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PREVENTION AND DIAGNOSIS OF CUTANEOUS MELANOMA: A SYSTEMATIC REVIEW OF RISK FACTORS AND EFFECTIVE STRATEGIES

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ABSTRACT

Objective: The general objective of this study is to analyze the scientific production on cutaneous melanoma, identifying the main risk factors, prevention methods and diagnosis of this pathology. Methodology: This is a systematic review focused on understanding the essential aspects of cutaneous melanoma. The research was guided by the question: "What are the main risk factors for the development of cutaneous melanoma, as well as the methods used for prevention and diagnosis?" To find answers, searches were performed in the PubMed database using five descriptors combined with the Boolean term "AND". This resulted in 99 articles, of which 15 were selected for analysis. Results: Melanoma is an aggressive form of skin cancer, with exposure to ultraviolet (UV) radiation being the main risk factor. The association between outdoor activities, use of indoor tanning and unprotected exposure to UV radiation highlights the vulnerability of young people and fair-skinned people. Awareness campaigns, use of protective clothing and sunscreens are essential in prevention. Early screening, including technologies such as digital dermoscopy, is essential for the detection of malignant lesions. However, the diagnosis of melanoma still faces challenges due to its clinical and histopathological variability. Conclusion: Primary

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prevention and education about the risks of sun exposure are crucial to reduce the incidence of melanoma. Improving photoprotection strategies and regulating the use of tanning beds are necessary measures. In addition, public policies and educational interventions must be intensified to promote changes in sun protection behavior, resulting in a sustainable reduction in skin cancer cases.

Keywords: Cutaneous Melanoma. Risk Factors. Prevention. Diagnosis.

INTRODUCTION

Melanoma is a neoplasm of melanocytes, cells that produce melanin (pigment) in the basal layer of the epidermis. Melanocytes derive from the neural crest and therefore express various signaling molecules and factors that favor metastatic migration and spread after cancerous transformation. Despite representing only 1% of skin cancers, melanoma is responsible for more than 80% of skin cancer-related deaths (MARKS, 2000).

The global incidence rate of melanoma has increased significantly over the past 50 years. Melanoma is the most frequent type of cancer in the young adult population, and its prevalence is quite high among the elderly. The incidence of melanoma differs according to sex. Adolescent women and young adults have a higher rate compared to men. This may be related, in part, to the greater use of artificial tanning beds, in addition to the deliberate exposure to the sun by women, who tend to adopt risky behaviors in search of tanning, influenced by socially established aesthetic standards. In fact, at older ages, the incidence rate of melanoma in men is higher than in women, probably because men are less likely to examine their own skin or see a dermatologist for evaluation. The World Health Organization (WHO) has stated that there is sufficient evidence to classify exposure to ultraviolet radiation (such as the use of tanning beds and sun exposure) as carcinogenic to humans (RAIMONDI; SUPPA; GANDINI, 2020).

There are four main histological subtypes of melanoma: superficial extension melanoma (70%), nodular melanoma (15-30%), lentigo maligna, melanoma (4-10%), and acral lentiginous melanoma (<5%). In addition to the skin, melanomas can also arise in the ocular, upper respiratory, gastrointestinal, and genitourinary systems. Although it accounts for only 5% of all skin cancers, melanoma has the highest mortality rate if not detected early (ŠERMAN et al., 2022). Cutaneous melanoma (CM) is the most aggressive and lethal form of skin cancer, occurring when unrepaired damage to the DNA of skin cells results in mutations or genetic defects that cause these cells to multiply rapidly, forming malignant tumors. CM accounts for about 5% of all skin cancers, but is responsible for approximately three-quarters of all skin cancer deaths (RAIMONDI; SUPPA; GANDINI, 2020).

Globally, CM incidence rates vary by up to 100 times between different situations, depending on ethnicity, with the highest rates seen in New Zealand and Australia. For this reason, these countries have intensified primary prevention actions, such as education campaigns on melanoma and awareness of the risks of excessive exposure to the sun, which has contributed to a reduction in the incidence rate (RAIMONDI; SUPPA; GANDINI, 2020) ŠERMAN et al., 2022). In Europe and the US, the incidence is proportional, and the lowest rates are recorded in south-central Asia. In Europe, the highest incidence rates of

CM were observed in Sweden and Denmark, while the lowest rates were recorded in Greece. These differences are mainly attributed to exposure to ultraviolet radiation and genetically determined phenotypic characteristics. The age group with the highest number of CM diagnoses is between 40 and 60 years, and the mean age at diagnosis and death are, respectively, 57 and 67 years. Incidence rates begin to grow from the age of 40, which makes CM a tumor that usually affects young and middle-aged people, almost a decade before most solid tumors, such as breast cancer, colon cancer, prostate or prostate dissemination (RAIMONDI; SUPPA; GANDINI, 2020).

