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Review

Epidemiology, Risk Factors, And Public Awareness Of Cancer: A Comprehensive Review

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Abstract

Cancer remains one of the leading causes of morbidity and mortality worldwide, with a growing burden projected in both developed and developing countries. This comprehensive review explores the epidemiology of cancer, examining global incidence, prevalence, mortality trends, and disparities across regions, age groups, and socioeconomic strata. Key risk factors contributing to cancer development including genetic predisposition, lifestyle behaviors (such as tobacco use, alcohol consumption, poor diet, and physical inactivity), environmental exposures, and infections are analyzed in depth. Special attention is given to modifiable risk factors and the role of early detection and prevention in reducing cancer-related deaths. Furthermore, the review assesses public awareness and understanding of cancer, identifying gaps in knowledge, attitudes, and practices that hinder effective prevention and timely diagnosis. It highlights the importance of educational campaigns, screening programs, and policy interventions in promoting awareness and behavioral change. By synthesizing current evidence, the review underscores the need for a multidisciplinary approach to cancer control that integrates epidemiological data, risk factor mitigation, and enhanced public engagement to reduce the global cancer burden.

Keywords: Cancer epidemiology, Global cancer burden, Cancer incidence prevalence, Cancer mortality trends, Cancer disparities.

INTRODUCTION

Cancer burden has been increasing worldwide. In India, one in nine people is likely to develop cancer in his/her lifetime. Lung and breast cancers were the leading sites of cancer in males and females, respectively. Among childhood (0-14 years) cancers, lymphoid leukaemia (boys: 29.2% and girls: 24.2%) was the leading site. The incidence of cancer cases is estimated to increase by 12.8 per cent in 2025 as compared to 2020. Thus, effective cancer prevention and control measures are urgently needed, as are improved technologies for early detection and treatment of cancer[1].

According to the Global Cancer Observatory (GLOBOCAN) estimates, there were 19.3 million incident cancer cases worldwide for the year 2020[1]. India ranked third after China and the United States of America. GLOBOCAN predicted that cancer cases in India would increase to 2.08 million, accounting for a rise of 57.5 per cent in 2040 from 2020[2].

Planning, monitoring, and evaluation of cancer control activities require recent statistics in any region. This is usually achieved through the Population-Based Cancer Registries (PBCRs). Cancer is not a nationally notable disease in India. Thus, the data collection from PBCRs involves active retrospective data abstraction, a laborious and complex process of analysis and reporting. Trained registry staff typically go to different resource centers (hospitals, vital statistics departments, and diagnostic laboratories) for collecting data on a standardized core form. This delays the process of real-time reporting and bringing out the most recent cancer statistics. Globally, there is usually a lag of 2-4 years between actual cancer registry data and the publication of results (*e.g.*, US cancer registry, GLOBOCAN[3,4]. Thus, providing estimates at periodic intervals is the best way to inform cancer prevention and control programmers. Hence, efforts to provide timely cancer estimates based on the recently available data for formulating appropriate cancer control measures are proposed[5,6].

The cancer generation is due to many factors, such as environmental influences, internal stress, and heredity[6–8]. The responsible factor varies from patient to patient and depends upon the type of cancer and geographical location[9]. The treatment needs are to be established adequately in each respective case. The change in environment (and climate) due to industrialization, along with living and food style, is considered one primary concerns for the increasing number of cancer incidences. However, a proper rational link still needs to be validated to establish any valid conclusive claim[10]. The affected organ of origin identifies the type of cells multiplying inadvertently. Increased prevalence in the different gender or populace has been observed with the occurrence of a particular kind of cancer. For example, breast cancer is most prevalent type of cancer in women worldwide, while lung and prostate cancers are the primary incidences in the male population. Lung cancer is the second major cancer in males and females when counted combined.

The socio-economic status of a specific region is a part of environmental factors that impacts the availability of medical facilities and more effective expensive drugs. Furthermore, improper use of pesticides, industrial waste disposal practices, and pollution control policies indirectly contribute to the quality of healthy living[11]. These factors directly account for a particular region's death and disease prevalence in a specific region. A glimpse reflects the relation of a disease with the socio-economic status of different parts of the world. The data reporting by different countries lags 2-4 years due to the time required for data collection, proper consolidation, and final reporting, along with varying delays in reporting death cases.

Herein, a trend analysis of the prevalence of cancer is presented based on the data recorded in different reviews and reporting sites and agencies. The review articles published recently were considered for extracting specific statistical data. The sites for international reporting agencies like the World Health Organization (WHO), International Agency for Research on Cancer (IARC), GLOBOCAN, American Cancer Society, and other countries' agencies were also used for the compilation of the statistics for this review discussion. Statistical analysis regarding the type of cancers, overall epidemiology as a relative inference from the data, and progress in therapeutics were included in the discussion. The main focus of this review is to generate an informed understanding via rational discussion from the data reported by different agencies and literature reports about the cancer incidences and deaths in the world and different regions and countries, along with the therapeutics development efforts.

Epidemiological Statistics [12]

Every country in the world has been burdened with the incidence of one or more types of cancer. The Global Cancer Observatory (GCO) (gco.iarc.fr) of the IARC records the global estimates of cancer incidences and deaths. The GLOBOCAN 2020 includes the data and interactive graphical visualization of datasets about cancer incidences and deaths from 185 countries in regional and sex-based data. The tabulation and graphical visualization of the GLOBOCAN data can be accessed via the Global Cancer Observatory (GCO).

Globally, an estimated 19.3 million incidences and 10 million deaths due to cancer were reported in GLOBOCAN 2020. Out of these total cases, the incidence of commonly diagnosed cancers worldwide was female breast (2.26 million cases, 11.7%), lung (2.21 million, 11.4%), and prostate cancers (1.41 million, 7.3%). The combined mortality due to cancer indicates the major causes of cancer death were lung (1.79 million deaths, 18% of total deaths due to cancer), liver (830,000, 8.3%), stomach (769,000, ~7.7%), and breast cancer (680,000, 6.9%).

