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Environmental Exposures and Cancer Risk: A Comprehensive Review

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Abstract: Environmental exposure is increasingly recognized as a significant cancer risk factor. This comprehensive review aims to provide an overview of current knowledge regarding the relationship between several environmental factors and the development of cancer. The complicated interactions between genetic predispositions and environmental factors in the etiology of cancer are highlighted in this study by looking at both known and newly discovered environmental carcinogens. The review covers a broad spectrum of environmental exposures, including occupational risks, dietary and physical activity habits, and toxins in the air and water. It also explores the molecular processes by which these exposures cause cancer, with particular attention to pathways including DNA damage, oxidative stress, and epigenetic changes. This review also discusses the differences in cancer risk associated with environmental exposures among various populations, highlighting the necessity of focused preventative and therapeutic measures. The results highlight how crucial it is to implement public health programs and regulatory regulations targeted at lowering environmental carcinogen levels and lessening their influence on the incidence of cancer. Considering an emphasis on developing precision medicine techniques and enhancing environmental health equality, future research directions are suggested further to clarify the complex links between the environment and cancer.

Keywords: environmental carcinogens, cancer risk factors, pollution and cancer, chemical exposures, epidemiological studies, carcinogenesis mechanisms, public health interventions

1. Introduction

Cancer is one of the leading causes of illness and death worldwide, accounting for nearly 10 million deaths from cancer-related causes and 19.3 million new cases of the disease in 2020 alone. The complicated etiology of cancer involves lifestyle decisions, genetic predispositions, and environmental exposure [1]. Among these, exposure to the environment is increasingly understood to be a major factor in cancer risk and to be responsible for a large amount of the cancer burden worldwide. Public health is increasingly at risk due to the accelerated rate of industrialization, urbanization, and lifestyle changes that have increased exposure to several environmental carcinogens [2].

Occupational hazards, air and water pollution, and lifestyle factors including exercise and nutrition are some of the most researched environmental exposures associated with cancer. For example, there is evidence linking air contaminants such as benzene, nitrogen dioxide (NO_2), and particulate matter (PM2.5) to lung cancer and other cancers. There is a connection between drinking water contaminants, such as arsenic and industrial chemicals, and bladder, liver, and skin malignancies. Additionally, workers in particular industries have a much higher chance of developing various malignancies due to occupational exposure to substances like asbestos, silica, and certain pesticides. In addition to environmental exposures, lifestyle variables such as drinking, smoking, and eating habits might raise one's risk of developing cancer [3].

It is essential to comprehend the processes by which these exposures cause carcinogenesis in order to create effective preventative and therapeutic plans. Oxidative stress, DNA damage, and epigenetic changes brought on by environmental carcinogens can result in mutations and dysregulated cell development. A microenvironment that is favorable to the development of cancer is also produced by chronic inflammation brought on by prolonged exposure to chemicals. There are still gaps in our understanding despite tremendous progress in identifying these pathways, especially with regard to the interaction of genetic and environmental factors and how they together affect cancer risk [4].

This study is significant because it provides a thorough synthesis of the available research on the relationship between environmental exposures and cancer risk, with a particular emphasis on differences between populations. Cancer susceptibility is influenced by exposure levels, geographic location, and demographic characteristics like age, gender, and race. Exposure to environmental carcinogens is generally higher in low-income and marginalized groups, which exacerbates health disparities and leads to unequal cancer outcomes. Targeted public health programs, sensible regulatory frameworks, and fair access to healthcare resources are all necessary to address these inequities [5].

This review aims to thoroughly understand the different environmental exposures linked to cancer, the biological processes that underlie carcinogenesis, and the implications of these findings

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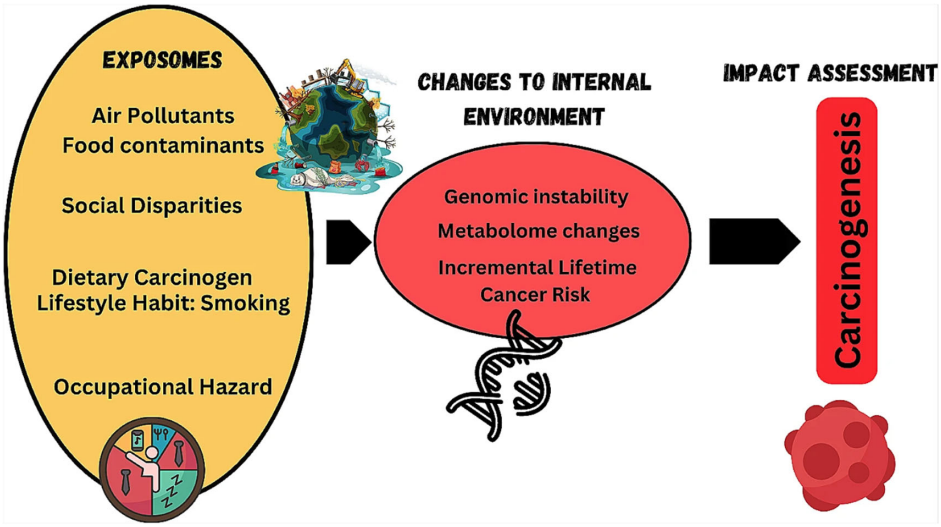

Figure 1. Impact of environmental factors on carcinogenesis

for general health (Figure 1) [6]. It emphasizes the need for comprehensive regulatory frameworks and public health measures designed to eliminate environmental carcinogens and ameliorate their impact on cancer incidence by exposing discrepancies in exposure and risk. The study highlights the significance of increasing precision medicine approaches and enhancing environmental health equity, while also identifying important areas for future research. By providing this synthesis, the review hopes to educate academics, policymakers, and healthcare professionals and aid in the creation of efficient plans to counteract the rising cancer incidence linked to environmental exposures [7].

This figure illustrates the pathway from various exposomes to carcinogenesis, emphasizing changes to the internal environment and subsequent cancer risk. Exposomes: Various environmental and lifestyle factors including air pollutants, food contaminants, social disparities, dietary carcinogens, smoking, and occupational hazards. Changes to Internal Environment: These exposomes induce genomic instability, metabolome changes, and increase lifetime cancer risk. Impact Assessment: The culmination of these changes contributes to the process of carcinogenesis, leading to the development of cancer.

