

RESEARCH ARTICLE

Melanoma in Iran: a Retrospective 10-Year Study

Samira Ferdosi¹, Mojtaba Saffari^{1,2}, Sharareh Eskandarieh^{3,4}, Raziye Alishahi¹, Mahsa Ghaffari Moghaddam¹, Alireza Ghanadan^{5*}, Reza Shirkoohi^{1*}

Abstract

Background: Melanoma, the most life-threatening type of skin cancer, is a malignant tumor initiating in melanocytes that rapidly metastasizes and causes death. **Materials and Methods:** In this retrospective study, samples were selected from patients' information files in our Cancer Institute in Tehran with a designed checklist. A total of 322 files were found from 2003 until 2012. Then the raw data were transferred to Statistical Package for Social Sciences (SPSS) software version 16 and additional analysis was performed by Students t-test. The important variables were considered according to the available information from history of pathology including age, gender, occupation, stage and location of tumor. **Results:** Our data showed that incidence of melanoma has been different in the studied 10-year period according to age. Also, incidence of melanoma was higher in men than women. It was more common in lower limbs. More commonly housewives among women and farmers among men were affected by melanoma. **Conclusions:** Taken together the descriptive data clarified general aspects of this disease for further screening and interventions.

Keywords: Melanoma - risk factors - Iran

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Introduction

Skin cancer is currently the third most popular individual malignancy. Its incidence rate is increasing globally due to living style and other conditions, for example environmental and behavioral alterations. As a type of skin cancer, melanoma is defined as a malignant tumor that commences in the melanocytes. It is the most hazardous kind of skin cancers and has resulted in many deaths (Garbe et al., 2008; Lobos et al., 2014). Up to one third of patients are in the stage IV of the disease with further metastases to the brain (Liebner et al., 2014). Total survival of patients in such stages will be 4-6 months (Lyle and Long, 2014).

The incidence of melanoma is increasing with age. It is more common in the eighth decade of life. However, the occurrence in people under 30 years old is not uncommon, which makes it a common cancer among the young people (Bishop et al., 2007). Generally, melanoma has been observed in men more than women. Nevertheless, it varies by age (increase of melanoma occurrence before 40 years old in women and after 40 in men) (Erdei and Torres, 2010; Roh et al., 2015).

Skin cancer has a wide range of risk factors. For instance in melanoma, a personal or family history of melanoma and large moles (more than 50) are crucial risk factors. Environmental factors such as sunlight

have shown to be important in all kinds of skin cancers (Azzarello et al., 2006; Bergman and Gruis, 2010; Li et al., 2014). Exposure to ultraviolet rays without protection can lead to melanoma (Saridi et al., 2014). Protection of skin from ultraviolet exposure is very important for melanoma prevention especially for people who work outside and are exposed for a long time (Houghton and Polsky, 2002). Melanoma has been generally found in any area of the skin, although it is more likely to initiate in specified regions. For instance, the most common area in men and women is the trunk (back and chest) and legs, respectively (MacKie et al., 2002; Cho et al., 2005).

Melanoma often initiates as a small mole in the body. Then it increases in size and its color might change (Swerdlow et al., 1986). The stage of melanoma is very crucial because of its management and prognosis (Tsaot et al., 2004). This study described a retrospective analysis of melanoma patients who had referred to our center in Tehran in order to achieve comprehensive information about the condition of melanoma during a 10-year period in Iran.

Materials and Methods

In this is retrospective study, all profiles of melanomapatients who had referred to the Cancer Institute our center in Tehran from 2003 to 2012 were

¹Group of Genetics, Cancer Research Center, Cancer Institute of Iran, ²Department of Genetics, Faculty of Medicine, ³Department of Dermatopathology, Razi Hospital, ⁴Brain and Spinal Cord Injury Research Center, ⁵MS Research Center, Neuroscience Institute, Tehran University of Medical Sciences (TUMS), Tehran, Iran *For Correspondence: rshirkoohi@tums.ac.ir; ghannadan@sina.tums.ac.ir

gathered. Thus, 322 profiles were collected. A checklist was prepared based on demographic information, risk factors, pathology, clinical stage, regional involvement and was filled with the information of the patients using Excel software (Microsoft 2013, USA). Data entry was rechecked by two different persons individually. Then raw data were transferred to statistical package for social sciences (SPSS) software version 16. The statistical analysis was performed by student t-test.

