



Melanoma in Iranian Childhood and Adolescence: An Analysis of 14 Patients

Azadeh Rakhshan ^{1,2}, Afshin Moradi ¹ and Elham Masoudi ^{1,2,*}

¹Cancer Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

²Department of Pathology, Shohada-e Tajrish Hospital, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

*Corresponding author: Cancer Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: e1.ma212@yahoo.com

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Abstract

Background: Skin cancer is the most common cancer in Iran. Given the importance of early diagnosis in treating early tumors, knowledge of the demographic and pathological findings of the disease is helpful.

Objectives: The aim of present study was to investigate the incidence, trend and risk factors of melanoma in Iranian childhood and adolescents.

Methods: The present retrospective study was performed between 2005 and 2014 on registered data in the National Cancer Registry System, Iran. The age group studied was patients 18 years or younger. Data included demographic status, risk factors, clinical and histopathological characteristics.

Results: The results showed that 8 (57.1%) of 14 patients were males. The mean age of the study population was 8.71 ± 6.02 years (range, 1 - 15 years). Ten (71.4%) patients were of Fars ethnic groups. In terms of tumor invasiveness, 13 (92.9%) patients were invasive and one (7.1%) patient was in situ. The growth phase of melanoma was vertical in 13 (92.9%) patients and radial phase in one (7.1%) patient. In terms of lymph node metastasis, it was observed in only one patient. Surgical treatment was performed on all patients. Melanoma histology was nodular in 3 patients and unspecified or unregistered in the rest. The most area of the tumor was in the head/neck and lower limbs.

Conclusions: According to the results, regardless of the differences in the specific coverage of the Iranian people, the distribution and statistical characteristics of malignant melanoma in Iran are almost similar to other countries in the world. Further studies are recommended to confirm the findings of the present study.

Keywords: Melanoma, Childhood, Adolescence, Iran, Cancer

1. Background

Cancer disease is the second leading cause of death in the world (1). According to the WHO, the death rate from cancer in Middle Eastern countries is estimated to increase by 80-100 percent in the next 15 years (2). Skin cancer is the most common cancer in the world. It constitutes 5.2 percent of all cancers, in Iran (3, 4). Skin cancer is classified into two groups: melanoma and non-melanoma (5). Melanoma is the deadliest form of skin cancer (6). Studies have shown that 65 to 90 percent of melanoma is due to sunlight and ultraviolet light, and DNA damage plays a major role in developing malignant melanoma (7). As approaches the equator, the incidence of skin cancer increases in a linear fashion, so that with every 10 degrees of latitude, its incidence doubles (8). The incidence of

melanoma clearly increases with age, so that at the age of 1 - 4 years, it reaches 1.1 people per million and at the age of 15 - 19 years, it reaches 10.4 people per million (9). Despite the increase in the number of new cases of melanoma (10), the resulting mortality rate seems to be declining (11). The main reason for this is attributed to the early detection of new cases, especially using tools such as dermoscopes, as well as more effective treatment methods (12). Studies have shown that the incidence of melanoma is slightly higher in girls and boys older than 4 years have a higher incidence of melanoma in the lower extremities, while girls older than 10 years have a higher incidence of cervical melanoma (13, 14). Also, the type of melanoma and the site of involvement appear to be different in different ethnic groups. For example, different types of acral lentiginous melanoma have been reported to be more common among Asians (15),

and the same is true of studies in Iran (16). The important point is the timely diagnosis of the disease and its correct treatment that increasing the patient's survival (17). The risk factors for melanoma in children and adolescents are less known (11). Melanoma in children older than 10 years is similar to adults, while under 10 years it seems to have a different etiology (18). The incidence of melanoma in an Australian study showed an increase for children under 14 between 1983 and 1996, followed by a significant decrease in the incidence, which could be due to sun protection training (10). Studies in Iran, based on histopathological criteria and demographic profiles including age, sex, and occupation of patients with melanoma have shown that the incidence and causes of melanoma have varied (19, 20).

2. Objectives

According to different factors causing the disease and the variability of symptoms according to similar studies, the aim of the present study was to investigate the incidence and risk factors of melanoma in Iranian childhood and adolescents for early diagnosis and prevention.

