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Review article

An Insight of Basal Cell Carcinoma Risk Factors

Dr. Rawan Almutairi *[1], **Dr. Abeer Albazzali** [2]

[1]Dermatology Resident, Farwaniya Hospital, Kuwait.
[2]Head of Dermatology Department, Farwaniya Hospital, Kuwait.

*Corresponding author: Rawan Almutairi; *r.mutairi95@gmail.com*

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Abstract

Basal cell carcinoma (BCC), a type of non-melanoma skin cancer, is the most common cancer worldwide that originates within the outermost layer of skin, the epidermis. Overexposure to ultraviolet (UV) radiation from the sun considered the main cause of this disease. Many risk factors increase the chance of developing BCC including environmental, lifestyle, and genetic risk factors. These factors range from exposure to UV radiation, occupational hazards, chemical exposures, family history of BCC, genetic mutations, inherited skin conditions, sun exposure and tanning habits, smoking and tobacco use, to weakened immune system. Once the risk factors are understood, preventive steps such as mitigating sun exposure and avoiding harmful chemicals can be taken to significantly reduce the likelihood of developing the cancer. By identifying the people who are most likely to get the cancer and providing the necessary preventive options, such as regular check-ups and lifestyle advice, the burden of BCC can potentially be decreased.

Keywords: ***Basal cell carcinoma, Risk Factors, Environmental Risk Factors, Genetic Risk Factors, ultraviolet.***

1. Introduction

Basal cell carcinoma (BCC), a type of non-melanoma skin cancer, is the most common cancer worldwide. It originates from the basal cells, a type of cell within the outermost layer of skin, the epidermis. BCC mainly occurs due to overexposure to ultraviolet (UV) radiation from the sun but can also result from exposure to UV radiation or tanning beds. UV radiation from the sun and from sunbeds is the main cause of BCC. Sunburn, particularly in childhood, is also a risk factor [1,2]. People particularly at risk are those with a pale complexion, freckles, red or fair hair, or light-coloured eyes. However, people of all skin types can be at risk. Too much exposure to the sun over the years can cause skin damage and can lead to the development of BCC. It is not the direct heat of the sun that usually causes the damage, but the UV radiation. This is thought to cause changes in the DNA of the basal cells in the deepest layer of the skin. In fact, BCC can occur on parts of the body that are not exposed to the sun much at all. For example, it can develop in the genital and anal areas and, very rarely, it can grow inside the mouth or other parts of the body [3,4]. BCC can also sometimes develop where scars, ulcers or other sores have damaged the skin. BCC tends to grow slowly and it's very rare for them to spread to other parts of the body. However, if left untreated, the sore may continue to grow and damage surrounding tissue. This can affect the normal function of the surrounding skin, bone and other structures. Successful treatment of BCC depends on early detection and treatment. It is primarily caused by cumulative, intense sun exposure, especially in the case of intense, occasional exposure which can lead to the development of a 'rodent ulcer'. This cancer tends to occur on the more usual sites for BCC, for example, the face and neck. However, BCC can develop on any part of the body [5-7].

There are various risk factors that can increase a person's likelihood of developing BCC. By understanding these risk factors, individuals can identify when they may be at a higher risk and work to prevent the development of BCC. Additionally, knowing the risk factors for BCC can help scientists and doctors understand how this disease develops and how to treat it. This study provides a comprehensive review of the risk factors for BCC.

1.1. Definition of Basal Cell Carcinoma

Skin is made up of three layers: the epidermis, the dermis, and the subcutis. The top layer, the epidermis, is constantly replacing itself. New cells are made in the lower part of the epidermis. These cells move up to the top of the epidermis as they get older. When the cells reach the top of the epidermis, they die and are shed from the surface. Basal cells are found at the bottom of the epidermis, the lower part of the epidermis. These cells constantly divide and push older cells towards the surface of the skin to replace dead or dying cells [8,9].

