RESEARCH ARTICLE

Breast Screening in North India: A Cost-Effective Cancer Prevention Strategy

Saumya Pandey*, Chandravati

Abstract

Objectives: Breast cancer is a leading cause of morbidity and mortality in women worldwide. Breast screening in normal and/or asymptomatic women is essential to reduce the burden of breast malignancies. Our study aimed to identify possible risk- and/or co-factors associated with breast screening in North Indian women. Methods: A public health research survey was conducted among 100 women of North Indian ethnicity during clinic visits in a 6-month timeline (April-October 2012). Demographic and clinical data, including mammography screening, were recorded in the questionnaire-based proforma after conducting a 10 minute interview. Written informed consent was taken from all the participants. Results: The mean age of the participants was 32.2±9.9 years. Out of 100 women, 6% had family history of breast disease. Breast-related complaints/malignancy, including galactorrhoea, mastitis, axillary lump, fibrocystic disease, fibroadenosis and adenocarcinoma were observed in 41% participants; age stratification revealed that 82.9% of this group (n=41) were <30 years, while 9.7% and 7.3% were >30 years and 30 years of age, respectively. 32% participants underwent mammography screening and 8% had breast ultrasound imaging. Age stratification in the mammography screening group demonstrated that 24 women were <40 years, while 7 women were >40 years. Conclusions: Our pilot study identified possible co-factors affecting breast screening in North Indian women. These findings may be beneficial in early detection of breast abnormalities, including malignancies in women susceptible to breast cancer, and thus aid in future design of cost-effective screening strategies to reduce the increasing burden of breast carcinoma in women worldwide.

Keywords: Breast cancer - cost-effective - mammography - prevention - screening

Asian Pacific J Cancer Prev, **14 (2)**, 853-857

Introduction

Breast cancer is a leading cause of morbidity and mortality in women worldwide; it is the second most common cancer in women after cervical cancer (Ferley et al., 2000). The age standardised incidence rate of breast cancer is 22.9 per 100,000; it is estimated that by 2030 the number of new cases of breast cancer in India will be approximately 200,000 per year (Datta et al., 2012). The Indian Council of Medical Research (ICMR)-Population Based Cancer Registry (PBCR) data reported that breast cancer is the commonest cancer among women in urban registries of Delhi, Mumbai, Ahmedabad, Calcutta, and Trivandrum constituting >30% of all cancers in females (ICMR, 2001). Hedau et al demonstrated 3 novel BRCA1 mutations including a founder Ashkenazi Jewish BRCA1 mutation in breast cancer patients of Indian ethnicity (Hedau et al., 2004).

Public health survey-based research studies are essential to increase breast cancer awareness by organizing effective breast screening programs for identification of possible cofactors/risk factors that may aid in early detection of breast malignancies in susceptible ethnic groups at the population level, and providing cost-effective multimodality treatment options. Breast self-examination, clinical breast examination (CBE), ultrasound and mammography are the preferred methods for breast screening. A majority of Indian breast cancer patients self-detect any clinically relevant breast abnormality such as a palpable lump, or at a stage when there are secondary manifestations such as local skin or chest wall changes and/or distant metastases (Agarwal et al., 2007). CBE is beneficial in confirming the presence of a dominant mass in breast region, documenting tumor size as well as determining the local extent of disease. Diagnostic mammography is usually advised to women who report symptoms on self examination or suspicious clinical findings on CBE to clarify as well as classify the nature of the target lesion; screening mammography is performed in target groups of asymptomatic women for identification of clinically significant malignant lesions and to facilitate early breast cancer detection. Further, diagnostic breast ultrasound refers to the use of ultrasound for assessment of targeted, localized findings on physical examination,

*Krishna Medical Centre, Rana Pratap Marg, Lucknow, Uttar Pradesh, India *For correspondence: e-mail saumyapandey6@yahoo.com*

mammography, or both (Guidelines for the International Breast Health and Cancer Control-Implementation, 2008).

