

# Comparative Study of Breast Cancer in Iran and India

**Shahzad Khorasani Esmaili**

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## Abstract

Breast cancer is a major health problem for women around the world, including case study is as each year more than 502,000 women. Because of the risk of this cancer will lose their lives. Breast cancer has ranked number one cancer among Indian and Iranian females. In this study enrolled two country patients, therefore prescription was analyzed for breast cancer, which showed that majority population was female. A retrospective analysis were done on breast cancer patients diagnosed for 2015 at the Cancer Research Centre of Shahid Beheshti University of Medical Sciences in Tehran, Iran and for India (PBCR (Population Based Cancer Registry) .we estimated the ASR for developing breast cancer among Iranian women at 17.1 per 100 000 person-years and for Indian females with age adjusted rate as high as 25.8 per100,000 women. The peak incidence rate for breast cancer were in the age group 45–54 years for both Iran and India. we excluded women with a diagnosis of benign lesion, intra lobular neoplasia, or intra ductal neoplasia. Intra ductal neoplasia represented the 17.6% of screen detected and the 14.4% of extra screening imaging-detected breast lesions, while it accounted for only the 2.5% of palpable lesions. Organized, invitational breast cancer screening in case study succeeded in detecting early-stage tumors, which have been consequently treated more frequently with breast and axillary conservative surgery, complementary breast irradiation, and eventual hormonal therapy. Age standardized incidence rates (ASR) of breast cancer in developed countries is nearly threefold higher than in developing countries. Iran and India have had one of the lowest incidence rates for breast cancer in the world, but during the last four decades increasing incidence rates of breast cancer made it the most prevalent cancer in Iranian and Indian women. After adjustment for age, Indian young women are at relatively higher risk of breast cancer than their counterparts in developed countries.

**Keywords:** Breast cancer, Age standardized incidence rates (ASR), early age, Iran, India

## Introduction

Breast cancer is the most common female cancer worldwide representing nearly a quarter (25%) of all cancers with an estimated 1.67 million new cancer cases diagnosed in 2012. This represents about 12% of all new cancer cases and 25% of all cancers in women. It is the fifth most common cause of death from cancer in women.

Breast cancer risk doubles each decade until menopause, after which the increase slows. However, breast cancer is more common after menopause. Survival rates for breast cancer vary worldwide, but in general rates have improved. This is because breast cancer is diagnosed at an earlier and localised stage in nations where populations have access to medical care, and progressive improvement in treatment strategies. In many countries with advanced medical care, the five-year survival rate of early stage breast cancers is 80–90 per cent, falling to 24 per cent for breast cancers diagnosed at a more advanced stage.

Most breast cancer subtypes are hormone-related. The natural history of the disease differs between those diagnosed before and after the menopause, which may be due to different kinds of tumor and possibly different effects of nutritional factors on hormones depending on menopausal status. Women from less developed regions (883 000 cases) have slightly more number of cases compared to more developed (794 000) regions. (Ferlay et al., 2015)

In India, although age adjusted incidence rate of breast cancer is lower (25.8 per 100 000) than United Kingdom (95 per 100 000) but mortality is at par (12.7 vs 17.1 per100 000) with United Kingdom. (Gupta et al., 2015)

There is a significant increase in the incidence and cancer-associated morbidity and mortality in Indian subcontinent as described in global and Indian studies. (Porter, 2009; Ali et al., 2011; Srinath Reddy et al., 2005; Balasubramaniam et al., 2013; Kaarthigeyan, 2012) Earlier cervical cancer was most common cancer in Indian woman but now the incidence of breast cancer has surpassed cervical cancer

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**Shahzad Khorasani Esmaili**

Department of pharmacy practice, Visveswarapura Institute of Pharmaceutical Sciences, Bengaluru, India

**Email:** shahzadkh411@gmail.com

and is leading cause of cancer death, although cervical cancer still remains most common in rural India. (Mousavi et al., 2009).

The prevalence of breast cancer is about one third of all cancers in women constitute the second most common cancer after lung cancer and the most common cause of cancer death among women (Mehrabani et al., 2008) and The incidence of the disease among Iranian women is increasing. With increasing life expectancy and the aging of the population in Iran is expected to increase the incidence of cancer will increase in the coming years (Berek, 2012; Henderson & Canellos, 1980).

