Role of cancer awareness in prevention of its outbreak: current scenario in Pakistan

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Abstract: Cancer is one of the major threats to mankind after heart diseases. In developing countries, malnutrition and parasitic infections are more serious but cancer has a unique significance because roughly one in the five persons on the face of earth expires due to this ailment. It is traditionally thought to be a disease that has a strong bond with industrial revolution, modern world and chemicals exposed life style on the planet. Excluding the other cancers, solely breast cancer contributes 45% of its cases and 55% deaths occur in low and middle income countries like Pakistan who are in the queue of that transition stage of modernism once faced by the nations. In this review, we discuss the epidemiology, causes, challenges, screening and managerial issues along with a bird's eye view of cancer status in Pakistan that might be helpful in devising preventive and treatment strategies in the future.

INTRODUCTION

The rate of cancer is mounting in Pakistan. Factors like paucity of health awareness and education, social and cultural norms, inadequate and outreach facilities, exposure to chemical pollutants are involved in reducing our immunity as a whole. Myriad barriers are identified as far as the cancer patients are concerned, economics and social status is one of the major hindrances in this regard in developing and low-income countries. Secondly late diagnosis of any sort of malignancy increases the chances of hopelessness. No doubt fewer hospitals, lack of technical expertise, government funding, persistency and continuality of public health policies are the other concerns in the augmented prevalence of cancer in our country.

Pakistani women like the regional countries; India and Bangladesh due to the resemblance in the culture and habitat. Occurrence of this malignancy is almost same in the West as well[1].

Neoplastic cells or tumors are classified according to the embryonic origin of tissues from which the tumor is derived. Carcinoma is the cancer that arises from ectodermal or endodermal tissues such as epithelial of internal organs, glands and skin. More than 80% cancer falls in this category. Similarly leukemia relates to hematopoietic cell and lymphomas affect the lymphatic system, a network of vessels and nodes that acts as the body's filter. The lymphatic system distributes nutrients to blood and tissue on one side and prevents foreign "invaders" from entering the bloodstream on the other.

There are more than twenty different types of lymphoma whose occurrence is 9%, while sarcomas are tumors that originate in bone, muscle, cartilage, fibrous tissue or fat with 1% of prevalence only[2].

Epidemiology

The most common cause of global increase in cancer is "Westernization" in the developing world[3] among which breast cancer is at its pinnacle in the west a decade before but now its rate of incidence in the eastern countries of third world is also increasing with the same pace. Pakistan is in its heydays regarding the outbreak of different types of cancer incidences which were never seen before.

It is estimated that 45% of the 1.35 million new cases diagnosed each year, and more than 55% of breast cancer related deaths occur in low and middle income countries[4]. It is expected that 1.7 million women will be diagnosed with carcinoma of breast in 2020 that will be 26% more than the current incidences particularly in the developing countries[5].

Trend of fast food and busy life routine which proved to be a gateway for all types of ailments especially due to the lack of exertion and physical exercise, the most obvious causes of ever happening diseases, as far as Breast cancer is the most prevalent cancer in women. Pakistan has a younger patient population with larger tumors, higher grades, and more advanced disease stage on presentation than does the United States. Receptor-negative tumors are also more common[6]. Carcinoma of the ovary is the most common cancer of gynecologic origin in Pakistan[7,8].

Consanguineous marriages might be one of the reasons of these two cancers. Pakistan has one of the highest rates of consanguinity in the world[9]. In general 58.7% and 62.7% consanguinity was observed in Pakistan but when observed more rigorously regarding the first cousin marriages it is 83.6% and 80.4% in two different studies of Karachi survey (KS) and demography and health survey (DHS) respectively. Similarly the mean coefficient of inbreeding in the children of the present

generation was 0.0316 in the Karachi survey and 0.0331 in the DHS[10]. The overall frequency of consanguineous marriages is 60–76% in Pakistan. Inbreeding is known to increase the risk of diseases caused by homozygosity of deleterious recessive genes. Parental consanguinity has been implicated in 60% of mortality and severe morbidity in Pakistani children born in Britain and autosomal recessive disorders affect 3.7% of all Pakistani children. An excess of childhood cancers was also reported among children of consanguineous marriages in Britain[11].

