




A Multicentre Observational Study on Risk Factors for Breast Cancer

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Abstract

Background Breast cancer is the most common malignancy in Indian women. There is scant data from Indian hospital-based populations on the prevalence of risk factors of this disease. We performed this study to quantify and analyze various epidemiological risk factors in Indian breast cancer patients.

Methods This was a multicenter collaborative study wherein breast cancer patients older than 18 years were served a structured questionnaire after informed consent. Patients or their relatives were required to fill out the questionnaire and those who were unable to read and write were excluded. Data were abstracted from case record forms and variables were descriptively analyzed.

Results Between January 2015 and February 2016, 800 patients were screened, of whom 736 patients with a mean age of 50.13 years were enrolled in the study. The mean number of pregnancies was 2.75 (0–11), the number (percentage) of women who had breastfed for more than 6 months was 628 (85.3) and 406 (55.1%) patients were post-menopausal at the time of breast cancer diagnosis. Of the enrolled patients, 91 (12.8%) had history of exposure to passive smoke, 13 (1.8%) had partners who were heavy smokers, 27 (3.7%) had history of oral contraceptive use, 4 (0.5%) had history of hormone replacement therapy, and 103 (14%) had undergone hysterectomy with oophorectomy.

Conclusion Our study contributes to the descriptive prevalence of some known risk factors in Indian breast cancer patients.

Keywords Breast cancer · Patients · Epidemiological factors

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Introduction

Breast cancer is the commonest cancer in women in India and its incidence is on the rise with more cases being detected with high-resolution imaging modalities. India has the largest estimated breast cancer deaths in the world. There have been several advances in the treatment of breast cancer both in chemotherapy and radiotherapy that have significantly improved the outcomes in the last few decades. It is also one of the cancers where definite risk factors have been identified, some modifiable and some unmodifiable. As prevention is always better than cure, it is important to identify women at higher risk of breast cancer to try and modify them to reduce the risk of breast cancer in the general population as well as to intensify screening strategies in high-risk women [1].

It is a well-known fact that first-hand smoking is associated with several types of cancers including breast cancer. There is a likely possibility that even second-hand smoking may be a risk factor for developing breast cancer, just as it is for lung cancer. This study was undertaken on the platform of FOGSI endocrine committee in association with Tata Memorial Hospital and a few other centers following the observation of one of the authors that many breast cancer patients had partners who were smokers. This observation was not revealed to any of the centers undertaking the data collection to avoid bias. Use of estrogen and progesterone therapy for various reasons has also been blamed as one of the risk factors for breast cancer. With this background, this multicenter study was initiated with the aim of identifying the various avoidable risk factors potentially associated with breast cancer.

Materials and Methods

The aim of this study was to analyze the various risk factors (previously known and unknown) that are prevalent in diagnosed cases of breast cancer who present to different participating hospitals.

This multicenter study was conducted over a period of 1 year from January 2015 to February 2016 at participating centers throughout India. All the women of age more than 18 years, diagnosed to have breast carcinoma with a histopathological confirmation were screened for the study. As this was a questionnaire-based study, patients who were literates, who could read and understand the translated questionnaire and were willing to participate in the study were included. Those patients who were unable to complete the questionnaire were excluded from the study. The study was conducted in accordance with Good Clinical Practices (GCP) as defined by the International Conference on

Harmonization (ICH) after approval from Tata Memorial Centre Institutional Ethics Committee. An informed written consent was taken prior to handing over the questionnaires to the participants. The questionnaire forms were distributed to all the centers. The completed questionnaire forms were sent to the principal investigator. Data were analyzed using SPSS version 24.0 and the prevalence of risk factors is being descriptively reported. In addition to risk factors, other variables of interest are also being descriptively reported.

Results

Total of 800 patients were screened for the study and 736 were enrolled after consenting. Data of 736 patients were analyzed. Salient results are summarized in Tables 1, 2, 3 and 4.

Eighty-five patients (11.5%) had history of exposure to passive smoke either at home or their office and 13 (1.8%) had partners who were heavy smokers. Only 27 patients (3.7%) had history of oral contraceptive usage, all of whom had used combined estrogen plus progesterone pills and only 4 patients (0.5%) had history of hormone replacement therapy out of whom one used estrogen-only preparation.

