

RESEARCH COMMUNICATION

Breast Cancer Trends in Indian Residents and Emigrants Portend an Emerging Epidemic for India

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Abstract

Purpose: As developing nations such as India become increasingly Westernized, incidence rates will increase for many cancers. Presently, breast cancer is the leading cancer site in female residents of India, but rates are considerably lower than in Western countries. Trends observed in Indian immigrants to the West may help predict changes expected in India. **Methods:** Data were obtained from Indian cancer registries, the SEER program in the USA, IARC scientific database, and published studies. Incidence, age at diagnosis, stage at diagnosis, and hormone receptor status in these three populations were compared for the period 1993-1999. **Results:** Age-adjusted (to world standard population) incidence rates (per 100,000) in Indian immigrants (47.0-61.0) were higher than in Indian residents (7.2-33.4) but lower than in Western whites (83.1-112.0). Compared to Indian residents, Indian immigrant cases tended to be older (49 years +), diagnosed at an earlier stage, and more often hormone receptor positive, sharing similarities with Western white women. **Conclusions:** The intermediate breast cancer trends exhibited by Indian immigrants may help predict future incidence trends amongst Indian (particularly urban) residents, which have major public health implications for India as urbanization and Westernization continue. We suggest adding demographic variables to cancer registry data, and additional studies on immigrant Indian populations.

Key Words: Breast cancer - incidence - immigrant - India - South Asian - Western - whites

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Introduction

Emigration from India to Western countries such as Canada, the UK, and the US continues to increase the number of Asian Indians in the West (see Table 1 for terminology describing ethnic subgroups). This group has shown one of the highest growth rates in these nations over the past two decades. As previous studies of breast cancer in immigrant Asian populations have shown, cultural changes can greatly impact the risk of breast cancer (Hedeen et al., 1999; Lin et al., 2002; Deapen et al., 2002; Hislop et al., 2007). As emigrants acculturate from their traditional diets and lifestyles their cancer incidence gradually changes towards that of the host country. Consequently, the distribution and determinants of chronic diseases such as cancer may be distinctly different in Indian emigrants compared to residents of India, and may indicate the changes in incidence to be expected within India as it becomes increasingly westernized.

According to the US Census Bureau, in year 2000 there were more than 1.6 million Asian Indians in the US, comprising 0.6% of the United States population (US Census, 2001). This is the third largest constituency of

Asians in the US, after Chinese and Filipinos, and has the largest growth rate of any Asian American population, doubling between 1990 and 2000. According to the 2001 UK census, the total number of Indians in the UK is over one million; it is the largest Asian ethnic group constituting 1.8% of the UK population, and approximately 22% of the total UK non-white population (UK Census, 2003). In spite of the large numbers of Asian Indians, cancer in this group has been only minimally investigated (Li et al, 2002; Hislop et al, 2007). This paper reviews trends in female invasive breast cancer incidence in residents of India, Indian emigrants to the West, and in Western populations.

Materials and Methods

The National Cancer Registry Program (NCRP) of the Indian Council of Medical Research (ICMR) has established thirteen population-based cancer registries in India, six of which have been functioning since the 1980s and seven which started functioning only recently (2003). Additionally, there are several population-based registries, which do not directly function under NCRP, situated in various geographical regions (Figure 1). We used data

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Figure 1. Network of Cancer Registries in India (Courtesy of Dr A. Nandakumar, ICRM)

published by the six registries of the NCRP established in the 1980s and six non-NCRP registries for the periods 1993-1997 and 1997-1999 to obtain age-specific and age-adjusted (to world standard population) incidence rates of breast cancer in women from various regions of India (Nandakumar et al., 2004). Additionally, data for approximately the same time period (1992-1999) from the Surveillance, Epidemiology, and End Results (SEER) Program of USA (SEER, 2001) were used to obtain age-specific and age-adjusted (to world standard population) incidence rates for US whites.

