important risk factor in the onset of MM and that incidence of severe intermittent exposure during childhood and adolescence may be particularly relevant to the latest onset of the disease. The evidence indicates that cumulative lifetime exposure to solar radiation is the most important cause of non-melanoma skin tumours in human beings⁵. The incidence is highest in those geographic areas where light-skinned people are

exposed to large amounts of sunlight. Depending on the circumstances of the exposure initiating or promoting effects predominant with UV light may vary. Intense UV exposure may be more likely to lead to initiating mutations and explains the relationship between erythema and UV exposures to the skin tumours. Chronic, lower-intensity UV light may have a predominant promoting effect and is the most noticeable in people who have already accumulated many initiating mutations, the elderly or the individuals with long sun-exposure histories⁶. Many people, including farmers, are occupationally exposed to solar UV radiation⁷.

The major sources of information on incidence of skin tumours are national cancer registries, but the exact incidence of non-melanoma and melanoma skin tumour in Bosnia and Herzegovina are unknown, as the united national cancer register does not exist.

Patients and Methods

The material for this study was collected from the Department for Dermatology and Venerology of the University Hospital Mostar. The study concerned the patients treated during the years 1997–2003. Only histologically verified skin tumours, (BCC, SCC, MM), were included in the study, which concerned 1676 patients, including 698 female, and 978 male. The study was conducted as a retrospective, contains the analysis of all available data on the occurrence of BCC, SCC, MM in the period from 1997 to 2001, while the prospective part relates to the period from 2002 to 2003. We analyzed: gender, age, occupation, skin type (all data available for 1676 patients), UV exposition (data available for 1015 patients) and occurrence of skin or other malignant disease in the family members (data available for 129 patients).

Statistic analysis was conducted upon χ^2 -test for estimation of expected value of incidence rate, Odds ratios (OR) for examination of risk occurrence in malignant skin tumour and for estimation with 95 percent confidence interval (%CI) the ration between risk factors and occurrence of malignant skin tumours. EPI statistic mathematic programme was applied.

Results

Table 1. presents the distribution of malignant skin tumours. Both, retrospective (1997–2001) and prospective parts of the study (2002–2003) included a total of

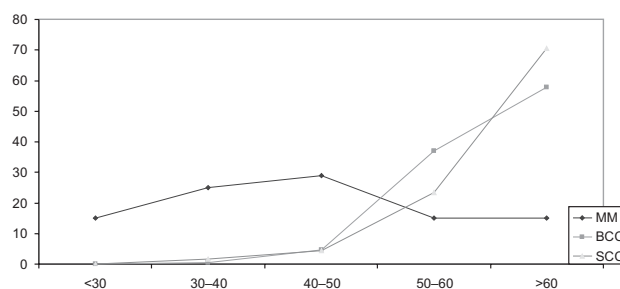


Fig. 1. Patient material classified by age range.

1148 patients with BCC, 444 patients with SCC and 84 patients with MM. Average rate of cumulative incidence was 622.83 %000 for BCC, it was 240.88 %000 for SCC and, it was 42.86 %000 for MM. Majority of patients with BCC (57.49%) and with SCC (62.61%) were male patients. There is a statistical significant discrepancy with regards to gender between retrospective and prospective part of the study for BCC ($\chi^2=4.17$ $p<0.05$), and SCC ($\chi^2=7.15$ $p<0.01$), while for MM such difference does not exist ($\chi^2=0.80$ $p=0.67$); ($p>0.05$, Anova test).

The great part of the patients with BCC (57.84%) and SCC (70.49%) are above 60 years of age. Difference between age groups for BCC is confirmed by $\chi^2=12.13$ and for SCC by $\chi^2=7.15$ ($p<0.01$). There is no significant statistical discrepancy among patients with BCC and SCC with regards to their age group neither in retrospective nor in prospective part of the study. The greatest number of patients with MM (34.52%) was in the age group from 40 to 50 years. There is statistically significant discrepancy of MM incidence in relation to the age of patients in both retrospective and prospective part of the study, $F=73.50$ $p=0.001$ (Tukey test), (Figure 1).

Incidence of skin tumours in relation to occupation of the patients was calculated with the rate of relative frequency. The results show that relative frequency of incidence of BCC and SCC for outdoor workers is bigger in comparison to relative frequency of incidence of the same diseases for indoor workers. On the contrary, a relative frequency of MM is lower for outdoor workers then for indoor workers (Table 2).