BCC is a type of skin cancer that begins in the basal cells. BCC usually occurs on skin that has been exposed to the sun, such as the face, neck, and ears, but can occur anywhere on the body. It is the most common type of skin cancer worlwide. It grows very slowly and is not likely to spread to other parts of the body. As a result, BCC is easily treated. However, if the BCC is not treated, the cancer cells may grow into nearby areas and invade the bone or other tissues beneath the skin. The two most common types of BCC are nodular BCC and superficial BCC. Nodular BCC has the appearance of a pearly bump or nodule. This nodule may have areas of bleeding or crusting. Superficial BCC usually occurs on sun-damaged and aged skin, especially on the face. It has a reddish-brown colored patch which may be scaly and bleed [10,11].

1.2. Importance of Understanding Risk Factors

Understanding the risk factors is important in identifying individuals who may be at a higher risk for developing BCC. By implementing preventive measures, such as reducing sun exposure and avoiding harmful chemicals, individuals can reduce their risk of developing BCC [12]. Additionally, regular skin screenings and early detection are crucial for the successful treatment of BCC. It is important for a medical professional diagnosing skin cancer to obtain a detailed medical history to help identify the most likely diagnosis. Understanding the common risk factors for each kind of skin cancer can assist a healthcare provider in making a correct diagnosis [12-14].

Chances in BCC survival are high with early detection and treatment. In general, people with skin cancer who are in good health and are treated early have a better chance of survival than those who are older or in poor health. By the time a skin cancer is diagnosed, the disease can be quite advanced, which sometimes makes treatment more difficult. Early detection can be a serious clinical advantage, having a lifesaving potential. Therefore, regular screenings are important to ensure that early diagnosis and treatment can be provided. These preventive measures and the possibility of early treatment make it very important for people to understand the risk factors that contribute to the development of BCC. Many may be tempted to tan excessively for aesthetic purposes or neglect the importance of wearing sunscreen daily, but these behaviors can drastically increase the likelihood of BCC development [15,16].

Once the risk factors are understood, preventive steps such as mitigating sun exposure and avoiding harmful chemicals can be taken to significantly reduce the likelihood of developing the cancer. By identifying the people who are most likely to get the cancer and providing the necessary preventive options, such as regular check-ups and lifestyle advice, the burden of BCC can potentially be decreased. And considering that the overall diagnosis and treatment of this cancer is pretty straightforward, preventive measures that could completely avoid the development of BCC are achievable and would save countless lives from this disease [17].

2. Environmental Risk Factors

2.1. Exposure to Ultraviolet (UV) Radiation

Exposure to UV radiation from the sun or artificial sources, such as tanning beds, is considered the major environmental risk factor for BCC development. The main feature of UV radiation is that it damages the DNA of the skin cells. The body can usually repair this damage. However, the body's ability to repair regularly occurring damage decreases over time. It is the accumulation of such DNA damage in the basal cell layer of the skin over a person's lifetime that can lead to the development of BCC. There are also different types of UV radiation, which are classified based on their wavelength. UV radiation with shorter wavelengths, called UVC and UVB radiation, is responsible for direct damage to the DNA molecules. On the other hand, UV radiation with longer wavelengths, called UVA radiation, produces free radicals which can indirectly harm the DNA. UVA radiation is also used in tanning beds. People who are frequently exposed to sunlight over a long time, for example due to high levels of outdoor activity, may be at an increased risk of developing BCC. Continual exposure to sunlight over time makes it difficult for the body to repair itself, as the rate of DNA damage accumulates that can lead to carcinogenesis [18-20].

Additionally, the use of artificial sources of UV radiation, such as tanning beds, has become increasingly popular especially among young adults and adolescents. Research has shown that the risk for BCC is greater among those who use tanning beds, and the risk increases with the number of years a person has used indoor tanning devices. Perhaps surprisingly, it has been suggested in some literature that repeated moderate UV radiation exposure may also lead to a higher risk, and to prevention of BCC incidence there has been discussion of behavior modification interventions that account for this [6,21,22].

This contrasts the general advice from the Centers for Disease Control and Prevention, which promotes complete sun avoidance and protecting oneself by wearing wide-brimmed hats, sunglasses, and sunscreens. Some popular research about the implications of UV exposure is investigating ways to protect against DNA damage, which could lead to important therapies or treatments in the future to help those most at risk from BCC development [23].