Breast cancer awareness programs in India are more concentrated in metropolitans and cities, but have not yet reached remote/rural areas of the country (Chopra, 2001; Agarwal et al., 2007). According to PBCR data (1997-2004) of Chittaranjan National Cancer Institute, a regional cancer centre in Kolkata, the total number of female breast cancer cases were steadily increasing from 1997-2001 and only slightly lower from 2002-2004; majority were observed to lie in the 40-49 year age group during the data collection timeline, and the next most commonly affected age group was 50-59 years (Datta et al., 2012).

Breast screening in normal and/or asymptomatic women is therefore essential to reduce the burden of breast malignancies in the western world as well as Asian nations, including India. Therefore, the present single-centre survey-based public health research study conducted during a 6-month timeline (April-October 2012) at Krishna Medical Centre, Lucknow, India aimed to identify possible risk- and/or co-factors associated with breast cancer screening, including mammography, in women of North Indian ethnicity.

Materials and Methods

Study design/setting

A public health survey-based research study was conducted at a single medical centre in India. The location of the breast screening study was Krishna Medical Centre, Lucknow in the state of Uttar Pradesh. We enrolled 100 women of North Indian ethnicity in our breast screening study conducted during May-October 2012.

Furthermore, only preoperative subjects of North Indian ethnicity, not undergoing chemo/radiotherapy were included in the study; exlusion criteria for enrollment included post-operative study subjects, pregnant women, presence of hereditary genetic disorders, ethnicity other than North Indian. Demographic and clinical data were recorded in a one-page clinical proforma. The study subjects were personally interviewed by the lead author in either Hindi or English, depending on the individual subject's preference for communication/interactive session for breast screening; each individual interaction/face-to-face interview was of 10-minute duration, wherein the response of the participants was carefully noted in the proforma. Breast screening was thereafter performed and/or recommended by the clinical expert (study co-author). Written informed consent, either signature, initials of full name, including first and family names, or thumb impression in case of illiterate women, was taken from all the participants of the breast screening single-centre study at the time of enrollment.

Public health research questionnaire

The survey questionnaire was prepared by the study authors after consulting relevant literature on the subject using Pubmed and Medline search databases; accordingly, the proforma included co-factors and/or risk factors for breast cancer susceptibility.

We interviewed the participants and assessed their response to questions/parameters such as name and age of the subject enrolled for screening; age at marriage; age at first pregnancy; geographical area (Lucknow or outside Lucknow); place of birth; marital status; dietary/food habits; education; profession (working woman or home-maker); breast complaints/malignancy or any significant clinically-relevant breast abnormality/change(s) such as fibroadenosis, adenocarcinoma, axillary lump, galactorrhoea, fibrocystic disease and mastitis; family history of breast malignancy; parity; menopause; self-reported use of contraceptives; religion; breast examination and screening.

Study subjects with suspicious breast abnormalities/clinical manifestations detected during breast examination were identified as possible average to high-risk group by the clinical expert, and were further advised/recommended mammography screening or ultrasound imaging to ascertain the nature of breast malignancy, either benign breast disease: fibroadenosis, or cancerous breast: adenocarcinoma.

Clinical data entry/management and analysis

The clinical data with essential variables, including breast screening history, collected during the survey-based research were carefully reviewed from each individual proforma (n=100) bearing the written consent of the breast screening participants, and entries were made using Microsoft Excel program; descriptive statistics for the continuous variables were given as means with standard deviations while those for categorical data were given as frequency distributions.

Results

Demographic profile(s) and response of breast screening participants to public health questionnaire

The present single-centre study included a total of 100 women of North Indian ethnicity from Lucknow and adjoining areas in the state of Uttar Pradesh. The mean age of the participants was 32.2±9.9 years. The response of breast screening participants to the public health questionnaire was well-defined with a high response rate (98%) during the 10-minute interaction sessions. Quality time was devoted to each screening participant so as to extract the maximum demographic as well as clinical information relevant for this pilot study.