In sex-disaggregated cancer incidences and deaths data, the most common cancers detected in men are lung (14.3%), prostate (14.1%), non-melanoma skin (7.2%), and stomach (7.1%) cancers, while in females the frequently diagnosed cancers are breast (24.5%), lung (8.4%), and cervix (6.5%) cancers

Mortality-wise, the most deaths in men occurred due to lung (21.5%), liver (10.4%), stomach (9.1%), and lethality in women was due to the breast (15.5%), lung (13.7%), and cervix (7.7%) cancers. The GLOBOCAN data with region-wise statistics indicate that Eastern Asia reported the most cases, 6.0 million (31.1% of the total),

with 3.6 million deaths (36.3%). North America reported 2.6 million cases (13.3%) with a 7% share of cancer deaths.

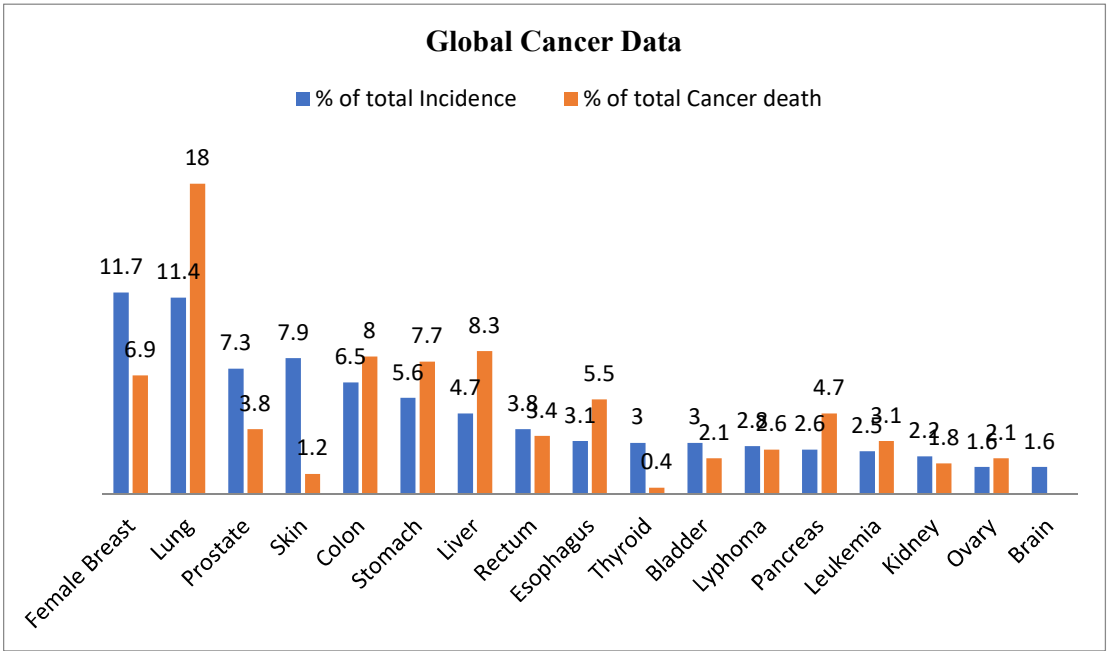

Fig 1: Representation of Global data of Incidence and Death % in India

Statistics Trend Projections[12–14]

Most agencies concerned with the cancer-related data reported analysis for the year 2024, at the time of the start of the COVID-19 pandemic. The emergence of the COVID-19 pandemic in early 2020 (from the first incidences in December 2019) has placed the world in a new order of lockdown nearly up to the end of 2021.The medical facilities and research units directed their resources towards the search for suitable and emergency medicine for COVID-19 treatment.

The medical staff got involved in controlling the infection. Furthermore, researchers potentiated efforts in developing viral medicines, 36–38 medical masks, sensors for detection, diagnostic kits, materials for surface neutralization from virus, and biologists oriented their efforts towards vaccine development.

In all these times, the other diseases received less attention, if not wholly ignored; hence, data reporting for cancer probably became a delayed objective of agencies. Keeping with the earlier trends reported in previous years, if projected for 2022, the data ratios can be considered with similar proportions as reported previously, assuming that the age-specific rate of cancer in 2022 would remain constant at the rates estimated in 2020.

However, the actual reflection depends upon final reports, including the impact of COVID-19 on statistics. The authors expect that the main variation would be in lung cancer cases, a major type of cancer incidence. During the lockdown period, the environmental factors, mainly the air quality, were changed.

Furthermore, COVID-19 mainly causes lung infections. Thus, the mortality due to lung cancer and COVID-19 might have been impacted considerably, and variance in data may be expected. The co-morbidity due to COVID-19 and other diseases has been observed during SARS-CoV-2 infection. The concerted data would provide an accurate reflection of incidences and mortality for the different types of cancers during and post-COVID-19 pandemic time.

Cancer

Cancer is characterized by uncontrolled cell growth and the acquisition of metastatic properties. In most cases, activation of oncogenes and/or deactivation of tumor suppressor genes leads to uncontrolled cell cycle progression and inactivation of apoptotic mechanisms. As opposed to benign tumors, malignant cancers acquire metastasis, which occurs in part due to the down-regulation of cell adhesion receptors necessary for tissue-specific cell–cell attachment, and up-regulation of receptors that enhance cell motility.

In addition, activation of membrane metalloproteases provides a physical pathway for metastatic cancer cells to spread. There are different mechanisms by which these genetic and cellular changes occur. The canonical mechanisms are mutation, chromosomal translocation or deletion, and dysregulated expression or activity of signaling pathways. These events may activate genes that promote dysregulated cell cycling and/or inactivate

apoptotic pathways. These processes are well described in the existing literature, and numerous excellent reviews are available on each topic[15].

