



Editorial

Cancer research in India: Challenges & opportunities

With changing lifestyle, improved longevity and better control of infectious diseases, non-communicable diseases have emerged as major health problems worldwide, more so in developing countries. After cardiac diseases, cancer has emerged as an important cause of morbidity and mortality in India. 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^{1,2}.

Magnitude & pattern of various cancers in India

The National Cancer Registry Programme was commenced by the ICMR in December 1981 and is a major source of information on cancer incidence and pattern in the country. Currently, there are 29 population-based cancer registries (PBCRs) and 29 hospital-based cancer registries. These cover about 10 per cent of India's population. Of these, 11 PBCRs are located in the North-East (NE) region. Age-adjusted incidence (per 100,000) rate for males is higher in the West - 631.9 in Brazil, 493.9 in USA - Michigan, compared to India 270.0 in Aizawl district and 149.4 in Delhi. Corresponding figures in females are 474.6 in Brazil, 363.3 in USA, 207.7 in Aizawl and 144.8 in Delhi (India) per 100,000, respectively³. The top five cancers among men are lung, head and neck region (mouth, tongue and larynx), prostate and oesophagus. While among women - breast, cervix, ovary, oral cavity and uterine cancer are most common³. The incidence of cervical cancer is declining over the past three decades in Delhi, Chennai, Bengaluru, Bhopal, Mumbai and Barshi PBCRs. The incidence of colon/rectum, lung, breast and prostate cancer is gradually rising in these registries³.

There is significant geographical variation in the incidence of cancer in India. For example, in the NE region, the incidence of cancer is highest in India,

for both sexes. In males, Aizawl district (located in Mizoram) reported highest cases while Papumpare district in Arunachal Pradesh had the highest number in females. Higher incidence of gallbladder cancer in north India and NE region compared to other parts, higher incidence of stomach cancer in Chennai and Bengaluru PBCRs, oesophagus cancer in Kashmir and NE region would indicate different aetiological factors operating, for example, environmental, diet, lifestyle and genetic factors⁴. Nearly 50 per cent of cancers in males and 15 per cent in females are related to the use of tobacco in different forms. These include cancers of aerodigestive tract (head and neck, lung and oesophagus), pancreas and renal and urinary bladder⁴. It is clear that the biggest measure to reduce the incidence of these cancers would be to reduce the consumption of tobacco. Specific cancer research programmes to focus on biology of population present in various States with PBCRs will help determine risk factors responsible and suggest strategies for prevention.

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.

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 India⁶.

Available data from randomized trials done in south India suggest that simple innovative methods such as visual inspection-based screening (for oral cavity)⁷, visual inspection with acetic acid application for cervical cancer⁸ 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 mammography⁹ 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 centres¹⁰. 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 use¹¹. 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.

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^{4,12}. 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 India¹³. 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)¹², and also Gujarat health scheme model¹³. The emphasis is now to educate people about these programmes.

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^{14,15}.

India has a large pool of individuals with genetic diversity (4000 anthropologically distinct groups and 22 languages)¹⁴. 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 therapy¹⁴. 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 areas¹⁶ 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^{14,15}.

Key priority areas for research

One of the important tasks would be to develop consensus on key priorities for cancer research in Indian context based on common cancers in males and females in a particular region. There is a need to focus research on prevention of some cancers with high incidence in certain areas, for example, gallbladder cancer in Gangetic belt, penile cancer in rural population, oesophageal cancer in NE region, colon cancer in Goa, stomach cancer in southern and northeast India⁴. Whether these regional differences in epidemiology are due to a difference in genomics and biology or due to differences in the prevalence of cancer risk factors or both are not yet known and would be an important area of research¹⁴. These cancers are rare in West and therefore, not a focus for large research programmes. Similarly, directing research for upcoming problems like lifestyle and obesity-related cancers would be timely.

Since most patients have advanced disease and poor performance status at presentation, research efforts to develop cost-effective protocols for palliative care would be meaningful. Developing protocols to less toxic regimens (*e.g.* metronomic therapy with minimal visits to a busy cancer centre)¹⁷ and minimizing need for imaging (*e.g.* computed tomography scan)¹⁸ in the follow up would be simple, yet important solutions. An active collaboration between investigators, funding agencies, industry and regulatory bodies would be important to understand needs of each other.

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.

Conflicts of Interest: None.

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