A Population Based Case Control Study on Breast Cancer and the Associated Risk Factors in a Rural Setting in Kerala, Southern India

P. PARAMESHWARI[1], K. MUTHUKUMAR[2], H. GLADIUS JENNIFER[3]

ABSTRACT

Introduction: The incidence of breast cancer is increasing in developing countries over three decades. Despite good health indicators breast cancer is a public health problem in Kerala with an annual incidence of 14.9/100000 population. Identifying the risk factors helps to reduce the incidence in future.

Method: A Population based case control study was conducted among all the breast cancer cases in the Arpookara Panchayat of Kottayam district in Kerala. 20 cases of breast cancer were paired with age matched controls from the same geographic area (ratio 1:4) with a total of 100 study participants. Data were collected by interviewing the participants using a pre tested structured questionnaire.

Analysis was done by the authors using SPSS version 16.0

Results: Age group of participants ranged from 32-70 years with mean age of 49.7 $\pm$ 10.39. Early menarche < 13 years [Odds Ratio =3.2, p= 0.03], being unmarried and single, family history of breast cancer [Odds Ratio = 3.5, p = 0.02], previous history of benign breast tumours [Odds Ratio =8.14, p= 0.04], breast feeding less than 2 years [Odds Ratio = 2.28, p = 0.01] were found to be the risk factors for the breast cancer and the birth of first child before 30 years [Odds Ratio =0.302, p = 0.03] was found to be a protective factor for breast cancer. 60% of cases belonged to lower socioeconomic status [Odds Ratio = 14.47, p = 0.03]. Despite high literacy status, significantly lower awareness about symptoms of breast cancer and self examination of the breast were noted [Odds Ratio =11.6, p= 0.03].

Conclusion: Awareness about symptoms of breast cancer and self examination of the breast were lacking in the study population. Health care personnel should be trained to spread the awareness of breast cancer in the community and to identify the vulnerable groups at the primary care settings itself. The policy makers can consider encouraging community participation by involving the non-governmental organizations, women self help groups and Public Private Partnerships in spreading the awareness of breast cancer.

INTRODUCTION

Breast cancer is the most common malignancy affecting one million women worldwide. It constitutes about 21% of all cancers with 519,000 annual deaths. About 900,000 women are diagnosed every year with the cancer [1]. Urbanisation, industrialisation, change in life styles and population growth have contributed to epidemiological transition with increasing incidence in developing countries at present.

Breast cancer is the second most common malignancy next to cervix cancer in India. An increase of 12% has been documented over past three decades in India now with annual incidence of 20.01/100000 population . Breast cancer contributes to about 60% of all cancers among women jointly with cancer cervix and ovary in India [2]. Breast cancer ranks first in urban areas and second in rural areas next to cervix cancer. In India, statistically significant increase in the trends of incidence of breast cancer is noticed [3]. Though the health indices in Kerala are far advanced in comparison to other states in India [4] the age adjusted cancer incidence among females is 97.4/100000 population according to population based cancer registry report in 2001.

Several risk factors for breast cancer have been well documented. Increasing age is considered as important risk for breast cancer. Prolonged exposure to endogenous estrogens such as early menarche, late menopause, exogenous hormones like oral contraceptive pills and hormone replacement therapy show high risk for breast cancer. Family history of breast cancer increases the cancer risk by two or three folds [5]. Breastfeeding has proved to be a protective effect for breast cancer [6]. Studies have proved that certain modifiable risk factors like unhealthy diet with high fat and physical inactivity resulting in overweight and obesity as increased risk for developing breast cancer in high income countries [7].

Majority of the risk factor studies conducted were hospital based and very few population studies have been done in the past on the risk factors of the breast cancer at the community level in India, particularly so in rural areas. The present study attempts to identify the various risk factors associated with breast cancer in Arpookara Panchayat of Kottayam district in Kerala, India.

METHOD

The first author conducted the study after informing the purpose of the study to each of the study participants and obtaining an informed written consent from the study participants, as the study addresses some of the sensitive personal issues of the participants.

Study Design: A community based case control study was conducted among the breast cancer cases with age matched controls in Arpookara Panchayat of Kottayam district in Kerala, India.

Study Area: Arpookara is a Grama Panchayat and is one of the field practice areas of the Government Medical College, Kottayam, Kerala, with a total population of 22,942 with females constituting about more than fifty percent of the population. It is located 9.58°N latitude and 76.52° E longitude.

Study Period: October 2012 – December 2012.

Study Population:

Cases

Inclusion Criteria

- Breast cancer cases of Arpookara Panchayat irrespective of their time of diagnosis, who have been registered in the cancer register of the Government Medical College, Kottayam.
- Able to give an informed consent.

Exclusion Criteria

- Those who were not willing to participate in the study.

Controls

Inclusion Criteria

- Those who were not having breast cancer in the Arpookara Panchayat.
- Belonging to the same age and geographical group.
- Able to give an informed consent.

Exclusion Criteria

- Those who were not willing to participate in the study.