According to the report of World Health Organization, the incidence of breast cancer has annually increased by 2% (Henderson & Canellos, 1980). According to the new statistics in Iran, 6160 breast cancers are diagnosed in the country each year and 1063 cases lead to death (Mousavi et al., 2007; Alizadeh et al., 2014). Although the incidence of breast cancer in Asian women is low compared to women in western countries, its incidence trend is considered higher. Breast cancer affects the Iranian women at least a decade earlier than women in developed countries and most of the patients with this disease are in the age of 40–49 years old in Iran (Shibuya et al., 2002). According to the statistics in 2007, at the time of diagnosis, 18% of patients were in stage I, 57% in stage II, 25% in stage III, 72% of patients had tumors larger than 2 cm and 63% had the involvement of lymph nodes at diagnosis (Mousavi et al., 2007). The symptoms of benign conditions are similar to those found in breast cancer and may cause great concern until evaluated and explained by a qualified health professional (Cardoso et al., 2012; Hosseini et al., 2012).

## Materials and Methods:

This study's data were obtained for Iran from the Cancer Research Center of Shahid Beheshti University of Medical Sciences in Tehran. The Cancer Research Center's team has been collecting clinical, pathological, biological, and demographic information on breast cancer patients since 1998. The Cancer Research Center is a major referral center for breast cancer patients. It has cases from all provinces of Iran. It has the biggest data records of breast cancer cases in the country and can be representative of all Iran.

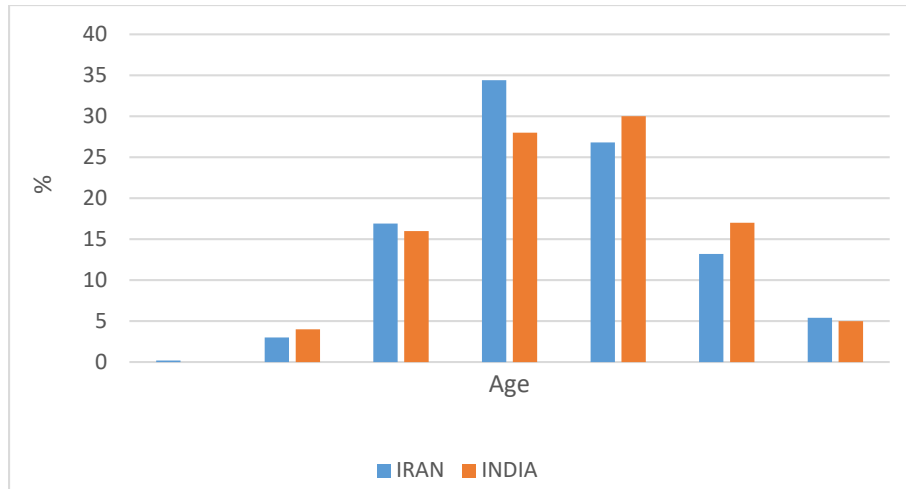
also in this study's data were obtained for India, Multiple sources from literature were used for gathering information and analysis of breast cancer. Information on crude rate (CR) and age adjusted rate (AAR) per 100,000 population was collected from National Cancer Registry Program reports 2012–2014 and twenty-five population-based cancer registries (PBCRs) across India (Bangalore, Barshi rural and expanded, Bhopal, Chennai, Delhi, Mumbai, Ahmedabad rural and urban, Aurangabad, Thiruvananthapuram) including North-East states (Cachar District, Aizawl District, Dibrugarh District, Kamrup Urban District, Manipur State, Mizoram State, Imphal). (Anonymou, 2016) National Cancer Registry Program reports on time trends in cancer incidence rates (1982–2010) from (Anonymou, 2016) PBCRs (Bangalore, Bhopal, Chennai, Delhi, Mumbai, Barshi, Thiruvananthapuram, Dibrugarh, Kamrup Urban District, Imphal West District, Ahmedabad Rural District and the states of Mizoram and Sikkim) were also used for projection of annual percentage change (APC) in burden of breast cancer. Besides many review articles were also screened for the filtering out of the data regarding epidemiology of breast cancer in Indian women.