Results

Melanoma was slightly prominent among men. Among the 322 rechecked profiles, 163 (50.63%) belonged to men and 159 (49.37%) belonged to women. (Figure 1). The data showed that the rate of melanoma in men and women is different for each year. The highest rate of melanoma was seen in year 2007 in both sexes (the number of women was a little more than men). The lowest rate was seen in

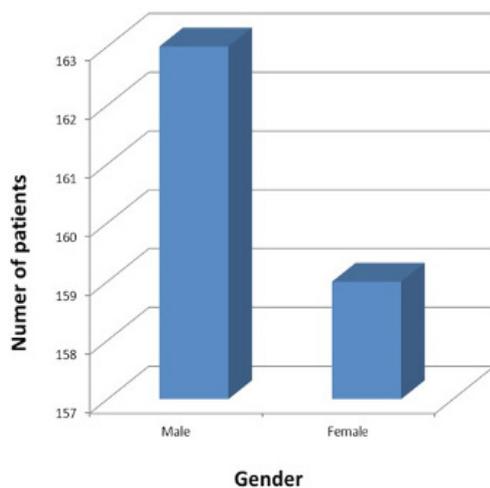


Figure 1. The Total Number of Men and Women in the Studied 10 Years (2003-2012)

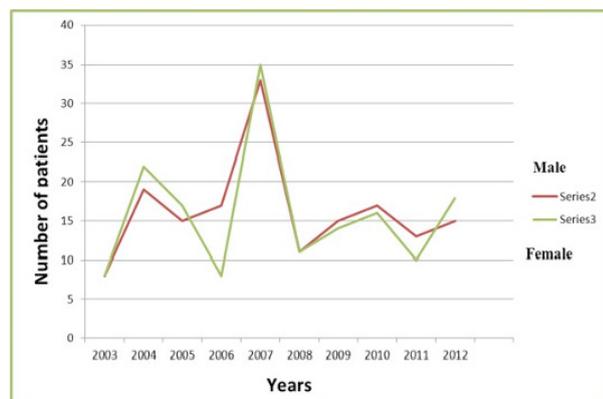


Figure 2. Numbers of Men and Women with Melanomas in Each Year (2003-2012)

year 2003 for men and in years 2003 and 2006 for women.

Melanoma had a relationship with age. The probability of melanoma in both sexes according to four age groups, i.e. from birth to 49 years old, 50 to 59 years old, 60 to 69 years old and from 70 years old and older, in Iran are shown in Table 1. (Figure 3) The number of patients varied in different age groups each year. (Figure 4) The highest number of patients in all age groups was seen in 2007 (the number of patients in from birth to 49 years old and 70 years old and older age groups was the same). The least number of patients was seen in from birth to 49 years old, 50 to 59 years old, 60 to 69 years old and 70 years old and older in years 2008, 2005, 2008 and 2006, respectively.

Comparing data of 2003 with 2012 has shown that the number of patients had increased specially in the 70 years old and older age group. In addition, after 2007 the

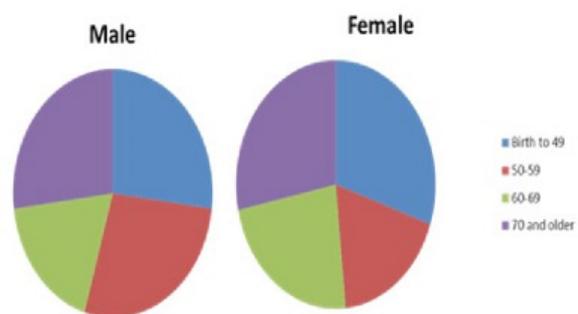


Figure 3. Rates of Melanoma in Both Sexes Based on Age Group

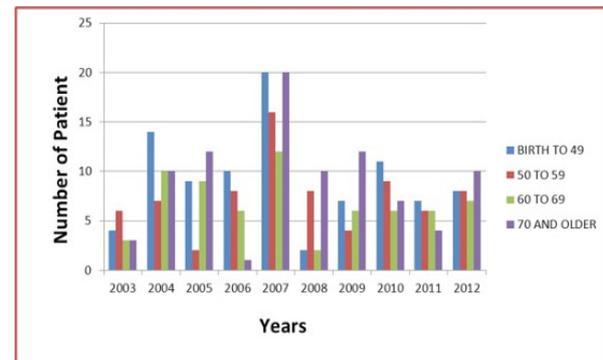


Figure 4. Number of Patients with Melanomas in Different Age Groups (2003-2012)

