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SKIN CANCER NON MELANOMA

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ABSTRACT

In Caucasians, nonmelanoma skin cancer (NMSC) is the most prevalent type of cancer, and its incidence is steadily rising globally. Seventy-five percent of NMSC cases are basal cell carcinoma (BCC), with the remaining majority of NMSC instances being squamous cell carcinoma (SCC). Although BCC metastases are very uncommon, high-risk SCC metastases can be lethal. We go over the causes, symptoms, and treatment of NMSC in this post.

Context: *The most common cancer in humans to be diagnosed is non-melanoma skin cancer. Skin carcinogenesis is still a poorly understood phenomenon. To better understand the mechanisms underlying malignancy, however, a number of investigations have been carried out; (2) Techniques: With an emphasis on actinic keratosis, squamous cell carcinoma, and basal cell carcinoma, we examined the most recent research on the etiology of non-melanoma skin cancer; (3) Findings: Numerous studies documented molecular and genetic changes that result in skin cancer that is not melanoma. The pathophysiology of non-melanoma skin cancer involves numerous risk factors, such as immunosuppression, UV radiation, and genetic and molecular changes.4) Conclusion Several studies have shown that genetic and molecular changes play a role in skin carcinogenesis, despite the fact that this process is still not entirely understood. Furthermore, a number of risk factors for non-melanoma skin cancer are now understood, making it possible to effectively prevent the development of non-melanoma skin cancer. Our review concentrated on molecular and genetic factors and thoroughly examined a number of factors associated with non-melanoma skin cancer, in contrast to earlier articles on the same subject.*

KEYWORDS: *Actinic Keratosis; Pathogenesis; Precancerous Conditions; Skin Neoplasms*

REVIEW OF LITERATURE

1) D Didona, G Paolino, U Bottoni, C Cantisani

Furthermore, a number of risk factors for non-melanoma skin cancer are now understood, making it possible to effectively prevent the development of non-melanoma skin cancer. Our review concentrated on molecular and genetic factors and thoroughly examined a number of factors associated with non-melanoma skin cancer, in contrast to earlier articles on the same subject.(2)

2) S Razi, M Enayatrad

Skin cancer is becoming more common in the nation. Therefore, health policy makers must give top attention to the plan for the prevention and control of this malignancy.(3)

3) J.Augustin, A.Kis, C.Sorbe, I.Schafer, M.Augustin

Our findings show that the prevalence of skin cancer in Germany is significantly influenced by sociodemographic characteristics, sunlight hours, and regional UV radiation. Clearly, one of the main determinants that should be addressed by preventive measures is individual behavior.(26)

4) Larisa Paramitha Wibawa, Melody Febriana Andardewi, Inge Adi Kristanti, Riesye Arisanty

The prevalence of BCC is rising in Dr. Cipto Mangunkusumo National General Hospital as compared to other forms. Establishing national skin cancer data in Indonesia requires a well-documented skin cancer registry.(25)

5) Rolf-Markus SZEIMIES, Colin A. MORTON, Alexis SIDOROFF and Lasse R. BRAATHEN, Photodynamic

A less invasive treatment with great esthetic outcomes is photodynamic therapy. In addition to being licensed for actinic keratosis in the US, methyl aminolevulinate-photodynamic therapy is already approved for actinic keratosis and basal cell carcinoma in Europe, Australia, and New Zealand.(9)

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6) Czarnecki D
The remainder of the population is the susceptible group. This article examines the NMSC death rate for sensitive populations and the general population since 1971.(17)

7) Samarasinghe, Venura; Madan, Bishal
Seventy-five percent of NMSC cases are basal cell carcinoma (BCC), with the remaining majority of NMSC instances being squamous cell carcinoma (SCC). Although BCC metastases are very uncommon, high-risk SCC metastases can be lethal. This article examines the causes, symptoms, and treatment of NMSC.(16)

INTRODUCTION

According to estimates from the American Cancer Society, the yearly incidence of nonmelanoma skin cancer (NMSC) in the United States is currently over one million instances, which is about equivalent to the total number of human malignancies. BCCs make up the great majority of non-malignant squamous cell carcinomas (NMSCs), while SCCs in about a 4:1 ratio. Many other nonmelanoma skin cancers are caused by a variety of other cell types present in the skin, such as Merkel cells, vascular endothelial cells, lymphocytes, mesenchymal stromal cells, and cells that make up the adnexal structures. Since these entities are rather rare compared to BCC and SCC, we won't discuss them here.(1)

