

Cancer: Its Symptoms, Challenges and Opportunities in Research in India: A Review

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Abstract

Cancer is uncontrolled division of the cells and has to capability to evade central endogenous control mechanism and as result of this spread to the surrounding tissue. The accumulating knowledge about development and progression of cancer can be used to develop more precise diagnostic and more effective and or less toxic cancer therapies. It is the second leading cause of death worldwide. After cardiac disease cancer has emerged as an important cause of mortality and morbidity in India. In 2019 annual cases grew by 23.6 million and 10 million deaths worldwide. The article compiled with the objective to know regarding the challenges and opportunities in cancer research in India.

Keywords: Cancer, cardiac disease, Mortality.

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INTRODUCTION

Cancer has existed for all of human history. The earliest written record regarding cancer is from circa 1600 BC in the Egyptian Edwin Smith Papyrus and describes breast cancer [1]. Hippocrates (460 BC – 370 BC) described several kinds of cancer, referring to them with the Greek word *karkinos* (crab or crayfish) [1]. This name comes from the appearance of the cut surface of a solid malignant tumor, with "the veins stretched on all sides as the animal the crab has its feet, whence it derives its name" [2] Galen stated that "cancer of the breast is so called because of the fancied resemblance to a crab given by the lateral prolongations of the tumor and the adjacent distended veins" [3].

Cancer refers to any one of a large number of diseases characterized by the development of abnormal cells that divide uncontrollably and have the ability to infiltrate and destroy normal body tissue. Cancer often has the ability to spread throughout the body. The word comes from the ancient Greek *καρκίνος*, meaning crab and tumor. Greek physicians Hippocrates and Galen, among others, noted the similarity of crabs to some tumors with swollen veins. The word was introduced in English in the modern medical sense around 1600 [4]. It is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body. Cancers comprise a large family of diseases

that involve abnormal cell growth with the potential to invade or spread to other parts of the body [5]. They form a subset of neoplasms. A neoplasm or tumor is a group of cells that have undergone unregulated growth and will often form a mass or lump, but may be distributed diffusely [6]. The progression from normal cells to cells that can form a detectable mass to outright cancer involves multiple steps known as malignant progression [7]. In 2015, about 90.5 million people worldwide had cancer [19]. In 2019, annual cancer cases grew by 23.6 million people and there were 10 million deaths worldwide, representing over the previous decade increases of 26% and 21%, respectively [8]. The most common types of cancer in males are lung cancer, prostate cancer, colorectal cancer, and stomach cancer. In females, the most common types are breast cancer, colorectal cancer, lung cancer, and cervical cancer [9]. In children, acute lymphoblastic leukemia and brain tumors are most common, except in Africa, where non-Hodgkin lymphoma occurs more often [10]. In 2012, about 165,000 children under 15 years of age were diagnosed with cancer. The risk of cancer increases significantly with age, and many cancers occur more commonly in developed countries [10].

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breast cancer, colorectal cancer, lung cancer, and cervical cancer. If skin cancer other than melanoma were included in total new cancer cases each year, it would account for around 40% of cases [22, 23]. In children, acute lymphoblastic leukemia and brain tumors are most common, except in Africa, where non-Hodgkin lymphoma occurs more often [12]. The risk of cancer increases significantly with age, and many cancers occur more commonly in developed countries. Rates are increasing as more people live to an old age and as lifestyle changes occur in the developing world [13]. The global total economic costs of cancer were estimated at US\$1.16 trillion per year as of 2010 [14]. According to The National Centre for Disease Informatics and Research of the Indian Council of Medical Research (ICMR) at Bengaluru, India, 1.45 million cases of cancer were estimated to be diagnosed in 2016. This burden is likely to become double in the next 20 years [15].

Symptoms

When cancer begins, it produces no symptoms. Signs and symptoms appear as the mass grows or ulcerates. The findings that result depend on the cancer's type and location. Few symptoms are specific. Many frequently occur in individuals who have other conditions. Cancer can be difficult to diagnose and can be considered a "great imitator. Symptoms may occur due to the mass of the tumor or its ulceration. For example, mass effects from lung cancer can block the bronchus resulting in cough or pneumonia; esophageal cancer can cause narrowing of the esophagus, making it difficult or painful to swallow; and colorectal cancer may lead to narrowing or blockages in the bowel, affecting bowel habits. Masses in breasts or testicles may produce observable lumps. Ulceration can cause bleeding that can lead to symptoms such as coughing up blood (lung cancer), anemia or rectal bleeding (colon cancer), blood in the urine (bladder cancer), or abnormal vaginal bleeding (endometrial or cervical cancer). Although localized pain may occur in advanced cancer, the initial tumor is usually painless. Some cancers can cause a buildup of fluid within the chest or abdomen.

The other symptoms may occur due to the body's response to the cancer. This may include fatigue, unintentional weight loss, or skin changes. Some cancers can cause a systemic inflammatory state that leads to ongoing muscle loss and weakness, known as cachexia. These symptoms are called systemic symptoms [16].

Another symptom includes the spread of cancer to other locations in the body. The dispersed tumors are called metastatic tumors, while the original is called the primary tumor. Almost all cancers can metastasize. Most cancer deaths are due to cancer that has metastasized [17]. Metastasis is common in the late stages of cancer and it can occur via the blood or the

lymphatic system or both. The typical steps in metastasis are local invasion, intravasation into the blood or lymph, circulation through the body, extravasation into the new tissue, proliferation and angiogenesis. Different types of cancers tend to metastasize to particular organs, but overall the most common places for metastases to occur are the lungs, liver, brain and the bones [18].