The role of epigenetics in carcinogenesis is less well defined. Recent studies suggest that epigenetic alteration may be another hallmark of cancer due to its role in the generation of cancer progenitor cells and subsequent initiation of carcinogenesis. Such modifications are covalent, and may affect histones or DNA residues. We recently suggested a new paradigm for cancer progression in which epigenetic changes play a key role in the development of these clinically significant cell features. Epigenetic changes can induce pro-cancer characteristics in even mutation-free cells [17]

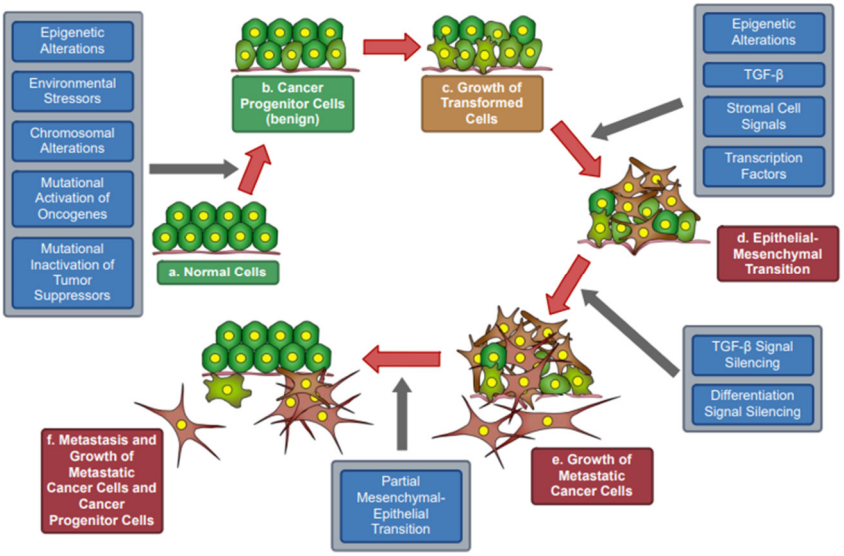

Fig 2: Cancer progenitor cells and progression of metastatic cancer[16]

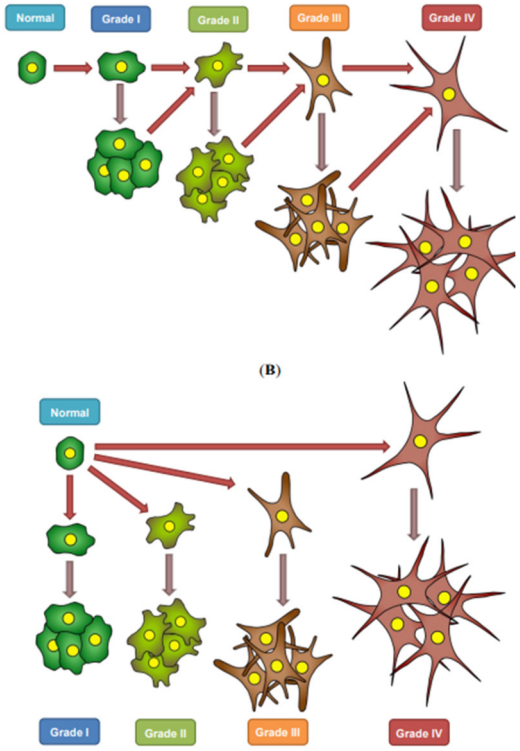

Fig 3: Model for the development of grade-specific cancers[16]

Types of Cancer

There are more than 100 kinds of cancer. It's not just 1 disease. Cancers are defined by the kind of cell they start in. Or they can be defined by the place in the body where they first started. Some cancers are of mixed types.

These are the most common categories of cancer that start in certain kinds of cells:

- **Carcinoma.** This is cancer that starts in cells that make up epithelial tissue. This tissue covers or lines the inside and outside surfaces of the body, like organs, glands, and the skin. Carcinoma usually forms a solid tumor. Carcinomas are the most common type of cancer. For instance, cancers that start in the lung, colon, breast, and prostate are most often carcinomas.
- **Sarcoma.** This is a cancer that starts in connective tissue cells. This includes blood and lymph vessels, cartilage, fat, muscle, tendon, and bone cells. For instance, osteosarcoma is the most common type of cancer that starts in the bone.
- **Lymphoma.** This cancer starts in a type of white blood cell called a lymphocyte. These cells are part of the immune system. Lymphoma cells can build up in lymph nodes and other lymph tissues. Lymphomas are grouped into 2 categories: Hodgkin lymphoma and non-Hodgkin lymphoma.
- **Leukemia.** This is called a blood cancer. It starts in the cells in the bone marrow that make blood cells. This type of cancer keeps the bone marrow from making normal red and white blood cells and platelets. (White blood cells are needed to fight infections. Red blood cells carry oxygen and carbon dioxide throughout the body. Platelets help the blood clot to prevent bleeding.

There are 4 main types of leukemia:

- Acute myelogenous leukemia (AML)
- Chronic myelogenous leukemia (CML)
- Acute lymphocytic leukemia (ALL)
- Chronic lymphocytic leukemia (CLL).

The terms myelogenous and lymphocytic mean the type of cells that are involved. Acute and chronic tell how fast the cells are growing.

- **Myeloma.** This type of blood cancer starts in the plasma cells of bone marrow. In some cases, the myeloma cells collect in 1 bone and form a single tumor. This is called a plasmacytoma. In other cases, the myeloma cells collect in many bones and form many tumors. This is called multiple myeloma.
- **Breast Cancer**[17,18]

Breast cancer is the leading cancer incidence worldwide, with an annual 2.26 million reported cases, 11.7% of total cancer cases, and 24.5 % of the cancers in females. It is also the leading cancer in the number of deaths in women (15.5% of annual cancer deaths in females).