SEER statistics were used to estimate the incidence of breast cancer in Indian immigrants to the US. The SEER racial/ethnic category "South Asians" is comprised primarily of Indians (Divan, 2004) and therefore serves as a good approximation for Indian immigrants and their descendents. For each five-year age group we estimated age-specific incidence rates by using the number of cases in South Asian women as the numerator, and the US census data for this ethnic group as the reference for the denominator. A similar approach has been used in comparative immigrant studies by other researchers in the past (Flood et al. 2000; Lee et al., 2007). Age-adjusted

Table 1. Terminology Used to Describe Ethnic Groups

Indian immigrants	Persons who themselves immigrated to the West from India, or are descendants of someone who immigrated from India.
Asian Indians*	Persons reporting India as country of birth/origin.
South Asians	Persons reporting origins in the Indian subcontinent (India, Pakistan, Bangladesh, Nepal, Sri Lanka, Bhutan, and Maldives).
Asian*	Persons reporting origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent
Indian residents	Citizens of India residing in India
Whites*	Persons reporting origins in any of the original peoples of Europe, the Middle East, or North Africa.

*Source: US Census Bureau. Available at: <http://www.census.gov/prod/cen2000/doc/sf4.pdf>. Accessed May 10 2007.

incidence rates in the UK and other nations for the corresponding period (1992-1999) were obtained from the International Agency for Research in Cancer (IARC)'s 'Cancer Incidence in Five Continents - Vol VIII' publication (Parkin et al., 2002).

Data for stage at diagnosis and hormone receptor expression were obtained from published studies. Since the acculturation pattern of Indian immigrants results in their lifestyles becoming more similar to Western whites rather than any other group such as blacks, we chose the Western white group for comparison in this paper. Only invasive breast cancer is discussed in this review.

Results

Breast Cancer Incidence in India

Age-adjusted breast cancer incidence rates in India (1997-1999 rates, world standard population) ranged from 7.2 to 33.4 per 100,000 (Table 2, 3) and were significantly lower than in Western countries such as the US for the same time period (Raina, 2005) (Table 3). However, breast cancer incidence rates in India are increasing in all regions. For example, the 1997 incidence rate of 27 per 100,000 in the Chennai registry in the South and 31 per 100,000 in the Mumbai registry in the West (Table 3) is a noticeable increase from the 1987 rate of 23 per 100,000 and 26 per 100,000 respectively (Nandakumar et al., 2004; Hebert et al., 2006). At the same time breast cancer has replaced cervical cancer as the leading cancer site in most registries (Pal and Mittal, 2004). This is particularly true in urban areas, but has occurred even in predominantly rural areas such as Eastern Rajasthan (covered by Ahmedabad registry-Figure 1) (Sharma et al, 1994). The lowest age-adjusted breast cancer incidence rate (7.2 per 100,000) was reported for the rural area of Barshi (in the Western Indian state of Maharashtra), and the highest rates (>30 per 100,000) were in metropolitan regions of Delhi and Mumbai (previously known as Bombay); the registry at

Table 2. Female Age-Adjusted Breast Cancer Incidence Rates from the 12 Registries in India (per 100,000 Women, Standardized to World Standard Population).

Setting	Registry	Incidence Rate	Years Covered
Rural	1 Barshi*	7.2	1997-1999
Semi-urban	2 Karunagappally	15.0	1993-1997
	3 Thiruvananthapuram	19.7	1993-1997
	4 Ahmedabad	19.1	1993-1997
Urban	5 Nagpur	24.2	1993-1997
	6 Bhopal*	24.8	1997-1999
	7 Pune (Poona)	26.9	1993-1997
Metropolitan	8 Bangalore*	25.0	1997-1999
	9 Kolkata	25.1	1998-1999
	10 Chennai*	27.0	1997-1999
	11 Mumbai*	31.3	1997-1999
	12 Delhi*	33.4	1997-1999
Range		7.2 - 33.4	

* NCRP registries. Source: Nandakumar A, Gupta PC, Gangadharan P, Visweswara RN (2004). Development of an Atlas of Cancer in India, First All India Report: 2001-2002. Bangalore, India: National Cancer Registry Programme (ICMR).

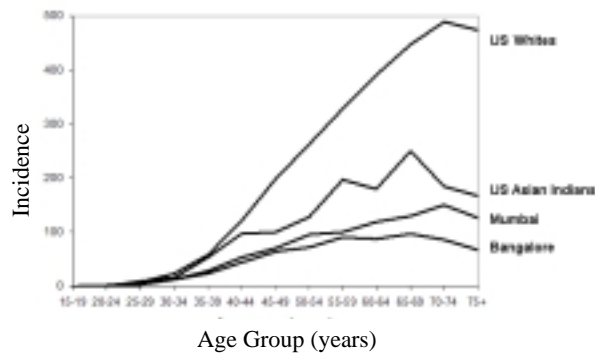


Figure 2. Female Age-Specific Breast Cancer Incidence Rates in US and India Populations (per 100,000 women). Source: ¹Nandakumar A, Gupta PC, Gangadharan P, Visweswara RN (2004). Development of an Atlas of Cancer in India, First All India Report:2001-2002. Bangalore, India: National Cancer Registry Programme (ICMR). ²Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*State Database: Incidence - SEER 11 Regions Public-Use, Nov 2001 Sub (1992-1999), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistic Branch.