The populations studied in this review include a wide range of demographic features and geographic areas, demonstrating the worldwide influence of environmental exposures on the risk of cancer. In terms of demographics, the research covered individuals from different age brackets, ranging from children to older adults, with a specific focus on those who are more susceptible to environmental influences, such as workers in industrial settings and people living in areas with high levels of pollution. Differences between genders were taken into account, specifically in malignancies that are known to have differences between males and females, such as breast and prostate cancer [8]. These studies covered many geographical regions, such as North America, Europe, Asia, and Africa providing valuable insights into the relationship between environmental exposures and cancer risk in distinct environmental and socio-economic settings. For example, research conducted in heavily industrialized locations mostly investigated the effects of being exposed to air pollution and chemical toxins. On the other hand, studies conducted in agricultural areas mainly concentrated on examining the consequences of being exposed to pesticides and herbicides. Potential risk factors for these populations encompass occupational exposures, particularly encountered by miners, manufacturing workers, and agricultural laborers, who are frequently at elevated risk due to extended contact with dangerous substances [9]. Furthermore, lifestyle factors such as smoking, nutrition, and the distinction between living in urban or rural areas were extensively examined in terms of their interaction with environmental exposures. This provided a detailed comprehension of how these factors jointly impact the risk of cancer in various populations. The comprehensive analysis of demographic characteristics enhances the results of our study, emphasizing the need for focused measures in reducing environmental cancer hazards [10].

Relevant exposure histories in the studies we reviewed encompass a wide range of environmental and lifestyle factors linked to cancer risk. These include prolonged exposure to air pollutants, such as particulate matter (PM) and industrial emissions, as well as occupational exposures to chemicals like asbestos, benzene, and pesticides. Additionally, lifestyle factors such as tobacco use, alcohol consumption, and dietary habits were considered, as these can interact with environmental exposures to influence cancer susceptibility. The studies also examined the cumulative effects of multiple exposures over time, highlighting the significance of both acute and chronic exposure histories in understanding cancer risk [10].

2. Methodology

In conducting this comprehensive review of environmental exposures and cancer risk, we utilized a methodical strategy to ensure the thoroughness and relevance of the included studies. Initially, we established the requirements of the analysis, concentrating on scholarly studies published in the last six years that examine the correlation between several environmental exposures, such as chemical pollutants, radiation, and lifestyle factors, and the likelihood of developing cancer. Our literature search was conducted utilizing numerous electronic databases, including PubMed, Scopus, and Web of Science. We used several terms linked to environmental exposures (e.g., “chemical pollutants”, “radiation”, “air pollution”) and cancer types (e.g., “lung cancer” and “breast cancer”) to locate relevant research. We applied inclusion criteria to choose studies that offered original

data, used strong epidemiological methodologies, and had unambiguous outcomes relating to cancer incidence or risk. Studies that did not fit these criteria, such as those lacking rigorous methods or concentrating on non-cancer outcomes, were eliminated.

Data extraction entailed a careful evaluation of the selected papers, where we noted the kind of environmental exposure, research population, study design, and major findings related to cancer risk. We gathered this data to discover common patterns, new trends, and gaps in the existing research. In cases where many research addressed similar exposures, we analyzed their results to establish consistency and strength of evidence. This review procedure also comprised a rigorous evaluation of the methodological quality of the included studies, evaluating aspects such as sample size, exposure assessment, and control for confounding variables. This allowed us to highlight the most credible findings and note potential limitations in the present corpus of research. Through this rigorous process, our evaluation intends to provide a thorough and fair assessment of the link between environmental exposures and cancer risk, with an emphasis on guiding future research and policy development.

3. Types of Environmental Exposures

3.1. Air pollutants

Air pollution is a major environmental issue that has been linked to several detrimental health implications, including several types of cancer. Although there are various kinds of air pollution, they can be broadly classified as natural or anthropogenic (caused by humans). Power plants, vehicle exhaust, industrial emissions, home heating systems, and agricultural activities are the primary human-caused sources of pollution. These activities result in the atmospheric discharge of several hazardous pollutants, including PM, nitrogen oxides (NOx), sulfur dioxide (SO_2), carbon monoxide, and volatile organic compounds (VOCs). Natural sources of air pollution include dust storms, volcanic eruptions, and wildfires; however, they occur less frequently [11].

PM is one of the most hazardous forms of air pollution because small particles (PM2.5 and PM10) have the ability to penetrate deeply into the respiratory system and reach the bloodstream (Figure 2) [12]. Black carbon, heavy metals, organic molecules, and other inorganic and organic components are often intricately mixed together to form these particles. Epidemiological studies have frequently demonstrated a significant correlation between long-term exposure to fine PM and an increased risk of lung cancer [13]. Furthermore, recent studies suggest that PM exposure may possibly contribute to the development of several cancers, including bladder and breast cancer, through mechanisms involving oxidative stress, DNA damage, and inflammation. One important class of air pollutants is NOx, which are mostly produced by vehicles and industry. NOx molecules, which include NO2 and nitric oxide (NO), can result in the development of ground-level ozone and secondary PM, both of which are harmful to human health. Lung cancer risk has been linked to long-term exposure to elevated NO2 concentrations [14]. Furthermore, NOx can exacerbate respiratory conditions and reduce the lung's ability to expel other carcinogens, which raises the risk of cancer.

A wide class of organic substances that readily evaporate into the atmosphere is known as VOCs. VOCs can be found in automobile emissions, industrial operations, paint and solvent use, and tobacco smoke. Benzene is one of the VOCs with the most well-established cancer-causing characteristics. There is no doubt that exposure to Benzene increases the incidence of leukemia, especially acute myeloid leukemia (AML). Reactive oxygen species (ROS) production, DNA damage, and bone marrow suppression are the processes via which benzene causes cancer. Another major air pollutant is SO_2, which is mostly created by burning fossil fuels and industrial operations [15]. Fine sulfate particles, which are produced when SO_2 interacts in the atmosphere, are the source of PM pollution. Even while the precise link between SO_2 exposure and cancer is less clear than it is for other pollutants, long-term exposure to high SO_2 levels may increase the risk of lung cancer through inflammatory pathways and respiratory tract irritation [16].

3.2. Water contaminants

The contamination of water is an urgent environmental problem that has serious effects on public health, including the prevalence of several types of cancer. Both natural processes and human activity can contaminate water supplies, resulting in the presence of dangerous compounds that provide major health hazards. Heavy metals, industrial chemicals, pesticides used on agriculture, and naturally occurring elements like arsenic and radon are among the common contaminants found in water. Numerous channels, such as agricultural runoff, industrial discharges, inappropriate waste disposal, and leaching from natural deposits, allow these pollutants to get into water supplies [17].

Studies have connected heavy metal contaminants like lead, cadmium, mercury, and arsenic that are present in water to cancer. In particular, the potent carcinogen arsenic is found naturally in groundwater in many places of the world. Long-term exposure to drinking water tainted with arsenic has been strongly linked to an increased risk of cancers of the skin, lungs, bladder, and kidney (Figure 3) [18]. Three factors contribute to arsenic-induced carcinogenesis: DNA damage, oxidative stress, and disruption of cellular signaling networks. In contrast, exposure to cadmium through contaminated water has been associated with prostate and kidney cancers, while exposure to lead has been linked to an increased risk of numerous cancers, including stomach, lung, and bladder cancer [19].