Sun exposure causes physical damage to the skin and also sunburn. These latter occurrences after intense exposure to the sun, resulting in an acute inflammatory response. Ultraviolet radiation is the main risk factor for malignant melanoma (MM) and non-melanoma skin cancer (NM-SCs). The incidence of both continues to increase globally. However, these cancers are among the most preventable. There are several photoprotection methods available, such as clothing with ultraviolet protection factors (UPF), specific clothing (gloves, hats) and the use of sunscreens. In addition, there are health promotion programs that carry out educational campaigns to encourage appropriate behaviors in relation to sun exposure (KLINIEC et al., 2023).

This systematic review article aims to compile and evaluate the existing scientific evidence on risk factors and the management of cutaneous melanoma. The intention is to provide a comprehensive and up-to-date view, which not only synthesizes current knowledge about the condition, but also identifies gaps in research and directs future investigations and clinical practices. By offering an in-depth analysis of the evidence, this work aims to serve as a resource for health professionals, researchers, and academics, helping to optimize preventive and diagnostic approaches to cutaneous melanoma.

METHODOLOGY

This is a systematic review that seeks to understand the main aspects of cutaneous melanoma, as well as to demonstrate the main risk factors related to the development of the condition and also the prevention methods, aiming to ensure a greater clinical elucidation of these pathologies. For the development of this research, a guiding question was elaborated through the PVO strategy (population, variable and objective): "What are the main risk factors for the development of cutaneous melanoma, as well as the methods used for the prevention and diagnosis of the condition?"

The searches were carried out through searches in the PubMed Central (PMC) databases. 5 descriptors were used in combination with the Boolean term "AND":

Melanoma, Family History of Melanoma, Risk Factors, Sun Exposure and Signs and Symptoms. The search strategy used in the PMC database was: Melanoma AND Family History of Melanoma; Melanoma AND Risk Factors AND Sun Exposure e Melanoma AND Signs and Symptoms. From this search, 99 articles were found, which were later submitted to the selection criteria. The inclusion criteria were: articles in English, Portuguese and Spanish; published in the period from 2019 to 2024 and that addressed the themes proposed for this research, in addition, review, observational and experimental studies, made available in full. The exclusion criteria were: duplicate articles, available in the form of abstracts, that did not directly address the proposal studied and that did not meet the other inclusion criteria.

After associating the descriptors used in the searched databases, a total of 99 articles were found. After applying the inclusion and exclusion criteria, 21 articles were selected from the PubMed database, and a total of 15 studies were used to compose the collection.

DISCUSSION

Melanoma is an aggressive skin cancer that develops from melanocytes, the cells that produce pigment in the skin. It remains the deadliest form of skin cancer. However, melanoma is potentially curable with early diagnosis and treatment. In the U.S., it is the 5th most common cancer and the deadliest form of skin cancer, accounting for about 80% of skin cancer-related deaths. Its incidence has continued to rise since the 1970s, with more than 1 million people living with melanoma. It also accounts for 1.7% of global cancers, with increasing incidence in developed countries. Although the 5-year relative survival rate has increased to 93.7%, survival for advanced-stage disease remains relatively low (29.8%) (NWAFOR et al., 2023).

Genetic risk factors include family history, light skin/hair/eye color, DNA repair defects, and several melanoma risk genes such as cyclin-dependent kinase inhibitor 2A (CDKN2A), CDK4, BRCA1-associated protein-1 (BAP1), telomere protection 1 (POT1), and telomerase reverse transcriptase (TERT). Mutations in these tumor suppressor genes confer high susceptibility to melanoma. In contrast, some genetic factors, especially when interacting with phenotypic and environmental risk factors, play a major role in melanoma susceptibility. For example, melanocortin receptor 1 (MC1R) R variants (D84E, R142H, R151C, I155T, R160W, D294H) are associated with the phenotype of fair skin and red hair color, which is prone to sunburn and has an increased risk of melanoma (YAMAUCHI et al., 2022).