Triple Negative Breast Cancer (TNBC), characterized by the absence of expression of estrogen receptor, progesterone receptor, and human epidermal growth factor receptor-2 in the cancerous cells, is one of the most malignant and aggressive forms of breast cancer, and it is accompanied by poor prognosis in patients. The use of cytotoxic chemotherapeutic drugs is an established treatment option as TNBC cells are unresponsive to hormonal therapy.

The TNBC type of breast cancer is reported to be most prevalent in African countries. It is also contested that data reporting from underdeveloped countries and respective projections of total cancers cases and deaths remain incomplete as the data only report consider the hospital-based cancer reports while people in many regions in underdeveloped and African countries either do not have access to medical facilities or large cases remain unreported (undiagnosed cancer cases) due to socio-cultural settings. The National Cancer Institute lists several FDA-approved chemotherapeutic drugs for breast cancer management.

A few selected drugs are capecitabine, docetaxel, doxorubicin, epirubicin, 5-fluorouracil (5-FU), gemcitabine, methotrexate, paclitaxel, tamoxifen citrate, thiotepa, and many other molecules from kinase inhibitors, cytotoxic anthracyclines, topoisomerase I inhibitors, and nucleosides. The list also includes trastuzumab, an antibody sold with the brand name Herceptin. A variety of therapeutics promises better control of breast cancer. Because of the lack of receptor expression in TNBC, its treatment remains the most challenging task.

The chemotherapeutic options are not so effective in the case of TNBC. The finding of a target is critical in treatment management. There is continuous ongoing research for the development of potent new therapeutics or improved chemotherapeutics options for TNBC. In a recent study, the live macrophage-delivered doxorubicin-loaded Liposomes have been reported for effective treatment of TNBC.

- **Lung Cancer**

Lung cancer continues to be present in all countries and most regions, with estimated annual incidences of 2.21 million, 11.4% of cancer cases, and a mortality of 1.79 million lung cancer patients every year. Lung cancer is one of the leading causes of cancer-related deaths in men and women. The segregation based on economic development shows no difference in lung cancer deaths in male patients in developed and underdeveloped countries. However, women from developed countries suffer a higher death rate due to lung cancer compared to developing nations. Lung cancer deaths are second only to breast cancer in women[19].

Table 1: Recently approved drugs for lung cancer treatment

Drug	Approved for	Approved on
Fam-trastuzumab-deruxtecan-nxki	unresectable or metastatic non-small cell lung cancer (NSCLC)	Aug 2022
Capmatinib	metastatic non-small cell lung cancer (NSCLC)	Aug 2022
Nivolumab	resectable non-small cell lung cancer (NSCLC)	March 2022
Atezolizumab	stage II to IIIA non-small cell lung cancer (NSCLC)	Oct 2021
Mobocertinib	metastatic non-small cell lung cancer (NSCLC)	Sept 2021

- **Prostate Cancer**:

Prostate cancer is one of the most prevalent malignancies in men, being the second most frequently diagnosed cancer among men globally, with about 1.41 million new diagnoses each year, which represents 14.1% of male cancer incidence[20]. This type of cancer occurs in the prostate gland, which is a part of the male reproductive organ, and usually grows slowly. However, virulent forms can metastasize to bones, lymph nodes, and other organs with increased morbidity and mortality[21,22]. Incidence rates are significantly higher in the developed world as a result of extensive Prostate-Specific Antigen (PSA) screening, better health infrastructure, and increased life expectancy[20,23].

Risk factors are rising age, African descent, family history, BRCA1/2 mutations, and lifestyle factors such as diet and obesity[21,24]. Diagnosis is most often obtained by PSA testing, digital rectal examination (DRE), prostate biopsy, and imaging studies such as multiparametric MRI or bone scan[25]. With early detection, the 5-year survival rate is greater than 90% [15].

Treatment approaches differ according to stage and cancer aggressiveness. Localized prostate cancer can be treated with active surveillance, surgery, or radiation, whereas advanced or metastatic disease is typically treated with androgen deprivation therapy (ADT), chemotherapy, or innovative hormonal and immunotherapies[26,27].

In the past several years, numerous newer drugs that target various features of prostate cancer biology have become approved, enhancing survival and quality of life.

Table 2: Drugs for Prostate Cancer

Drug Name	Drug Class / Mechanism	Indication	FDA Approval Year
Leuprolide	GnRH agonist	Androgen deprivation in advanced PCa	1985
Bicalutamide	Antiandrogen	Metastatic prostate cancer	1995
Docetaxel	Chemotherapy (Taxane)	Metastatic hormone-refractory PCa	2004
Abiraterone acetate	CYP17 inhibitor	Metastatic castration-resistant PCa	2011
Enzalutamide	Androgen receptor inhibitor	Metastatic CRPC and nmCRPC	2012
Sipuleucel-T	Cancer vaccine (immunotherapy)	Asymptomatic or minimally symptomatic CRPC	2010
Apalutamide	Androgen receptor inhibitor	Non-metastatic CRPC	2018
Darolutamide	Androgen receptor inhibitor	Non-metastatic CRPC	2019
Olaparib	PARP inhibitor	BRCA-mutated metastatic CRPC	2020
Relugolix	Oral GnRH receptor antagonist	Advanced hormone-sensitive PCa	2020

- **Colorectal Cancer**

Colorectal cancer (CRC) (colon + rectum) accounts for more than 1.85 million cases annually (9.8% of the total cancer cases) and causes an estimated 850,000 deaths (9.2% of total cancer-related deaths) annually. CRC is the third most common cause of cancer mortality worldwide. A recent report has projected about 3.2 million cases of colorectal cancer in 2040, with China and the United States as the leading countries in the number of incidences in the next 20 years[28].