3. Methods

3.1. Ethical Considerations

All patients' information were collected in accordance with the applicable principles of research ethics committees of Shahid Beheshti University of Medical Sciences with the ethical code of IR.SBMU.MSP.REC.1398.281.

3.2. Study Population

The present retrospective study was performed on the information of patients registered in the National Cancer Registry System (NCRS), in Iran. The period of the studied cases was from 2005 to 2014. The criterion for selecting patients was the histopathologic diagnosis corresponding to melanoma and age under 18 years. Information was collected in two ways. First, there was recorded information including age, sex, tumor location, type of tumor invasiveness, melanoma growth phase, treatment method, etc. Second, the information requested over the phone, such as eye color, hair color, skin color, ethnic groups, benign moles, history of sunburn, use of UV solarium, xeroderma pigmentosum disease, history of immunodeficiency, and genetic disorders. Patients over 18 years of age, non-skin melanoma, and non-melanoma skin cancer were excluded from the study. Furthermore, the information received from the NCRS was not fully detailed and the pathology report was available only for 5 cases.

3.3. Statistical Analysis

Results were presented as Means \pm SD. All statistical analyses were performed using SPSS software, version 18.

4. Results

In the present study, 16 patients were included in the study that 2 of whom were excluded due to the uncertain primary location of tumor.

The results showed that of 14 patients, 8 (57.1%) patients were males. The mean age of the study population was 8.71 ± 6.02 years. The minimum and maximum ages were 1 and 15 years, respectively. Four patients had a congenital mole at the melanoma site and the rest had no mole. Also, one person had dysplastic mole, 4 people did not have dysplastic mole and the rest were not identified or registered. Details are given in Table 1. These results showed that there were no benign moles, history of sunburn, use of UV solarium, xeroderma pigmentosum disease, history of immunodeficiency, and genetic disorders in these patients.

5. Discussion

Melanoma is one of the most dangerous types of skin cancer and is known as the deadliest form of skin cancer in adolescents and young adults (15 - 29 years) (6). The disease is caused by sunlight, UV, and other causes. Melanoma grows rapidly over weeks to months. Most malignant melanomas are caused by intense sun exposure in the white population (18). Many risk factors for melanoma have been identified, but these studies have been performed mainly on adults and limited studies have been performed on childhood and adolescence, especially in Iran (19). In this regard, in the present study, the risk factors for skin melanoma in childhood and adolescence in Iran were investigated. Given that the prevalence of melanoma in children and infants is rare, we had to use the National Cancer Registry in recent years to collect data.

The results of the present study showed a low prevalence of melanoma in the childhood and adolescence population in Iran so based on the data of the NCRS from 2005 - 2014, 14 patients were identified and included in the study. Of these, 57 percent were male and 43 percent were female, with a mean age of 8 years. These results were in line with the study conducted by Noorbala et al. (20). They documented that the prevalence of melanoma was lower in Iran than in other countries and the incidence was higher in males than females. Also, Ferdosi et al. reported that the incidence of melanoma was higher in males than females and 26-30 percent of all cases were under the

Table 1. Demographic and Clinical Characteristics of Study Subjects

Variables/Sample Type	No. (%)
Eye color	
Black	9 (64.3)
Brown	5 (35.7)
Hair color	
Black	10 (71.4)
Brown	4 (28.6)
Skin color	
White	9 (64.3)
Wheaten	3 (21.4)
Dark	2 (14.3)
Ethnic groups	
Fars	10 (71.4)
Fars-Arab	1 (7.1)
Turk	1 (7.1)
Lurs	1 (7.1)
Baloch	1 (7.1)
Tumor location	
Chest wall	1 (7.1)
head and neck	5 (35.7)
Genital	2 (14.2)
lower limb	5 (35.7)
upper limb	1 (7.1)
Tumor invasiveness	
Invasive	13 (92.9)
Insitu	1 (7.1)
Melanoma growth phase	
Radial	1 (7.1)
Vertical	13 (92.9)
Skin ulcers	
Yes	2 (14.2)
Unspecified or unregistered	12 (85.8)
Lymph node metastasis	
Yes	1 (7.1)
No	4 (28.4)
Unspecified or unregistered	9 (64.5)
Satellite nodules	
Yes	1 (7.1)
No	4 (28.4)
Unspecified or unregistered	9 (64.5)
Therapeutic method	
Surgery	13 (92.9)
Surgery and chemotherapy	1 (7.1)
Symptoms	
Tumor enlargement	9 (40.9)
Pain	5 (22.7)
Ulcer	3 (13.6)
Itching	3 (13.6)
Bleeding	2 (9.2)
Family history of cancer	
Yes	
Gastrointestinal	2 (14.2)
Liver	1 (7.1)
Larynx	1 (7.1)
No	10 (71.6)
Melanoma histologic subtype	
Nodular	3 (21.3)
Unspecified or unregistered	11 (78.7)

