Editorials

Breast Cancer: An Indian perspective

Public health perspective in a non-communicable chronic disease requires attention to yardsticks such as incidence, mortality, survival, quality of life and cost-effective adoption of technology. Breast cancer is no exception. Because of its tryst with this ailment decades earlier, the developed world has much to convey to the developing world, including India. It will be instructive to consider the effect of various interventions on the above-mentioned end-points in the developed world and plan appropriate healthcare policies in India.

Incidence

The incidence of breast cancer has been increasing in India in the past few years and has overtaken uterine cervical cancer as the commonest cancer in women in metropolitan cities. This has been due to an increase in the incidence of breast cancer and a gradual decline in that of cervical cancer. The increase in the incidence of breast cancer has been minimal in women <40 years of age (average annual percentage change [AAPC] 0.3%) and modest in those between 40 and 50 years (AAPC 1%). The greatest increase has been in post-menopausal women >50 years of age (AAPC 1.4%; Table I; Arun Kurkure, personal communication). The incidence of breast cancer in the USA followed a similar pattern, with the greatest increase in women >50 years of age.[1] Although not well studied across populations, it is likely that many features of urbanized lifestyle are responsible for this increase. Despite the similarity in temporal trends in incidence, the actual crude and age-adjusted incidence of breast cancer (Table I) and the general population pyramid are remarkably different between India and the West (Fig. 1) with profound implications for public health perspective and discourse. As >80% of the female population in India is <50 years of age, in contrast to just over 50% in the USA, it is inappropriate to expect public health interventions that have been proven effective in older women in the West to work equally well in

TABLE I. Age-specific incidence rates of breast cancer in Mumbai, 1976–2005

Age (years)	1976–80		1981–85		1986–90		1991–95		1996–2000		2001–05	
	n	ASR	*n*	ASR	*n*	ASR	*n*	ASR	*n*	ASR	*n*	ASR
25–29	60	3.6	87	4.5	89	4.1	107	4.5	110	4.2	105	3.7
30–34	109	8.6	161	10.8	197	11.5	252	13	261	11	265	11.2
35–39	216	19.5	296	22.5	368	23.6	451	24	481	23.6	504	22.1
AAPC (25–39 years) 0.3%												
40–44	270	32.7	368	37.7	484	42.8	605	46.9	652	42.3	806	46.3
45–49	330	47.6	417	49.9	492	52.4	665	60.2	823	61.6	946	60.8
AAPC (40–49 years) 1%												
50–54	296	56.3	385	60.9	588	81.9	657	78.7	757	76.2	1006	87.5
55–59	226	65.9	323	75.2	385	72.7	566	91.4	615	84	755	91.4
60–64	209	66.7	260	68.3	355	78	537	100.4	587	93.6	722	99.3
65–69	152	81.9	178	77	287	104.9	355	101.6	499	105.3	589	98.0
70–74	83	63.1	103	63.7	180	95.3	286	120.4	324	104.3	416	105.6
AAPC (50–74 years) 1.4%												

ASR age-specific rate AAPC average annual percentage change Source: Mumbai Cancer Registry

