

## **INTRODUCTION**

## **1.1. Cancer**

Cancer is one of the most dangerous diseases in today's modern world. Cancer is formed when normal cells lose their normal regulatory mechanisms that control growth and multiplication[1]. Abnormal growth of tissue is called neoplasm and when neoplasm also forms a mass, it is called as tumor. Neoplasm may not always be associated with tumor formation. These tumors can be of two types benign and malignant [2]. Benign tumors are non cancerous and are not life threatening. These kind of tumors grow slowly, composed of normal cells and do not spread to other tissues. Whereas malignant tumors grow fast (uncontrolled growth) and break off from mother tissue and spread to other tissues through blood and lymphatic system. The process of spreading is known as metastasis and at new site the growth continues to result in a condition known as metastatic cancer [3].

Based on tissue types, cancer may be classified as sarcoma, lymphoma, leukemia, adenoma and carcinoma as discussed below [4].

Sarcoma: It includes cancer of bone, cartilage, fat, muscles and other connective tissues.

Lymphoma: It includes cancer of lymph nodes and immune system tissues.

Leukemia: It includes cancer of bone marrow and often accumulates in blood stream.

Adenoma: It includes cancer of the glandular type of tissue like thyroid cancer.

Carcinoma: It includes cancer of lung, breast, pancreas and colon.

### **1.1.1 Carcinoma**

Carcinoma is most common type of cancer. Carcinoma arises from epithelial cells and may invade adjacent tissue, organs and metastasizes all organs. Breast, prostate, pancreatic, lung and colon cancers are some examples of carcinoma.

**Colorectal cancer:** Colorectal cancer starts in the colon or rectum hence named as colon cancer or rectal cancer, depending on where it starts. Colon and rectal cancers are often grouped together as they have common signs and symptoms. Most colorectal cancers begin as uncontrolled growth on the inner lining of the colon or rectum called a polyp. Some of the polyps may develop as cancer over the course of time, but not all. The transformation into a cancer depends on the kind of polyp and conditions, for example, hyperplastic polyps and inflammatory polyps are not pre-cancerous.

**Pancreatic cancer:** Pancreas has two types of cells: exocrine and endocrine. Most of the cells in the pancreas form the exocrine glands and ducts which are involved in secretion of pancreatic enzymes that are released into the intestine help to digest foods (especially fats). Endocrine cells are arranged in small clusters called islets (or islets of Langerhans) and are involved in production of important hormones like insulin and glucagon.

The exocrine cells and endocrine cells of the pancreas form different types of tumors. Exocrine cancers are by far the most common type of pancreatic cancers. Tumors of the endocrine pancreas are rare and contribute to 5% of all pancreatic cancers.

**Lung Cancer:** When cancer starts from lung tissue it is caused as primary lung cancer and if cancer starts in another part of body and metastasizes to the lung, it is called secondary lung cancer. About 80 to 85% of lung cancers are non-small cell lung cancers (NSCLC) and rest 10 to 15% are Small Cell Lung Cancer (SCLC). These two types of lung cancers have been defined by the size of abnormal cells and the particular way the cancer spreads [5].

Small cell lung cancer, also called oat cell cancer, is so called because under the microscope, the cancer cells look small and are mostly filled with the nucleus. It is mainly caused by smoking and is very rare for non-smokers to develop it. It is highly metastatic and spreads fast.

Non small cell lung cancers are of three types viz: adenocarcinoma, squamous cell cancer and large cell carcinoma. Since these behave in a similar way and also respond to treatment in a different way than small cell lung cancer, they are grouped together as NSCLC.

**Adenocarcinoma:** Adenocarcinomas are most common primary lung cancers (upto 40% of lung cancers). It usually develops in mucus making cells in the lining of the airways and often found in the outer areas but slowly grows to other parts of lungs.

**Squamous cell (epidermoid) carcinoma:** Squamous are flat cells, lining the inside of the airways in the lungs. It accounts for 25% of total lung cancers and often found near the centre of the lung in one of the main airways (the left or right bronchus). It has been often linked to smoking.

**Large cell (undifferentiated) carcinoma:** Here, the carcinoma cells look large and rounded under a microscope. large cell carcinoma tends to grow and spread quickly and is difficult to treat. It accounts approximately for 15% of the lung cancer cases.

Other subtypes: A few less common types of lung cancers are sarcomatoid carcinoma, adenosquamous carcinoma and lung carcinoid tumors.

### **1.2 Cancer: facts and figures**

As per reports of International Agency for Research on Cancer (IARC), in 2012, 14.1 million new cancer cases were reported along with 8.2 million cancer deaths worldwide. The global burden of cancer is expected to grow to 21.7 million as new cancer cases and 13 million cancer deaths in 2030. The future burden will probably be more because of the adoption of western lifestyles, such as smoking, poor diet, physical inactivity etc. This estimate does not include carcinoma except urinary bladder, nor does it include basal cell or squamous cell skin cancers as these are not required to be reported to cancer registries. During 2005 to 2011, relative rate of 5-year survival for all cancer diagnosed patients was 69%, up from 49% during 1975-1977. Improvement in survival is because of early diagnosis of certain cancers and improvements in treatment strategies [6] [7].