The relative risk of melanoma, in fact, doubles in individuals with first-degree relatives with melanoma and increases with the number of family members affected. In addition, patients with familial melanoma often have an early onset of melanomas and develop multiple primary melanomas. Multiple primary melanomas tend to develop sporadically in 5% of those who have had a melanoma, compared to 19% in patients who have a family history of melanoma (ZOCCHI et al., 2021).

CDKN2A is by far the most commonly mutated gene that causes inherited melanoma. Germline mutations increase the risk of melanoma by 65 times. Mutations in the CDKN2A gene are rare in sporadic cases, but have been implicated in up to 30% of inherited melanomas (MARKS, 2000) (TOUSSI et al., 2020). This tumor syndrome was first described in the 1960s by Lynch and Krush as multiple mole syndrome and familial atypical melanoma (FAMMM) and by Clark and colleagues as BK5 mole syndrome or dysplastic nevus syndrome. Both groups described families with multiple clinically atypical nevi, melanomas, and, in a subset of patients, pancreatic cancer (TOUSSI et al., 2020).

The average age of melanoma diagnosis in patients with CDKN2A mutation is between 30 and 40 years, while that of the general population is around 50 years. Although the onset of melanoma at a young age is quite common in individuals carrying CDKN2A mutations, it cannot be considered a predictor of the presence of the mutation; less than 1% of individuals diagnosed with melanoma before the age of 40 are, in fact, positive for this mutation (ZOCCHI et al., 2021).

The screening and surveillance of patients with high-risk CDKN2A mutation remains an ever-evolving area of clinical research. For patients with cutaneous melanoma, a surveillance program including skin, scalp, oral mucosa, and genitals, an examination every three/six months (or annually based on the patient's risk factors) is recommended. In this context, a dermoscopic comparative approach seems to be particularly useful, and sequential digital dermoscopic imaging can help diagnose early melanomas (ZOCCHI et al., 2021).

One of the most common mutations is the BRAF gene, the inhibition of which has demonstrated a beneficial anti-tumor reaction against melanomas The BRAF gene is located on chromosome 7 (7q34) and encodes the BRAF protein that is involved in the activation of the mitogen-activated protein kinase (MAPK) pathway, leading to the regulation of cell growth, differentiation, proliferation, and apoptosis. BRAF has been identified as a commonly mutated gene in human tumors, mutations have been detected in nearly 50% of malignant melanomas (SAWADA; NAKAMURA, 2021).

UV radiations are one of the main extrinsic risk factors for all types of skin cancer and particularly affect areas most frequently exposed to the sun, such as the head and neck, contributing to almost 80% of reported cases. However, about a quarter of cases are reported in anatomical parts of the body that are not often directly exposed to the sun, and this highlights that discontinuous exposure to sunlight, whether intense or for a long period of time, also contributes to tumor formation (SAEED et al., 2024).

UVR can be separated into four ranges – UVA1 (340-400nm), UVA2 (320-340 nm), UVB (280-320 nm), and UVC (200-280 nm) – with the majority of UVR reaching the skin's surface falling into the previous three categories due to the filtering effects of atmospheric ozone. UVR exposure damages epidermal DNA through multiple mechanisms. Direct damage occurs when DNA itself acts as a photophore and absorbs energy from the incident UVR. DNA has a maximum absorption in the UVC region at approximately 260 nm, with substantial absorption in the UVB region and in the UVA regions as well. Because the minimum UVC reaches the Earth's surface, most of the direct DNA damage is attributed to radiation in the UVB spectrum. Although UVA is a less potent mutagen, natural sunlight contains 20-100 times more UVA, which leads to a higher dose compared to UVB. In addition, UVA is less filtered through car windows and protective clothing and penetrates deeper into the epidermis due to its longer wavelength. Increased penetration also contributes to dermal changes that result in photoaging of the skin (SUOZZI; TURBAN; GIRARDI, 2020).

A study conducted in Canada estimated the current attributable and future preventable burden of melanoma related to UVR exposure and UVR-modifiable risk behaviors. They estimated that 62.3% of melanomas in Canada were attributable to UVR exposure and that 29.7% were attributable to the combination of sunburn (7.4%), sunbathing (17.8%) and indoor tanning (7.0%). They also concluded that a 50% reduction in UVR-modifiable behavior could prevent about 11,980 cases of melanoma by 2042 (RAIMONDI; SUPPA; GANDINI, 2020).