Kidney and bladder under the genito-urinary system and hematological chronic myeloginous leukemia (HCML) while other cancer which are with highest rate in Pakistani females are breast and ovarian while prostrate in males [13]. In respect to reported cases in different hospitals, male cancers accounted for 47.7% which are leukemias, non-Hodgkins lymphoma and lungs, while female cancers reported 52.2% of the total cases, in which breast cancer is the most common cancer accounting for 38.5% followed by 13.6% ovarian cancer[14].

Breast cancer

Breast cancer is the most prevalent cancer in the world whilst among the Asian countries Pakistan is at its highest rate. Approximately 5 to 10 % of breast cancers are inherited. Which are due to germ-line mutations in the *BRCA1* (MIM 113705) and *BRCA2* (MIM 600185) genes. Mutations in these genes are responsible for familial clustering for the majority of breast and ovarian cancer families and for about one-half of site-specific breast cancer families[15]. Regarding the putative causes, its outbreaks are associated with delayed parity, reduced trend of breast feeding, donning of dark colored bra specially black in color which absorbs virtually all spectrum of light and facilitate to being more prone to mutations, early menarche which is according to some traditional thought is by induced milking by milkmen through the injection of some hormones at the time of milking. Intake of such sort of milk perturbing the hormonal balance in the body and early signs of puberty and secondary sex characters that should be self regulated in accordance to the phase of age especially in the urban areas of Punjab and Sind province of Pakistan which are confronting the scarcity of milk.

Ovarian and cervical cancer

It is sixth most common cancer and the seventh cause of death among cancers in women in the world and emerges with 204,000 cases and 125,000 deaths. which is 4.0% and 4.2% in reported cases and deaths respectively[16]. At least 10% of ovarian cancers are hereditary which evolved the germ line mutation.

There is little information on the possible role that recessive genes play in adult cancer. A study in Pakistan has described an association between consanguinity and the risk of breast cancer[12]. Study of the Pakistani population offers the potential to explore the contribution that consanguinity makes to breast and ovarian cancer rates. The most common maladies in this list which are categorized on the basis of organ, as far as the gastrointestinal tract is concerned are esophageal, stomach, liver, gall bladder and anal, vaginal, ovarian and prostrate under the gynecology.

BRCA1and BRCA2 genes like breast cancer. Human papillomavirus (HPV) was also being noticed as a major causative agent for cervical carcinomas. Based on their oncogenic potential, HPV subtypes have been divided into high- and low-risk. HPV screening in Pakistani female patients is not being commonly practiced and as a consequence, the degree of HPV prevalence and its correlation with cervical cancer is unknown. There is strong relationship between HPV infection and cervical cancer among Pakistani women and results of some of the studies underscore the need to implement regular HPV screening. An early diagnosis of HPV infection will allow better health management to reduce the risk of developing cervical cancer[17]. Regarding the prevention, the vaccines of its two subtypes 16 and 18, which cause 70% of cervical cancer[18] have been developed and being controlled by vaccination.

Leukemias

Leukemia accounts for some 300,000 new cases each year (2.8% of all new cancer cases) and 222,000 deaths in the world. This rather high ratio of deaths/cases (74%) reflects the poor prognosis of leukemia in many parts of the world, where somewhat complex treatment regimes required are not available. Pakistan is confronting the scarcity of medical related facilities but instead in the front line to combat against these cancers. Proportion of T cell acute lymphoblastic leukemia (TALL) among known acute lymphoblastic leukemia (ALL), Pakistani patients are 17.22% and similar to that reported in the region as well. Mean age of the TALL patients was 17.2 years and it is higher in adults than in children (21.95% vs 14.17%). Overall there are more male patients affected by TALL (25/36 or 69.40%) than females (11/36 or 30.60%). The female to male ratio among TALL patients is 1:2.27. However, the proportion (%) of TALL in females is higher than males (18.96% vs. 15.82 %) i, e, 1.2:1. The CD7 was found to be the most sensitive among both adults & children. It is positive in 94.4% of the TALL cases[19].