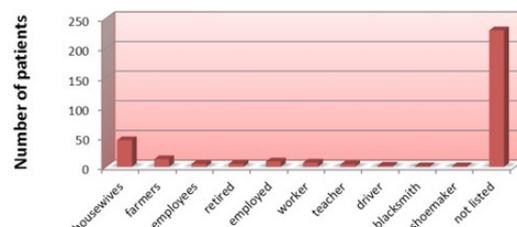


Figure 5. Studied Patients' Occupations

Table 1. Probability of melanoma in both sexes basic of age in this study

Gender	Birth to 49 years old	50 to 59 years old	60 to 69 years old	70 years old and older
Male	26.9% (44 in 163)	27.6% (45 in 163)	18.4% (30 in 163)	26.9% (44 in 163)
Female	30.1%(48 in 159)	18.2% (29 in 159)	23.2% (37 in 159)	28.3% (45 in 159)

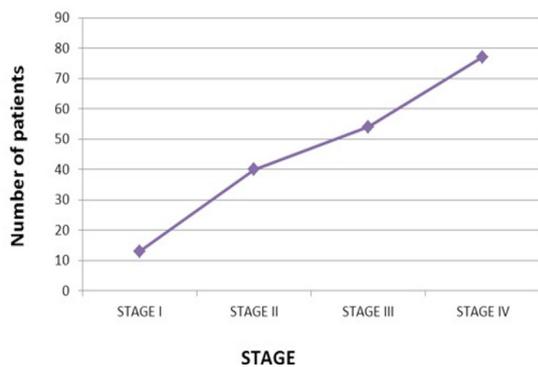


Figure 6. Rates of Melanomas in Different Stages (I-IV)

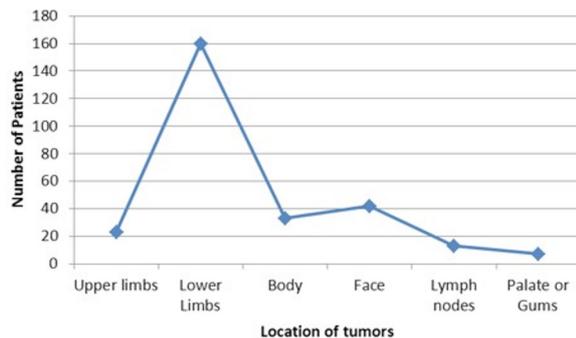


Figure 7. Frequency of Tumor Localization

number of patients was different in all age groups. For example, in 2008 and 2009 incidence of melanoma had increased in 70 years old and older age group, but in 2010 and 2011 this rate had increased in from birth to 49 years old age group. Again in 2012 this rate had increased in 70 years old and older age group. In 2003 the highest occurrence of melanoma was seen in 50 to 59 years old age group, in 2004 and 2006 in from birth to 49 years old age group, and in 2005 in 70 years old and older age group. Consequently, the rate of melanoma decreased among individuals after 2007 and in each year melanoma had occurred in different age groups.

Melanoma was more common in housewives. Regarding jobs, there were 45 cases of housewives (48.91%), 13 farmers (14.13%), five employees (5.43%), five retired (5.43%), nine employed (9.78%), seven workers (7.60%), four teachers (4.34%), two drivers (2.17%), one blacksmith (1.08%), and one shoemaker (1.08%). A number of 230 profiles (71.42%) had not recorded information about the patient's job. All housewives were women and did not work outside the home and all infected farmers were men. (Table 2)

Approximately, 184 patients from the total of 322 cases had complete information about the clinical stage of their illness (57.14%). Stage IV of melanoma was seen more in lower limb. (Figure 6)

Melanoma was more common in lower limbs. Location of tumor was determined only in 278 (86.33%) patients. Melanoma in lower limbs was seen in housewives and farmers. (Table 3) The most common areas for incidence of melanoma in lower limbs were in the heel of foot (48 patients, 17.26%) and sole of foot (38 patients, 13.66%), respectively. Also, the less common area for melanoma

has been seen in palate or gums. (Figure 7)

Discussion

Melanoma survival is different in both genders and women usually have longer survival than men (Joose et al., 2011). High incidence of melanoma has been reported in United State, Scandinavia, Australia and New Zealand and it has been recorded as the third cause of cancer. The lowest incidence is related to south-central Asia (Gajda and Kaminska, 2014). Results have shown that there is difference in the incidence rate among men and women. The incidence of melanoma is moderately higher in men than women.