Most outdoor physical activities increase exposure to UV radiation, which translates into an elevated risk of skin cancer. Special attention should be paid to certain disciplines, especially water sports, which are associated with even greater exposure. As presented above, water sports seem to be addressed more frequently in the available literature on the association between outdoor physical activity and skin cancer. Individuals who participate in water sports are exposed not only to UV radiation but also to the removal of sunscreens (KLINIEC et al., 2023).

Fair skin is defined by skin types I-IV according to Fitzpatrick, Per unit of skin area, the highest densities of melanoma occur in places with greater sun exposure, such as the face, head, and neck. The association between UV radiation and the development of melanocytic nevi is also well established. The increased frequency of sunny vacations is associated with a large increase in melanocytic nevi in children. A high number of melanocytic nevi is associated with an increased risk of developing melanoma (GARBE et al., 2024).

The International Agency for Research on Cancer (IARC) has classified indoor tanning as a group 1 carcinogen, placing it alongside cigarette smoke within the most potent group of carcinogens. A recent meta-analysis found that more than 10,000 cases of melanoma can be attributed to indoor tanning in the United States, Europe, and Australia. Although indoor tanning rates have declined in recent years, there were still an estimated 7.8 million women and 1.9 million men involved in indoor tanning in the United States in 2015. (SUOZZI; TURBAN; GIRARDI, 2020).

Growing evidence links tanning bed use to melanoma development, especially when tanning bed use began during adolescence. It is estimated by a meta-analysis that individuals who started using tanning beds before the age of 3 had a 15% increase in melanoma risk compared to individuals who had never used a tanning bed. The Australian Melanoma Family Study was conducted at various latitudes to determine associations between early-onset melanoma and tanning bed use. A total of 604 cases and 479 control groups were included in the experiment. The results indicated that women (24%) were more likely than men (8%) to use tanning beds. Tanning salons (83%), gyms (72%), private homes (60%), and beauty salons (55%) were the most common places for indoor tanning. A total of 18% of controls and 23% of case groups reported indoor tanning. The average age for the first use of indoor tanning was 22 years, the first reported was 14 years for cases and 16 years for controls. The average total use of tanning beds was the same regardless of the age of first use. Compared to control groups that never used indoor tanning, those who did were reported to be easy tanners, were women, and had lower lifetime exposure to environmental UV rays. Indoor tanning use was moderately correlated with higher socioeconomic status, lower total sun exposure in childhood, and higher amounts of lifetime sunburn that caused blisters. Outdoor leisure time, skin color, family history, and level of education were not associated with artificial tanning (RAYMOND-LEZMAN; RISKIN, 2023).

Participants who used tanning beds were 41% more likely to develop melanoma compared to those who did not. There were correlations between earlier first use of tanning beds and the development of melanoma. Using tanning beds more than 10 times had twice

the risk of melanoma compared to those who did not use tanning beds. In addition, using tanning beds more than 10 times led to a fourfold increase in melanoma diagnoses for participants aged 18 to 29 years than for individuals with melanoma diagnosed between 30 and 39 years. About 76% of melanomas for the 18-29 age group were associated with the use of tanning beds. Only 13% of melanomas in the 30-39 age group were associated with the use of tanning beds (RAYMOND-LEZMAN; RISKIN, 2023).

In addition to being a carcinogen, indoor tanning has been implicated as an addiction disorder. Some groups have suggested that indoor tanning is a type of substance-related disorder, adapting scales for alcohol dependence to study the phenomenon. Interventions to decrease tanning rates included restricting minors' access to indoor tanning, excise taxes on indoor tanning, and medical advice on the risks of UVR exposure (SUOZZI; TURBAN; GIRARDI, 2020).

Since the 1970s, many epidemiological studies have focused on the possible relationship between female endocrine traits and melanoma, but there has been considerable debate about the potential impact of hormones on melanoma risk. Some studies suggest that a woman's reproductive history may affect her risk of melanoma, leading to speculation that the development of female melanoma may also be influenced by hormonal changes during pregnancy. One study also found that women who had their first child after age 30 had an increased risk of melanoma after adjusting for oral contraceptive use, while another study found that menarche before age 14 also significantly increased the risk of melanoma. Two studies have identified an association between early delivery and a reduced risk of melanoma (SUN et al., 2020).