- **Leukemia**

Leukemia is a cancer of blood-forming tissues, including bone marrow, involving white blood cells. It has different types, such as acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), and chronic lymphocytic leukemia (CLL), which affect different age groups. With an estimated annual 474,519 cases of leukemia contributing 2.5% of total cancer incidences, it is a rare disease that accounts for many incidences[12].

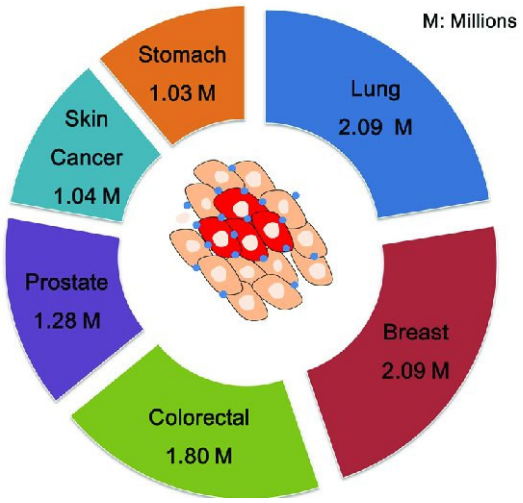

Fig 3: Types of Cancer[29]

Pathophysiology of Cancer[30]

Pathophysiology is a combination of two medical terms: pathology and physiology. Pathology involves the study of structural and functional changes in cells, tissues, or organs that are caused by a particular disease. On the other hand, physiology explores the functions of the human body. Therefore, pathophysiology can be defined as the study of fundamental changes in the body's physiology, resulting from a disease.

For instance, the pathophysiology of the tumor explores the underlying changes in the body that result from the tumor or metastasis of cancer cells. Therefore, the pathophysiology of cancer includes the physical and hormonal changes associated with cancer and paraneoplastic syndrome. In general, cancer occurs in four main stages. The pathological stage of cancer is determined through biopsy (removal of small body tissue for laboratory examination) where the cancerous cells are compared to normal cells. The four main stages of cancer are:

- Stage 1 — Cancer is normally localized in a small area
- Stage 2 — The size of the cancer increases
- Stage 3 — The size of the cancer becomes larger and starts spreading to some parts of the body, including the lymph nodes
- Stage 4 — Cancer has grown and has spread to most parts of the body

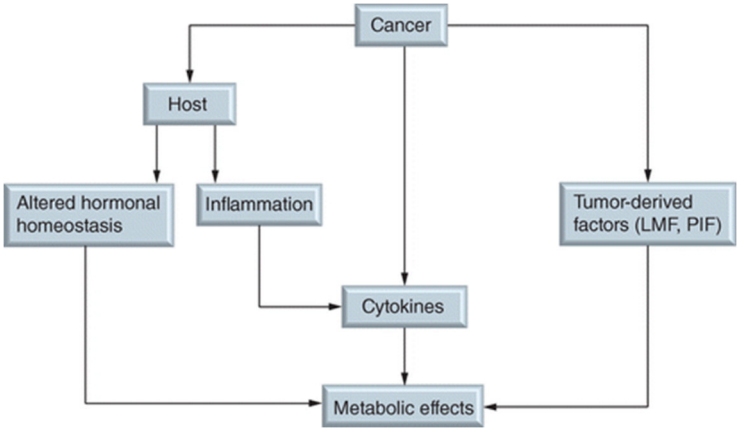

Fig 4: Pathophysiology of Cancer

Risk Factors

Cancer is a complex disease acted upon by a spectrum of modifiable and non-modifiable risk factors. Knowledge of these is essential for prevention and detection at an early stage.

Lifestyle Determinants: Habits like the use of tobacco, heavy alcohol intake, inadequate nutrition, lack of physical activity, and sun exposure over extended periods increase cancer risk. The use of tobacco alone causes about 24% of cancer-related deaths worldwide[31]. Physical activity and obesity have also been identified with higher risks of several cancers like breast, colorectal, and endometrial cancers[32].

Genetic Causes: Inherited mutations in genes may predispose a person to developing some cancers. For example, mutations in the BRCA1 and BRCA2 genes have increased risks of breast cancer and ovarian cancer. History in the family is an important factor, and those with a close relative who has developed cancer are at increased risk[33].

Infectious Agents: There are some viruses which are known to increase the risk of cancer. Human papillomavirus (HPV) is associated with cervical and other cancers, while hepatitis B and C viruses cause liver cancer. Epstein-Barr virus (EBV) is also associated with lymphomas, and human immunodeficiency virus (HIV) raises the risk of Kaposi's sarcoma and some lymphomas[34].

Environmental and Occupational Exposures: Exposure to environmental or occupational carcinogens, like asbestos, benzene, and formaldehyde, can increase cancer risk. Radon gas, an environmentally occurring radioactive gas, is a major cause of lung cancer in non-smokers. Occupational exposures in painting, construction, and agricultural industries may also pose elevated risks[35].

Age and Other Non-Modifiable Factors: Increasing age is an important risk factor, and the majority of cancer cases present in people aged above 65. Gender and ethnicity may also play a role in cancer vulnerability, with some cancers being more common within specific populations[36].

Prevention and Early Detection: Some risk factors are uncontrollable, but numerous others are. A healthy lifestyle-tobacco avoidance, reduced alcohol, balanced diet, regular exercise, and skin avoidance of excessive exposure to the sun-can decrease the risk of cancer drastically. Routine screening tests, including mammograms, colonoscopies, and Pap smears, can identify precancerous lesions or cancers in their early stages, increasing curability[37].