## Result and Discussion

This study enrolled two country patients, therefore prescription was analyzed for breast cancer, which showed that majority population was female.

A retrospective analysis was done on breast cancer patients diagnosed in 2015 at the Cancer Research Center of Shahid Beheshti University of Medical Sciences in Tehran and India (PBCR (Population Based Cancer Registry) Thus, the profiles of women with breast cancer were evaluated in this study. All the studied patients were followed up in 2015. We excluded all men from our analyses (Figure 1).

Mean age of the patients were 49 ( $\pm 14.58$ ) year, most of them were between 40 and 50 years old. the demographic details of study population are listed in Table 1. Age group in Figure 1.



**Fig. 1:** breast cancer in different age group

According to the ASR (The age-standardized incidence rate) for women aged  $\geq 50$  years in Iran and India were 83.8 per 100 000 person-years. Using data derived from these registries and considering the whole population of Iran and India, we estimated the ASR for developing breast cancer among Iranian women at 17.1 per 100 000 person-years and for Indian females with an age-adjusted rate as high as 25.8 per 100,000 women and mortality 12.7 per 100,000 women. The peak incidence rate for breast cancer was in the age group 45–54 years for both Iran and India (Figure 1). The mean age of patients at the time of diagnosis was 0.84 [standard deviation (SD) 14.4; median 49; mode 50] years.

**Table 1:** Incidence rates of breast cancer among women in Iran and India (2015)

	Age	Cases %	Crude Rate	ASR	SE	Rank a
Iran	below 20	1	3.4	4.2c	0.68	1
	20 -30	3	10	7.6c	0.57	1
	30-40	17	11.2	16.9b	0.82	1
	40-50	34	20.5	23.9a	0.84	3
	50-60	27	10.1	19.6b	0.84	2
	60-70	18	4.7	17.2b	0.84	1
	70-80	6	2.8	9.1	0.84	1
India	below 20	0	3.4	1.5c	0.68	1
	20 -30	3	10	7.4c	0.42	1
	30-40	17	11.2	16.5b	0.82	2
	40-50	34	22.5	24.2a	0.84	3
	50-60	29	10.8	19.1a	0.84	3
	60-70	13	4.7	17b	0.84	1
	70-80	6	1.8	9.1	0.84	1

a Breast cancer compared to rank of cancer at other sites.

b Significantly higher than for the rest of the provinces,  $P < 0.05$ .

c Significantly lower than for the rest of the provinces,  $P < 0.05$ .

ASR = age standardized rate per 100 000 (direct method, world standard population).

SE = standard error.

Our study demonstrates that the ASR of breast cancer is low (17.1/100 000 person years for Iran and for India 83.8 per 100 000 person-years), as it is in most Asian countries: 20.6, 21.8 and 33.3 for Eastern, South-Central and Western Asia respectively (Ferlay et al., 2002; Parkin & Fernández, 2006). This is in contrast to North America and Europe where the highest rates of breast cancer are observed (99.4 per 100 000 person-years for North America and 82.5, 62.4, 84.6 and 42.6 per 100 000 person-years for Northern, Southern, Western, and Central and Eastern Europe respectively) (Ferlay et al., 2002; Hankinson & Hunter, 2002). The difference has been attributed to variations in lifestyle and environmental exposure (Parkin et al., 2002; 20] and in part to the presence of screening programs detecting early invasive cancers in the more affluent regions (Parkin et al., 2002; Breast & screening, 2005). Age-adjusted incidence rates for breast cancer peaked in Iranian women aged 45–54 years. This agrees with the findings of other limited studies previously conducted in the country (Harirchi et al., 2004; Harirchi et al.,

2000). Similar findings have been reported in a number of Asian countries such as Pakistan [49.8 (SD 13.9) years] ( Malik, 2002) and Lebanon [49.8 (SD 13.9) years] ( El Saghir et al., 2002). In contrast, in the United States of America, the highest incidence rate is among women aged 75–79 years and the median age at the time of diagnosis is 61 years (Breast, 2009). Similarly, in the United Kingdom cancer of the breast becomes more common with age, approximately 80% of cases occur in women over the age of 50 years, with the peak in the 50–64 years' age group (Sadjadi, 2003). table1