In 2012, 14,738 new cases of melanoma were reported in Australia and New Zealand. Among them, 8499 (57.66%) were men and 6239 (42.33%) were women. In Scandinavia (Sweden, Norway, Finland and Denmark), the highest rate of melanoma was recorded in Sweden (2911 new cases including 1456 (50.01%) men and 1455 (49.98%) women). A number of 4094 cases of melanoma were reported the same year in south-central Asia (2294 (56.03%) men and 1800 (43.96%) women) (Ferlay J, 2012). According to the American Cancer Society, 76,690 new cases of melanoma were diagnosed in United State in 2013 (45,060 (5%) men and 31,630 (4%) women) (Siegel et al., 2013). In 2014 this number was 76,100 in United State (43,890 (5%) men and 32,210 (4%) women) (Azoury and Lange, 2014).

According to an epidemiological study in Minnesota the incidence of melanoma is rapidly increasing among the young generation, especially women born between 1970 and 2007 (eight and four times increase in young women and men, respectively) (Reed et al., 2012). According to our results the incidence of melanoma was higher in men than women. This is in line with the results from United Stated, Australia and Scandinavia. Because of limitation in sample collection, it is difficult to compare our study with others. A national survey is needed to make a comparison of the incidence of melanoma regarding gender.

According to the American Cancer Society, the average age of diagnosis in melanoma for men and women is 63 and 56 years old, respectively (Siegel et al., 2012). There is a relationship between gender and age in incidence of melanoma. The incidence rate of melanoma in United Stated was categorized into four age groups: a) from birth to 49 years old: 0.4 in men and 0.5 in women, b) 50 to 59 years old: 0.4 in men and 0.3 in women, c) 60 to 69 years old: 0.8 in men and 0.4 in women and d) 70 years old and older: 2.1 in men and 0.9 in women. Of course, women were also affected before the age of 45 years old, while men older than 60 years old were also affected (2014).

Additionally, according to a study in Scotland from 1979-2003, the incidence of melanoma had increased in both sexes and all age groups, but the highest rate of melanoma was seen at the age of 60 years old and older in both genders (MacKie et al., 2007). The molecular mechanisms can be associated with age of incidence. For example, data has shown that an individual with BRAF mutation is affected in a younger age group (Bauer et al.,

2011; Long et al., 2011). Nevertheless, according to our data the highest rate of melanoma was in 50 to 59 years old age group for men (27.6%) and from birth to 49 years old age group for women (30.1%) (Table 1, Figure 3).

The relationship between occupation and rate of melanoma was observed in several studies. Some occupations have high risk of incidence. For example, pilots and cabin crew have approximately twice the incidence of melanoma compared to general population (Sanlorenzo et al., 2015a; Sanlorenzo et al., 2015b). In the Nordic countries, airline crews especially pilots had a higher than expected rate of melanoma because of over exposure to sun light (natural ultraviolet radiation) (Pukkala et al., 2002). Also, artificial ultraviolet radiation source can increase the risk of melanoma (Swerdlow et al., 1988).

Our data showed that the highest rate of melanoma is in housewives and farmers. The incidence of melanoma is higher among housewives. Although different possible factors such as genetic predisposition and environment still remain unknown, it is more likely that because of hormonal alteration during their different life periods (such as pregnancy) women have several stimulants for melanin excess which may increase the incidence of melanoma in early stages of pregnancy (Karagas et al., 2006). Also, individuals such as ranchers, farmers, and construction workers who are exposed to sunlight for long hours and those who work with different chemicals have a higher risk factor (Malak et al., 2011).

Clinical staging is critical for treatment and survival. According to a study in Turkey on 98 patients, 23 were in stage I, 36 in stage II, 22 in stage III and 17 in stage IV (Uysal-Sonmez et al., 2013). In another study, from patients with melanoma who registered in surveillance, epidemiology, and end results (SEER) and implemented surgery (that is primary treatment), 31% were in stage I, 46% in stage II, 53% in stage III and 9% in stage IV (Siegel et al., 2012).