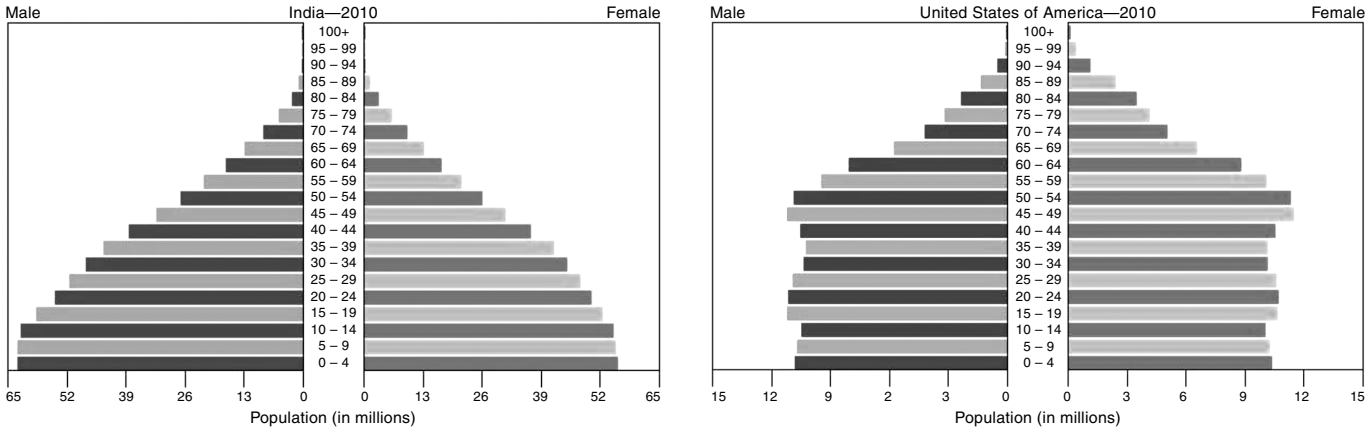

FIG 1. Population pyramids of India and the United States of America in 2010. *Source: US Census Bureau*

India. For example, with identical test characteristics (sensitivity and specificity), routine screening mammograms will lead to many more false-positive results in a low incidence country such as India than in the higher incidence societies of the West. These facts are often overlooked when passionate debates rage on the utility of such interventions.

It will be useful to reflect on the causes of the increasing incidence of breast cancer in India. Of special note is the fact that, unlike in the West, this is a real increase uncontaminated by overdiagnosis due to mass screening of an asymptomatic population. The increasing incidence in India is due to an increase in the age at first childbirth, decreasing trend in urban mothers for prolonged breastfeeding, increasing obesity and awareness and willingness among women to seek medical care in the presence of breast symptoms. While the societal trend towards reduced fertility is non-modifiable (even desirable!), it is possible to educate young Indians about the appropriate age to initiate childbearing (perhaps best before 30 years of age) and the importance of breastfeeding, not only for the child but also for the mother. This will require education and an enabling environment that allows young working women the privilege of temporary recusal from work without long term effects on their careers. Obesity is the other potentially modifiable risk factor that requires multidimensional preventive attention with major health benefits that extend beyond cancer prevention. Societal and public health intervention in these areas has the potential to reverse much of the increase in the incidence of breast cancer that has been observed in the West.

Systematic population-based screening is one additional reason for the increase in incidence of breast cancer in western societies. All screening procedures (clinical breast examination, mammography) have this effect on incidence that varies in magnitude from 30% to 40%.[2] This is evident in all screening trials in which the incidence increased by 30%–40% in the first 5 years in the screened arms and about half of that difference persisted beyond 10 years of initiation of the study. One explanation for this phenomenon is detection of occult indolent cancers by screening that are not destined to ever have a clinical impact, the so-called problem of overdiagnosis. Therefore, it is important to apply the yardsticks of reduction in breast cancer mortality (preferably all-cause mortality) while planning public health interventions such as screening. Based on this talisman it would be hard to justify the introduction of populationwide breast cancer screening, especially using expensive and imperfect techniques such as mammography, in India at present.

Mortality

Death rate per 1 00 000 population is the best indicator of the magnitude of a problem and its interaction with public health interventions and/or treatment. Breast cancer is one of the highest contributors to mortality in women in developed countries because of its high incidence. It would be a misfortune (and lack of foresight) if India travels

the same road in the next few decades. Mortality can be reduced by reducing the incidence of disease or improving treatment outcomes. There are two conventional methods of improving outcome in breast cancer—early detection by screening and improving treatment or its delivery. Screening has been shown to reduce the mortality of breast cancer in women >50 years of age but the results between 40 and 50 years of age are controversial. Of note, only 13% of the Indian population is >50 years of age. In one elegant trial[2] the combination of mammography and physical examination (compared with physical examination alone) did not reduce the mortality from breast cancer. There is no direct comparison in a randomized trial, of physical examination and health education. The Mumbai study[3] with 1 50 000 women will answer this question but until then clinical breast examination can be a reasonable public health intervention for downstaging breast cancer in women >50 years of age. This will require integration of preventive oncology services in the primary healthcare programme with defined referral pathways, a difficult but not insurmountable task. Mammography requires considerable investment in equipment and expertise, is beset with the problem of overdiagnosis and probably inappropriate for populationwide implementation as a screening measure in India. There is also a need to explore novel screening methods that are more likely to detect clinically important cancers at an earlier stage.

Improvement in treatment modalities and their delivery is known to have a positive effect on breast cancer mortality and survival.[4] However, there is lack of reliable documentation of cause-specific mortality in India. No registry other than the Mumbai Cancer Registry reports on mortality. There is an urgent need to link municipal and government death records with cancer registries to derive reliable and meaningful conclusions about the disease and its interaction with treatment.