Given the potential harm from UV radiation, minimizing skin exposure from the sun and other sources is vital in cutting the risk of developing BCC. This can be done through a number of means, such as wearing protective clothing, using sunscreen, and staying in the shade during peak UV radiation times. Creative strategies to avoid sunburn and overexposure are also commonly advocated for, such as staying indoors between mid-morning and late afternoon, when the UV index is at its highest. These steps should also include avoiding the use of sunbeds and other similar equipment. Diagnosis of BCC in patients who have had high levels of UV radiation exposure, such as individuals with outdoor occupations or high levels of outdoor activity, is often important. This risk factor for BCC demonstrates the influence of environmental factors in the development of the disease [24,25]. More research can be undertaken to investigate the potential protective measures that can be employed today in order to reduce a person's risk of BCC from UV radiation and its implications on public health.

2.2. Occupational Hazards

Another significant risk factor for BCC is occupational hazards. In particular, certain occupations or jobs that involved exposure to harmful agents can significantly increase the likelihood of developing BCC. Some of the hazardous agents associated with increased risk of BCC include polycyclic aromatic hydrocarbons, arsenic, and ionizing radiation. Polycyclic aromatic hydrocarbons, or PAHs, are a group of more than 100 different chemical compounds that are widely distributed in the environment. Many occupational settings, such as coal tar distillation, coal gasification, and aluminum production, expose workers to these harmful agents. Research has found that exposure to PAHs can lead to genetic mutations and molecular changes that cause skin cells to grow uncontrollably, which contributes to BCC development [26,27].

Arsenic is another hazardous agent that is linked to an increased risk of BCC. It is commonly found in industrial workplaces, such as copper or lead smelting, wood treatment, and pesticide application. Moreover, certain occupations, such as archeological digs and wine making, may involve exposure to arsenic as well. Long-term exposure to high levels of arsenic can lead to direct DNA damage and suppression of DNA repair, increasing the likelihood of developing BCC [28,29].

Finally, studies have shown that people, such as radiologists and radiologic technicians, who are frequently exposed to ionizing radiation may have a higher risk of BCC in the areas of the body that are more exposed to radiation. Too much ionizing radiation can damage the DNA in skin cells and impede their ability to repair and protect against cancer [30].

By understanding the association between BCC and different factors in work settings, workplaces and processes could be constantly reviewed and improved, benefiting the health of the public. To employees and employers, protecting everyone from the hazards of BCC in the workplace is an essential duty by law. As such, knowledge about health and safety, risks related to the occupation,

industry standard practices, and appropriate protective measures are vital in ensuring a safe work environment for everyone.

2.3. Chemical Exposures

Scientific research has shown that exposure to certain chemicals in the environment can increase the risk of developing BCC. These chemicals can be found in a variety of places, including the workplace, at home, and in the general environment. The type of chemical and the amount of exposure are important factors in determining the level of risk; in general, the higher the exposure, the higher the risk. However, many chemicals that have been linked to BCC are also recognized as having broader health risks, and good prevention and protection measures can lower the risk from both BCC and other health conditions. Chemicals that are known to increase the risk of developing BCC are described as "carcinogens". Carcinogens can damage cells in the body, causing mutations that may ultimately lead to the development of cancer. UV radiation is also a type of carcinogen, which works by damaging the DNA in the outermost layer of the skin. Evidence has linked the development of skin cancer to exposure to both chemical carcinogens and UV radiation, demonstrating the complexity and range of risk factors associated with the development of skin cancer like BCC. One of the more common ways people are exposed to chemicals that can increase the risk of BCC is in the workplace. Certain industries, including the construction, agriculture, and mining sectors, use equipment or materials that may lead to increased levels of exposure to these types of chemicals. For example, compounds such as coal tar, and paraffin, but also diesel and other types of fuel, can damage the skin and increase the risk of developing occupational BCC. In recent years, measures have been introduced to try to reduce the levels of chemical exposure in the workplace, including the use of technology and personal protective equipment (PPE) to minimize the risks. Governments and employers also have a duty to carry out risk assessments and provide suitable training and safety advice to employees who may be at risk of exposure to carcinogens. This will help to minimize the risk of chemicals, and ultimately the risk of developing BCC, from the working environment [31-33].