Discussion

We report here a cross-sectional prevalence of risk factors and other variables of interest in breast cancer patients surveyed at multiple hospitals in India. The mean age of this cohort was 50.3 years which is consistent with previous observations of lower average age of breast and other cancer patients in India and other developing countries compared to that in developed countries [2, 3], likely due to differences in age structure of the populations.

About 16.8% of patients were working or had worked earlier, while 58.4% were housewives. About 11.5% of the patients had history of exposure to passive smoke out of whom approximately three-fourths (76.4%) were exposed at home. Although several cohort studies found questionable

Table 1 Menarche, pregnancy, and breastfeeding

Variable	Number (<i>n</i> = 736)
Mean age, years (range)	50.13 (22–92)
Mean weight, kg (range)	61.77 (30–123)
Mean age at menarche, years (range)	13.69 (9–42)
Mean number of pregnancies, (range)	2.75 (0–11)
Breastfeeding for more than 6 months, number (%)	628 (85.3%)
Breastfeeding for 4–6 months, number (%)	16 (2.2%)

Table 2 Marital status, occupation, menopausal, and hysterectomy status

Variable	Number	Proportion (%) out of 736
Marital status		
Married	688	93.5
Unmarried	13	1.8
Divorced	01	0.1
Widows	28	3.8
Data missing	06	0.81
Occupation		
Housewives	430	58.4
Service	99	13.5
Retired	07	1
Student	01	0.1
Self-employed	13	1.8
Others	07	1
Data missing	179	24.3
Menopausal status		
Pre-menopausal	147	20
Post-menopausal	406	55.1
Not known	33	4.5
Post-chemo-amenorrhoea	150	20.4
Hysterectomy and oophorectomy status		
Yes	103	14
No	632	85.9
Not applicable	1	0.1

evidence of an association between breast cancer risk and first-hand smoking [4], many studies performed later did find a definite relationship [5]. The data regarding second-hand smoke and breast cancer risk are limited. The Canadian Expert Panel on Tobacco Smoke and Breast Cancer Risk concluded that there was a consistent causal relationship between second-hand smoke and pre-menopausal breast cancer risk [6]. The European Prospective Investigation into Cancer and Nutrition has conducted the largest cohort study till date on smoking and breast cancer and it was found that there was an increased risk of breast cancer in former and current smokers as well as women who were currently exposed to passive smoking [7].

Smoking is less prevalent in Indian women as compared to the Western population but there is higher use of smokeless tobacco such as mishri, snuff, ghutka, and khaini. Our cohort had only 1.2% women using smokeless tobacco which we feel is lesser than the actual incidence because of the tendency of Indian women to deny history of tobacco use. The role of smokeless tobacco in breast cancer has not been well evaluated as that of smoking. The incidence of smokeless tobacco use among partners in our cohort was 4.6%. It is very well known that tobacco chewing is strongly

Table 3 Mastalgia, benign breast, and gynecological conditions and comorbidities

Variable	Number	Proportion (%)
Benign breast diseases		
Pre-menstrual breast pain	155	21.0
History of drainage of breast abscess	50	6.8
History of benign breast disease	09	1.2
Earlier history of FNAC of breast lesion	73	9.9
History of excision of breast lump	57	7.7
History of nipple discharge	70	9.5
Gynecological conditions		
Abnormal uterine bleeding	61	8.3
Polycystic ovary disease	14	1.9
Endometriosis	01	0.1
Fibroid uterus	49	6.7
Comorbidities		
Diabetes mellitus	114	15.5
Hypertension	151	20.5
Obesity	101	13.7
Thyroid disorders	79	10.7
Ovarian cancer	02	0.3
Other cancers	10	1.4

associated with oral cancers but there are also studies that suggested that breast cancer is about eightfold more common in smokeless tobacco users [8]. In another study conducted in the Satara district of Maharashtra, the incidence

Table 4 Diet, addictions, passive smoke exposure, hormone use, and family history of cancer

Variable	Number	Proportion (%)
Diet		
Non-vegetarian	408	55.4
Vegetarian	323	43.9
Data regarding diet missing	05	0.7
Addictions		
Present	07	01
Smoking	01	0.1
Tobacco chewing	09	1.2
Alcohol	00	00
Partner addictions		
Present	174	23.6
Smoking	68	9.2
Tobacco chewing	34	4.6
Alcohol	33	4.5
Alcohol + tobacco	39	5.4
Family history of cancer		
Family history of breast cancer	45	6.1
Family history of endometrial and other cancers	70	9.5

of smokeless tobacco use was 58.9% and the risk of getting breast cancer was 1.7 times higher as compared to women who did not use tobacco [9].