Clinically, the increase in the number of melanocytic nevi and the presence of atypical nevi have been recognized as risk factors for the development of melanoma. In a meta-analysis on nevi as risk factors for melanoma, the highest risk (about 7-fold) for melanoma was observed in individuals with more than 100 nevi. The existence of several atypical nevi was correlated with a six-fold increased risk of melanoma formation compared to the absence of atypical nevi. It is believed that this dose-dependent correlation between nevi counts and melanoma implies that nevi may represent precursor lesions in the evolution of melanoma. However, the risk of a single nevus progressing to melanoma is very low (annual risk less than 0.0005%), so most nevi will remain stable and will not turn into melanoma (SHREBERK-HASSIDIM; OSTROWSKI; FISHER, 2023).

Congenital nevi are a classic example of Nevi-associated Melanoma (NAM). They are typically present at birth or in the first few years of life. This type of nevus is usually caused by an activating mutation in the MAPK pathway, primarily the NRAS gene. Large,

giant congenital nevi (>20 cm) have a significantly increased risk of melanoma formation, with an estimated lifetime risk of 10–15%, but likely requiring additional mutational events (in addition to NRAS) and/or genomic changes to progress (SHREBERK-HASSIDIM; OSTROWSKI; FISHER, 2023).

The WHO classification emphasizes the distinction between melanoma that develops de novo versus melanoma that arises from a benign precursor lesion, namely NAM. Importantly, although NAM and melanoma de novo largely represent separate clinical, histological, and molecular entities, there is an overlap. For example, although LMM and nodular melanoma most commonly occur de novo, a small percentage may occur in association with a precursor of nevus [18,19]. On the other hand, although SSM is enriched in NAMs, about one-third of SSM cases occur de novo. Survival, when normalized to Breslow depth, a key parameter for invasion and risk of relapse, is similar in NAM and de novo melanoma To date, no reports have examined the differences between response to immunotherapy in patients with metastatic melanoma whose primary melanoma was de novo versus nevus-associated (SHREBERK-HASSIDIM; OSTROWSKI; FISHER, 2023).

Primary prevention can be described as any type of prevention that decreases the possibility of cancer development in humans, and this is further subcategorized at the collective and individual level. Rather than being limited to the private sector, primary prevention can be part of an overall approach that also includes the implementation of prevention-related regulations, guidelines, and campaigns, as well as proactive organizational, administrative, and community measures and programs. Primary prevention includes avoiding excessive UV radiation, which has a chance to reduce the genetic and epigenetic risk factors described above. Promoting sun-safe behaviour is the main aid to avoid the harmful effects caused by UV radiation (SAEED et al., 2024). Reducing the incidence of skin cancer can be achieved through behavioral changes in childhood, but devising strategies is difficult as most data on UV exposure in children is limited, and especially from interviews and surveys. It has been suggested that schools are the best resource for implementing changes and educating children about UV exposure (RAYMOND-LEZMAN; RISKIN, 2023).

Given that UVR is the leading environmental risk factor for the development of skin cancer – as well as for sunburn and signs of photoaging that include rhytids, telangiectasia, and depigmentation – dermatologists employ a multi-pronged approach to minimize UVR exposure (SUOZZI; TURBAN; GIRARDI, 2020). Adequate UV protection includes a combination of the following measures in order of importance: avoiding intense UV sun exposure, avoiding the use of tanning devices, physical protection with clothing, a wide-

brimmed hat and sunglasses, and the use of sunscreens for uncovered skin. These measures are particularly important for children and adolescents and remain valid throughout life (GARBE et al., 2024).

Avoiding high/intense UV exposure is the first pillar in UV protection. The UV index quantifies the intensity of solar UV radiation reaching the Earth's surface, on a scale of 1 to 11+. According to the World Health Organization, sun protection measures are advised from the UV 3 index (moderate). UV intensity is highest 2 h before and after solar noon and accounts for 50–75% of the daily UV flux. Therefore, people are advised to seek shade during these times of the day (for UV index 3–7) or to stay indoors (UV index 8 or higher). Indoor tanning devices are another avoidable source of strong UV exposure. Legislation prohibiting the use of commercial tanning facilities is in place in Brazil, Australia, and Iran, and is being considered in other jurisdictions as a low-cost policy intervention that can reduce melanoma and other skin cancers (GARBE et al., 2024).