The majority of patients with melanoma in our study were diagnosed at stage IV (Figure 6). Moreover, the number of patients increased with stage (13 in stage I, 40 in stage II, 54 in stage III and 77 in stage IV). Most melanoma patients were in the final stage (IV). It is critical for high risk people to refer to clinics while they are in lower stages of the disease.

The involved area of body was also related age and sex. Some organs of the body have a higher risk for melanoma. A study in British Columbia in 1991-1992 showed that amongst 1033 men younger than 50 years old with melanoma, the disease forms most often in back and upper arm, and as for men older than 50 years old it occurs in ear, face, neck and back. In women younger than 50 years old it is limited to the back and in women older than 50 years old it occurs more often in face, upper arm and leg (Elwood and Gallagher, 1998). Between 1987-1993, a study on residents of mainland eastern Australia reported that over 10,000 individuals were diagnosed with melanoma on the upper and lower limbs (Green et al., 1996). In another study in Denmark in 1978-1982, the highest rate of melanoma in men was in back, followed by face, scalp, neck and chest. In women the highest rate

of melanoma was seen in the leg, followed by face, scalp, neck and back (Osterlind et al., 1988). A case-control study in the UK and Australia has reported melanoma more commonly on palms and soles in individuals exposed to pesticides (MacKie et al., 2009). Our data has shown that in both genders, younger and older than 50 years old, melanoma is most often seen in lower limbs in different body areas (heel and sole of foot) although the exact cause(s) are unknown. Some possibilities may be pesticides and lifestyle.

In conclusion, This study was a 10-year retrospective description of melanoma condition in patients who had referred to a center in Tehran. The results can help to design a screening or prevention plan. Different screening programs can be developed for to find more risk factors in future.

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References

- 2014. Cancer Facts. & Figures 2014 [Online]. American Cancer Society. Available: www.cancer.org.
- Azoury SC, Lange JR (2014). Epidemiology, risk factors, prevention, and early detection of melanoma. *Surg Clin North Am*, **94**, 945-62.
- Azzarello LM, Dessureault S, Jacobsen PB (2006). Sunprotective behavior among individuals with a family history of melanoma. *Cancer Epidemiol Biomarkers Prev*, **15**, 142-5.
- Bauer J, Buttner P, Murali R, et al (2011). BRAF mutations in cutaneous melanoma are independently associated with age, anatomic site of the primary tumor, and the degree of solar elastosis at the primary tumor site. *Pigment Cell Melanoma Res*, **24**, 345-51.
- Bergman W, Gruis NA (2010). Management of melanoma families. *Cancers (Basel)*, **2**, 549-66.
- Bishop JN, Harland M, Randerson-Moor J, et al (2007). Management of familial melanoma. *Lancet Oncol*, **8**, 46-54.
- Cho E, Rosner BA, Colditz GA (2005). Risk factors for melanoma by body site. *Cancer Epidemiol Biomarkers Prev*, **14**, 1241-4.
- Elwood JM, Gallagher RP (1998). Body site distribution of cutaneous malignant melanoma in relationship to patterns of sun exposure. *Int J Cancer*, **78**, 276-80.
- Erdei E, Torres SM (2010). A new understanding in the epidemiology of melanoma. *Expert Rev Anticancer Ther*, **10**, 1811-23.
- Ferlay J SI, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray, F. 2012. Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Online]. Lyon, France: International Agency for Research on Cancer; 2013.
- Gajda M, Kaminska-Winciorek G (2014). Do not let to be late: overview of reasons for melanoma delayed diagnosis. *Asian Pac J Cancer Prev*, **15**, 3873-7.
- Garbe C, Terheyden P, Keilholz U, et al (2008). Treatment of melanoma. *Dtsch Arztebl Int*, **105**, 845-51.
- Green A, McCredie M, Giles G, et al (1996). Occurrence of