Table 2 :Description of the Population in the Different Groups in Iran and India

Characteristic	Screening		Imaging		Palpable Lesion	
	India	Iran	India	Iran	India	Iran
<b>BMI, kg/m2 (SD)</b>	26.31	27.47	24.9	25.84	25.1	25.49
	Patients, %		patients, %		Patients, %	
	India	Iran	India	Iran	India	Iran
<b>Tobacco smoker <sup>a</sup></b>	8.1	7.9	4.9	4.7	5.8	5.7
<b>Familial history of breast cancer <sup>a</sup></b>	31.1	28.6	29.2	28.7	37.1	36.3
<b>Estroprogestinic therapy <sup>a</sup></b>	21	20	29	28.1	26	25.1
<b>Menopause <sup>a</sup></b>	96.2	97.9	83	83.8	75.2	75.7
<b>Surgical treatment (first procedure)</b>						
<b>Conservative</b>	83.2	84.1	74	75.6	47.2	47.4
<b>Mastectomy</b>	15.9	15.9	24	24.4	53	52.6
<b>Axilla surgery</b>						
<b>CALND</b>	33.6	33.8	49.1	49.5	78	80
<b>SLNB</b>	66	65.6	48	47.1	16	15
<b>None</b>	0.5	0.6	3.2	3.4	5	5
<b>Surgical treatment (second procedure)<sup>b</sup></b>						
<b>Nothing</b>	75.9	76.5	67.2	68.9	69	72
<b>Conservative</b>	16.2	15.2		14.8		10.1
<b>Mastectomy</b>	8.4	8.3	16.8	16.3	18.1	17.9
<b>Neo adjuvant therapy</b>	6	5.7	0.55	0.5	17	16
<b>Adjuvant therapy <sup>a</sup></b>						
<b>Radiotherapy</b>	75.3	76.3	62.3	63.6	47.4	48.9
<b>Chemotherapy</b>	27.2	26.3	37.4	36.3	52.2	51.1
<b>Hormonal therapy</b>	85	85.3	83	83.3	73	73.2

an abbreviation: BMI ¼ body mass index; CALND ¼ complete axillary lymph node dissection; SLNB ¼ sentinel lymph node biopsy.

a Sample size varies because of incomplete data.

b Sample size varies because only conservative treatment were eventually treated by a second procedure.

we excluded women with a diagnosis of benign lesion, intra lobular neoplasia, or intra ductal neoplasia . Intra ductal neoplasia represented the 17.6% of screen detected and the 14.4% of extra screening imaging-detected breast lesions, while it accounted for only the 2.5% of palpable lesions; therefore, we decided to exclude it from data analysis because of its better prognosis and its consequently probable influence on the survival analysis. In fact, it is well-known that the screening benefit of mortality reduction is accompanied by the harm of over diagnosis, defined as the detection at screening of a cancer that would not have otherwise become clinically evident in the woman's lifetime. (Bleyer & Welch, 1998; Independent, 2012).

Collected data included the following patient's characteristics: age at diagnosis, body mass index (BMI), familial history of breast cancer, fertility status, eventual use of estroprogestinic therapies. Tumor characteristics were considered as follows: histological type, TNM classification and stage, nuclear grading, Mib1/Ki-67 proliferation index, hormone receptors status including estrogen receptor(ER), progesteron receptor (PR) and Her2/neu expression, eventual involvement of extra axillary lymph nodes (internal mammary chain or sub clavary ones), and other microscopic features evaluated in the new classification by (Arnone et al., 2005).