Common contaminants found in water include industrial chemicals such as trichloroethylene (TCE), polychlorinated biphenyls (PCBs), and different solvents. PCBs can linger in the environment and damage water systems. They were formerly widely utilized in electrical equipment and other industrial applications. Epidemiological studies indicate that exposure to PCBs is associated with an increased incidence of liver, breast, and melanoma cancer. TCE is a solvent that is used in industrial cleaning and degreasing; non-Hodgkin lymphoma, liver, and kidney cancer have all been related to it. By entering the body through the consumption of tainted water, these chemicals can cause reactive intermediates that can damage DNA and interfere with cellular functions, ultimately resulting in cancer [20]. Agricultural pesticides are a significant type of water contamination that may cause cancer. Hazards to human health can arise from pesticides that seep into surface and groundwater, including atrazine, glyphosate, and organochlorines. A common herbicide, atrazine, has been connected to a higher risk of prostate and breast cancer. The carcinogenicity of glyphosate, a chemical widely used in agriculture, has been an issue of research. A connection between glyphosate and non-Hodgkin lymphoma has been suggested by certain research. Three main pathways that pesticides use to cause cancer are immune system regulation, oxidative stress, and endocrine disruption [21].

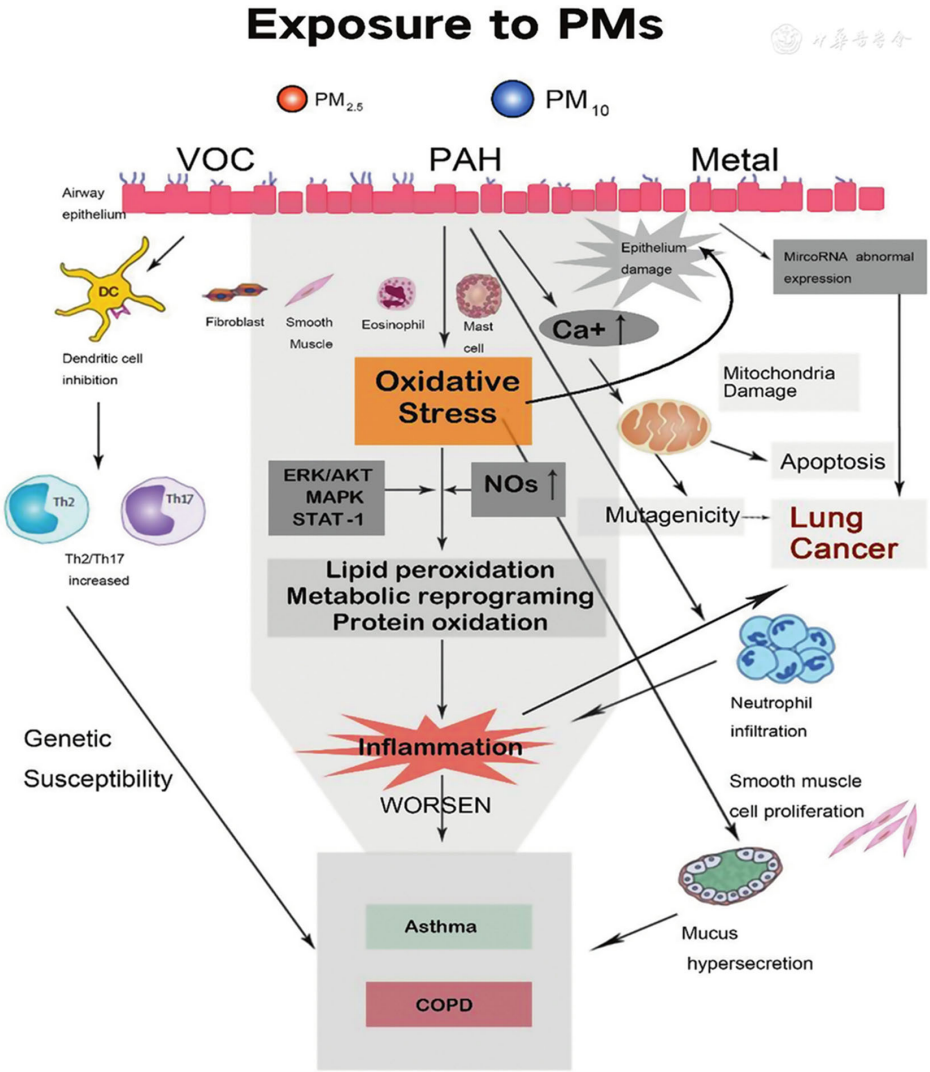

Figure 2. Basic mechanism of exposure to PM2.5 impairs the human respiratory system
Note: PM: particulate matter; VOC: volatile organic compounds; PAH: polycyclic aromatic hydrocarbon; ERK: extracellular regulated protein kinases; MAPK: mitogen-activated protein kinase; STAT-1: signal transducers and activators of transcription-1; COPD: chronic obstructive pulmonary disease.

Additionally harmful is drinking water contaminated by radon and fluoride, two naturally occurring contaminants. Radon, a radioactive gas that may dissolve in water and is inhaled when contaminated water is used for cooking or washing, is a well-known risk factor for lung cancer. Fluoride has been connected to bone cancer (osteosarcoma) in several studies; however, the data are still conflicting. Fluoride is good for dental health in tiny doses, but hazardous in large levels. In summary, a variety of compounds can considerably raise the risk of cancer in water, which is why they are referred to as pollutants [22]. The carcinogenic load of contaminated water is exacerbated by heavy metals, industrial chemicals, agricultural pesticides, and naturally occurring elements like arsenic and radon. These pollutants cause cancer through a variety of routes, including oxidative stress, endocrine disruption, and DNA damage (Table 1). Comprehending the origins and consequences of water pollutants is essential for formulating efficacious rules on water quality and public health initiatives aimed at reducing the risk of cancer linked to exposure to water [23].

3.3. Occupational hazards (industrial and agricultural exposures cancer prevalence in workers)

The incidence of cancer among laborers in both agricultural and industrial settings is significantly influenced by environmental factors. Workers in industrial settings are frequently exposed to a wide range of carcinogenic compounds, including formaldehyde, asbestos, benzene, and heavy metals like chromium and cadmium. Mesothelioma is a rare but fatal cancer that affects the lining of the heart, abdomen, or lungs. It was once often used for its insulating properties, but it is now understood that asbestos is the cause of the illness. Inhaling asbestos fibers over an extended period also raises the risk of lung cancer. A solvent that is widely used in industrial operations, Benzene, has been directly associated with hematologic cancers, especially AML. The use of formaldehyde as a preservative and in the production of resins has been linked to leukemia and nasopharyngeal cancer, underscoring the serious hazards involved with long-term work-related exposure to these substances [24].