Intrinsic risk factors	Non-intrinsic risk factors	
	Endogenous risk factors	Exogenous risk factors
❖ Random errors in DNA replication	❖ Biologic aging ❖ Genetic susceptibility ❖ DNA repair machinery ❖ Hormones ❖ Growth factors ❖ Inflammation ❖ etc.	❖ Radiation ❖ Chemical carcinogens ❖ Tumour causing viruses ❖ Bad lifestyles such as smoking, lack of exercise, nutrient imbalance ❖ etc.
[Unmodifiable]	[Partially modifiable]	[Modifiable]

Fig 5: Risk Factors[38]

Genes affect Cancer Growth

Cancer is a gene disease at its essence. Whatever cancer cells exist will have genetic alterations, or mutations, on how cells develop and grow. Less than half of these mutations are inherited from one's parents, but most occur sporadically due to exposure to the environment, lifestyle, or random errors during DNA replication [39,40].

There are three basic categories of genes that lead to cancer development:

1. Oncogenes: Proto-oncogenes are regular genes responsible for activating normal growth, cell division, and differentiation. They encode proteins such as growth factors, receptor tyrosine kinases, signal transducers, and transcription factors. If these types of genes become mutated such as via point mutations, gene amplification, or chromosomal translocations they become oncogenes, and the outcome is ongoing, unregulated cell signaling [39,41]. A point mutation in a RAS gene (e.g., KRAS) generates a protein trapped in the "active" GTP-bound state. It results in continuous activation of downstream pathways like MAPK and PI3K-AKT, causing proliferation independent of growth stimuli[39]. HER2/ERBB2, which is commonly amplified in breast cancer, causes overexpression of receptor tyrosine kinases, increasing mitogenic signals[41].

Table 3: Oncogenes examples and its Mechanisms

Oncogene	Cancer Types	Mechanism
KRAS	Colon, lung, pancreas	Constitutive activation of RAS/MAPK signaling
BCR-ABL	Chronic myeloid leukemia (CML)	Fusion gene with tyrosine kinase activity
MYC	Burkitt's lymphoma	Promotes transcription of growth genes
HER2	Breast, gastric	Gene amplification leads to overactive receptor

2. Tumor Suppressor Genes: Tumor suppressor genes are the brakes that prevent cells from dividing uncontrollably. They are also sentinels of DNA damage, cell cycle regulators, and inducers of apoptosis. Cancer occurs when these genes are silenced by loss-of-function mutations. In contrast to oncogenes (where a single mutant allele is enough), both alleles of a tumor suppressor gene usually need to be lost before cancer can occur this is known as Knudson's two-hit hypothesis[42].

Example: TP53 Activates DNA repair proteins, halts cell cycle (by p21), and induces apoptosis when damage is irreversible. Mutated in >50% of all human cancers[43,44]. RB1 Suppresses E2F transcription factor, thus preventing G1/S transition. Loss leads to uncontrolled replication. APC Regulates β-catenin destruction. Mutation leads to constitutive WNT signal, linked with familial adenomatous polyposis (FAP) and colorectal cancer.

Table 4: Major Tumor Suppressors

Gene	Function	Cancer Type
TP53	DNA damage response, apoptosis	Lung, breast, colon, sarcomas
RB1	Cell cycle arrest	Retinoblastoma, osteosarcoma
APC	Wnt signaling inhibition	Colorectal cancer
BRCA1/2	DNA double-strand break repair	Breast, ovarian cancers

3. DNA Mismatch Repair Genes: Mismatch repair (MMR) genes fix mistakes that are being made during DNA replication such as base mismatches or insertion-deletion loops. When these genes are defective, replication errors are not fixed, and this leads to a mutator phenotype and microsatellite instability (MSI), a characteristic of several types of cancers[45].

Key MMR Genes: MLH1, MSH2, MSH6, PMS2 These genes all come together to form protein complexes that recognize and repair mismatches[45]. Mutations can be heritable (e.g., Lynch syndrome) or acquired (epigenetic silencing in sporadic colorectal cancer). Lynch Syndrome (Hereditary Nonpolyposis Colorectal Cancer HNPCC): Because of germline mutations in MMR genes. Increased lifetime risk of neoplasms of the colon, endometrium, ovary, stomach, and urinary tract. MSI testing and immunohistochemistry are diagnostics[46].

Integration: How Mutations Drive Cancer results not as the result of a single genetic change but through the sequential accumulation of many mutations that undermine mechanisms of normal cell control. These mutations include critical genes and pathways, allowing cells to acquire the features necessary for malignant transformation[39,47]. Among the necessary alterations is apoptosis loss, typically resulting from TP53 gene mutation. In normal cells, p53 acts as a "guardian of the genome" to trigger cell death on detecting severe DNA damage. p53 loss permits genetically unstable cells to grow and survive[43,44].

The other characteristic is the ability of sustained proliferation, possibly due to proto-oncogene mutations such as RAS. In its mutated form, the RAS proteins are constitutively active and continually transmit signals that favor uncontrolled cell division even in the absence of growth stimuli from the outside.

Parallel to this, cancer cells are made immortal by telomerase enzyme activation, which shields telomeres and provides for unlimited replicative capacity a property lost by normal somatic cells with advancing age as a result of progressive telomere shortening. For satisfying their increased growth demands, cancer cells also induce angiogenesis, the formation of new blood vessels, to a great extent by overexpression of vascular endothelial growth factor (VEGF). This mechanism ensures a proper supply of oxygen and nutrients to the growing tumor mass.