Challenges and Opportunities

Clinical Research

Although a notable progress in this field has been made in the recent years, there is a need to develop proper clinical research environment. This includes exposing graduate and postgraduate medical students, community physicians and medical college teachers about translation clinical research, and developing adequate infrastructure. Indian pharmaceutical industry has made phenomenal growth in the field of generic molecules; they need to invest in the development of new molecules and India centric cancer research. India has a large pool of individuals with genetic diversity (4000 anthropologically distinct groups and 22 languages) [19]. This provides an opportunity to study environmental influences on drug metabolism (such as smoking, alcohol and use of herbal medicine), variation in drug targets (for example, higher incidence of activating mutations of epidermal growth factor receptor in lung cancer in patients from Asia), and genetic polymorphism in drug-related genes. Indian population is unique in terms of genetics, culture, languages and food habits. Well-planned genome-wide association studies may yield insights into disease aetiology and potential responses to therapy. In the era of precision medicine, it will be important to define risks or susceptibility of certain population or ethnic subgroups for high incidence of cancer seen in these areas and also from treatment point of view if these subgroups need dose modification or special precaution during the treatment. Translational studies involving imaging, pathology, gene expression profiling, sequencing, bioinformatics and detection of circulating tumour cells can be done in few centres, and then data generated can be evaluated for its translation at other centres [20].

Infrastructure

One of the major reasons for not being able to implement screening programme in India has been lack of workforce - physicians, health workers, technical staff and pathologist to review pathological material. The preference of healthcare personnel to work in urban settings has also resulted in unequal distribution of healthcare centres and practitioners. Many tertiary care centres (not all) have a comprehensive team of professionals comprising medical, radiation and surgical oncologists, pain and palliative care experts and auxiliary services, for example, diagnostics and pathological tests. A complex team like this is yet to be a reality in rural India [21]. Available data from

randomized trials done in south India suggest that simple innovative methods such as visual inspection-based screening (for oral cavity) visual inspection with acetic acid application for cervical cancer may be useful and cost-effective methods of screening for these two common cancers. Similarly, for breast cancer self-examination or examination by a physician may be alternative methods to screening mammography which are doable for early detection of breast cancer, as detection in early stages is amenable for treatment with curative option with less morbidity. Ultimately, the screening programmes can bring down the incidence of some of the common cancers in India. There has been effort by the Government of India (GOI) to establish regional cancer centres in rural areas, and upgrade medical colleges with oncology department. Under the National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Disease and Stroke, the GOI has allocated ₹ 120 crores each for the establishment of 20 State-level cancer centres. The GOI has also allocated 20 million USD to develop 23 new tertiary care centres and to strengthen 27 regional cancer centres¹⁰. Under the ‘Pradhan Mantri Swasthya Yojna’, eight new cancer centres would be set up in various parts of country and 58 existing medical colleges would be upgraded in a phased manner. This is a mammoth task and will take some years before this translates into standard care and survival benefit. One solution to this problem might be setting up and improving primary care services in rural areas and educating people about cancer, environmental pollution, clean drinking water, healthy diet and avoid tobacco use.

Several non-government organizations are engaged in increasing public awareness, supporting screening, early detection, patient and family support services and palliative care by providing home care [22]. There is a need to consolidate and strengthen their role in national cancer control programme. Further, the ICMR has taken initiative to publish consensus documents on common cancers in India to improve quality and standardized cancer care. These are expert and evidence-based guidelines to promote uniformity and to ensure the quality of treatment across cancer centres in India. In recent years, the government has tried to address these issues by establishment of the National Health Mission and insurance schemes such as Rashtriya Swasthya Bima Yojna (a central government initiative); Rajiv Aarogyasri Scheme (an Andhra Pradesh government initiative); Vajpayee Arogyashree Scheme (a Karnataka government initiative) and also Gujarat health scheme model¹³. The emphasis is now to educate people about these programmes.

Delay in Diagnosis

Almost 75-80 per cent of patients have advanced disease (Stage 3-4) at the time of diagnosis⁵. This has been attributed to the late presentation which in turn is due to low level of awareness in the

population and among community physicians, lack of screening programmes, lack of diagnostic facilities locally and vast distances to travel to reach a major tertiary cancer centre, financial constraints and stigma associated with the diagnosis. The situation is even worse in rural areas (69% of total population) where patients and families have to travel a long distance to reach a tertiary care oncology centre. Lack of place to stay, long time taken for investigations, limited finances, language and cultural differences are also some of the limitations⁴. As per data from rural-based PBCRs, the incidence of cancer is low in rural India compared to urban PBCRs². Even the pattern of cancers in rural PBCRs is different compared to those in urban PBCRs, suggesting a different policy/approach to adopt in rural areas.

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translates into standard care and survival benefit. One solution to this problem might be setting up and improving primary care services in rural areas and educating people about cancer, environmental pollution, clean drinking water, healthy diet and avoid tobacco use. Experienced health practitioner, researchers and physicians should concentrate on early detection of cancer, as cure rates are high, if cancer is detected in early stage.

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Way Forward

Cancer in India is emerging as a major cause of morbidity and mortality. Some of the key features include young age (generally one decade younger compared to the western population), advanced disease, poor performance status and possibly more aggressive phenotype. While many tertiary cancer centres have state of the art diagnostic workup and treatment protocols, this is yet to reach to a standard level in many other regional cancer centres and hospital in smaller towns. Focussing on epidemiological research, screening for certain cancers and clinical trials India-centric common cancers may provide solutions for improvement in outcome. A planned and teamwork approach at the institution level and collaboration with different research teams are likely the key to success.

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