Survival

Clinical trials in adjuvant radiation and systemic therapy (chemotherapy and endocrine therapy) have shown modest improvement in cure rates at a reasonable cost. It is now necessary to disseminate this evidence as guidelines[5–7] and improve compliance for effectiveness. The gains derived from these treatments are implementable due to their feasible cost of delivery. The systemic treatment with the greatest worldwide impact on breast cancer mortality has been tamoxifen. It has been repeatedly shown to be effective in preventing relapses even decades after its administration.[8] Its appropriate use is hampered in India due to lack of reliable oestrogen receptor testing. There is an urgent need to make quality pathology testing available to all centres treating breast (and other) cancers throughout India, perhaps on a defined referral basis. The high cost-effectiveness of treatments such as tamoxifen is not true of targeted therapies such as trastuzumab that have also led to better cure rates, but at a prohibitive cost. At present, <5% of eligible patients are able to access the latter treatments. It will be important to improve accessibility to such interventions through reduction in their cost and evaluation of novel schedules such as short term perioperative or postoperative use.[9]

Quality of life and cost-effectiveness

Breast-conserving surgery is the standard of care in early breast cancer with proven long term equivalence to modified radical mastectomy in terms of survival and a positive impact on the quality of a woman's life. In India the rates of conservation are dismal (<10%) except in a few centres where it varies from 30% to 70%.[10] The possible reasons include lack of adequate radiation facilities, lack of surgical expertise and the non-availability of essential multidisciplinary inputs such as adequate imaging and pathology. This situation needs rectification. Other surgical advances such as sentinel lymph node technique have also been shown to improve the quality of life by reduction in the incidence of arm oedema in patients in whom full lymph node dissection is avoided. However, because of the requirement for radioisotope facilities, steep learning curve and the lack of local validation in large, well-conducted studies, its widespread applicability remains doubtful. Other forms of reduced axillary surgery that are less technology intensive such as untargeted low axillary sampling or four lymph node biopsy have also been shown to reduce arm oedema, have low false-

negative rates (<10%) and are more feasible and cost-effective.[11–14] A prospective comparison of all these techniques is currently being done at Tata Memorial Hospital, Mumbai and will define the local standard of care for axillary surgery in the near future. In the context of cost-effectiveness, uncritical adoption of new technologies such as positron emission tomography and newer forms of radiation delivery, without adequate evidence of impact on survival, toxicity or quality of life is also likely to be cost-ineffective.

Research agenda and delivery of care

Research efforts in India have to be multidimensional and interconnected. The industry should (and will) test products from its laboratories with adequate protection of intellectual property. Healthcare professionals should (and often do not) conduct well-designed clinical trials that test cost-effective treatment options. There must be adequate cross-talk between industry and the academia that is sorely lacking at present.

Delivery of care would vastly improve with uniform implementation of evidence-based guidelines and will impact immediately on mortality from breast cancer. The guidelines need to be contextual to the Indian circumstances and appropriately flexible in catering to variable levels of infrastructure and expertise. Since 2003, Tata Memorial Hospital, Mumbai has conducted annual conferences with the express aim of evolving such guidelines. The meetings focus on collation of high quality evidence in relation to pre-identified clinical problems in breast cancer with incisive discussion on their feasibility and applicability in various settings. Robust evidence that can be implemented in rural, urban and semi-urban locales is adopted as a guideline and that which can be implemented only in tertiary hospitals is recorded as a referral guideline. The evidence is then put into a matrix as per its robustness and applicability and is collated as minimum, optimum and optional to guide healthcare planners.[5–7] These guidelines are revisited every year to incorporate new evidence.

An important area of concern is the inadequate and unequal availability of specialist expertise in the delivery of breast cancer care. Specialist care has been shown to improve outcomes in many cancers[15] including breast cancer.[16] There is a need to initiate fellowship programmes in breast diseases with subsequent accreditation to treat breast cancer in metropolitan India and stipulated requirement of training for semi-urban and rural areas.

The way forward

India faces considerable challenge in provision of adequate care to a large number of breast cancer patients at present. Especially challenging is to abridge the wide disparity in healthcare delivery across geographic and socioeconomic divides. An even greater challenge is to prevent the increasing incidence of breast cancer in India. This will require efforts in researching and preserving those aspects of our lifestyle that have historically resulted in a low incidence of breast cancer, only a small fraction of that seen in the West. Concerted multidimensional action and leadership, as outlined above, is required.

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