The most common malignancy to be diagnosed is non-melanoma skin cancer (NMSC). Although any kind of skin cell can become the source of a skin cancer, 70% of all NMSC instances are basal cell carcinoma (BCC), and 25% are squamous cell carcinoma (SCC). Both BCC and SCC have a fair prognosis, especially when identified early, despite differences in development patterns, behavior, and probability of spreading.(2)

Skin cancer risk is influenced by a combination of environmental, genetic, and personal factors. Personal and genetic traits that affect skin cancer risk include factors like skin color, eye color, hair color, age, and sometimes immune system deficiencies. Environmental factors include prolonged outdoor activities, changes in lifestyle, heavy alcohol consumption, a diet high in fat, exposure to UV radiation, and living at lower latitudes. Although skin cancer is one of the most common cancers, it is also one of the most preventable. The earlier preventive measures are taken, the greater the impact in reducing the risk. This type of cancer is particularly prevalent in Iran, where there has been little comprehensive research on its trends.(3)

EPIDEMIOLOGY OF SKIN CANCER

Squamous Cell Carcinoma

Squamous cell carcinoma (SCC) is a type of malignant epithelial tumor that often begins as a localized form called carcinoma in situ within the skin's outer layer (epidermis). Over time, it can develop into an invasive cancer. SCC is the most common type of cancer in the mucous membranes and areas where the skin transitions to mucosa, accounting for about 20% of all skin cancers. These tumors usually spread through the lymphatic system and grow aggressively. The same risk factors linked to actinic keratosis (AKs) also contribute to the development of SCC. In the United States, around 200,000 new cases of SCC are diagnosed each year. A study estimates that a Caucasian man born in 1994 has a 9% to 14% chance of developing SCC in his lifetime, while the risk for white women is estimated to be between 4% and 9%.(4)

Skin Cancer Pathophysiology

The development of skin cancer is influenced by multiple factors. The primary cause of both malignant melanoma and non-melanoma skin cancer (NMSC) is ultraviolet radiation (UVR) from sunlight. UVR is made up of two main types of rays: ultraviolet A (UVA) and ultraviolet B (UVB). UVA rays penetrate deeper into the skin and can cause more significant damage, such as the breakdown of skin fibers (elastosis). UVB rays are mainly responsible for sunburns or erythema. UVR leads to various harmful effects, including DNA damage, gene mutations, suppression of the immune system, oxidative stress, and inflammation.(5)

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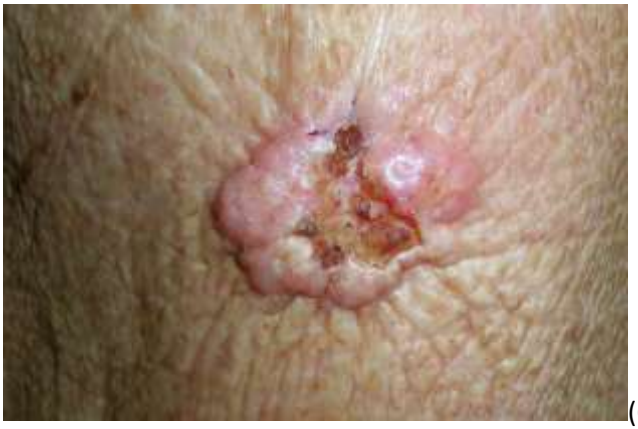
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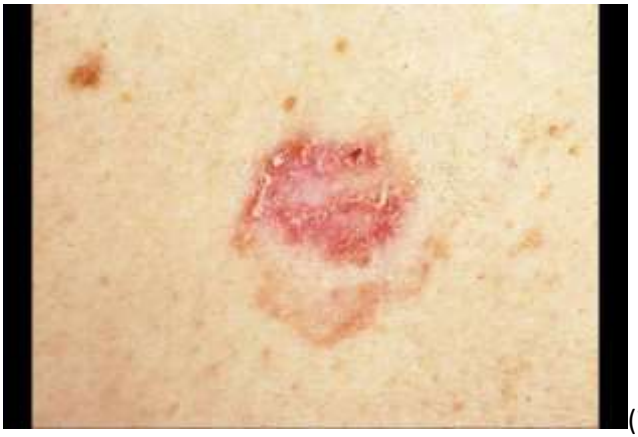
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MECHANISM OF ACTION