Physical protection through clothing, a hat and sunglasses is the second pillar of UV protection. Epidemiological studies have repeatedly found a reduced risk of sunburn, development of nevi in children, and melanoma through sun protection through clothing compared to sunscreens. The protective properties of garments vary with the type of fiber (polyester, nylon > wool, silk, > cotton), the density of the weave, the color (dyes contribute to UV blocking), the design (e.g., long sleeves, a collar), and the incorporation of UV absorbers. Clothing with a high UV protection factor is particularly useful in conditions of high UV exposure, such as outdoor sports and water sports. The field of photoprotection of fabrics, however, has evolved substantially in recent years. The key to the study of tissue photoprotection is the concept that fabrics inevitably contain small spaces (so-called interstices) between fibers through which UVR can permeate. As a general rule, fabric should cover 94% of an area (i.e., 6% or fewer interstices per area) to achieve a UV protection factor (UPF) of 15. UPF refers to the ratio of average effective UV irradiation through air to average effective UV irradiation transmitted through a tissue in question (GARBE et al., 2024) (SUOZZI; TURBAN; GIRARDI, 2020). Hats should have wide brims to protect the head, face, neck, and ears (GARBE et al., 2024).

The application of high-protection sunscreens to uncovered areas of the skin represents the third pillar of UV protection. Two randomized, prospective, community-based clinical trials conducted in Australia, follow-up after 10 years revealed a significantly lower number of melanomas in the sunscreen group. In conclusion, when the UV index is expected to reach 3 or more, it is recommended to apply broad-spectrum sunscreens daily (UVB+UVA) (Sun Protection Factor 30+ - 50+) to the face, ears, scalp (if uncovered), neck,

and all parts of the body not covered by clothing. Public health organizations, including the WHO, recommend that sunscreen be reapplied every 2 to 3 hours, although some authors have pointed out that reapplying with a frequency of up to 20 minutes can significantly increase UVR protection in real-world trials. Early innovations in application frequency involved adding a variety of compounds to make sunscreen water-resistant (e.g., through the use of polymers including acrylates/polytrimethyloxymethacrylate, butylated BVP, and others). Current efforts are focused on creating sunscreen particles that can covalently bind to the stratum corneum (GARBE et al., 2024).

Commercially available topical sun protection formulations use active agents that fall into two main classes: organic molecules that primarily absorb UVR energy and inorganic (or physical, mineral-based) molecules that additionally reflect UVR. Organic sunscreen agents (including PABA and derivatives, cinnamates, benzophenones including oxybenzone, avobenzone, octocrylene, salicylates including homosalate and octisalate, among others) are molecules that usually contain one or more aromatic rings, capable of absorbing and distributing energy from the incident UVR. Inorganic sunblocks (titanium dioxide and zinc oxide) also absorb UVR, although this effect is superimposed on a second mechanism of incident UVR dispersion. Although inorganic sunscreens are popular for their lower penetration into the living epidermis (Langerhans cells, keratinocytes, and melanocytes) and, therefore, for a lower risk of inducing allergic contact reactions, their light-spreading property results in formulations with a propensity to leave a whitish tint on the patient's skin, making them less cosmetically pleasing (SUOZZI; TURBAN; GIRARDI, 2020).

Coloring these formulations with universal skin tone shades helps combat the whitish tint and enhance the cosmetic. In addition, micronization technology has enabled the manufacture of smaller zinc oxide and titanium dioxide particles, reducing the intensity of the off-white hue and improving cosmetic favorability. This micronization process, however, raises some concern as to the increased deposition of these particles within the hair follicles and the increase in their penetration into the living epidermis. To date, no studies have demonstrated significant penetration of micronized particles into the fabric and inorganic sunscreens have been deemed "generally recognized as safe and effective" by the FDA. Organic sunscreens carry a higher risk of inducing an irritant or allergic contact dermatitis, but in general, they are more cosmetically appealing and continue to be the most popular products on the market today (SUOZZI; TURBAN; GIRARDI, 2020).