Non-hodgkin lymphoma

Advances in molecular biology, genetics and immunology have resulted in extensive changes in the classification of lymphoid tumors in the last few decades. The World Health Organization (WHO) classification distinguishes tumors primarily by cell lineage defined by immunophenotype and groups together lymphomas and leukemias, acknowledging that some solid tumors also pass through circulating leukemic phases. Three broad categories are now recognized: B-cell neoplasms, T/NK-cell neoplasms, and Hodgkin disease. Lymphocytic leukemias fall within the B-cell neoplasm group.[20] According to one of the epidemiological study, A total 780 specimens were collected within five years from the cases classified as adult Non Hodgkin's lymphoma (NHL). Out of which 596 (76.4 %) were diagnosed as diffuse large B cell lymphoma (DLBCL). The gender ratio was 2.3:1 (M:F) and the median age was 47.2 years with an age range of 15-85 years. Nodal-NHLs constituted 42.2 % of all adult NHLs with the cervical lymph nodes as the most frequent nodal site of presentation[21].

Lungs cancer

Major cause of this malady is smoking alike rest of the world. Other causes include lethargic life style, lack of body exertion, industrial effluents and pollutants in the environment. According to histological type, human pappiloma virus (HPV-16) was detected in 8/18 (44%) squamous cell carcinomas (SQCs), which were mainly from Pakistan; 0/38 (0%), the results support the notion that HPV-16 infection is highly associated with SQCs in Pakistan[22]. This cancer has been the most common in the world since 1985 to 2002. There were 1.35 million new cases representing 12.4% of all new cancers. It was also the most common cause of death with 1.18 million deaths or 17.6% of the world in total. Geographic patterns of lung cancer incidence and mortality are very much influenced by past exposure to tobacco smoking while geographic pattern in women reflects rather different historical patterns of smoking from those in men. The proportion of lungs cancer cases due to tobacco smoking can be estimated by comparing observed incidence or mortality in different areas with that expected based on rates in nonsmokers from several large cohort studies[23].

Oral cavity cancer

Pakistan is premier in the occurrence of this cancer in the world due to chewing the betel and areca (plant material) smokeless tobacco especially in the Sind province[24]. There are significant variation in the distribution of site-specific cancer mortality and incidence by region. A curb on the use of tobacco and areca nut would reduce the epidemic levels of this malignancy by 43.7% and 17.8% in males and females respectively. WHO estimates put these figures at 45% and 18.5% for males and females respectively[25]. Another study conducted in Karachi ranked second in all malignancies among both males and females with the highest reported incidence in the world. Chewing the products of betel, areca and tobacco are the main etiological risk factors other than the usage of alcohol. These products include paan, chaalia, gutka and naswar, because of the ancient history of these products, their usage is socially acceptable in some of the sections of South Asian societies[26].

Prostate cancer

Worldwide prostate cancer ranks third in cancer incidence and sixth in mortality. The incidence of prostate cancer is low in Pakistan with a figure of 3.8% of our male population but increased dramatically in near the past. The most likely explanation for this is lower life expectancy and no screening for prostate cancer in Pakistan [25]. Prostrate-Specific antigen PSA is very effective as a tumor marker for prostatic cancer. It is useful for monitoring therapeutic efficacy, staging, prognosis, tumor volume evaluation, detection of recurrent disease, differential diagnosis, confirmation of tissue of prostatic origin and in some cases for screening and early diagnosis as well. Both radio immuno sassay (RIAs) and immuno radiometric assay (IRMAs) have been developed for PSA[27,28]. According to another study's notion that as in many countries of the world, prostatic adenocarcinoma is extremely common in Pakistan. It is the third commonest malignancy in males, comprising almost 7% of all malignant neoplasms[29].