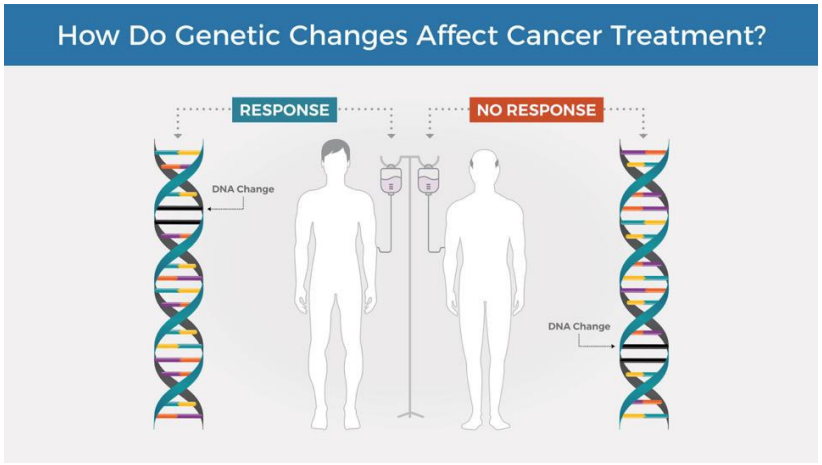

Fig 6: Genetic changes affect cancer treatment

Treatment of Cancer

Treatment of cancer is a comprehensive method that needs an individualized and systematic plan based on the type of cancer, site of cancer, stage, genetic profile of the tumor, and patient's overall health. Treatment can be curative, palliative, or control-oriented in its goal. A multidisciplinary treatment typically integrates various treatment modalities which include surgery, radiation therapy, chemotherapy, hormone therapy, immunotherapy, targeted therapy, stem cell transplantation, hyperthermia, and photodynamic therapy to attain optimal results[48–50]

Surgery continues to be one of the most successful therapies, especially for solid tumors that are diagnosed early and localized. Surgical oncology seeks to remove the tumor mass with a border of surrounding normal tissue to ensure against recurrence. Improvements in surgical methods, including laparoscopic and robotic surgery, have enhance accuracy and decreased recovery time.

Radiation therapy (RT) uses ionizing radiation to induce irreparable DNA injury in highly proliferating cancer cells, resulting in apoptosis or mitotic catastrophe. It may be delivered externally using linear accelerators or internally with brachytherapy. Fractional does enable maximum tumor control while limiting damage to normal tissue. Stereotactic body radiotherapy (SBRT) and intensity modulated radiotherapy (IMRT) provide better precision, particularly in complicated anatomical areas like the brain or spine[51]

Chemotherapy is a systemic therapy in which cytotoxic agents are used to destroy rapidly growing cancer cells. Though effective in numerous types of cancers, its lack of selectivity causes major side effects since it targets normal fast-dividing cells such as those in the gastrointestinal tract, bone marrow, and hair follicles. Chemotherapy may be neoadjuvant (preoperative), adjuvant (postoperative), or palliative, and in many instances, it is administered with radiation or target therapies for synergism. Resistance to drugs, both intrinsic and acquired, continues to pose the greatest challenge

Hormonal therapy is directed against cancers that are dependent on hormonal stimuli for growth, including breast and prostate cancer. In hormone receptor-positive breast cancer, treatment includes Tamoxifen (a selective estrogen receptor modulator) or aromatase inhibitor (such as anastrozole) to inhibit estrogen signaling. In prostate cancer, androgen deprivation therapy (ADT) through LHRH agonists or antiandrogens decrease the level of testosterone, hence inhibiting tumor growth. Hormone therapy is usually better tolerated comparted to chemotherapy but could have long-term effects such as osteoporosis and cardiovascular complications[52].

Immunotherapy is a shift in the paradigm of oncology, which utilizes the body's immune system to identify and kill cancer cells. Immune checkpoint inhibitors (e.g., pembrolizumab, nivolumab) inhibit proteins like PD-1/PD-L1 or CTLA-4 utilized by cancers to avoid immune surveillance. CAR T-cell therapy involves the manufacture

of a patient's T-cells to produce chimeric antigen receptors for tumor antigens. Immunotherapy has provided dramatic outcomes in cancers like melanoma, lung cancer, and Hodgkin Lymphoma, though it may be followed by immune-related adverse events (irAEs) due to excessive activation of the immune system[53].

Targeted therapy addresses molecular abnormalities of cancer cells. Through the selective inhibition of major oncogenic pathways, these therapies achieve specificity with reduced side effects compared to conventional chemotherapy. Such treatments include EGFT inhibitors in lung cancer, BCR-ABL inhibitors such as imatinib in CML, and HER2-targeting drugs such as trastuzumab in breast cancer. Resistance may occur via secondary mutations or redundance of pathways, requiring combination treatments or next-generation inhibitors[48,54]

Stem cell transplantation (SCT) is primarily applied to hematologic malignancies. High-dose chemotherapy or radiation treats the patient with ablative therapy, and then autologous or allogenic stem cells are infused to reconstitute hematopoiesis. Allogenic SCT has a graft-versus-leukemia effect but also has risks like graft-versus-host disease (GVHD). It has indications such as acute leukemia, lymphoma, multiple myeloma, and bone marrow failure syndromes[55].

Hyperthermia therapy is an adjuvant therapy where regional or whole-body temperatures are raised (usually 40–45°C) to improve cell killing of tumors. Heat causes disruption of protein and DNA structures in cancer cells and also potentiates chemotherapy and radiation. Methods involve microwave, radiofrequency, or ultrasound hyperthermia. Clinical trials have been promising despite being experimental in treating recurrent breast cancer, melanoma, and soft tissue sarcomas[51].

Photodynamic therapy (PDT) employs a photosensitizer activated by a particular wavelength of light to produce reactive oxygen species (ROS) with consequent cell death. PDT is utilized mainly for surface or luminal cancers like skin, esophageal, and bladder cancers. It has the benefit of being non-invasive, with little systemic toxicity, but availability is restricted by the penetration depth of light and photosensitizing side effects [56].