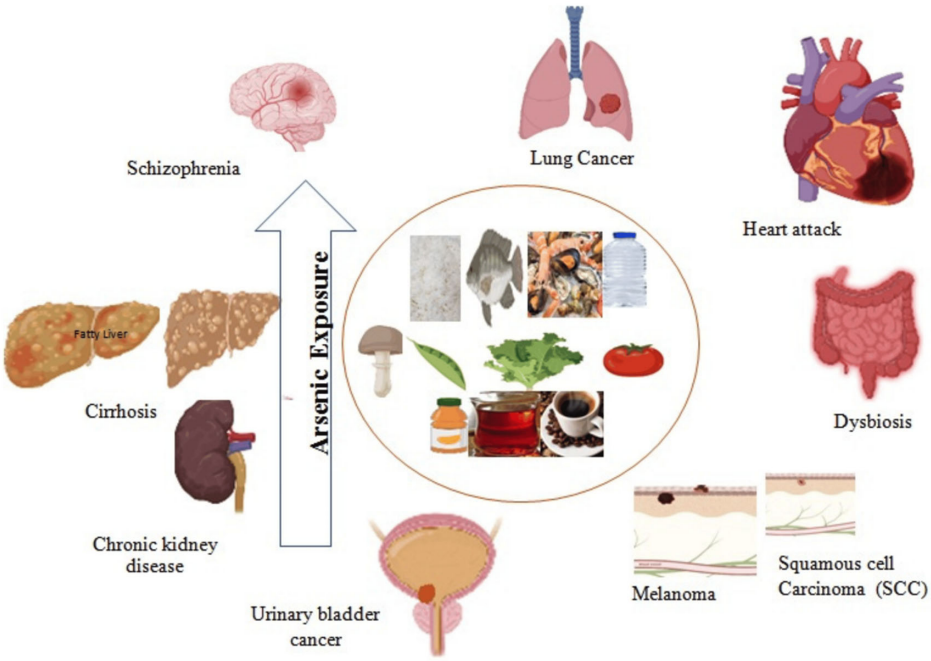

Figure 3. Exposure to arsenic induces both acute and chronic side effects, including dysbiosis, cirrhosis, schizophrenia, fatty liver, chronic renal disease, cardiovascular disease, and various cancers

Table 1. Carcinogenic pollutants in contaminated water

Pollutant type	Examples	Sources	Routes to cancer
Heavy Metals	Lead, Mercury, and Cadmium	Industrial discharge, mining, and agricultural runoff	Oxidative stress and DNA damage
Industrial Chemicals	Benzene and Dioxins	Manufacturing processes, waste disposal, and spills	Endocrine disruption and DNA damage
Agricultural Pesticides	Atrazine and Glyphosate	Agricultural runoff and pesticide application	Endocrine disruption and oxidative stress
Naturally Occurring Elements	Arsenic and Radon	Geological formations and groundwater contamination	DNA damage and oxidative stress

In addition to chemical exposures, industrial workers may also be subjected to physical agents such as ionizing radiation and electromagnetic fields. Ionizing radiation can directly damage DNA and induce a variety of diseases, including leukemia, thyroid cancer, and breast cancer. It is utilized in nuclear power plants, medical imaging, and some manufacturing operations. Even while the connection between electromagnetic fields and cancer is less clear-cut, study on the topic is still underway, particularly in relation to possible links with brain tumors [25]. Contrarily, the main exposures for agricultural laborers are to pesticides, herbicides, and other agrochemicals, which have been connected to a higher risk of developing a number of cancers. Carcinogenic pesticides include carbamates, organochlorines, and organophosphates. For instance, organophosphates have been connected to leukemia and non-Hodgkin lymphoma, but exposure to organochlorines, such as DDT, has been connected to prostate and breast cancer (Table 2). These substances frequently cause endocrine disruption, oxidative stress, and genetic alterations as their modes of carcinogenesis [21].

Moreover, agricultural laborers are frequently exposed to ultraviolet (UV) radiation due to their prolonged outdoor employment, which increases their risk of acquiring melanoma and non-melanoma skin cancers. The combined effects of chemical exposure and UV radiation significantly raise the risk of cancer for these individuals. When compared to the general population, epidemiological studies have consistently demonstrated greater cancer prevalence among workers exposed to certain occupational hazards. For example, workers in shipyards and construction had greater rates of mesothelioma and lung cancer because of prior asbestos exposure [26]. Similarly, leukemia and lymphoma rates among chemical plant workers are higher and are linked to their exposure to solvents like benzene. Agricultural laborers additionally experience a higher incidence of skin cancer, non-Hodgkin lymphoma, and leukemia, highlighting the effects of UV light and pesticide exposure [27]. The chances of cancer linked to occupational exposures can be significantly decreased by taking preventive measures. These include tightening laws governing the use of drugs known to cause cancer, enhancing workplace safety procedures, and offering workers protective gear and routine health examinations. Furthermore, encouraging knowledge and awareness of workplace dangers might enable employees to actively reduce their exposure [3].

Table 2. Carcinogenic pesticides and their health impacts

Pesticide class	Examples	Associated cancers	Modes of carcinogenesis
Carbamates	Carbaryl and Aldicarb	Various cancers (less specific associations)	Endocrine disruption, oxidative stress, and genetic alterations
Organochlorines	DDT ad Chlordane	Prostate cancer and breast cancer	Endocrine disruption, oxidative stress, and genetic alterations
Organophosphates	Malathion and Parathion	Leukemia and non-Hodgkin lymphoma	Endocrine disruption, oxidative stress, and genetic alterations

3.4. Lifestyle factors (diet, physical activity, and cancer risk)

The diet of an individual and level of activity are two major lifestyle factors that affect their risk of cancer. Dietary habits in particular have a substantial impact on the occurrence of cancer since different foods and dietary patterns have been linked to a higher or lower risk of developing specific malignancies. Diets high in red and processed meats have long been associated with an increased risk of colon cancer. These foods may be carcinogenic because they include carcinogens such as nitrites and nitrates, which are used to prepare meats, and heterocyclic amines and polycyclic aromatic hydrocarbons, which are created when food is cooked at a high temperature [28]. Conversely, diets rich in fruits, vegetables, whole grains, and legumes are associated with a decreased risk of several cancers, such as colon, breast, and stomach cancer. The high fiber, vitamin, mineral, and phytochemical content of these plant-based diets has immune-stimulating, antioxidant, and anti-inflammatory properties that may help ward off the onset of cancer. Alcohol use is another dietary factor that influences cancer risk. Alcohol consumption has been linked to an increased risk of cancer in the mouth, throat, esophagus, colon, and liver. Alcohol causes carcinogenesis through a number of mechanisms, including the conversion of ethanol to the recognized carcinogen acetaldehyde and the generation of ROS, which can damage DNA and other cellular components. Additionally, alcohol may impede the body's ability to absorb and utilize vital nutrients, increasing the risk of cancer [29].