Reactive oxygen species (ROS), particularly singlet oxygen, are generated when a photosensitizer is activated by light of the right wavelength. These ROS can disrupt cellular functions or lead to cell death, either through necrosis or apoptosis, depending on their concentration and the specific area of the tissue they affect. Interestingly, there is limited data on the cancer-causing potential of ALA/MAL photodynamic therapy (PDT), with only two case reports, which may have been coincidental. Additionally, a recent study showed that long-term use of topical ALA with blue light exposure did not result in skin tumors in a hairless mouse model. The damage from this treatment mainly targets the tumor, as ALA or MAL preferentially sensitizes growing, iron-deficient tumor cells of epithelial origin, leading to good cosmetic outcomes with minimal risk to surrounding healthy tissue. Unlike systemic photosensitizers, which cause damage to the tumor's blood vessels, ALA/MAL-PDT targets the tumor itself.(9)

Formulation Table

Characteristics of the dataset (10)

Types	Train_Sep	Test	Valid Sum
Melanoma.	5341	1781	8903
Nonmelanoma	5341	1781	8903

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Rising Incidence of Melanoma Varies by Subsite and Sex

The data shows notable differences in melanoma rates between sexes and body sites over time. For example, the rate of melanoma in the arm among white individuals increased by 71% in males (from 1.4 to 2.4 per 100,000) and by 41% in females (from 1.7 to 2.4 per 100,000) between the periods of 1973–1977 and 1983–1987. In the leg, the rate increased by 43% in females (from 2.3 to 3.3) and by 37% in males (from 0.8 to 1.1). The most significant rise occurred in the trunk area, with a 70% increase in males (from 3.0 to 5.1) and a 76% increase in females (from 1.3 to 2.3). Overall, melanoma rates are increasing at all major sites, particularly on the trunk, and these trends are similar for both sexes.(11)

Genetics of Non-Melanoma Skin Cancer and New Candidate Genes

Researchers are continuing to explore the genetic factors that contribute to the development of various cancers, focusing on aspects such as genomic stability and genetic variations that can affect the expression of oncogenes and tumor suppressor genes. In the case of cutaneous carcinomas, UV radiation-induced DNA damage is a key characteristic. It is estimated that just one hour of UV exposure can cause between 100,000 and 200,000 DNA lesions, which, if not properly repaired, can disrupt critical cellular processes like transcription and replication. Recent studies have also shown that non-melanoma skin cancer (NMSC) lesions can accumulate mutations that drive more aggressive cancer forms. The ability of cancer cells to adapt allows them to escape normal cellular control mechanisms.(12)

NMSC and Ultraviolet Radiation

A study conducted in Beijing explored the connection between surface UV radiation and air pollution levels using the TUV4.4 radiative transfer model. The findings showed that the average ozone content in the atmosphere is higher during winter and spring, and lower in summer and autumn. Interestingly, there is an inverse relationship between ozone levels and ground-level UV radiation, meaning that as ozone levels increase, UV radiation decreases. Additional data indicated that UV radiation is reduced by more than 50% on days with high air pollution. In conclusion, the study suggests that in Beijing, there is a clear link between the decrease in UV radiation reaching the ground and the increased levels of ozone and nitrogen oxides in the lower atmosphere.(13)

Radiotherapy

For some patients with non-melanoma skin cancer (NMSC) who cannot undergo surgery, radiotherapy can be an effective treatment alternative. However, its overall success rate is lower compared to methods like Mohs micrographic surgery (MMS) or standard excision with set margins. A meta-analysis by Rowe et al. found a 5-year cure rate of 91.3% for basal cell carcinoma (BCC), while another study showed a 5-year cure rate of 90% for squamous cell carcinoma (SCC). In cases where full surgical removal of the tumor is not possible due to advanced disease, radiation therapy may be used as a palliative option or as additional treatment after surgery, especially for tumors with nerve involvement.(14)

MATERIALS AND METHODS

The Australian Bureau of Statistics (ABS) provided the population data for Australia. Every five years, there is a census, and everyone is required by law to participate. Although the population's countries of birth were noted in every census, the 2001 census was the first to record the population's ancestry [18]. Data on all births and deaths in Australia for the calendar year are provided by the ABS every year. Children born in Australia have their parents' country of birth listed, but not their heritage. Each fatality that was caused by skin cancer is identified as either melanoma or non melanoma skin cancer.(15)

