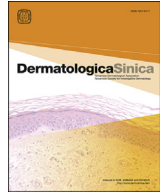


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ORIGINAL ARTICLE

Sun-related risk factors, perceived seriousness of disease and accompanying non-melanoma skin cancer in patients with actinic keratoses

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ABSTRACT

Background: Actinic keratoses are the most common premalignant skin lesions worldwide. They are of public health importance since their presence has been associated with the significantly increased incidence of non-melanoma skin cancers (NMSCs), especially when they are numerous and have coalesced into an area with severe photodamage. The current study aimed to evaluate the relationships between sun-related risk factors, perceived seriousness of actinic keratosis (AK), skin cancer examination (SCE) history, and newly detected NMSC in AK patients.

Methods: In this descriptive, cross-sectional, case–control study, firstly we examined the demographics, phenotypic traits, sun exposure history, cancer history and newly detected NMSC with full-body skin examinations in AK patients (n = 198) and controls. Secondly, the effects of these parameters, AK knowledge and AK-related clinical findings on the perceived seriousness of AK, SCE history and the presence of newly detected NMSC in AK patients were evaluated.

Results: The presence of newly detected NMSC was significantly higher in patients aged ≥ 65 years, with personal or family skin cancer history, higher AK severity and photoaging grade; however, it was observed that these cases did not perceive AK as a serious illness and did not visit a physician for an SCE previously.

Conclusion: This is the first study evaluating sun-related risk factors, knowledge and perceived seriousness of disease and SCE findings of AK patients in Turkey. Our results indicate that national health awareness campaigns and skin cancer scanning programs should be developed especially for the patients under the sun-related risks of AKs and NMSC occurrence.

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Introduction

Actinic keratosis (AK) is the most common type of precancerous skin lesions worldwide. They are clinically characterized by a slow growth rate <1 cm, ranging from indistinct scaly erythematous macules to hyperkeratotic papules on the sun-exposed areas such as face, scalp, forearms, and hands. The incidence of these lesions which usually develop because of long-term cumulative exposure to sunlight and ultraviolet (UV) rays in susceptible individuals gradually increases in the middle-aged and older adults.^{1,2}

AKs and non-melanoma skin cancers (NMSCs; basal cell carcinoma/BCC, squamous cell carcinoma/SCC) have a very similar genetic and environmental expression profile.² Moreover, AKs are regarded as precursor lesions of cutaneous SCCs, and their presence is associated with the significantly increased incidence of NMSCs, especially when they are numerous and have coalesced into an area with severe photodamage.^{1,2} Since NMSCs are by far the most common forms of cancer in humans and account for nearly 90% of all skin cancers, both the early diagnosis and prevention of AKs are of great value to reduce further morbidity and mortality.^{3–8}

In a previous study including AK patients, different perceptions were reported in the wake of an AK diagnosis, such as worries about the condition worsening over time, fear of its progression to skin cancer, guilt and sadness associated with UV-related activities, and/or a relaxed attitude due to an active decision or ignorance.⁴

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However, it was identified in general public studies that the awareness of AK disease, its relationship with skin cancer, the rates of regular skin cancer examination (SCE) and full body skin examination (FBSE) were low.^{1,9–11} Although AKs are reported to be premalignant lesions most frequently observed (78.3%) in the geriatric age group in Turkey,⁹ there is not a comprehensive study evaluating sun-related risk factors, perceived seriousness of the disease, and SCE findings of AK patients.

In the first stage of this study, we aimed to examine the demographic data, phenotypic traits, sun-related acquired risk factors, personal and family history of cancer and newly detected NMSC in AK patients comparatively with the control group. In the next stage, we planned to determine the relationships between the variables such as AK-related clinical findings and AK knowledge in addition to the above-mentioned findings identified in AK patients, and perceived seriousness of AK, history of SCE and presence of newly detected NMSC.