Exercise has a correspondingly large impact on the risk of cancer. Regular exercise has been shown to reduce the risk of several cancer types, including endometrial, prostate, colon, and breast cancers. Engaging in physical activity has numerous preventive advantages. Workout helps control hormone levels, including insulin and estrogen, which when elevated can hasten the development and spread of cancer [30]. Physical activity reduces the incidence of cancer in addition to reducing inflammation, enhancing immune response, and helping to maintain a healthy body weight. Conversely, obesity is a recognized risk factor for certain malignancies, such as colon, renal, pancreatic, endometrial, and breast cancers. The creation of sex hormones and adipokines, as well as chronic inflammation and insulin resistance, are some of the processes via which obesity increases the risk of cancer by promoting cell proliferation and inhibiting apoptosis. Therefore, in order to prevent cancer, it is imperative to maintain a healthy body weight through a balanced diet and regular exercise [31].

In addition, dietary habits and physical exercise can combine with genetic predispositions to modify the risk of cancer. People who have a family history of specific cancers can be especially vulnerable to the cancer-causing consequences of an unhealthy diet and inactivity. Consequently, people who are more genetically predisposed should emphasize the importance of leading a healthy lifestyle. In summary, dietary practices and physical activity levels significantly influence cancer risk. The risk of many cancers is increased by alcohol consumption and diets high in processed and red meats and low in fruits and vegetables [32]. On the other hand, plant-based diets offer defensive advantages. Frequent exercise lowers the risk of cancer by affecting immune system performance, hormone modulation, and maintenance of body weight. It is crucial to address these lifestyle variables through individual behavior modification and public health activities in order to effectively prevent cancer and promote overall health [24].

4. Mechanisms of Carcinogenesis

4.1. Oxidative stress and DNA damage

Carcinogenesis is the process by which healthy cells transform into malignant ones; it is mostly brought on by oxidative stress and damage to DNA. Oxidative stress results from an imbalance between the body's ability to detoxify or repair the damage caused by ROS and their creation. ROS are naturally occurring byproducts of cellular metabolism, particularly in the mitochondria. They include non-radical species such as hydrogen peroxide and free radicals such as superoxide anion ($O_2^{\bullet-}$) and hydroxyl radical ($^{\bullet}OH$). Little amounts of ROS are required for cell communication and homeostasis, but excessive ROS levels can cause major damage to proteins, lipids, and nucleic acids, among other components of cells. The damage that ROS induce to DNA is a critical step in the genesis of cancer [33]. ROS's interaction with DNA bases and the sugar-phosphate backbone can cause a variety of DNA infections, such as base changes, single- and double-strand breaks, and cross-linking. The creation of 8-oxo-2'-deoxyguanosine (8-oxo-dG) is one of the most common types of oxidative DNA damage. If left unrepaired, this damage can result in GC to TA transversions during DNA replication. This mutagenic lesion, which is frequently found in malignant tissues, is a sign of oxidative stress. The aggregation of these mutations accelerates the development of malignancy by activating oncogenes or inactivating tumor suppressor genes [34].

In order to repair damaged DNA and lessen the consequences of oxidative stress, the cell has created a variety of defense mechanisms. Antioxidant enzymes such as glutathione peroxidase, catalase, and superoxide dismutase neutralize ROS, while DNA repair pathways like nucleotide excision repair and base excision repair (BER) rectify oxidative DNA damages. However, oxidative damage builds up and increases the risk of carcinogenesis and genomic instability when these defense systems are overworked or compromised. Defects in crucial DNA repair proteins, such as

those implicated in BER, have been linked to an increased risk of multiple cancer types, underscoring the importance of these processes in maintaining the integrity of the genome [35]. Chronic inflammation is another environment where oxidative stress fosters the growth of cancer. Inflammatory cells, such as neutrophils and macrophages, release a lot of ROS and reactive nitrogen species (RNS) as part of the immune response. Although these reactive species are meant to eliminate pathogens, they can also harm nearby tissues, including DNA. The pro-inflammatory cytokines that encourage cell division and survival in combination with this ongoing DNA damage foster an environment that is favorable to the formation of cancer. Chronic inflammatory conditions like hepatitis, ulcerative colitis, and Helicobacter pylori infection have been shown to raise the risk of cancer, demonstrating the interaction between oxidative stress, inflammation, and carcinogenesis [36].

Additionally, environmental variables such as exposure to ionizing radiation, UV light, and certain chemicals can aggravate oxidative stress and DNA damage (Figure 4) [37]. For example, ionizing radiation generates ROS by radiolysis of water, resulting in severe DNA damage that, if not appropriately repaired, results in mutations and cancer. UV radiation mostly causes cyclobutane pyrimidine dimers to form, but it can also produce ROS, which increases the load of mutagenicity [38].

4.2. Epigenetic modifications

Epigenetic modifications, which are heritable differences in gene expression without altering the underlying DNA sequence, have a substantial impact on the processes of carcinogenesis. Histone modifications, DNA methylation, and non-coding RNA-associated gene silence are some of these changes that help regulate gene activity. Oncogenes and tumor suppressor genes are both silenced or activated by aberrant epigenetic modifications that contribute to the onset and progression of cancer [38]. One thoroughly investigated epigenetic alteration is DNA methylation, which involves the insertion of a methyl group to the cytosine ring's fifth carbon. DNA methylation patterns are tightly controlled in normal cells, helping to preserve genomic stability and control gene expression. These patterns, however, become dysregulated in cancer cells. Oncogenes and genomic instability can result from hypomethylation, whereas tumor suppressor genes can be silenced by hypermethylation of CpG islands in promoter regions. For example, it has been demonstrated that the promoter region of the p16INK4a gene, a crucial tumor suppressor involved in cell cycle regulation, is hypermethylated in a range of cancers, including those of the breast, lung, and colorectal areas. Because of this epigenetic silencing, p16INK4a cannot be transcribed, which promotes unchecked cell growth [39].