For the diagnosis, the clinician examined the 3D avatar both in a broad overview and a detailed, zoomed-in view, enabling them to assess each lesion from multiple angles. To ensure consistency between the two devices, the clinician was provided with precise details about the number and locations of lesions for each patient. The diagnostic results from dermoscopy and the 3D-TBP zoomed-in view were compared to histopathology to assess their accuracy. Rather than choosing from a range of possible diagnoses, the clinician recorded a specific suspected diagnosis along with a confidence level for each device. The diagnoses were categorized into basal cell carcinoma (BCC), squamous cell carcinoma (SCC), in-situ SCC, other malignant lesions, and benign lesions.The final diagnosis was based on histological results when available. Tumors with clear diagnoses were removed, while benign lesions were treated locally without the need for histological examination. In cases where the diagnosis was uncertain, punch biopsies were performed. Punch or excision biopsies were only used for lesions suspected to be superficial BCC or in-situ SCC if the doctor had low confidence in the diagnosis. Only lesions with histopathological confirmation were included in the calculation of the imaging devices' sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy; clinical diagnoses without histopathological confirmation were excluded.(16)

This retrospective analysis used electronic medical records from kidney transplant patients at Rabin Medical Center. It focused on all adult patients (aged 18 and older) who received a kidney transplant between January 1, 2005, and December 31, 2010. These patients

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were closely monitored by nephrologists at the kidney transplant clinic, and they also attended at least one annual check-up at the transplant dermatology clinic. Patients who experienced graft loss or death within the first year after their transplant, or who were diagnosed with non-melanoma skin cancer (NMSC) in that same period, were excluded from the study. There was no reliable data available regarding the incidence of NMSC before the transplant or details on skin phenotype unrelated to their ancestral background.(17)

DISCUSSION

Although non-melanoma skin cancers are sometimes thought of as non-aggressive tumors, this is only true for tiny lesions that get prompt, appropriate treatment. Locally, both BCCs and cSCCs are distinguished by varying rates of destructive development and tissue invasion. In the case of cSCCs, distant invasion has a low rate of metastasis, while regional tissue invasion happens less frequently through lymph node metastasis [37–39]. Despite having a very low death rate, these tumors are very common and represent a significant worldwide health burden. Furthermore, they are associated with a high rate of morbidity, especially when they impact parts of the face that are sensitive to cosmetics, which frequently calls for difficult reconstructive procedures(18)

Martincorena et al. conducted a study that looked for somatic mutations using ultra-deep sequencing of 74 cancer-related genes from skin biopsies of normal skin taken from sun-exposed eyelid areas across 234 samples from four individuals. They found that the mutation rate in these samples was typical for UV radiation (UVR) exposure, with an average of two to six mutations per megabase per cell, which is similar to the mutation rates seen in many cancers. They observed a high frequency of specific mutations, including CC>TT dinucleotide changes and C>T mutations. Notably, 20% of normal skin cells carried a mutation in the NOTCH1 gene, making it the most frequently altered gene in the study. In skin squamous cell carcinoma (SCC) and other cancers, both copies of NOTCH1 are often inactivated, typically through point mutations and changes in the gene's copy number. Other commonly mutated genes include RBM10,FGFR3, CDKN2A, and NOTCH2.(19)

CONCLUSION

The incidence of Basal Cell Carcinoma (BCC) is increasing at Dr. Cipto Mangunkusumo National General Hospital compared to other types of skin cancer. To establish comprehensive national data on skin cancer in Indonesia, it is essential to create a well-maintained skin cancer registry.(20)

RESULT

An analysis was conducted using data from 70.1 million insured individuals. In 2009 and 2015, the age-adjusted rates of malignant melanoma (MM) and non-melanoma skin cancer (NMSC) were 284.7 and 1126.9 cases per 100,000 insured individuals, respectively, in 2009, and 378.5 and 1708.2 per 100,000 in 2015. There were significant regional variations in prevalence, ranging from 32.9% to 51.6%. The multivariate analysis showed that there were statistically significant positive correlations between the prevalence of MM/NMSC and higher levels of wealth and education.(21)

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