Karunagapally, a semi-urban area in Southern India, reported an intermediate incidence rate of 15 per 100,000. Nearly 80,000 new cases of breast cancer are reported annually by the Indian registries (Sinha et al., 2003). This number is projected to exceed 100,000 by the year 2010 (Saxena et al., 2002), when the population of India will be about 1.16 billion (World Health Organization, 2000).

Table 3. Female Breast Cancer Incidence Rates for Indian Residents, Indian Immigrants, and Western Populations (per 100,000 women, standardized to the world population)

Population	Location	Years Covered	Incidence Rate
Indian residents ^a	Karunagapally Delhi	1993-1997	15.0
		1997-1999	33.4
Immigrant Asians and descendants			
South Asian ^b	UK	1990-1992	46.6
South Asian ^c	California (USA)	1993-1997	66.6
South Asian ^d	USA	1992-1999	61.0
Western			
All ^e	England (UK)	1993-1997	74.4
White ^d	US	1992-1999	98.3
White ^d	San Francisco, California (USA)	1992-1999	112.0

Sources: a. Nandakumar A, Gupta PC, Gangadharan P, Visweswara RN (2004). Development of an Atlas of Cancer in India, First All India Report: 2001-2002. Bangalore, India: National Cancer Registry Programme (ICMR). b. Winter H, Cheng KK, Cummins C, Maric R, Silcocks P, Varghese C (1999) Cancer incidence in the south Asian population of England (1990-92). *Br J Cancer* 79: 645-54. c. Jain RV, Mills PK, Parikh-Patel A (2005) Cancer incidence in the south Asian population of California, 1988-2000. *J Carcinog* 4:21. d. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 11 Regions Public-Use, Nov 2001 Sub (1992-1999), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch e. Parkin DM, Whelan S, Ferlay J, Teppo L, Thomas D. Cancer Incidence in Five Continents, Vol. VIII. Lyon: IARC Scientific Publication, 2002

Consequently, breast cancer is emerging as a serious public health concern for India.

Age-specific breast cancer incidence rates in most Indian registries, for example Mumbai and Bangalore (Figure 2), show a steep increase during premenopausal years (age 15-49) after which the rates plateau (Yeole and Kurkure, 2003), a pattern typical of more traditional societies. A study conducted in 2003 at a cancer hospital in Delhi reported that breast cancer was most prevalent in the 30-40 year age group, accounting for 40% of cases (Goel et al., 2003). At Tata Memorial Hospital (Mumbai), one of the largest cancer hospitals in India with a hospital-based cancer registry, 63% of cases were in premenopausal women (ages 15-49) (Desai et al., 2000). These observations reflect both the young age at diagnosis and the large number of younger people in Indian populations, where proportionately fewer women are in the over 60 age group. Most breast cancer cases in India present with advanced disease (Chopra, 2001). More than 50% present with stage III or IV (Hebert et al., 2006) (American Joint Committee on Cancer (AJCC) system) and in some areas as many as 70% of cases are locally advanced (stage III) at diagnosis (Goel et al., 1995).

Comparison with Immigrants and Western Populations Incidence

As shown in Table 3, the comparatively low risk for breast cancer in Indian women becomes much greater when they emigrate from India to Western nations. Age-adjusted breast cancer incidence rates (standardized to world standard population) for Indian immigrant women were 47 per 100,000 in England (1990-1992) (Winter et al., 1999) and 61 per 100,000 in the US (1992-1999) (Jain et al., 2005), notably higher than the 26 to 33 per 100,000 in most Indian cancer registries (1993-1997) (Nandakumar et al., 2004), but relatively lower than in Western nations such as the US (83.1 to 112 per 100,000 for white women in the various SEER registries during the same time period) (SEER, 2001) and the UK (74 per 100,000) (Parkin et al., 2002). Similarly, in California, an American state with a large Asian Indian population, the incidence of invasive breast cancer among South Asian women (composed mainly of Indian immigrants) has grown substantially over the last decade to become more similar to the rates in white women in California (Jain et al., 2005).