Histone changes that affect chromatin structure and the regulation of gene expression include acetylation, methylation, phosphorylation, and ubiquitination. Depending on the precise modification and where it is located, these post-translational modifications on histone tails can either stimulate or repress transcription. Histone acetyltransferases (HATs) mediate histone acetylation, which is typically linked to transcriptional activation, whereas histone deacetylases (HDACs) eliminate it. The equilibrium between HAT and HDAC activity may be upset in cancer, which can result in abnormal expression of genes essential for cell division and survival [40]. For example, the inhibition of tumor suppressor genes and the promotion of oncogenesis have been linked to the overexpression of HDACs. In an attempt to recover normal acetylation levels and activate dormant tumor suppressor genes, HDAC inhibitors are being studied as possible therapeutic agents in the treatment of cancer [40].

Non-coding RNAs, or ncRNAs, have become an increasingly important part as regulators of epigenetic modifications and gene expression. This is especially the case for microRNAs (miRNAs) and long non-coding RNAs (lncRNAs). Short, non-coding RNA molecules called miRNAs have the ability to attach to messenger RNA (mRNA) complementary regions and cause translational suppression or mRNA destruction. Cancer frequently exhibits dysregulation of miRNAs, which can act as tumor suppressors or oncogenes. For instance, miR-21 targets several tumor suppressor genes to promote tumor development and metastasis, and it is commonly overexpressed in a variety of malignancies. Non-coding RNAs (lncRNAs) are longer transcripts that can influence the expression of particular genes by interacting with chromatin-modifying enzymes. For instance, it is known that the lncRNA HOTAIR targets specific genomic sites for recruitment of polycomb repressive complex 2, which causes histone H3 lysine 27 methylation and gene silencing, both of which promote the progression of cancer.

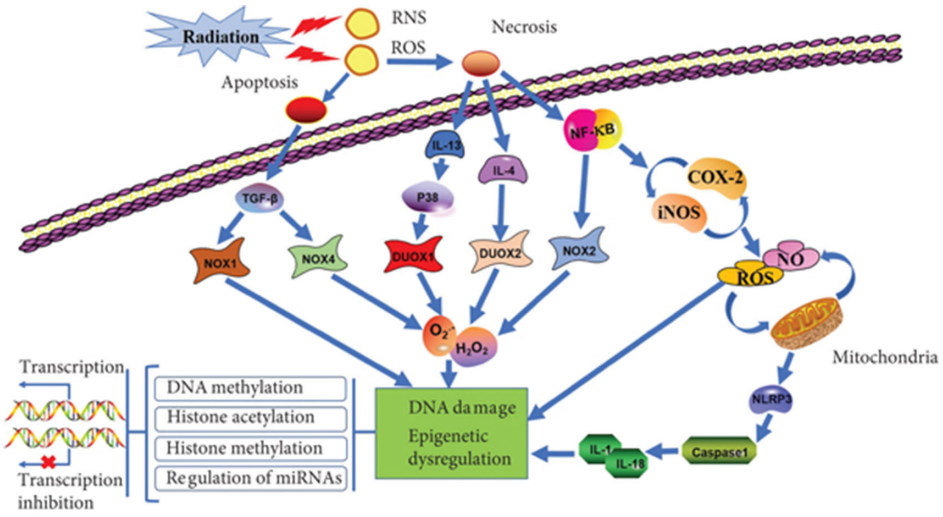

Figure 4. The processes of inflammatory response, epigenetic regulation, and redox system activation after radiation exposure

The environment of gene regulation in cancer can become even more complex due to the interaction between several forms of epigenetic alterations. For instance, repressive chromatin states can be created and maintained by the interaction of histone changes with DNA methylation, strengthening the silencing effect of tumor suppressor genes. Chromatin remodeling complexes are important in nucleosome repositioning, and their dysregulation can also be linked to anomalies in gene expression profiles in cancer. Epigenetic modifications—which affect gene expression without changing the DNA sequence—are essential to the mechanisms underlying cancer [41]. Tumor suppressor genes can become silent and oncogenes can become activated when normal gene regulation is disrupted by aberrant DNA methylation, histone changes, and non-coding RNA activity. Understanding these mechanisms reveals prospective targets for therapeutic intervention and sheds light on the genesis of cancer. Novel cancer treatments that can reverse aberrant epigenetic states and restore normal cellular activity may be developed thanks to advancements in epigenetic therapeutics, such as DNMT inhibitors and HDAC inhibitors [42].

4.3. Inflammatory pathways

The mechanisms of carcinogenesis mostly depend on inflammatory pathways, which establish a connection between chronic inflammation and the onset and spread of cancer. Chronic inflammation is a condition marked by an ongoing immunological response that can be brought on by autoimmune illnesses, infections, or prolonged exposure to irritants. This ongoing inflammatory state fosters the growth of cancer by producing a microenvironment that is favorable to cellular change, proliferation, and survival [43].

The persistent inflammation at the molecular level causes immune cells, such as macrophages, neutrophils, and T cells, to continuously release pro-inflammatory cytokines, chemokines, and growth factors. These signaling molecules activate key transcription factors, such as nuclear factor-kappa B (NF-κB) and signal transducer and activator of transcription 3 (STAT3). As a mediator in the process of inflammation-induced carcinogenesis, NF-κB is essential. When NF-κB is activated, it moves to the nucleus and starts to produce genes related to angiogenesis, metastasis, cell proliferation, and survival. Therefore, by allowing malignant cells to evade apoptosis and continue growing unchecked, continuous NF-κB activation promotes a pro-tumorigenic environment [44].

ROS and reactive nitrogen species (RNS), which are also produced during inflammation, have the direct ability to harm lipids, proteins, and DNA. Carcinogenesis is driven by chromosomal instability, epigenetic changes, and genetic mutations brought on by the oxidative and nitrosative stress that follows. For example, NO, which is produced by inflammatory cells like macrophages, can combine with superoxide to make peroxynitrite, a strong mutagen that causes base changes and breaks in DNA strands. These genetic insults have the ability to inactivate tumor suppressor genes or activate oncogenes, which makes it easier for normal cells to develop into malignant ones [45].

Chronic inflammation generates an environment conducive to malignant transformation and disrupts tissue homeostasis. Prostaglandins, IL-6, and tumor necrosis factor-alpha are a few examples of inflammatory mediators that stimulate cell division and inhibit apoptosis. For example, IL-6 stimulates the Janus kinase/STAT3 pathway, resulting in the production of genes that support the survival and growth of cells. Numerous malignancies, such as hepatocellular carcinoma and colorectal cancer, have been shown to overexpress IL-6 and have persistently activated STAT3, which emphasizes their involvement in connecting inflammation and carcinogenesis [43].

