Editorial

Discrete implementation of cancer from the NCD program and concurrent opportunities for research

Introduction

The disease trajectory for cancers is unique to the organ and cell types. The long latency of the majority of cancers offers opportunities for screening of precancerous lesions and subsequent early detection of the malignancy. Treatment is more effective in cancers detected in an early stage, which is evident in case of breast, cervical, colorectal and oral cancers. The shared risk factors for non-communicable diseases (NCDs) although important in the causation of cancer, are insufficient in its prevention. This editorial explores the rationale of a cancer specific agenda disparate from the NCD control program, and suggests priorities for cancer research. The objective is to discuss distinct considerations for effective implementation of cancer control programs.

Cancer heterogeneity

The heterogeneity of cancer is due to its etiology, pathology and geographical distribution. Some of the common cancers in Africa, Asia and South America are due to infections with hepatitis B and C viruses (HBV and HCV), HPVs and Helicobacter pylori.[1] Infection as a cause of cancer provides opportunities for prevention. The UN Political declaration [2] promotes the inclusion of vaccination against cancer related infections, and such an intervention is measurable and achievable. Given the lack of vaccine against HCV, we need to prioritize our research towards effective low-cost treatments for chronic HBV and HCV carriers.

In cancers, the spectrum of biological changes is infinitely variable. The biological attributes (or acquired capabilities) of neoplastic cells are controlled at different spatial and temporal scales. [3] The complex dynamics of cancer is due to the cellular heterogeneity of the tumor, response of the immune system, metabolic reprogramming of cancer cells, non-linear coupling of the evolving genetic diversity of cancer cells, and the immunosuppressive and inflammatory state of the tumor microenvironment (TME) which promote the growth of tumor.[4] Its treatment includes a multi-modal approach: human resource (Oncology Physicians, trained Nurses and Pharmacists), infrastructure, medicines, imaging modalities, supportive therapies (blood transfusion, pain control) and palliative care. The rationale for multi-disciplinary team work includes the increasing complexity of treatment decisions.

The cancer morbidity of a particular geographic region is impacted by the shared environmental and behavioral risk factors for NCDs. Given the significantly higher total cancer-related mortality in low- and middle-income countries (LMIC), especially among people <65 years of age, the unique issues faced by these Countries include premature mortality and lost years of productivity which in-turn have greater economic impact. [5] WHO's comprehensive Global Action Plan for the prevention and control of NCDs 2013-20 [6] recognizes the four key components to control cancer: prevention, early detection and diagnosis, treatment and palliation.

Relevant issues

Interventions which are beneficial in resource-rich settings cannot be extrapolated to resource constrained settings. The debate in high income countries (HIC) includes the harm caused by a false-positive cancer screening test, which in-turn leads to significant wait-times for additional imaging tests and/or tissue biopsy which ultimately might result in a benign finding. However, the optimal approaches in LMIC for cancer screening include population-based screening or a high-risk approach or an opportunistic case-finding. [7] LMIC will find it onerous to prioritize early detection (screening, surveillance) as a strategy, as it will strain the limited downstream resources. [5] Also, much of the infrastructure in LMICs' was built as a response to addressing communicable diseases, maternal & child health and malnutrition. Other priority areas for cancer management in LMIC include strengthening of health infrastructure, training of professionals and their retention, provision of affordable and effective treatment (including those for childhood cancers), adequate access to palliative care, and quality of life among cancer survivors.

Strategies for screening could differ among the developed and

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developing countries, as illustrated with breast cancer where-in mammography is the chosen program in the former and awareness/clinical breast examination are the programs in the latter. The beneficiaries of a screening program are not necessarily patients, and subsequently they may not become diseased. The yield is high when such programs are population based, with a high coverage approach and rigorous quality-control procedures. High quality specimens from a cervical cancer screening program include a cellular sample from the transition zone. This process includes topical rotation of the spatula, retrieving the sample, preservation on a slide (or liquid based medium) including spreading and fixation. Such appropriate techniques provide cytotechnologists an ideal chance to detect the abnormal cells. [9] Some activities included in quality assurance process include performing control samples on each run of tests, testing against external standards, double testing of some abnormal results, and identifying the normal range and extent of variability in the test results. [10] Any lesions detected following screening for cancers, may not imply subsequent progression to disease status.

Targeted surveillance can benefit the high-risk group of individuals (those with precancerous conditions and/or risk of familial inheritance). This issue is evident among people with a family history suggestive of hereditary non-polyposis colorectal cancer (HNPCC) and familial adenomatous polyposis (FAP). The challenge of colorectal cancer prevention among such high-risk individuals includes surveillance appropriate for these syndromes, irrespective of whether genetic testing is available or uninformative. The guidelines for such a program will be markedly different from those for people with average risk. [10]

Lead-time bias is the period by which screening advances the diagnosis of disease, and it accounts for the improved survival of screen detected cases. Another bias which needs to be considered while evaluating cancer programs includes length-biased sampling, which occurs among rapidly progressive cancers. An appropriate indicator includes the cancer-specific mortality rate (Cancer deaths per 1000 screened) rate, which is computed regardless of the interval between detection and death[8].

There are many facilitators and barriers for implementing cancer prevention strategies in healthcare settings. The uptake of HPV vaccination among adolescent girls is influenced by behavioral and health system-based factors, and cultural sensitivities influence cervical cancer screening programs. After a positive result on screening test, adherence to treatment regimen is also influenced by social factors. Successful implementation of such programs relies on awareness initiatives and community empowerment. The psychological and financial consequences of a false positive screening test include the stress and downstream diagnostic and therapeutic expenditure respectively. Thus, evaluation of public health interventions assumes importance and mandates further research into health systems.

Cancer statistics and registries provide information on geographical heterogeneity, and temporal trends which potentially generate etiological hypotheses. They also enable the identification of the process and outcomes of cancer management, which in-turn enables the quality assessment of cancer control iterations. A comprehensive health information system ensures improvement of efficiency of health services through better management at all levels. The IARC's Global Initiative for Cancer Registry Development [11] facilitates the coverage and quality of cancer registration in LMIC.

Priority areas for research

The structure and behavior of a tumor can be quantitatively modeled using a mathematical framework. Cancer research in LMIC should prioritize the risk factors prevalent in their geography. It is important to study exposure over the life course, including early stage of life. It is imperative to invent effective early detection methods, given the rising incidence of breast cancer in women and prostate cancer in men. The focus areas in cancer research include its prevention and implementation, and further exploration of the causal factors in prostate cancer, colorectal cancer, leukemia, lymphoma and renal cancer. Other areas of research include cancer risk among individuals living with HIV, given their susceptibility to other cancer-associated chronic infections. Also, there is a compelling need to reduce exposure to aflatoxins.

Conclusion

This editorial conceptualizes a unique cancer control program which is disparate from the NCD program. Among other approaches for NCD management, cancer demands a complementary approach given its specific features. Implementation of such a program in LMIC entails distinct cogitation, with focus on prevention, risk reduction and relevant research. With regard to cancer management, evidence for priority setting process is aided by the research findings. Political declarations tend to shape the cancer research agenda.

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