- melanomas on the upper and lower limbs in eastern Australia. *Melanoma Res*, **6**, 387-94.
- Houghton AN, Polsky D (2002). Focus on melanoma. *Cancer Cell*, **2**, 275-8.
- Joose A, de Vries E, Eckel R, et al (2011). Gender differences in melanoma survival: female patients have a decreased risk of metastasis. *J Invest Dermatol*, **131**, 719-26.
- Karagas MR, Zens MS, Stukel TA, et al (2006). Pregnancy history and incidence of melanoma in women: a pooled analysis. *Cancer Causes Control*, **17**, 11-9.
- Li WQ, Han J, Widlund HR, et al (2014). CXCR4 pathway associated with family history of melanoma. *Cancer Causes Control*, **25**, 125-32.
- Liebner DA, Walston SA, Cavaliere R, et al (2014). Radiation necrosis mimicking rapid intracranial progression of melanoma metastasis in two patients treated with vemurafenib. *Melanoma Res*, **24**, 172-6.
- Lobos-Gonzalez L, Aguilar-Guzman L, Fernandez JG, et al (2014). Caveolin-1 is a risk factor for postsurgery metastasis in preclinical melanoma models. *Melanoma Res*, **24**, 108-19.
- Long GV, Menzies AM, Nagrial AM, et al (2011). Prognostic and clinicopathologic associations of oncogenic BRAF in metastatic melanoma. *J Clin Oncol*, **29**, 1239-46.
- Lyle M, Long GV (2014). The role of systemic therapies in the management of melanoma brain metastases. *Curr Opin Oncol*, **26**, 222-9.
- MacKie RM, Bray C, Vestey J, et al (2007). Melanoma incidence and mortality in Scotland 1979-2003. *Br J Cancer*, **96**, 1772-7.
- MacKie RM, Bray CA, Hole DJ, et al (2002). Incidence of and survival from malignant melanoma in Scotland: an epidemiological study. *Lancet*, **360**, 587-91.
- MacKie RM, Hauschild A, Eggermont AM (2009). Epidemiology of invasive cutaneous melanoma. *Ann Oncol*, **20**, 1-7.
- Malak AT, Yildirim P, Yildiz Z, et al (2011). Effects of training about skin cancer on farmers' knowledge level and attitudes. *Asian Pac J Cancer Prev*, **12**, 117-20.
- Osterlind A, Hou-Jensen K, Moller Jensen O (1988). Incidence of cutaneous malignant melanoma in Denmark 1978-1982. Anatomic site distribution, histologic types, and comparison with non-melanoma skin cancer. *Br J Cancer*, **58**, 385-91.
- Pukkala E, Aspholm R, Auvinen A, et al (2002). Incidence of cancer among Nordic airline pilots over five decades: occupational cohort study. *BMJ*, **325**, 567.
- Reed KB, Brewer JD, Lohse CM, et al (2012). Increasing incidence of melanoma among young adults: an epidemiological study in Olmsted County, Minnesota. *Mayo Clin Proc*, **87**, 328-34.
- Roh MR, Eliades P, Gupta S, et al (2015). Cutaneous Melanoma in Women. *Int J Womens Dermatol*, **1**, 21-5.
- Sanlorenzo M, Vujic I, Posch C, et al (2015a). The Risk of Melanoma in Pilots and Cabin Crew: UV Measurements in Flying Airplanes. *JAMA Dermatol*, **151**, 450-2.
- Sanlorenzo M, Wehner MR, Linos E, et al (2015b). The risk of melanoma in airline pilots and cabin crew: a meta-analysis. *JAMA Dermatol*, **151**, 51-8.
- Saridi MI, Rekleiti MD, Toska AG, et al (2014). Assessing a sun protection program aimed at Greek elementary school students for malign melanoma prevention. *Asian Pac J Cancer Prev*, **15**, 5009-18.
- Siegel R, DeSantis C, Virgo K, et al (2012). Cancer treatment and survivorship statistics, 2012. *CA Cancer J Clin*, **62**, 220-41.
- Siegel R, Naishadham D, Jemal A (2013). Cancer statistics, 2013. *CA Cancer J Clin*, **63**, 11-30.
- Swerdlow AJ, English J, MacKie RM, et al (1986). Benign melanocytic naevi as a risk factor for malignant melanoma. *Br Med J (Clin Res Ed)*, **292**, 1555-9.
- Swerdlow AJ, English JS, MacKie RM, et al (1988). Fluorescent lights, ultraviolet lamps, and risk of cutaneous melanoma. *BMJ*, **297**, 647-50.
- Tsao H, Atkins MB, Sober AJ (2004). Management of cutaneous melanoma. *N Engl J Med*, **351**, 998-1012.
- Uysal-Sonmez O, Tanriverdi O, Esbah O, et al (2013). Multicenter evaluation of patients with cutaneous malignant melanoma in Turkey: MELAS study. *Asian Pac J Cancer Prev*, **14**, 533-7.