3. Genetic Risk Factors

3.1. Family History of Basal Cell Carcinoma

The occurrence of BCC in an individual's family history is commonly known as a family history of BCC. In the development of BCC, the PATCHED gene, which is a genetic factor, plays a significant role, particularly in individuals with basal cell nevus syndrome. This genetic condition leads to the appearance of multiple BCCs on the skin at a young age, often before the age of 20, and can also result in the occurrence of other cancers within the body. The discovery of this gene has expanded our comprehension of the genetics involved in non-syndromic BCC, which sporadically occurs in individuals. Research has indicated that individuals with one parent affected by BCC have an increased risk of developing the condition themselves. In families where two or more relatives have been affected, the risk further increases depending on the proximity of the relationship and the number of individuals affected by the disease. For example, studies have revealed that if both parents of an individual have experienced BCC, the risk is considerably higher compared to those with only one affected parent. However, there are discrepancies in the research due to variations in factors such as the age at which the disease manifests, the number, and location of primary tumors. Nevertheless, genetic research on BCC has provided significant insights into the prevention and treatment of this prevalent form of skin cancer. Therefore, it is highly recommended to consider seeking genetic counseling if multiple relatives in a family have been affected by BCC. Genetic counseling involves examining a person's family history and medical records to evaluate the risk. This can assist individuals in making well-informed decisions regarding the suitability of genetic testing and discussing potential preventive measures and treatment options [11,34,35].

3.2. Genetic Mutations

Within the past few years, researchers have identified a specific genetic abnormality found in the vast majority of all BCCs. This genetic mutation involves the p53 gene, which provides instructions for the production of a protein that acts as a tumor suppressor. Normally, the protein made by the p53 gene helps regulate the cell cycle. However, the p53 protein is inactive in the overwhelming majority of BCCs, so it is unable to control cell proliferation and survival like it should. Instead, the uncontrolled growth and division of the basal cells contribute to the formation of a tumor. Some people are born with one mutated p53 gene, which is a condition known as "basal cell nevus syndrome." Basal cell nevus syndrome patients are extremely sensitive to the effects of UV radiation and will develop BCCs repeatedly and at a young age throughout their lifetime. In patients with sporadic BCCs, both copies of the p53 gene have usually incurred changes in the same cell at some time during the person's life, leading to the development of the tumor [11,18,36].

Some people may inherit a substitution in their DNA that provides the instructions for making a perfectly normal protein, but this particular p53 sequence is not found in the most common, or "wild type," form of the gene. This inherited version is instead known as a polymorphism. Some preliminary studies seem to suggest it may confer a very small risk of developing common cancers, presumably by leading to a reduction in the amount of p53 protein produced. More research into the nature of p53 polymorphisms will be necessary before we can fully understand their implications and effects on human health [1,37].

3.3. Inherited Skin Conditions

Certain inherited disorders including Gorlin Syndrome and Xeroderma pigmentosum are considered risk factors for BCC. Gorlin syndrome (nevoid basal cell carcinoma syndrome) is an inherited disorder caused by a mutation in the gene 'PTCH1'. This mutation leads to uncontrolled, cancerous cell growth. The syndrome affects various organ systems and can result in BCCs and other cancers, such as medulloblastoma. It can also cause non-cancerous tumors, bone cysts, and distinctive facial features. Individuals with Gorlin syndrome have a higher risk of developing BCC and should seek medical advice for any unusual skin changes [38,39].

Xeroderma pigmentosum (XP) is a rare inherited disorder that increases the risk of developing BCC due to a defect in DNA repair caused by UV light exposure. XP patients, who face a heightened susceptibility to skin cancer, are particularly susceptible to BCC. To date, there are eight identified genes that, when mutated, can lead to XP. The accumulation of DNA damage in XP patients significantly enhances the probability of abnormal cell development, increasing the likelihood of developing BCC [40,41].