Results of the study have shown that the majority of patients with BCC (70.29 %) had skin type I and II. The number of patients with BCC in relation to the skin type has a significant statistical discrepancy $\chi^2=33.10$ ($p<0.001$). The risk of getting BCC is higher for the persons

TABLE 1
PATIENT MATERIAL CLASSIFIED BY YEAR OF DIAGNOSIS, GENDER AND TYPE OF SKIN TUMOUR

	1997–2001		2002–2003		Total		Grand Total
	Men	Women	Men	Women	Men	Women	
BCC	415	314	245	174	660	488	1148
SCC	181	102	97	64	278	166	444
MM	25	31	15	13	40	44	84

TABLE 2
MALIGNANT SKIN TUMOURS ASSOCIATED WITH OCCUPATION

Type of skin tumour	1997–2001				2002–2003				Total
	Outdoor workers		Others		Outdoor workers		Others		
	N	RF	N	RF	N	RF	N	RF	
BCC	396	0.5945	333	0.5050	239	0.5704	180	0.4296	1148
SCC	195	0.6890	88	0.3109	105	0.6521	56	0.3479	444
MM	18	0.3214	38	0.6782	8	0.2857	20	0.7142	84

N – number of patients, RF – relative frequency

TABLE 3
MALIGNANT SKIN TUMOURS ASSOCIATED WITH SKIN TYPES

Type of skin tumour	1997–2001		2002–2003		Total
	Skin type		Skin type		
	I and II	III and IV	I and II	III and IV	
BCC	509	220	298	121	1148
SCC	199	84	102	59	444
MM	43	13	21	7	84

TABLE 4
MALIGNANT SKIN TUMOURS ASSOCIATED WITH UV RADIATION

Type of skin tumour	1997–2001		2002–2003		Total
	UV P	UV O	UV P	UV O	
BCC	395	101	301	82	879
SCC	58	12	28	8	106
MM	7	1	18	4	30

UV P – permanent UV radiation, UV O – occasional UV radiation

with skin type I and II than for the persons with skin type III and IV, OR=1.50 (95% CI 1.30–1.72). Also, majority of patients with SCC (68.79 %) have a skin type I and II. There is an obvious statistical discrepancy with regards to the number of persons with SCC and a skin type $\chi^2=55.45$ ($p<0.001$). Influence of skin type I and II to the incidence of SCC is higher than skin type III and IV, OR=2.10 (95% CI 1.72–2.57). In the retrospective part of the study 76.19% of the patients with MM had the skin type I and II, while in the prospective part of the study 23.81% of the patients with MM had the same skin type. There is a statistically significant discrepancy $\chi^2=23.05$ ($p<0.001$) with regards to the skin type between retrospective and prospective part of the study. Incidence of MM in the persons with skin type I and II is higher than in the persons with skin type III and IV, and it is OR=3.20 (95% CI 1.94–5.29), (Table 3).

From the total of 879 patients with BCC, and based on the results of the study, 79.18% of them stated they had different kinds of outdoor occupation, related to the long-term and chronic sun exposure or to intermittent sun exposure in their youth. According to the results

gathered from the personal history of patients with BCC there is an obvious statistical discrepancy between the number of patients and frequent exposure to UV radiation, $\chi^2=29.80$, ($p<0.001$), OR=3.81 (95% CI 3.24–4.49) for incidence of BCC in the persons exposed to chronic UV radiation. The results show that long term exposure to UV radiation over the years leads to the increased incidence of SCC. According to the data from the personal histories on the sample of 106 patients with SCC, we proved that the incidence of SCC (81.13%) is more frequent in the persons who were exposed to chronic UV radiation. The results showed that there is significant statistical discrepancy between the number of patients with SCC and exposure to UV radiation, $\chi^2=37.60$ ($p<0.001$), OR=3.91 (95% 2.45–6.25).

From the total of 30 patients with MM and based on the data from their personal histories, 83.33% confirmed they were exposed to sun for longer time and without any protection, and suffered from severe sunburns provoked by inadequate sun exposure. Results for incidence of MM and exposure to UV radiation show that there is significant statistical discrepancy, $\chi^2=12.03$ ($p<0.001$). Influ-

TABLE 5
MALIGNANT SKIN TUMOURS ASSOCIATED WITH FAMILY HISTORY OF MALIGNANT TUMOURS

Type of skin tumour	1997–2001		2002–2003		Total
	MST	OMT	MST	OMT	
BCC	54	12	27	10	103
SCC	9	1	2	0	12
MM	9	1	4	0	14

MST – malignant skin tumours, OMT – other malignant tumours

ence to the incidence of MM and long term exposure to UV radiation, in comparison to others is 12.03 times bigger (95 % CI 1.91–13.06), (Table 4).

The study shows there is a significant statistical discrepancy between incidence of BCC and malignant skin tumours in the family $\chi^2=8.16$ ($p<0.001$) OR=13.00 (95% CI). There is also a significant statistical discrepancy between the incidence of SCC in the tested groups $\chi^2=6.75$ ($p<0.001$), OR=11.00 which shows higher risk for the incidence of SCC in the families with the same type of skin tumours. Relation of the incidence of BCC and SCC with other malignant diseases, according to our results, is statistically insignificant. The results of the study with regard to MM show significant correlation between the incidence of malignant skin tumours in the same family, $\chi^2=8.64$ ($p<0.001$). Incidence of MM in the same family and incidence of malignant skin tumours is OR=13.01 (95% CI 1.17–76.15), (Table 5).