Table 1 depicts the demographic details of breast screening subjects, collected during questionnaire-based interview; study subjects with breast abnormalities, such as nodules, excess fat in axilla, inflammation, precancerous lesions as well as family history of breast malignancy, were further stratified and referred for digital mammography.

Out of a total of 100 women recruited in the study, 6% presented with significant family history of breast disease. Breast-related complaints/abnormalities and malignancy, including galactorrhoea, mastitis, axillary lump, fibrocystic disease, fibroadenosis and adenocarcinoma were observed in 41% participants; moreover, fibroadenosis was diagnosed in 30 screening participants and adenocarcinoma was confirmed in 1

Table 1. Demographic Details of Breast Screening Subjects Collected During Questionnaire-Based Interview

Demographic data		Breast screening subjects (N=100)
Mean Age (±s.d.)		32.2 (±9.9)
Mean Age at Marriage (±s.d.)		21.9 (±4.3)
Mean Age at First Pregnancy (±s.d.)		24.1 (±3.9)
Mean Age at Menarche (±s.d.)		13.6 (±0.9)
Geographical area	Lucknow	23
	Outside Lucknow	66
	Not known	11
Place of Birth	Lucknow	13
	Outside Lucknow	75
	Not known	12
Marital status	Married	76
	Unmarried	17
	Not known	7
Food Habits	Vegetarian	44
	Non-Vegetarian	46
	Not known	10
Education	≥ High School	67
	≤ High School	23
	Not known	10
Profession	Housewife	51
	Working woman	21
	*	28
Breast malignancy	Yes	40
	No	60
Family history of breast malignancy		
	Yes	6
	No	90
	Not known	4
Parity (average, incuding live+still births+abortion(s))		3
Menopause	Yes	4
	No	96
Contraceptives	Yes	21
	No	61
	Not known	18
Mammography	Yes	32
	No	66
	Not known	2
Breast screening	Malignant breast/breast-related complaints	41
	NAD	59
Religion	Hindu	88
	Muslim	12

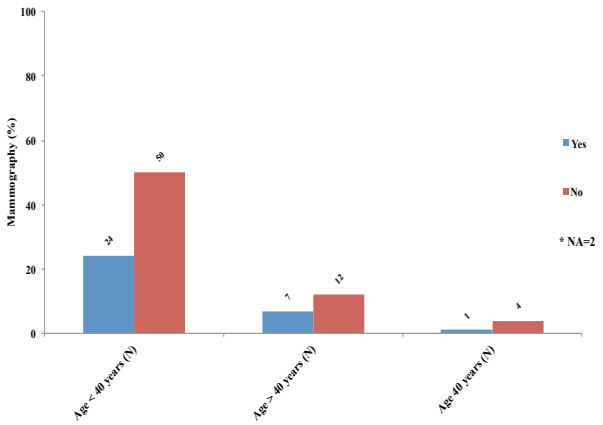

Figure 1. Mammography Screening in North Indian Women

participant. Further age stratification was performed and we observed that 82.9% of this group (n=41) were <30 years, while 9.7% and 7.3% were >30 years and 30 years of age, respectively.

Mammography screening

Study subjects with suspicious breast abnormalities/ clinical manifestations detected during breast examination were identified as possible average to high-risk group by the clinical expert; they were further advised/ recommended mammography screening or ultrasound imaging to ascertain the exact clinical nature of breast malignancy, either benign breast disease: fibroadenosis, or cancerous breast: adenocarcinoma. 32% participants underwent mammography screening and 8% had breast ultrasound imaging for confirmation of malignant breast disease. Age stratification in the mammography screening group demonstrated that 24 women were <40 years, while 7 women were >40 years (Figure 1).