age of 49 years (19). The most important reasons for the low prevalence of melanoma in Iran are factors such as geographical area and sunlight, genetic factors, skin color, and type of clothing that can be effective in this field.

In the present study, factors such as benign moles, history of sunburn, use of UV solarium, xeroderma pigmentosum disease, history of immunodeficiency, and genetic disorders were investigated and no one was reported in patients. However, Nayman et al. reported that risk factors such as abnormal skin nodules, moles, skin burns from work-related accidents, sunburn, bright eye color, and light skin color can be involved in developing melanoma (21). It seems that not using the solarium at a young age and less exposure of children to the sun, has a significant impact on the low prevalence of melanoma in this group.

Currently, most symptoms included itching, ulcers, bleeding, enlargement, and sudden deformity. On the other hand, our results showed that the highest frequency of tumor sites was in the chest wall and lower limb. In this regard, Ferdosi et al. showed a high prevalence of tumors in the lower limb and the next most common areas were the heel and sole of the foot (19). Paradelo et al. reported that the disease is most common in the limbs and head/neck (22).

The majority of melanoma cases in this study were invasive. This factor indicates the dangerousness and rapid spread of the disease (6).

In 14 patients, only the pathological information of 5 patients was available, of which in terms of histopathological subtypes, all were nodular and the rest were unknown. However, Juhl et al. reported that 11.8, 14.9, and 73.2 percent of melanoma cases were nodular, lentigo, and superficial types, respectively (23). Also, Rahnema et al. reported that 20 percent of all melanoma cases were nodular, 16 percent in situ, and 36 percent in acral lentiginous (24). Accordingly, due to the uncertainty of the major histopathological status of patients in this study, it seems that a broader and more detailed study is needed to summarize the prevalence of different histopathological subtypes of melanoma. Among all patients, only one patient had a satellite nodule and 4 patients did not have a nodule and in the rest of the patients the satellite nodule status was unknown. Also, among the 5 patients from whom we had pathological information, only one of the patients had lymph node metastasis. In this regard, the results of previous studies indicated that lymph node metastasis is one of the most important risk factors for exacerbation of the disease in pediatric melanoma (18, 25). However, in this study, due to limited clinical information and patient classification, it was not possible to investigate the relationship between the presence of

these risk factors and the prognosis of the disease. The results showed that in 4 patients there was a congenital mole and in one person there was a dysplastic mole. In this regard, de Sa et al. reported that 22 percent of patients with melanoma have congenital moles and 25 percent have acquired moles (25). Based on the results of previous studies and as mentioned in previous sections, such moles are considered as a factor with a worse prognosis and its report is clinically important.

Also, the results of the present study showed that the highest incidence of the disease was in Fars ethnic group. According to the latest report on ethnicity statistics in Iran, more than 65% of Iran's population belongs to Fars ethnic group (26). Therefore, this finding could be justified in terms of population distribution by ethnicity in the country.

All patients had used surgical treatment, however, information was limited and detailed information on the type of surgery (limited or extensive surgery, etc.) was not available. In this regard, Noorbala et al. reported that using surgical treatment is more common in Iran than other treatments (20). Generally, the present study provides an overview of the prevalence of melanoma among children. Due to the low prevalence of melanoma in children in Iran and also due to the fact that present study was conducted in the first years of cancer registration in Iran with some missing data in the records, further studies are recommended to confirm the findings of the present study.