Up to about age 34, breast cancer age-specific incidence patterns are similar for women in Indian and Indian immigrant women; after that, rates gradually increase in Indian immigrant women to almost twice the rates seen in India (Figure 2) and retain something of the post-menopausal plateau typical of more traditional cultures. This pattern contrasts markedly with the continued rise with age seen in Western women (e.g. US white women), who have almost twice the Indian immigrant rate by age 49 and over thrice the Indian rate by age 70+. The notably higher age-adjusted incidence rate in Indian immigrants to the West, compared to residents of India, can be considered primarily due to the higher incidence of breast cancer in post-menopausal age groups, consistent with partial acculturation to western lifestyles.

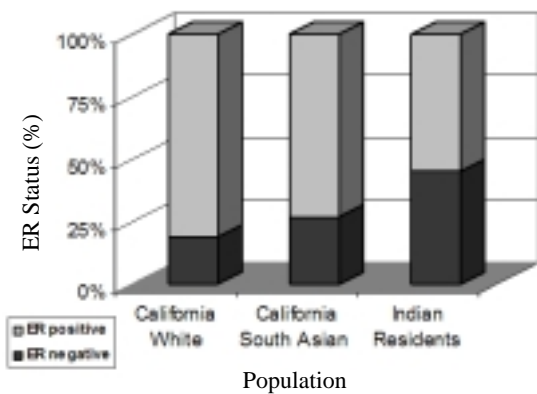


Figure 3. Estrogen Receptor Expression (ER) in Breast Cancer Cases age 50 and Above. Sources: ¹Li et al (2002). Differences in Breast Cancer Hormone Receptor Status and Histology by Race and Ethnicity among Women 50 Years of Age and Older. *Cancer Epidemiol Biomarkers Prevent*, **11**, 601-7. ²Desai et al (2000)

Stage at diagnosis and hormone receptor status

Breast cancer in India tends to be more advanced and/or aggressive at diagnosis than in the West. Whereas nearly 50-70% of invasive breast cancer cases (where stage is reported) in India present at an advanced stage (stages III or IV) (Goel et al., 1995; Hebert et al., 2006), the corresponding proportion for US white women is only 13-15% (Pineda et al., 2001). Studies conducted using Indian hospital-based cancer registry data also suggest that breast cancer in India tends to be estrogen receptor (ER) expression negative. Among women 50 years and older, of cases for which hormone receptor data were available only 45 to 55% of invasive breast cancer cases in India were ER positive (Desai et al., 2000; Redkar et al., 1992) compared to about 81% for whites in California (Li et al., 2002) and the US overall (SEER, 2001) and 73% for South Asians in California (Li et al., 2002) (Figure 3). This of course reflects the combination of the higher incidences in immigrant and western postmenopausal women, and relatively more women in the older age groups in which ER positive cancer predominates, but may also indicate culturally relevant etiologic differences (Potter et al., 1995). It is interesting to note that a study conducted in Mumbai, India, reported significant differences in hormone receptor status between women belonging to different communities. Christians had the highest and Muslims had the lowest proportion of ER positive tumors, with Hindus intermediate. As in the West, prevalence of ER positive cancers increased with age. The mean age of the Christian women with breast cancer was also significantly higher than that of the Hindus and Muslims, which, according to the authors, at least partially explains the difference in ER positive proportions (Redkar et al., 1992). Studies conducted in US also indicate that Indians and Pakistanis are only 30 to 70% as likely to present with ER and progesterone receptor positive breast cancer as are their white counterparts (Li et al., 2002) but age differences may also affect this observation. In discussing this it is important to be aware that for a large number of cases, ER status data are missing in sources from both the

West and India, and it is unclear whether the same receptor assay methods and cut-points are used to determine positive versus negative hormone receptors status.