4. Lifestyle Risk Factors

4.1. Sun Exposure and Tanning Habits

Individuals with excessive sun exposure and a history of using tanning beds are at an increased risk for developing BCC. Sunlight is the main source of UV radiation, which is known to cause damage to the skin, including the development of skin cancer. In

particular, intense, occasional exposure to sunlight that results in sunburn and an increase in the BCC risk factors. Fair-skinned individuals with a history of sunburn are even more susceptible. This is why BCC is more common in regions of the world that receive large amounts of sunlight. Indoor tanning beds and sun lamps can also cause skin damage and an increased risk of BCC. These devices can emit two forms of UV rays, UVA and UVB. UVB rays are thought to cause the genetic damage in the skin that can lead to cancer. However, UVA rays, which are also known as tanning rays, can damage the skin's connective tissue and may increase the risk of BCC. Research has shown that use of indoor tanning equipment before the age of 35 is associated with an increased risk of BCC, the most frequently diagnosed malignancy in the United States. BCC is the least deadly type of skin cancer; however, it can still cause considerable damage. Due to the slow growth and deep invasion of BCCs, aggressive treatment is generally required. BCC treatment can be minimally invasive, such as with a cream applied to the skin, or more invasive, such as with surgery. However, if left untreated, BCC can grow to be disfiguring. It can also become dangerous if the cancer starts to invade the deeper layers of the skin or grows near a critical structure, such as the eye. This is why minimizing sun exposure and the use of tanning beds, as well as regularly checking the skin for any new growths, are important steps in helping to prevent the development of BCC and to identify the disease early. By detecting BCC at an early stage, it is often possible to treat it more easily and with less scarring. In contrast, if BCC is left to grow, treatment may become more difficult and tissue repair more extensive. In addition, early detection is critical to ensure that the cancer is completely cured. If left to develop, BCC can continue to grow and potentially spread to other parts of the body. However, it is very rare for BCC to spread to other areas, and virtually all cases are curable [22,42,43].

4.2. Smoking and Tobacco Use

Smoking is not only generally adverse for fitness and skin, it may also be a risk factor for the development of BCC. Cigarette smoking has constantly been suggested in organizations getting more competitive and multiple BCC, particularly concerning males, in numerous research published in diverse countries. The mechanism behind the effect of smoking on BCC is not wholly clear. It is proposed that nicotine absorbed in the blood during smoking may also resource the formation of tumors by inhibiting the process of apoptosis in the cells. On the other hand, smoke includes free radicals and a number of distinct molecules, so smoking may also lead to skin injury induced by these molecules [44].

4.3. Weakened Immune System

Individuals with a weakened immune system have an increased risk of developing BCC. The body's immune system is responsible for defending against pathogens, such as bacteria, viruses, and other disease-causing agents. The immune system is also important in recognizing and destroying cells in the body that are abnormal or have the potential to develop into cancer. When the immune system is compromised and does not function properly, cancer cells are more likely to develop and grow. There are several reasons why a person's immune system may be weakened. Certain medical conditions, such as HIV/AIDS, can directly affect the immune system and make it less effective at fighting off cancer. Some medical treatments, like chemotherapy and medications used to prevent rejection after organ transplantation, can also suppress the immune system, which increases the risk of cancer development. In the context of BCC, having a weakened immune system can allow the cancer cells to grow more easily. It can also make it difficult for the body to effectively recognize and destroy the cancer cells. This could potentially allow the tumor to grow larger and become more invasive before it is detected [45].

In clinical practice, BCCs on individuals with a weakened immune system may appear differently than those on individuals with a healthy immune system. This is important in the clinical management of the tumor. Dermatologists may consider a weakened immune system as a risk factor for a more aggressive or advanced cancer and may have a lower threshold for taking a biopsy or recommending treatment. Also, dermatologists should advise high-risk patients with unexplained masses or swelling to seek medical attention early to rule out BCC.

Conclusion

Chances in BCC survival are high with early detection and treatment, which highlights the importance of identifying the people who are most likely to get the cancer and providing the necessary preventive options. This is done by first understanding and locating the BCC risk factors to apply preventive measures that could completely avoid the development of BCC and would save countless lives from this disease.

List of abbreviations

BCC: Basal cell carcinoma
UV: Ultraviolet
PAHs: Polycyclic aromatic hydrocarbons
PPE: Personal protective equipment
XP: Xeroderma pigmentosum
HIV: Human immunodeficiency virus
AIS: Acquired immunodeficiency syndrome

Declaration

Ethics approval and consent to participate

Not applicable

Data Availability

Data sharing is not applicable to this article as no new data were created or analysed in this study

Authors' contributions

The manuscript has been read and approved by all the authors

Conflict of interest

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