5.1. Conclusions

Melanoma has a low prevalence in Iranian childhood. It seems that lifestyle may play a role. Future studies are recommended for establishing the results. In addition, regardless of the differences in the specific coverage of the Iranian people, the distribution and statistical characteristics of malignant melanoma in Iran are almost similar to other countries in the world.

Footnotes

Authors' Contribution: Study concept and design: Rakhshan and Moradi; Acquisition of data: Moradi; Analysis and interpretation of data: Masoudi and Rakhshan; Drafting of the manuscript: Masoudi; Critical revision of the manuscript for important intellectual content: Rakhshan; Statistical analysis: Masoudi; Administrative, technical, and material support: Rakhshan and Masoudi; Study supervision: Rakhshan and Moradi.

Conflict of Interests: The authors have no conflicts of interest to declare.

Data Reproducibility: The data presented in this study are openly available in one of the repositories or will be available on request from the corresponding author by this journal representative at any time during submission or after publication. Otherwise, all consequences of possible withdrawal or future retraction will be with the corresponding author.

Ethical Approval: IR.SBMU.MSP.REC.1398.281.

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References

- Shojaie Tehrani H. [Epidemiology of acute noncontiguous and contiguous diseases]. Tehran, Iran: Samat; 2007. 153 p. Persian.
- Omar S, Alieldin NH, Khatib OM. Cancer magnitude, challenges and control in the Eastern Mediterranean region. *East Mediterr Health J.* 2007;**13**(6):1486-96. [PubMed ID: 18341198]. <https://doi.org/10.26719/2007.13.6.1486>.
- Azizi F, Hatami H, Janghorbani M]TEP. [Epidemiology and control of common diseases in Iran]. Tehran, Iran: Eshtiagh Publications; 2000. p. 602-16.
- Mirzaei M, Razi S, Ghoncheh M, Hafshejani AM, Salehiniya H. Skin cancer incidence rate and trend in 2004-2008 in Tehran province. *Dermatology & Cosmetic.* 2014;**5**(4).
- Cullen JK, Simmons JL, Parsons PG, Boyle GM. Topical treatments for skin cancer. *Adv Drug Deliv Rev.* 2020;**153**:54-64. [PubMed ID: 31705912]. <https://doi.org/10.1016/j.addr.2019.11.002>.
- Bergman PJ. Melanoma. *Clinical Small Animal Internal Medicine.* Wiley; 2020. p. 1347-52.
- Saraiya M, Glanz K, Briss PA, Nichols P, White C, Das D, et al. Interventions to prevent skin cancer by reducing exposure to ultraviolet radiation: a systematic review. *Am J Prev Med.* 2004;**27**(5):422-66. [PubMed ID: 15556744]. <https://doi.org/10.1016/j.amepre.2004.08.009>.
- Wakeford R. The cancer epidemiology of radiation. *Oncogene.* 2004;**23**(38):6404-28. [PubMed ID: 15322514]. <https://doi.org/10.1038/sj.onc.1207896>.
- Fattouh K, Ducroux E, Decullier E, Kanitakis J, Morelon E, Boissonnat P, et al. Increasing incidence of melanoma after solid organ transplantation: a retrospective epidemiological study. *Transpl Int.* 2017;**30**(11):1172-80. [PubMed ID: 28700114]. <https://doi.org/10.1111/tri.13011>.
- Armstrong BK, Gillespie JA, Leeder SR, Rubin GL, Russell LM. Challenges in health and health care for Australia. *Med J Aust.* 2007;**187**(9):485-9. [PubMed ID: 17979607]. <https://doi.org/10.5694/j.1326-5377.2007.tb01383.x>.
- Arozarena I, Wellbrock C. Phenotype plasticity as enabler of melanoma progression and therapy resistance. *Nat Rev Cancer.* 2019;**19**(7):377-91. [PubMed ID: 31209265]. <https://doi.org/10.1038/s41568-019-0154-4>.
- Shenenberger DW. Cutaneous malignant melanoma: a primary care perspective. *Am Fam Physician.* 2012;**85**(2):161-8. [PubMed ID: 22335216].
- Wong JR, Harris JK, Rodriguez-Galindo C, Johnson KJ. Incidence of childhood and adolescent melanoma in the United States: 1973-2009. *Pediatrics.* 2013;**131**(5):846-54. [PubMed ID: 23589817]. [PubMed Central ID: PMC3639457]. <https://doi.org/10.1542/peds.2012-2520>.
- Diepgen TL, Mahler V. The epidemiology of skin cancer. *Br J Dermatol.* 2002;**146** Suppl 61:1-6. [PubMed ID: 11966724]. <https://doi.org/10.1046/j.1365-2133.146.s61.2.x>.