#### **Indian context**

With more than 1,300 deaths reported every day, cancer in India has become one of the major causes of death. National Cancer Registry Program (NCRP) of the Indian Council of Medical Research (ICMR) estimates that, cancer mortality rate in the country increased by about six percent from 2012 to 2014. In 2014, 4,91,598 people died out of 28,20,179 cases, while in 2013 it was 4,78,180 deaths out of 29,34,314 cases, and in 2012, around 4,65,169 people lost their lives due to the disease out of 30,16,628. In India, large number of ageing population, unhealthy lifestyle and diet, use of tobacco and tobacco products, lack of diagnostic facilities, are some of the factors that have attributed to increase in the number of cancer deaths. As per ICMR, India is likely to have over 17.3 lakh new cases of cancer and over 8.8 lakh deaths by 2020, due to cancers of breast, lung, colon and cervix etc. [8] [9].

### **1.3 Available treatment options for cancer**

The treatment depends on type of cancer and how advanced it is. Some people with cancer may have one treatment while others may have combination of treatments. Type of treatments are: surgery, radiation therapy, chemotherapy, immunotherapy, targeted therapy, hormone therapy, stem cell transplant and precision medicine [10].

**1.3.1 Surgery:** Surgery is used to remove cancer that is contained in one area, causing pain and pressure. It works best for solid localized tumors and may be followed by other treatment such as chemotherapy. It may be used as Cryosurgery, Lasers, Hyperthermia and Photodynamic therapy [11].

**1.3.2 Radiation therapy:** At high doses, radiation can kill or slow down the growth of cancer cells. It has two types: external and internal beam therapy. It treats a specific part of body such as chest for cancer in lung. In internal beam therapy, source of radiation is put inside the body and radiation source could be liquid or solid (brachytherapy) [12].

**1.3.3 Chemotherapy:** Chemotherapy means treatment with cell killing (cytotoxic) drugs. Cytotoxic drugs may be used alone or in combination with other treatments. There are more than 100 drugs currently available and new ones are being developed all the time. Chemotherapy may also be used along with combination of radiotherapy, surgery, hormone therapy and immunotherapy. Selection of chemotherapeutic agent depends on the type, place and mechanism of cancer spreading. Examples of drugs include Cisplatin, Carboplatin, paclitaxel, Gemcitabine, Etoposide etc.

**1.3.4 Immunotherapy:** Immunotherapy is a type of cancer treatment that helps the immune system to fight against cancer. By giving monoclonal antibodies, T-cell transfer, interferons and interleukins and with certain vaccines, immunity can be boosted [13].

**1.3.5 Hormone Therapy:** Hormones are natural substances made by glands in our bodies through endocrine system. They have lots of effects and one of these is controlling the growth and activity of certain cells and organs. Hormone therapy for cancer means use of medicines to block the effects of hormones where cancer cells use these hormones to grow. Breast, prostate, womb, ovarian and kidney cancers respond well to hormone therapy [14].

**1.3.6 Stem Cell Transplant:** Stem cell transplant (also called peripheral blood stem cell transplant) is a treatment which is used in leukaemia, lymphoma and myeloma. High doses of chemotherapy, sometimes with whole body radiotherapy not only kills the cancer cells but also kills the stem cells in the bone marrow. Stem cells are very early stage of blood cells in the bone marrow that develop into red blood cells, white blood cells and platelets [15]

**1.3.7 Precision Medicine:** Precision medicine is an approach of patient care that allows doctors to select treatments based on a genetic understanding of their disease or simply called personalized medicine. The idea of precision medicine is not new, but recent advances in science and technology have helped speed up the pace of this area of research particularly in cancer. Even so, different people may respond differently with the same treatment for same type of cancer. With precision medicine, if cancer has a genetic change, it can be targeted with a known drug [16].

**1.3.8 Targeted Therapy:** Chemotherapy drugs cannot differentiate normal cells and cancer cells. Targeted therapies are designed specifically to attack specific cancer cells by attaching to or blocking targets that appear to be involved. Patient with advanced lung cancer with certain molecular biomarkers may receive treatment with a targeted drug along with chemotherapy. Molecules which are involved in the cell signaling process are very important in designing targeted therapy. These processes or signals can be disrupted by targeted therapy. Targeted therapy includes enzyme inhibitors, apoptosis-inducing drugs, angiogenesis inhibitors and small molecule inhibitors [17]. Targeted cancer therapies are sometimes called "molecularly targeted drugs" or "molecularly targeted therapies". Targeted therapies differ from standard chemotherapy in several ways. Targeted therapies act on specific molecular targets that are associated with cancer, whereas most standard chemotherapies act on all rapidly dividing cancerous cells. Targeted therapies are deliberately chosen or designed to interact with their target, whereas many standard chemotherapies were identified because they are cytotoxic. Moreover, targeted therapies are often cytostatic (that is, they block tumor cell proliferation), whereas standard chemotherapy agents are cytotoxic (that is, they kill tumor cells) [18].

The comparison of above treatment strategies can be summarized as below:

Type of treatment	Advantage	Disadvantage
Surgery	Type of cancer, its stage, size, distribution and location	Pain in the part of the body that was operated, Infection, early stage, detached cells pass elsewhere in the body
Radiation Therapy	Painless, boost the outcomes of surgical or other treatment	Affects normal cells, tissue damage, expensive, long time treatment, stage
Chemotherapy	Destroy tumors, boost the outcomes of surgery or radiotherapy, Cancer cell are more sensitive	Kill normal cells, shorten the survival of patients, treatment usually causes nausea, hair loss and fatigue
Immunotherapy	Boost the body's immune system and in that way induce your body's immune system to attack cancer cells.	Severe allergic reaction
Hormone therapy	Form of targeted drug therapy, breast cancer, prostate cancer, thyroid cancer and endometrial cancer	Planned on a personal basis, affects the hormone level
Precision medicine	Optimized therapy	Genetic understanding required
Targeted therapy	Cell signaling process, molecularly targeted	Indirect treatment, resistance