Colorectal cancer

In Asia the most evident increase have been in Singapore and Miyagi [30]. While in Pakistan this carcinoma is 25.4% in male and 20.1% in female [31]. Colorectal cases are increasing gradually due to our living style and feeding habits. No doubt there are genetic causes as well but chronic constipation where it leads to anal fissure and fistula like medical ailments along with cancer cases are also raising. There are strong internal correlations between risk of large bowel cancers and per capita consumption patterns of meat, fat (specifically animal fat) and fiber. Epidemiologic studies found consistent evidence that physical inactivity, excess body weight, and a central deposition of adiposity have a major influence on risk of colon cancer. The risk of colon cancer is quite labile to environmental change is evident from the study of migrants; when populations moved from low-risk to high-risk areas,

the incidence of colorectal cancer increases rapidly within the first generation, implying that dietary and other environmental factors constitute a major components of risk[32].

Early diagnosis, screening and prevention

Utmost in early diagnosis in any sort of malignancy is the awareness about that particular cancer or those must be more conscious that have tendency of cancer is their family history. Early detection and population based screening is comparatively expensive in Pakistan [33] because of the different restraints of well equipped health care infrastructure, state-of-the-art medical detection machinery and gizmo. The estimated annual incident cancer cases in Pakistan in year 2000 on the basis of Karachi cancer registry (KCR) data were 138,343 for males and 135,054 for females; approximately twice the number cited by WHO for the same year [25]. It has The Breast Health Global Initiative (BHGI) was founded in order to develop feasible, cost-effective and culturally specific guidelines for low-and middle-income countries (LMCs). The guidelines were constituted of four levels of resources which include basic, limited, enhanced and maximal. The basic-level resources were constituted of basic breast health awareness through education and self-examination and a clinical breast exam (CBE). The limited level includes CBE in addition to diagnostic ultrasound with or without mammography within limited financial means and modest health care systems. The third level involves mammography screening and the maximal level includes population-based mammographic screening [35]. Using this stepwise-based approach, advancement in LMCs health care systems may be achieved.

Pathological and clinical presentation

The vast majority of cancers (about 80%) are considered sporadic, meaning that there is no clear cause. For some reason, certain normal genes begin to mutate, multiplying rapidly and becoming malignant. According to another study "mutational screening of the exons did not reveal any pathogenic mutation. These results along with the results of the nodes) enhances the detection but with minimal rate of recovery. Histopathology of the patient needs to be considered before choosing the mode of treatment. Cytopathological along with several advanced imaging technologies that include the use of CT scan, PET scanning, MIBI scanning as well as MRI can be used for the well before diagnosis and prognosis[36,38].

Availability of health care expertise

Modified radical mastectomy after or without neoadjuvant chemotherapy is the most commonly used procedure as far as breast cancer is concerned[39].

been reported in a recent study conducted in Pakistan that the knowledge of availability of screening for cervical cancer amongst general population is only 5% and merely 2.6% of the sample have been conducted Pap test [34]. Another issue of inadequacy of mammography facility is prevailing in each and every hospital all around the Pakistan. Leading hospitals of Lahore city are Skoukat Khanam Cancer Hospital and Research Center (SKCH&RC), Institute of Nuclear Medicine and Oncology Lahore (INMOL) along with Agha Khan University Hospital Karachi (AKUH) are playing key role in awareness campaigns at least in the urban and suburbs of these provincial capital cities. Due to different reasons of impracticality in our prototype society, media in this regard can play an important role to educate the common people especially in the breast cancer self examination is concerned. previous Pakistani studies for both *BRCA1* and *BRCA2* genes were summed up to prepare a Pakistani database. Percentage involvement of these genes was estimated; about 9% of these cancers show alterations in *BRCA1* gene while 3% have shown *BRCA2* variants. The remaining 88% of breast and ovarian cancers can be attributed to the involvement of other genes[9,10].

There are several environmental influences like diet, obesity, cigarettes and long-term exposure to chemicals that may cause gene mutations to occur. In fact, a large number of cancers are preventable because most of these factors can be controlled with healthy lifestyle choices. In a recent Pakistani study, the clinical presentation of patients was highest in advanced stages III and IV amounting to 65.7% in poor societies and 43.6% in middle- and high-income societies of the country[36]. Both of these values are significantly higher than the 18.9% and 11.3% incidence of stage III and IV among African-Americans and American Whites respectively[37]. Cancer in the last stage along with metastasized ability (when neoplastic cell able to cross the basal lamina and enters in the blood capillaries or in lymph.