Testing for biomarkers typically has become necessary in precision oncology to allow clinicians to detect actionable mutations, make predictions regarding responses to treatment, and track disease progression. EGFR, ALK, BRAF, and KRAS mutations biomarkers have become standard-of-care testing in cancers such as non-small-cell lung cancer (NSCLC), guiding the administration of targeted therapies. Likewise, PD-L1 expressionor MSI status determines eligibility for immunotherapy. Next-generation sequencing and liquid biopsies are transforming the landscape by offering non-invasive, complete molecular profiling[57].

Table 5: Treatment types of Cancer

Treatment Type	Mechanism	Indications	Side Effects
Surgery	Physical removal of tumor	Localized solid tumors	Pain, infection
Radiation Therapy	DNA damage via ionizing radiation	Brain, breast, prostate, others	Fatigue, skin irritation
Chemotherapy	Cytotoxic drug-induced cell death	Most systemic cancers	Nausea, immunosuppression
Hormone Therapy	Blocks hormone receptors or synthesis	Breast, prostate	Hot flashes, osteoporosis
Immunotherapy	Stimulates immune system	Melanoma, lung, kidney	Autoimmune-like symptoms
Targeted Therapy	Inhibits specific cancer-driving mutations	NSCLC, CML, breast cancer	Diarrhea, liver toxicity
Stem Cell Transplant	Replaces damaged marrow	Leukemia, lymphoma	GVHD, infection risk
Hyperthermia	Heat-induced damage	Breast, melanoma, soft tissue tumors	Burns, discomfort
Photodynamic Therapy	Light-activated cell destruction	Skin, esophageal, bladder	Photosensitivity
Biomarker Testing	Genetic/molecular profiling	All cancers	Minimal

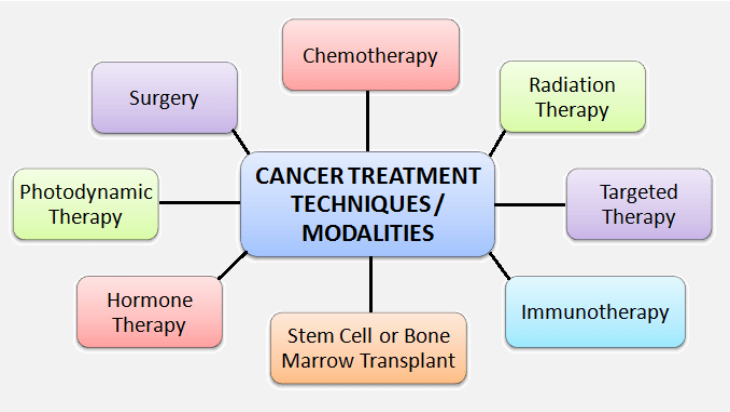

Fig 7: Cancer treatment[58]

Prevention of Cancer

Prevention of cancer is a complex proves that entails changing lifestyle habits and reducing exposure to the environment in order to decrease the chances of getting the disease. Sizeable research shows that a large percentage of cases of cancer are preventable if one takes protective action. First among these interventions is to stop the use of tobacco. It is still the most preventable source of cancer globally, accounting for about 80% of cases of lung cancer and substantially raising the risk for cancers of the oral cavity, larynx, esophagus, stomach, kidney, bladder, pancreas, and cervix. A healthy body weight, achieved through a balanced diet and regular exercise, is also important. Obesity has been associated with the heightened risk of various cancers such as those of the esophagus, colorectum, breast, endometrium, and kidney. Exercise of moderate intensity for a minimum of 30 minutes everyday not only contributes to weight reduction but also reduces the risk of cancer independent of its effects on weight. Nutritional choices are an important component of cancer prevention. Fruits, vegetables, whole grain diets offer protective effects, and excessive intake of red and processed meats is implicated in raising cancer risk. Reducing alcohol consumption is also important, as consumption of alcohol has been conclusively implicated in cancer of the mouth, esophagus, breast, and colorectum. Immunization with oncogenic viruses, including Human papillomavirus (HPV) and hepatitis B virus (HBV), provides solid defense against cancers of the cervix and liver. Exposure to carcinogens in the environment and workplace, such as ultraviolet (UV) radiation, ionizing radiation, and indoor and outdoor pollutants like radon, also causes cancer risk. Applying protection measures, like the use of sun protection, safe handling of medical radiation, and reducing exposure to indoor and outdoor pollutants is crucial.

Fig 8: Prevention of Cancer[59]

CONCLUSION

Cancer is still a powerful worldwide health problem, and its occurrence has been increasing as a result of the combined effect of genetic, environmental, and lifestyle factors. This review has shed light on the heterogeneity and dynamism of cancer, thereby stressing that cancer is not a uniform disease but a group of more than a hundred unique malignancies, each with a unique pathophysiology, clinical pattern, and therapeutic strategy. The cancer burden is high among developed and developing countries, and future projections see it increasing in a sustained manner, requiring immediate and persistent public health interventions. Knowledge of the epidemiology of cancer, risk factor identification, and public awareness constitute the pillars of prevention and early detection. Molecular biology has given us profound insights into the genetic and epigenetic processes of cancer initiation, such as the function of oncogenes, tumor suppressor genes, and mismatch repair genes. These have been translated into new modalities of diagnosis, prevention, and treatment, such as precision medicine, immunotherapy, and biomarker-based treatment. In spite of these advances, issues continue to exist in access to early diagnosis, uniform cancer care, and fair distribution of new therapies, especially in low- and middle-income nations. Improvement requires reinforcement of cancer registries, development of multi-institutional cooperative groups, and investment in infrastructure, education, and community outreach. Prevention through lifestyle change, vaccination, environmental control, and screening is the best and cost-effective strategy to limit its burden. With the dawn of personalized medicine and integrative oncology, the approach that integrates the latest science with community-based health programs will be instrumental in lowering cancer's morbidity and mortality globally.

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