Discussion

Breast cancer is an emerging public health problem globally, including India. Breast screening in normal and/or asymptomatic women with significant clinical manifestations of disease is thus essential to reduce the burden of breast cancer and accordingly identify disease susceptible individuals in a specific ethnic population. Our single-centre public health research survey conducted in a timeline of 6 months during May-October 2012 at Krishna Medical Centre, Lucknow, India had an active participation of 100 study subjects. The response of the participants was assessed using a well-designed public health research questionnaire; it may be noted that each participant was educated about the primary purpose of the pilot study and thereafter written informed consent was taken. We observed that the mean age of the participants was 32.2±9.9 years. Breast screening was conducted using clinical breast examination, fine needle aspiration cytology/core biopsy, mammography and ultrasound imaging. Out of a total of 100 participants, 32% had undergone mammography. Moreover, breast-related complaints and/or benign/malignant breast, including fibroadenosis, adenocarcinoma, axillary lump, galactorrhoea, fibrocystic disease and mastitis were diagnosed in 41% survey participants; age stratification in this group (n=41) showed that 82.9% were <30 years, while 9.7% and 7.3% participants were >30 and 30 years of age, respectively. Age stratification in the mammography screening group (n=32) demonstrated that 24 women were <40 years, while 7 women were >40 years. Determining the precise age for recommending the initiation of regular mammography screening in women has been slightly controversial; after a comprehensive review of literature on mammography screening using Pubmed and Medline, we decided to stratify the mammography screening data according to age at 40 years and the basis for this particular selection criteria i.e. mammography screening age </> 40 years was the recommendation guideline(s) recently provided by the Society of Breast imaging and the ACR on the use of mammography screening (Lee et al., 2010).

Among the possible risk- and /or co-factors, age of the subject appears to be an important risk factor in breast cancer susceptibility in North Indian population. According to a Mumbai-based study, a significant proportion of Indian breast cancer patients are reported to

be younger than 35 years of age; however, this proportion varies between 11% (Tata Memorial Hospital at Mumbai) (Dinshaw et al., 2006) to 26% (SGPGIMS Lucknow) (Agarwal et al., 2007). A comparatively younger age has been associated with larger breast tumor size, higher number of metastatic lymph nodes, poor grade of tumor, lower rates of hormone receptor-positive status, earlier and more frequent locoregional recurrences, and poorer overall survival (Shavers et al., 2003; Mathew et al., 2004). Shin et al. (2010) investigated the incidence trends for invasive breast carcinoma in women aged ≥20 years from 15 registries in Eastern (China, Japan, the Republic of Korea, Taiwan) and Southeastern Asia (the Philippines, Singapore, Thailand) for the timeline 1993-2002; the study reported that breast cancer incidence rates increased gradually over time in all populations included in the research programme. Moreover, incidence rates were observed to be relatively high in Southeastern Asia and became progressively lower along a south to north gradient, with a four-fold geographic variation within the study populations; age-specific incidence curves demonstrated patterns that gradually changed according to incidence rates. Interestingly, breast cancer incidence among Asian women residing in the United States was 1.5-4 times higher than the corresponding incidence rate in the women's respective countries of origin. Overall, the research group suggested that breast cancer incidence is expected to continue to increase for the next ten years in Asia.

Almost one-third of breast cancer patients are believed to have familial disease pattern, and approximately 5% are supposed to be hereditary, with BRCA1 and BRCA2 gene mutations as the major genetic causes. A detailed assessment of the screening subjects' response in our questionnaire demonstrated that 6% of the subjects had significant family history of breast malignancy in first degree relatives, either mother or sister. In another Indian breast cancer study involving 226 patients, 20.7% had a positive family history (Saxena et al., 2005). It may be noted that there have been conflicting data regarding the association of family history of breast malignancy in susceptible individuals at the population level and some studies have reported a lower rate of familial pattern of breast cancer in patients of Indian ethnicity.