Major reason behind this practice could be related to the advanced stage that patients present with and the low number of radiation centers, because radiation therapy is important in the treatment of breast cancer after breast conserving surgery[40,41].

Radiation center facility can help us to devoid this burden of all sort of cancer by early detection so that patient revival rate can be enhanced at the early stage of the disease. Mostly in Pakistan patient presents in the hospitals with stage IIIa and IIIb when tumor has attain the level of 62%. On the other

hand public awareness campaign can act as catalyst in early detection e.g. in the cervical cancer which is 98% due to HPV infection according to an Indian study[42].

Promising managerial initiatives

Genetic testing is gaining acceptance worldwide and has been established throughout North America and much of Europe. Genetic counseling, especially in country like Pakistan having one of the highest rates of consanguinity [9 10] is being practiced by many health professionals. However its expansion into the health policy and training regimes of health care providers is needed. The awareness about the genetic testing as a tool for preventive and treatment-oriented remedy is limited.

Prevention and treatment strategy

Up to 85% of cancers can be prevented by avoiding environmental risk factors like smoking, prolonged sun exposure, alcoholic abuse and malnutrition. Of course, things like age, race, gender and family history cannot be changed, but knowing your personal cancer risk can help you to devise a prevention strategy with regular screenings and healthy lifestyle choices. Having one or more risk factors for cancer doesn't mean you will get cancer. In fact, many people considered high risk never develop cancer while others with no known risk factors become ill.

Location, size and stage of the tumor as well as patient's overall health determine which treatment or treatments he will receive. Many new treatments, including cancer vaccines and gene therapy are being studied in clinical trials. A team of specialists required to meet patient's individual needs. The team may include a medical oncologist, a surgeon, a radiation oncologist, a pathologist, a pharmacist, a dietician and other health care professionals to coop the putative complexities in the course of successful recovery of this ailment.

Unfortunately, many types of cancer don't display any obvious symptoms or cause pain until well advanced. Because early-stage cancer symptoms tend to be subtle, they are often mistaken for signs of other less threatening diseases. Here are the seven warning signs of cancer: Changes in bowel or bladder habits, a sore that does not heal, unusual bleeding or discharge, thickening or lump in the breast or any other part of the body, indigestion or difficulty swallowing, an obvious change in a wart or mole and nagging cough or hoarseness.

Hierarchy of most prevalent twelve cancers in both sexes are stomach, lungs, breast, colon/rectal, cervix/mouth/pharynx, esophagus, liver, lymphatic, prostrate, bladder and leukemia[43]. Every sort of malignancy can be treated as the stage of presentation and availability of resources. There are defined cascade of treatment given by the BHGI according to which there are four or five major types of cancer treatment: surgery, radiation therapy, chemotherapy and immunotherapy. These therapies can be used either alone or in combination with each other.

Methods of cancer treatment

Surgery is the oldest form of cancer treatment. About 60% of cancer patients will undergo some sort of surgery, either by itself or in combination with other therapies. Chemotherapy uses powerful drugs to kill cancer cells, control their growth or to relieve pain symptoms.

Radiation uses large doses of high-energy beams or particles to destroy cancer cells in a specifically targeted area. Immunotherapy also known as biologic therapy stimulates the body's own defense systems to fight cancer. Gene Therapy identifies missing or defective genes that cause cancer or increase cancer risk, and replaces them with normal copies.

Conclusion

Significant advancements are made in cancer care worldwide, patients in Pakistan still present at an advanced stage. Fewer screening and diagnosing facilities, lack of care, management and treatment of those who are diagnosed with cancer, are serious issues to be addressed without further delay. SKMCH&RC along with two other INMOL and AKUH are in continuous endeavor to cope with this dilemma in the public health sector, but still there is a huge task for the health policy makers, medical professionals and researchers to streamline the process of timely diagnosing the cancer and to find ways and means to tackle this issue with untiring efforts and actions. Antecedent use of unconventional therapies before seeking any medical advice is widespread. There is a dire need to educate the public to augment awareness about cancer prevention and treatment.

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