Discussion

The research on incidence of malignant skin tumours was conducted in the area of West Herzegovina. According to the data collected by the Statistical Institute, the total population in the tested area, in December 2002 was 184, 318. Population was predominantly rural. During the testing period from 1997 to 2003 a total of 1676 cases was diagnosed. The smallest number of cases was registered in 1997, but it gradually increased with the highest number registered in 2003. The reason for this may be that the patients were treated, and especially in the beginning of the research, in other medical institutions mostly located in the Republic of Croatia. This mainly refers to the cases of malignant melanoma.

The majority of patients suffered from BCC (1148), and this confirms the fact that is the most frequent malignant tumour. This skin tumour is, by far with SCC, the most common form of tumours in humans and in 2002, an estimated 1 million Americans were diagnosed with these tumours⁸. Average rate of cumulative incidence for MM in this study was 42.86 %000. Reported incidence (1998–2002) vary for Europa, it is the highest in Scandinavia countries (Norway, Sweden, Denmark), and in eastern Europa. North America shows the incidence 19.4/10⁵, but the highest is in Queensland, Australia 55.8/10^{5,9}.

The results of the study show that the majority of patients suffering from BCC and SCC were predominantly male patients. There appears to be a gender related difference in the development of tumours. Previous studies, as well as a recent report of the »Surveillance, Epidemiology and End Results« (SEER) program of the National Cancer Institute, revealed that the tumours incidence for all sites are greater in males compared to females^{9,10}. These gender differences appear to hold true for non-melanoma skin tumours as well. Epidemiological studies have reported the development of significantly more non-melanoma skin tumours in male than female, with the American Cancer Society reporting approximately twice the incidence of these tumours development in male compared to female and a threefold greater incidence of SCC in males compared to females^{11,12}. When gender is examined BCC and SCC are more prevalent in male subjects, especially in the early decades of life when occupational exposure may vary based on sex¹³. All European countries report a higher incidence of MM in females than males as in this study, in contrast to Australasia and North America where males have a higher incidence¹⁴.

One of the most important factors is the age. All epidemiological studies indicate that the skin tumours increase in prevalence with advancing age. This study confirms the fact that the patients suffering from BCC or SCC are above 60 years old. Among Caucasians it was found that the prevalence rate was less than 10% in the third decade of life, but more than 80% when people were examined in the seventh decade of life^{15,16}. Patients suffering from MM who were part of this research fell mostly into the age group from 40 to 50 years old. Important factor is sun exposure at childhood. The average patients suffering from BCC and SCC are elderly patients with fair skin and a history of excessive sun exposure.

A part of the study considers occupation and how it influences the incidence of malignant skin tumours. Male tended to have occupations that required them to spend more time out in the sun and overall male are less likely to use sun protection than female. Occupational exposure to ultraviolet light does show a strong relationship between cumulative sunlight exposure and skin tumours¹⁷. This study shows that the majority of patients suffering from BCC and SCC were outdoor workers. This was an expected result, because the tested sample was predominantly rural and agricultural. The given

results confirm that the persons with occupational outdoor exposure have higher incidence rates of BCC and SCC than their indoor worker counterparts. Outdoor work is associated with increased risk of SCC in South Europe with an odds ratio of 1:6¹⁸. On the other hand, persons who work indoors have a higher incidence of MM in comparison to those who work outdoors. Patients with MM in the study mostly belonged to indoor workers. Other important features of melanoma is related to the risks in higher socioeconomic groups. A number of studies have reported that, in contrast to SCC of the skin, MM are more prevalent in the wealthier strata of society. Studies from the USA and UK show that the incidence of MM in age-matched sections of the population is higher in those with a higher income and other measures of affluence¹⁹. This may be due to the greater opportunity of the more affluent for recreational sun exposure and sunny holidays in the winter months.

The mechanisms for induction vary between the types of skin and tumour. Skin tumours is less common in darkly pigmented persons than in light skinned Caucasians but is often associated with increased morbidity and mortality²⁰. Malignant skin tumours, both non-melanoma and melanoma, are mostly present in persons with skin types I and II (as per Fitzpatrick²¹). The epidemiological similarities include the concentration in white population with light pigmentation and in those who live in sunny areas. The person's sun sensitivity correlates best with those who are fair skinned, have light-coloured eyes (blue, green) and red or blond hair. This study showed significant associations between skin types. A significant majority of patients with malignant skin tumours had the skin types I and II.