Angiogenesis and metastasis are facilitated by chronic inflammation, which modifies the tumor microenvironment. One of the pro-inflammatory cytokines, vascular endothelial growth factor, encourages the formation of new blood vessels as long as the growing tumor has enough oxygen and nutrients. Furthermore, inflammatory cells' production of matrix metalloproteinases breaks down the extracellular matrix, which promotes tumor invasion and metastasis. Chemokines such as CCL2 and CXCL12 also draw immune cells to the tumor site, where they provide cancer cells survival signals, which can ironically promote tumor development and dissemination. The relationship between persistent inflammation and cancer is exemplified by certain illnesses [46]. For example, Helicobacter pylori infections in the stomach can lead to chronic gastritis, which increases the risk of gastric cancer by causing the stomach to continuously create ROS and inflammatory mediators that damage the stomach epithelium. In a similar vein, the hepatitis B and C viruses cause chronic hepatitis, which increases the risk of hepatocellular carcinoma in people by causing persistent liver inflammation and cirrhosis [47].

5. Regulatory and Public Health Implications

5.1. Current regulatory policies

The regulations that govern a variety of organizations, such as food safety, pharmaceuticals, environmental protection, and healthcare delivery, greatly influence how public health is shaped and how regulatory issues are handled. These regulations provide the foundation for guaranteeing the efficacy, safety, and caliber of goods and services while also defending the interests of the general public's health. However, in order to effectively address new challenges and ensure optimal public health outcomes, regulatory frameworks must constantly adapt and refine them in response to globalization, emerging health threats, technological advancements, and changing societal needs [48].

Food safety regulatory authorities, like the Food and Drug Administration (FDA) in the US and the European Food Safety Authority in Europe, are in charge of creating and implementing laws to ensure the security of food products consumed by the general public. Aspects of the food supply chain that are covered by these regulations include food production, processing, labeling, and distribution. In order to handle new food-borne dangers, stop food fraud, and improve transparency and traceability across the supply chain, regulatory regulations need to be tightened and harmonized in light of the globalization of food trade and the growing complexity of food supply chains. In order to optimize the impact on public health, regulatory agencies are also using risk-based techniques more frequently to prioritize resources and initiatives. These approaches center on high-risk foods and toxins [49].

Regulations in the field of environmental protection are designed to lessen the negative impacts that pollution, chemical exposure, and climate change have on ecosystems and public health. To regulate pollutant emissions, handle hazardous materials, and protect natural resources, agencies such as the Environmental Protection Agency in the US and the European Environment Agency in Europe set rules and regulations. Regulatory policies are changing to include concepts of sustainability, circular economy, and ecosystem-based approaches to solve interconnected environmental and health difficulties as worries over air and water quality, biodiversity loss, and climate change grow. In addition, regulatory bodies are working more

closely with the public health and environmental sectors—as well as with industry, academia, and the healthcare sector—to promote cross-sectoral alliances and pool resources and knowledge [50].

Regulations play a crucial role in the pharmaceutical and healthcare industries in guaranteeing the security, effectiveness, and caliber of medical supplies and services. The European Medicines Agency, the World Health Organization (WHO), the FDA, and other regulatory bodies assess and approve drugs, vaccines, medical devices, and biologics for market authorization. These organizations evaluate clinical trial data, manufacturing procedures, and post-marketing surveillance thoroughly in order to determine the benefit-risk profile of medical products and to decide on regulations based on solid evidence [51]. For integrating cutting-edge treatment techniques like gene therapies, cell-based therapies, and personalized medicine while upholding strict standards for patient safety and product quality, regulatory rules must be flexible and adaptive due to the quick speed of scientific innovation.

5.2. Public health initiatives

Through focused interventions and policies, public health initiatives are essential in addressing societal health issues and advancing population well-being. These programs cover a broad spectrum of approaches to illness prevention, healthy behavior promotion, and better access to healthcare services. They have important ramifications for public health and regulations in a number of areas. Public health programs, such as immunization campaigns and tobacco control measures, have a significant impact on regulatory practices and public health results [52].

One important area where public health initiatives have regulatory implications is disease prevention and management. As an illustration, immunization efforts have a significant role in preventing infectious diseases as well as reducing the burden they place on public health systems. Regulatory agencies such as the WHO and the US Centers for Disease Control and Prevention are crucial in evaluating and approving vaccines for safety and efficacy, in addition to enforcing vaccination laws and regulations. These programs reduce the overall transmission and incidence of infectious diseases within communities by promoting herd immunity and shielding individuals from infections that can be prevented by vaccination [53].

Additionally important to preventing chronic diseases like diabetes, obesity, and cardiovascular disease is the promotion of healthy behaviors and lifestyles through public health efforts. For example, tobacco use reduction regulations have been crucial in lowering smoking rates and the incidence of disorders linked to tobacco use. Tobacco taxes, smoke-free laws, and prominent warning warnings on cigarette packaging are a few examples of measures that work well to discourage new smokers and promote quitting. Initiatives that support physical exercise and a healthy diet, like built environment interventions and nutrition education programs, also have regulatory ramifications for marketing laws, food labeling, and urban planning guidelines. By reducing the burden of chronic diseases on public health systems, these initiatives help to create environments that encourage healthy choices [54].

Furthermore, public health initiatives are essential for reducing healthcare inequalities and advancing health equity among diverse populations. Improving access to healthcare services through legislative initiatives, such as the US Affordable Care Act and Medicaid expansion, has a significant impact on improving health outcomes and reducing disparities for disadvantaged populations. Initiatives that address the social determinants of health, such as housing, education, and work, may have an impact on policies related to social welfare, economic development, and social justice. By addressing the root causes of health inequalities and inequities, these initiatives contribute to the creation of more equitable and inclusive societies where everyone has the opportunity to realize their full potential in terms of health [55].

5.3. Recommendations for policy improvement

To ensure that interventions are effective, promote positive health outcomes for a variety of populations, and address regulatory and public health concerns, recommendations for policy change are crucial. With important ramifications for regulatory practices and public health outcomes, these proposals cover a variety of tactics targeted at improving public health programs, fortifying regulatory frameworks, and tackling new health concerns [56]. To begin with, in order to fully address complex health concerns, there is a need for increased collaboration and coordination among regulatory agencies, healthcare providers, legislators, and other stakeholders. Policymakers can create more comprehensive approaches to regulatory decision-making and public health programming by establishing partnerships and utilizing group knowledge and resources. This will guarantee that interventions are supported by research, sensitive to cultural differences, and adapted to the needs of a variety of populations [57].