Methods

Study design

AK patients aged >18 years, who had applied to our Outpatient Department of Dermatology between January 2014 and October 2016, were included in this descriptive, cross-sectional and case–control study. We clinically defined AKs as discrete lesions with ill-defined borders, dry surface, roughness on palpation and color varying from gray to reddish brown. AK diagnosis was also confirmed histopathologically by taking an incisional skin biopsy from the most distinct lesion. Cases with a non-malignant and non-tumoral skin condition (e.g. contact dermatitis, seborrheic dermatitis, psoriasis vulgaris, tinea pedis) affecting less than <5% of the body surface area were selected as the control group. The controls were gender and age (± 2 years) matched with the patients. Criteria for excluding the patients and the controls from the study were: presenting evidence of immunosuppression (e.g. due to specific conditions with significant reduction in immune response, such as organ transplant recipients, AIDS or an active malignancy), genetic syndromes predisposing to cancer (e.g. xeroderma pigmentosum, basal cell nevus syndrome, familial atypical multiple melanoma syndrome), presence of personal skin or non-skin cancer history detected within the last one year, communication deficit, being bedridden, diffuse skin dermatoses and those who had daily used potentially photosensitizing (e.g. thiazide diuretics, cardiac drugs) or immunosuppressive medications for more than 3 months, who were treated for AKs on some occasion or who had been submitted to phototherapy previously. Due to the possible protective effects of the NSAIDs against AK/NMSC development, current regular users of NSAIDs (individuals who had taken any type of NSAID two or more times per week for at least 1 year) were also excluded. The study protocol was approved by the Local Ethical Committee, which follows the guidelines set by the Declaration of Helsinki. All subjects provided a written informed consent to participate in the study. The demographic findings and the medical history of all the participants were collected by a 15-min face-to-face interview method. The self-report questionnaires, which consisted of only close-ended questions in a written form, were handed out to participants at our department.

Data collection

All study participants

The basic demographic questionnaire of all participants included information on their gender, age and educational level (low, ≤ 5 years; medium, 6–8 years; high, ≥ 8 years). Natural hair color at a

young age, eye color and self-estimated skin type (type I “always burns, never tans” to type IV “rarely burns, always tans” according to Fitzpatrick’s classification of sensitivity to sun exposure) among the phenotypic traits were questioned. Among the acquired sun-related risk factors, the histories of sun exposure due to an occupation and/or an outdoor leisure activity for more than 2 h per day, between 10.00 a.m. and 4.00 p.m., in the months of May to September, lasting for ten years or more (in certain individuals, e.g. farmers, gardeners, foresters, construction workers, sailors, fishermen, policemen, sports teachers)^{12,13} and ≥ 1 episode of severe painful sunburn (which is defined by the presence of blisters or pain for at least two days) were recorded. Furthermore, the personal and family histories of skin and non-skin cancers were evaluated.

All participants also completed a self-report questionnaire including the sun habits/sun protection behaviors developed in line with the literature.¹⁴ This questionnaire included a set of eight questions on exposure to UV radiation, with response alternatives presented on a five-point Likert-type scale. A mean total UV exposure score (ranging from 8 to 40) was calculated. A low score represented a low level of sun exposure, and a high score represented a high level of sun exposure (Supplementary Fig. 1).

In all participants, Glogau photoaging grades (type I “no wrinkles” to type IV “only wrinkles”) were determined by a dermatological examination. They also underwent an FBSE by experienced dermatologists focusing on the presence of NMSCs. Physicians performing the FBSE were blinded to the previous skin cancer history of the participants. During the FBSE, a magnifying glass and fluorescent light were used to examine all areas of skin except for those covered by the underwear. Any lesions suspicious of NMSCs were confirmed histopathologically.

AK patients

The duration, total number, clinical distribution, and the severity degree (grade I/mild: flat, pink macule without signs of hyperkeratosis and erythema, slight palpability, and AK felt better than seen; grade II/moderate: a large number (≥ 5) of visible, small, pink to reddish papules with moderate thickness or a small number (< 5) of thick, rough scaly erythematous plaques; grade III/severe: a large number (≥ 5) of obvious, very thick and hyperkeratotic lesions) of AK lesions were determined in patients. Thereafter, as shown in Supplementary Table 1, the patients were asked to fill out another self-report questionnaire including three questions related to perceived seriousness of AK, the history of previous SCE, and AK knowledge (from sources including television, magazines, newspapers, posters/leaflets in public places, pharmacies, workplace, schools, the internet, family/friends and healthcare professionals such as practitioners, dermatologists and/or surgeons, etc.) similarly to the literature.¹⁰

Statistical analysis

The statistical analyses were performed with the SPSS/PC software (Version 23.0 for Windows; SPSS Inc., Chicago, Ill). The compliance of the variables with normal distribution was examined with visual (histogram and probability plots) and analytical methods (the Kolmogorov–Smirnov/Shapiro–Wilk tests). Descriptive analyses were presented with the mean and standard deviation for continuous variables and with percentage distribution for categorical variables. The two sample Student’s *t*-test was used to compare the mean values of normally distributed quantitative variables as the two samples were obtained independently. The Mann–Whitney *U* test was used if the variables were not normally distributed. Qualitative variables were analyzed with the chi-squared test and Fisher’s exact test. $P < 0.05$ was considered significant in all analyses.

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