Early identification and screening are the two main elements of secondary prevention, which ultimately led to the early detection of tumors or malignancies in their

early stages. Secondary prevention of skin cancer includes interventions that help detect cancer at an early stage and treat it, to prevent deterioration and the formation of new sites. Skin self-checks, as well as professional skin examinations, are vital to check for the early signs of any skin lesions. Methods such as dermoscopy and digital mole surveillance can also increase the efficiency of identifying early-stage melanomas and other malignant skin diseases. Another secondary prevention approach includes raising awareness of the need to detect diseases as early as possible, and creating awareness of the signs to look out for in skin cancer is equally essential. The option of mobile health technologies has increased the accessibility of early diagnosis services, where teledermatology has also been considered to have added positive value driving the unprecedented outcomes (SAEED et al., 2024).

Diagnosing melanoma can be challenging because it can present in a variety of ways, such as a new or changing mole, a mole or lump that looks different from other moles on the skin, or a sore that doesn't heal. In addition, the various cytomorphological presentations of melanoma represent an immunohistological challenge. This is because its immunohistomarkers can resemble those of other tumors, such as germ cell tumors, neuroendocrine tumors, and other carcinomas. Clinical examination and biopsy are the main tools used to diagnose melanoma.

The first step in diagnosing melanoma is the recognition of atypical lesions. The ABCDE method is a simple acronym designed to assist the general public and medical professionals in identifying potential melanomas based on their characteristics. The letters represent five important characteristics of an aberrant skin lesion: asymmetry, irregular border, color variability/change, diameter, and progression. These features are often associated with melanomas that are early or in situ. Asymmetry refers to irregularity in the shape of the lesion, in which one half differs from the other. Edge irregularity refers to the blurring, notching, or unevenness of the edge of the lesion. Color variability/change refers to the lesion having a range of colors, such as various shades of brown or black, or gradually becoming darker or paler. Diameter refers to the extent of the lesion, typically greater than 6 millimeters. Changes in the size, shape, color, or texture of the lesion over time are called evolution/evolution. Once a lesion is identified as potentially malignant, a biopsy is performed, and the tissue is analyzed under a microscope to confirm the diagnosis. Dermoscopy can be used to improve the accuracy of tissue sampling (NWAFOR et al., 2023).

The gold standard for diagnosing melanoma is histopathological examination. A pathologist examines the biopsy sample under a microscope to determine if the lesion is

malignant. A typical melanoma under a tissue microscope can be described using several descriptions. When a pathologist examines a melanoma under a microscope, he or she typically looks for several defining characteristics of the tumor. For example, melanocytic cells arranged in layers and nests and the presence or absence of perineural invasions. Other characteristics include the number of lymphocytes, or TILs (tumor-infiltrating lymphocytes), present within the lesion. The presence of TILs may indicate that the immune system has recognized melanoma cells as abnormal and is attacking them. The pathologist may describe TILs as "fast," "non-fast," or "absent" and may also use the terms "mild" or "moderate." Other defining features of melanoma under a tissue microscope include the type of melanoma, the depth of invasion, the presence or absence of ulceration, the mitotic count, the presence or absence of regression, and the presence or absence of satellite lesions. The pathologist may also look at the type of specimen, the procedure used to remove the lesion, the location and side of the body where the lesion was located, the subtype of melanoma, the margin of excision, the size of the tumor, and whether the tumor is in situ or invasive (NWAFOR et al., 2023).

CONCLUSION

Exposure to ultraviolet (UV) radiation continues to be the main risk factor for the development of skin cancer, especially melanoma. The association between outdoor activities, indoor tanning, and unprotected exposure to UV radiation reinforces the need for continuous awareness campaigns and preventive interventions, especially among young people and fair-skinned people, who are more vulnerable. The results of this review highlight the importance of primary prevention, with a focus on sun insurance, use of protective clothing, and appropriate sunscreens. In addition, regulating the use of tanning beds and educating about the dangers of indoor tanning are essential measures to reduce the incidence of melanoma, particularly in young women

Early screening and the use of technologies such as digital dermoscopy and teledermatology emerge as valuable tools for the early detection of malignant skin lesions. However, there are still challenges related to the accurate diagnosis of melanoma, due to its clinical and histopathological variability. Future research should focus on improving photoprotection strategies, including the development of more effective sunscreens that have greater cosmetic adherence, as well as studies exploring the effects of intermittent and low-level UV exposures in underexposed populations. Finally, educational strategies and public policies must be improved to achieve rigorous changes in sun protection behavior, changing a sustainable reduction in skin cancer cases.

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