The most important causative factor is a long term sun exposure. There is a clear relation between solar radiation and skin tumour. Non-melanoma skin tumour is consistent with the concept that its risk is proportional to the cumulative dose of UV radiation received²². More important are the individual features such as sun sensitivity and inability to tan, the tendency to sunburn rapidly. Cumulative UV radiation exposure is an important factor in determining the occurrence of BCC and SCC, which is also obvious from this study. Since the majority of patients were from the population group involved with agriculture and were constantly exposed to UV radiation, and also fell into older age group (above 60), this confirms the fact that cumulative dosage of UV radiation is crucial for the development of non-melanoma skin tumours. Intermittent rather than long-term sun exposure is closely linked with melanoma development. Majority of patients with MM also belong to the group that was often exposed to UV radiation, but in a different manner. They, from the early childhood, intermittently exposed to the sun with common redness of skin and burning. Short, intermittent burning episodes of sun exposure have been identified as a major melanoma risk factor, so some of the increase could be attributed to greater opportunities for burning of pale, non-acclimatised Caucasian skin²³. It is probably easier to study intermittent expo-

sure in population where many people have little regular exposure but indulge in binge type sun exposure during holidays and recreational activities²⁴. It could be argued that the relatively low risk of melanoma seen in the outdoor workers and presented above, in contrast to the high skin surface sun exposure dosage of these workers, occur because these individuals have considerable natural protection against UV radiation due to the skin thickening and melanin distribution²⁵. Skin reaction to sun exposure and occurrence of sunburns, especially second degree burns, as well as the spots are the risk factors for the development of MM. Erythema is a marker for the most damaging type of UV exposure. It is also likely that sunburns have a strong influence on skin tumour risk because sunlight acts more like an initiator when it induces erythema than when it does not²⁶. The epidemiological evidence suggests that the effect of long continued exposure such as that received by persons with outdoor occupations is different qualitatively as well as quantitatively from the effect of intermittent exposure²⁷.

There is the relation between non-melanoma skin tumours and a family history of skin tumours. There have been previous indications that patients with BCC and SCC may run an increased risk of experiencing other malignancies^{28,29}. This study shows significant statistical relation between the suffering from malignant tumours and their occurrence in the families of patients. On the contrary, we were not able to prove the relation to other malignant tumours. The reason for that may be in a small number of persons tested in this segment. Personal history of MM is an important information pointing to an increased risk of secondary MM. Personal history of non-melanoma skin tumour can also be a prognostic factor for MM³⁰.

Conclusion

To conclude, the majority of patients suffering from non-melanoma skin tumours, BCC and SCC, were predominantly male patients. On the other hand, there was a higher incidence of MM in females than in males. This study confirms the fact that the patients suffering from BCC or SCC are above 60 years old, while patients suffering from MM fall mostly into the age group of 40 to 50 years old. Because of the fact that majority of non-melanoma skin tumours has been diagnosed in older outdoor workers, the main cause of this skin tumour is the sun exposure and its risk is proportional to the cumulative dose of UV radiation received. Intermittent burning episodes of sun exposure have been identified as a major melanoma risk factor and majority of patient suffering from MM were indoors workers. It is clear that there is sufficient evidence of the obvious correlation between melanoma and non-melanoma skin tumours and other malignant tumours. A clear understanding of the risk factors for development of these tumours, further research into preventing and treating these tumours and more effective tracking records may help to begin reversing the current trend of new cases being reported each year.

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NAJČEŠĆI TUMORI KOŽE POVEZANI S ULTRAVIOLETNIM ZRAČENJEM NA PODRUČJU ZAPADNE HERCEGOVINE

SAŽETAK

Incidenција nemelanomskih i melanomskih tumora kože danas je u porastu. Različiti etiološki čimbenici učestvuju u pojavi bolesti. Sunce je prepoznato kao jedan od prvih uzročnika, a dugotrajno izlaganje ultravioletnom zračenju igra važnu ulogu u nastanku tumora kože. Nemelanomski tumori kože, *carcinoma baseocellulare* (BCC) i *carcinoma spino-cellulare* (SCC) su najučestaliji tumori kože uobičajeno smješteni na suncu izloženoj koži. U *melanoma malignum* (MM), najagresivnijem tumoru kože, izlaganje suncu također igra važnu ulogu. Naša studija istražuje povezanost tumora kože i ultravioletnog zračenja na području Zapadne Hercegovine i uključuje 1676 bolesnika s tumorima kože u razdoblju od 1997. g. do 2003. g. Studija istražuje incidenciju i čimbenike rizika koji su etiološka veza bolesti i izlaganja suncu: zanimanje, izloženost sunčevom zračenju, tip kože i pojava istih tumora u obitelji. Bosna i Hercegovina nema točne podatke o broju bolesnika s tumorima kože, jer još uvijek ne postoji jedinstveni Referentni centar za tumore kože.