Discussion

Currently, Indian immigrant women exhibit patterns in breast cancer incidence and disease characteristics that are approximately intermediate between Indian residents and Western white populations. Thus, Indian immigrants provide an opportunity to study the effects of lifestyle changes on incidence, mortality and even histopathologic characteristics. However, few researchers have studied breast cancer in this group. One of the most common reasons cited is that Western cancer registries tend to categorize all sub-populations of Asian origin as one group, even though they are culturally and racially heterogeneous. Indian or South Asian ethnicity has been added only recently as a category in routinely collected cancer data by the UK and the US (Farooq and Coleman, 2005) and even where it is included the information is not validated (Lin et al., 2002). As a result, data on specific ethnic groups are difficult to obtain. There is also some ambiguity over classification by ethnicity in government data such as census data. Asian Indians are included in the group South Asians or even lumped with all Asians in national data such as the US National Center for Health Statistics (NCHS) data and the US Agency for Health Care Research and Quality (AHRQ) data (Wingo et al., 2005).

This results in difficulties in determining the reference population for calculation of population-specific incidence and mortality rates, a problem we call 'the denominator dilemma'. Some studies have used place of birth and/or name to infer Indian ethnicity (Barker et al., 1990; Winter et al., 1999; Jain et al., 2005; Hislop et al., 2007) but a standard has not yet emerged. Another (possibly important) phenomenon noted by some authors is the practice of some Indian immigrants to return to India for definitive diagnosis and treatment after a finding of suspected cancer (Blesch, 1999). These cases are not included in the host country statistics, which may notably diminish the available incidence rates for this sub-section of the population. This observation emphasizes that current data for breast cancer in Indian immigrants have their limitations and should therefore be interpreted with caution.

It should also be kept in mind that the data on breast cancer incidence rates in India have limitations as well, under-reporting being one of them. Large areas of the population, particularly the rural areas, are not yet sufficiently covered by the existing cancer registries and therefore the patterns of cancer in several rural areas are still largely unknown (Nandakumar et al., 2004). This limits the accuracy of such comparative studies, but likely does not detract in a meaningful way from overall interpretations.

In future, the inclusion of variables such as country of birth or country of origin in all cancer registry data in the West would greatly facilitate an understanding of all cancers in immigrant populations, as has been well discussed by Wingo et al (2005). With better cancer

statistics, screening and counseling programs could be better-designed and implemented to decrease morbidity and mortality and improve survival and quality of life in immigrant women. Studies of Indian immigrants and Indian residents are warranted in order to better analyze the dynamics of this emerging public health concern. Incorporating immigration data, such as date of immigration, would allow estimation of the effects of latency and cultural/lifestyle adaptation.

In this paper we have attempted to capture some key aspects of this issue. Our finding that immigrant Indian women exhibit cancer patterns intermediate between Indian residents and Western white women is consistent with previous research studies of cancer in immigrant populations to the West (Yavari et al., 2006; Hislop et al., 2007). In developing nations such as India, rapid urbanization and modernization are resulting in dramatic lifestyle changes, including delayed marriages and child bearing, fewer children, earlier age at menarche and later age at menopause, westernization of the diet, reduced physical activity, and greater utilization of breast cancer screening. Our investigation of breast cancer incidence in Indian immigrants to the West likely foreshadows changes which will occur, albeit somewhat more slowly, in India. Interestingly, this trend may have been anticipated by studies on the Parsis, a unique cultural and religious subgroup concentrated in the Mumbai area. Their breast cancer age-specific incidence rates in the 1970's were much higher than in the Greater Bombay (Mumbai) population, almost as high as seen in the Connecticut tumor registry for the same time period. Demographically and culturally, they share the older age population structure and many of the reproductive pattern characteristics of Western populations (fewer children, late marriage, later childbearing, etc.) (Jussawalla et al., 1981; Sampat et al., 1978).

The increases in incidence over the past few decades in India are beginning to mimic those changes which previously occurred in the West. These trends together underscore the urgency for countries such as India to develop policies and infrastructure for early detection and improved medical care before breast cancer becomes the 'epidemic' it is in the West.

Currently, breast cancer in Western whites, Indian immigrants and Indian residents differs not only in age-adjusted incidence rates, but also in age-specific incidence and tumor characteristics such as hormone receptor status and stage. In general, the proportion of hormone receptor positive breast cancer cases found at older ages is notably higher among Indian immigrants than among Indian residents, more similar to that seen in Western whites. With the rapid changes in environmental and lifestyle currently occurring in India, especially in metropolitan areas, future patterns of breast cancer can be expected to increasingly resemble those in the West, an observation with tremendous public health implications for India. It is abundantly clear that more studies on migrant Indian populations would be very helpful in regard to developing control strategies, as would inclusion of place of birth and even duration in the host country in the national cancer data.

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