Second, regulatory rules that place a higher priority on health promotion and prevention than on reactionary treatments are required. Investing in preventative measures can have significant long-term benefits in terms of lowering healthcare costs, improving population health outcomes, and boosting general well-being. Examples of these projects include vaccination programs, tobacco control campaigns, and chronic disease prevention initiatives. Through public-private partnerships, financing sources, and policy incentives, regulatory regimes should encourage and support preventive initiatives [58]. Thirdly, in order to lessen gaps and advance health equity among varied groups, regulatory policies should give priority to health equity and address social determinants of health. This entails putting laws into place that deal with systemic obstacles to health equity, enhance access to healthcare services, and address socio-economic disparities. Principles of equality, diversity, and inclusion should also be incorporated into regulatory frameworks' decision-making procedures to guarantee that all members of society—especially the underprivileged and marginalized—benefit from policies and interventions [59].

Moreover, regulatory regulations must be flexible and sensitive to new risks to public health, developments in technology, and changes in the demands of society. In order to handle new public health concerns, policymakers should create adaptable regulatory frameworks that can be swiftly adjusted to changing conditions, foresee difficulties down the road, and encourage innovation. To expedite decision-making and the implementation of effective actions, this may include establishing mechanisms for quick response, data sharing, and cross-sector collaboration [60]. Transparency, accountability, and stakeholder involvement should also be given top priority in regulatory policies in order to boost public confidence in the regulatory system. Integrating community members, advocacy groups, and industry representatives into the policymaking process enables policymakers to guarantee that regulatory decisions are based on a range of viewpoints, accurately represent the interests and concerns of impacted communities, and are viewed as just and lawful [61].

6. Future Research Directions

The findings of our studies on the relationship between environmental exposures and cancer risk have important

implications for public health and environmental management policies. Our research highlights the importance of implementing stronger restrictions on pollutants and chemicals that are known to cause cancer, by determining the crucial environmental elements that lead to the development of cancer. Policymakers can utilize this information to design or enhance regulations that restrict exposure to these deleterious compounds in both occupational and public environments. Furthermore, our findings could provide valuable insights for the creation of public health initiatives focused on increasing knowledge about environmental risks while promoting behaviors that minimize exposure. To further research, it is necessary to investigate the complex interactions between genetic predisposition and environmental influences in the progression of cancer. Conducting research on the impact of diverse exposures on cancer development in different groups, including individuals with genetic predispositions, is essential for the development of individualized preventative measures. Also, it is important for research to prioritize the identification of biomarkers that indicate exposure and early-stage cancer. This strategy has the potential to enhance detection techniques and enable more precise therapies. It is crucial to broaden research efforts to encompass emerging environmental hazards, such as microplastics and endocrine disruptors, to gain a comprehensive understanding of and effectively reduce potential cancer risks in the future. By focusing on these specific areas, future research can offer more comprehensive insights that can enhance policy and prevention initiatives.

Novel avenues for research and innovation in the fields of biomedical and public health are being explored by means of emerging fields of study. The development of precision medicine techniques, which try to customize medical care and preventative measures to individual features like genetic composition, environmental exposures, and lifestyle choices, is one such area. Precision medicine promises to improve patient outcomes, optimize therapeutic approaches, and reduce healthcare inequities by utilizing advancements in genetics, bioinformatics, and tailored diagnostics [62]. Future studies in this field might clarify the genetic and environmental factors that contribute to a person's vulnerability to a disease, create predictive models for risk assessment tailored to each individual, and examine the efficacy of targeted treatments across a range of populations. Further study on improving environmental health equality is necessary, especially in view of the mounting issues around environmental pollution, climate change, and social determinants of health. With an emphasis on correcting gaps in exposure to environmental risks and access to resources that promote health and well-being, environmental justice concepts emphasize the equitable distribution of environmental benefits and costs. Subsequent investigations should delve into inventive approaches to appraise and alleviate environmental health hazards in susceptible populations, advocating for environmental justice policies and measures, and reviewing how environmental rules affect health equity results.

Also, to advance environmental health equity research and turn findings into workable policies and practices, interdisciplinary approaches integrating environmental science, social epidemiology, and community participation will be crucial [63]. Also, cutting-edge approaches and technologies present fascinating chances to deepen our comprehension of intricate disease processes and create fresh approaches to enhance public health. Systems biology, AI, and digital health are a few fields that show promise in clarifying the fundamental causes of illness, finding biomarkers for early diagnosis and prognosis, and refining treatment plans via tailored treatments [64]. Future directions in research could include using wearable sensors and mobile health applications to monitor health outcomes in real-time, integrating multi-omics approaches to characterize the molecular basis of disease phenotypes, and leveraging big data analytics to uncover hidden patterns in health data. Researchers can pave the way for revolutionary advancements in environmental health equity and precision medicine by embracing interdisciplinary collaboration and innovation. This will ultimately advance the objective of improving health outcomes and reducing health disparities for all populations [65].

7. Conclusion

To sum up, this comprehensive review has clarified the complex relationship between environmental exposures and cancer risk by combining data from a variety of research and highlighting the main mechanisms behind carcinogenesis. We have looked at prevalent toxins, their sources in the environment, and the cancer risks they pose Our results highlight how important it is to understand these exposures and reduce them to reduce the global cancer burden. We have also looked at how biological processes like oxidative stress, DNA damage, epigenetic changes, and inflammatory pathways, as well as lifestyle choices and occupational risks, mediate the carcinogenic consequences of environmental exposures. Our study highlights the critical need for multidisciplinary research projects that clarify the relationships between environmental exposures and the development of cancer and pinpoint populations that are more vulnerable. Researchers can contribute to the creation of focused therapies and public health policies aimed at lowering the incidence of cancer and improving health outcomes by clarifying the intricate interactions between biological pathways and environmental variables. Furthermore, our results highlight the need of maintaining a preventive stance against cancer by limiting exposure to carcinogens and encouraging healthy living and environmental sustainability.

Our study highlights the critical need for multidisciplinary research projects that clarify the relationships between environmental exposures and the development of cancer and pinpoint populations that are more vulnerable. Researchers can contribute to the creation of focused therapies and public health policies aimed at lowering the incidence of cancer and improving health outcomes by clarifying the intricate interactions between biological pathways and environmental variables. Furthermore, our results highlight the need of maintaining a preventive stance against cancer by limiting exposure to carcinogens and encouraging healthy living and environmental sustainability.

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Ethical Statement

This study does not contain any studies with human or animal subjects performed by any of the authors.

Conflicts of Interest

The authors declare that they have no conflicts of interest to this work.

Data Availability Statement

The data that support this work are available upon reasonable request to the corresponding author.

Author Contribution Statement

Rufus Oluwagbemileke Ajayi: Conceptualization, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization. **Taiwo Temitope Ogunjobi:** Methodology, Formal analysis, Resources, Data curation, Writing – original draft, Writing – review & editing, Supervision.

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