15. Chang JW, Yeh KY, Wang CH, Yang TS, Chiang HF, Wei FC, et al. Malignant melanoma in Taiwan: a prognostic study of 181 cases. *Melanoma Res.* 2004;**14**(6):537-41. [PubMed ID: 15577327]. <https://doi.org/10.1097/00008390-200412000-00016>.
16. Yaghoobi R, Rafiei R, Savad Dar F, Latifi SM. [Malignant Melanoma in Khouzestan: Study of 62 cases]. *Iran J Dermatol.* 2002;**5**(3):7-14. Persian.
17. Gambichler T, Scholl L, Stucker M, Bechara FG, Hoffmann K, Altmeyer P, et al. Clinical characteristics and survival data of melanoma patients with nevus cell aggregates within sentinel lymph nodes. *Am J Clin Pathol.* 2013;**139**(5):566-73. [PubMed ID: 23596107]. <https://doi.org/10.1309/AJCPG83CMAVFBWLC>.
18. Carr S, Smith C, Wernberg J. Epidemiology and Risk Factors of Melanoma. *Surg Clin North Am.* 2020;**100**(1):1-12. [PubMed ID: 31753105]. <https://doi.org/10.1016/j.suc.2019.09.005>.
19. Ferdosi S, Saffari M, Eskandarieh S, Raziye R, Moghaddam MG, Ghanadan A, et al. Melanoma in Iran: a Retrospective 10-Year Study. *Asian Pac J Cancer Prev.* 2016;**17**(6):2751-5. [PubMed ID: 27356685].
20. Noorbala MT, Mohammadi S, Noorbala M. Cutaneous malignant melanoma in central Iran: a 20-year study. *Iran Red Crescent Med J.* 2013;**15**(8):690-4. [PubMed ID: 24578836]. [PubMed Central ID: PMC3918193]. <https://doi.org/10.5812/ircmj.5364>.
21. Nayman T, Bostan C, Logan P, Burnier MJ. Uveal Melanoma Risk Factors: A Systematic Review of Meta-Analyses. *Curr Eye Res.* 2017;**42**(8):1085-93. [PubMed ID: 28494168]. <https://doi.org/10.1080/02713683.2017.1297997>.
22. Paradelo S, Fonseca E, Pita-Fernandez S, Kantrow SM, Diwan AH, Herzog C, et al. Prognostic factors for melanoma in children and adolescents: a clinicopathologic, single-center study of 137 Patients. *Cancer.* 2010;**116**(18):4334-44. [PubMed ID: 20549825]. <https://doi.org/10.1002/cncr.25222>.
23. Juhl AL, Byers TE, Robinson WA, Morelli JG, Crane LA. The anatomic distribution of melanoma and relationships with childhood nevus distribution in Colorado. *Melanoma Res.* 2009;**19**(4):252-9. [PubMed ID: 19543126]. [PubMed Central ID: PMC2995701]. <https://doi.org/10.1097/CMR.0b013e32832e0b81>.
24. Rahnama Z, Meymandi SS, Nasiri N. Cutaneous melanoma in a desert climate zone: a retrospective study of 125 cases. *Int J Dermatol.* 2010;**49**(4):406-9. [PubMed ID: 20465695]. <https://doi.org/10.1111/j.1365-4632.2010.04290.x>.
25. de Sa BC, Rezze GG, Scramim AP, Landman G, Neves RI. Cutaneous melanoma in childhood and adolescence: retrospective study of 32 patients. *Melanoma Res.* 2004;**14**(6):487-92. [PubMed ID: 15577319]. <https://doi.org/10.1097/00008390-200412000-00008>.
26. Ekhtiyari M. [Race distribution in Iran]. *Ircat*; 2011. Persian. Available from: <http://ircat.blogfa.com/post/55>.