Apart from age and family history of breast malignancy, there may be other possible risk- and/or co-factors in breast cancer susceptibility in Indian women (Agarwal and Ramakant, 2008; Leong et al., 2010; Mittra et al., 2010). Our questionnaire therefore included parameters such as age at marriage, age at first pregnancy, menarche, geographical area, place of birth, marital status, dietary intake/food habits, education, profession, parity, menopause, use of contraceptives, breast screening including clinical breast examination/mammography/ultrasound and religion (Table 1); however, we did not observe any significant association of these factors in malignant breast disease. This may be attributed to the relatively small sample size in the study (n=100); we wish to further clarify that this precise sample size number was achieved in a significantly small timeline (n=6 months) at a single medical centre/clinic based in Lucknow. Therefore, to gain a better understanding of the various risk- and/or co-factors involved in identifying breast cancer susceptible individuals in the North Indian population and accordingly recommend mammography or ultrasound imaging, it may be worthwile to pool clinical data/samples from other active breast cancer screening research groups in Lucknow, such as medical universities and/or tertiary care hospitals after drawing a formal consensus and/or public health policy for clinical data management so as to increase the sample size and draw more definitive conclusions in comparatively low-resource settings in Asia unlike the Western world that possesses a relatively superior and more advanced/sophisticated healthcare infrastructure in screening modalities. Reliable population-based cancer survival data are essential for accurate assessment of the effectiveness of cancer screening programmess, distribution of cancer therapy and prevalent cancer cases (Tanaka et al., 2009).

The present study had some strengths as well as limitations. The study subjects enrolled in our breast screening public health research survey were of North Indian ethnicity, thereby reducing the possibility of heterogeneity in terms of population admixture. Our questionnaire was well-designed and the response of the participants was assessed after devoting quality time (10 minute) during the interview (conducted in English or Hindi, depending on the educational background/socioeconomic status of the subject) as part of the breast screening campaign. The study also had some limitations; these included lack of response/assessment regarding body mass index, Estrogen Receptor (ER)+/- and Herceptin (Her)-2/neu status, prior and/or current usage of non-steroidal anti-inflammatory drugs (NSAIDS), Tamoxifen, aromatase inhibitors such as Letrozole or anti-estrogen therapy in malignant breast disease. A relatively small percentage of participants, 32%, underwent mammography screening and 8% ultrasound imaging; this may be attributed to the high cost factor associated with these screening modalities. We would like to comment that there was poor or no response from the survey participants regarding variables such as socioeconomic status/monthly income, and this could be one of the important factors for the relatively low mammography screening rate (32%) in North Indian women.

In conclusion, our public health survey-based research study achieved moderate success in a 6 month study timeline. Our pilot study strongly advocates well-designed questionnaire-based survey as an effective initial screening strategy for breast cancer awareness, control and prevention in North Indian women. However, cost-effective breast screening protocols with a wider population coverage are warranted so as to reduce the burden of cancer of the breast in women worldwide. Moreover, mammography screening should be promoted by educating women about the benefits of breast screening. Future comprehensive research studies in the breast cancer field may help in identification of susceptible individuals in Indian population at pre-malignant/early stages of breast cancer, thereby reducing the burden of disease in women. Breast cancer prevention using cost-effective preventive screening modalities should be advocated in ethnically

diverse populations.

Author contributions, Dr. Pandey conceptualized the study, conducted the survey and interviewed patients, reviewed data, prepared figures/tables and drafted the manuscript; Dr. Chandravati helped in study design, performed/recommended breast screening/clinical diagnosis and referred subjects for public health questionnaire-based interview.

Acknowledgements

We acknowledge the assistance provided by the support/clinical staff of Krishna Medical Centre, Lucknow during the survey-based study. We would like to thank Dr. Anurag Khare for his valuable inputs, clinical insights and expert suggestions/comments on breast screening, especially mammography, during manuscript preparation.

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