In our cohort, 20% patients were pre-menopausal, 55.1% were post-menopausal, and 20.4% had post-chemotherapy amenorrhoea. A considerable minority of patients (14.3%) were hysterectomized and had also undergone oophorectomy at the time of diagnosis of breast cancer. Although no inference can be drawn about the risk factor implications of these data, it is therapeutically important from the point of view of choice of endocrine therapy (aromatase inhibitors versus tamoxifen). In this cohort, 14 (1.9%) patients had polycystic ovary disease, one patient had endometriosis, and 49 (6.7%) patients had fibroid uterus.

In terms of breast symptoms, 21% of our patients had history of premenstrual mastalgia. 6.8% of the patients had history of breast abscess drainage and 1.2% had documented benign breast disease. Benign breast diseases which include non-proliferative lesions, proliferative lesions without atypia, and atypical hyperplasias are said to be risk factors for later breast cancer [10] with the highest risk with proliferative or atypical lesions [11, 12].

In our group, 55.4% of the patients were non-vegetarians while 43.9% were vegetarians. It is difficult to assess the impact of diet on risk of any cancer in general. One systematic review and meta-analysis found an association between increased consumption of red and processed meats and high-fat diet [13]. One study supported a protective role of vegetarian diet against breast cancer [14]. A large American study suggested that even among the vegetarians, those on a vegan diet were at a much lower risk of breast cancer [15]. The reasons for this are unclear but the probable explanations could be consumptions of beneficial plant constituents, the avoidance of red and processed meats and the maintenance of ideal body weight among vegetarians [16]. Vegetarians in Asia consume more soy products for their high protein content and this has been shown to reduce the risk of breast cancer [17].

It is worth pointing out that the design of our study did not include unaffected controls so assessing the impact of any factor on the risk of breast cancer is not possible. However, our study contributes to the descriptive prevalence of some known risk factors as well as other variables of interest, such as burden of comorbidities and others, in a breast cancer cohort.

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Author Contributions SK: Chair, FOGSI endocrinology committee, conceptualizing the hypothesis, index cases, editing and modifying the manuscript, review of literature, and relevant additions. MB: wrote the

first draft of the manuscript, and did analysis and interpretation of data. PP: collection, analysis, data interpretation, and manuscript writing. SG: collection, analysis, data interpretation, and manuscript writing. SC: respective center in charge data compilation, and providing cases. SK: respective center in charge data compilation, and providing cases. SG: respective center in charge data compilation, and providing cases. TT: chair of FOGSI breast diseases committee, coordinator, and conceptualizing the article. PP: collection, analysis, data interpretation, and manuscript writing. DJ: collection, analysis, data interpretation, and manuscript writing. YK: collection, analysis, data interpretation, and manuscript writing. SG: collection, analysis, data interpretation, and manuscript writing.

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Compliance with Ethical Standards

Conflict of Interest All authors declare that they have no conflict of interest.

Human and Animal Rights All procedures were conducted in accordance with ethical standards and as per the Declaration of Helsinki 1964 and its later amendments.

Research Involving Animals Research does not involve animals.

Informed consent Informed consent was obtained from all participants included in the study.

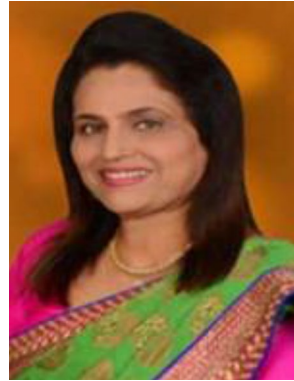
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