Interventions made in patients with breast cancer diagnosed through screening began in 2006. Before and after screening introduction the number of operations for invasive breast cancer has not changed (respectively 21.6 vs. 21.5 interventions / month). After the introduction of screening 20% of invasive cancers were diagnosed by screening and significantly decreased the prevalence of cancers diagnosed by physical examination of the breast (56.0% ante screening vs. 44.5% post screening period).

the study of two country (Iran, India) population were divided into 3 groups as follows: group A) screen-detected breast cancers (including lesions detected by mammography, ultrasound or breast objective examination within the biyearly, organized, regional screening program); group B) extra screening imaging-detected breast cancers (including lesions detected by mammography or ultrasound, which the women underwent spontaneously, for example in case of familial history of breast cancer out from the age range of the screening, or yearly within the interval between 2 screening invitations, or even simply for personal choice); group C) cancers detected by extra screening breast objective examination (including palpable mass, cutis retraction, breast ulceration, nipple discharge, and mastitis carcinomatosa).

If we compare patient's characteristics in the 3 groups [Table 2], the despite the similar mean age at diagnosis (about 61 years old), women in their fertile age were more frequently diagnosed to have a breast cancer by extra screening objective examination (24.3%) than by breast screening (2.1%) or extras screening breast imaging (16.2%). And, considering that breast screening in our region is offered to women between 50 and 69 years of age, it does not surprise that almost the totality of screen-detected breast cancers (97.9%) is diagnosed after menopause.

Taking into consideration the surgical treatment, the majority of screen-detected breast cancers were treated with breast conservative surgery (77.1% excluding 15.9% of primary mastectomies and 7.0% of radicalization mastectomies) and sentinel lymph node biopsy (65.6%). Women of group B and C underwent only breast conservative surgery in the 63.2% and 38.9% of cases respectively, and sentinel lymph node biopsy in the 47.1% and 15.0% of cases respectively, and this prevalence resulted significantly different among the 3 groups.

Moreover, a great number of women in two countries (Iran, India) population underwent regular breast imaging controls out from the screening program, and the earlier detection of breast cancer in these cases may be explained just by the increased women awareness about this topic. Furthermore, it is not possible to exclude that, even if the screening would have diagnosed group C cancers, their unfavorable biologic behavior would have anyway correlated with a worse prognosis. In this perspective, an analysis of interval cancers would be more helpful, defined as breast cancers that occur in the age-specific screening population during the interval between 2 consequent screening invitations. In fact, interval cancers represent a group of very biologically aggressive tumors with a rapid grow and worse prognostic factors, and their incidence may be a good indicator of screening effectiveness.

## Conclusion

Breast cancer is the most common invasive cancer in women, and the second main cause of cancer death in women, after lung cancer. After skin cancer, breast cancer is the most common cancer diagnosed in women. Breast cancer can occur in both men and women, but it's far more common in women.

According to various studies, reproductive patterns in study area, such as older age at menarche, earlier age at first pregnancy, greater number of pregnancies, and longer duration of breast-feeding (as a religious belief), have probably given rise to the low risk of breast cancer among women (Robert et al., 2004). Lifetime exposure to endogenous sex hormones may play an important role in the pathogenesis of breast cancer. Menarche at over 14 years results in lower exposure of breast epithelium to estrogens and progesterone (Robert et al., 2004). Mean age of the patients were 49 ( $\pm 14.58$ ) year, most of them were between 40 and 50 years old.

the ASR (The age-standardized incidence rate) for women aged  $\geq 50$  years in the Iran and India were 83.8 per 100 000 person-years. Using data derived from these registries and considering the whole population of the Iran and India, we estimated the ASR for developing breast cancer among Iranian women at 17.1 per 100 000 person-years and for Indian females with age adjusted rate as high as 25.8 per 100,000 women. The peak incidence rate for breast cancer were in the age group 45–54 years for both Iran and India.

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If we compare patient's characteristics in the 3 groups, the despite the similar mean age at diagnosis (about 61 years old), women in their fertile age were more frequently diagnosed to have a breast cancer by extra screening objective examination (24.3%) than by breast screening (2.1%) or extras screening breast imaging (16.2%). In conclusion, breast cancer screening in two country (Iran, India)

population resulted in a significant survival gain at 5 years from the diagnosis, but a longer follow up should be necessary to confirm this data, and further studies are required in order to evaluate interval cancers in order to better assess breast screening effectiveness in our population.

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