Breast cancer cases in Arpookara Panchayat who have been registered in the cancer register of the Government Medical College, Kottayam irrespective of their time of diagnosis were considered for this study and the 20 breast cancer cases belonging to this locality were included in the study. According to the Family register in Arpookara Panchayat, there were 5692 families in Arpookara Panchayat with the population of 22942. From this Family register, Controls belonging to age group between 30–70 years from Arpookara panchatyat itself, were selected by simple random technique with the help of random number table. Before being enrolled in to the study, it is ensured that the controls were free from breast cancer. In our study for each case, four age matched controls free from breast cancer were selected from the same Panchayat hence 20 cases and 80 controls in the ratio of 1:4 were included in the study thus making a total of 100 subjects.

The questionnaire containing particulars with regard to socio demographic factors like age, marital status, education, occupation, family income, religion, menstrual and reproductive health history viz., age at menarche, age at first child birth, abortions, menopausal status, family history of breast cancer, previous history of benign tumours, oral contraceptive intake and awareness regarding symptoms of breast cancer and breast self examination, initially drafted in English, translated to Malayalam, the local language of the study participants and then pre–tested to assess the suitability with regard to duration, language appropriateness and question comprehensibility. With the help of the grass root level workers of the health care delivery system viz. Accredited Social Health Activitist (ASHA) and Anganwadi workers of the Panchayat, all the study participants were interviewed at their residence.

Analysis was done using SPSS version 16.0. Quantitative variables were compared using student t-test. Chi-square test was used to find significance of categorical variables. The risks were estimated by using odds ratio (OR) & their 95% confidence interval.

RESULTS

Age group of cases ranged from 32-70 years. The mean age of cases and controls were 49.7 and 49.6 years respectively [Table/Fig-1]. More than 95 % of study subjects were literate with at least 8 years of schooling. In the present study almost 72% of cases belong to lower socio–economic status [OR =14.47 (1.28 -162) p = 0.03].

[Table/Fig-2] shows that 55% of the cases attained menarche before 13 years of life which was significantly associated with increased risk of breast cancer [OR =3.2 (1.18 -8.8) (p=0.03). Marital status showed a statistically significant difference (p=0.001) between

cases and controls suggesting that being single or unmarried as risk factor for breast cancer. 98% of study subjects delivered their first child before 30 years which reduces the risk of breast cancer [OR =0.302 (0.1 -0.4) p < 0.03]. 4 cases and 27 controls had abortion in the past. 13 cases (65%) and 39 controls (48.8%) had attained menopause. Out of that 40% of cases and 37.5% of controls attained menopause after 45 years. However the above variables were not statistically significant.

From the [Table/Fig-3], it is evident that 45% of cases and 18 % of controls reported to have positive family history of breast cancer. Increase in breast cancer risk was seen among cases with family history of breast cancer [OR =3.5 (1.27 -10.8) p < 0.02]. 30 % of cases had previous history of benign tumours which was highly significant [OR =8.14 (2.03 -32.62) p = 0.04]. 88% of study subjects had breast fed their child for more than two years with an average of 4.5 and 5.6 years for cases and controls. Breast feeding for less than two years or absence of breast feeding as in nulliparous women increased the risk of breast cancer [OR =2.28 (1. 48 -18.8) p = 0.01]. Out of 3% of the study subjects had a history of OCP intake in the past and 65% of cases were overweight and obese based on BMI and these two variables did not show any significance with breast cancer. 47% of study subjects had significantly less awareness about symptoms of breast cancer and self examination of the breast [OR =11.6 (1.2-112) p = 0.03].

And the [Table/Fig-4] shows the risk factors associated with breast cancer from the present study are early menarche, being single or unmarried, family history of breast cancer, previous history of benign breast tumours, breast feeding less than two years or absence of breast feeding and poor awareness of the symptoms of breast cancer. Giving birth to first child before 30 years was a protective factor against breast cancer in our study.

DISCUSSION

Breast cancer is associated with various risk factors. Despite

Variables	Cases (n=20) n (%)	Control (n=80) n (%)	p value
Age (years) <40 40-49 50-59 >60	5 (25%) 6 (30%) 4 (20%) 5 (25%)	20 (25%) 24 (30%) 16 (20%) 20 (25%)	0.065
Socio Economic Status I II III IV V	1 (5%) 1 (5%) 6 (30%) 10 (50%) 2 (10%)	1 (1.2%) 1 (1.2%) 2 (2.2%) 62 (77.8%) 14 (17.6%)	0.03*

[Table/Fig-1]: Socio Demographic Variables of the Study Participants
p < 0.05 - Significant *

Variables	Cases (n=20) Number (%)	Controls (n=80) Number (%)	p value
Age at menarche (years) < 13 ≥ 13	11 (55%) 9 (45%)	22 (27.5%) 58 (72.5%)	0.032*
Marital status Single Married	4 (20%) 16 (80%)	1 (1.2%) 79 (98.8%)	0.001*
Age at first child birth (years) < 30 ≥ 30	18 (90%) 2 (10%)	80 (100%) -	0.038*
Abortions Yes N	4 (20%) 16 (80%)	27 (33.5%) 53 (66.2%)	0.095
Menopausal status Yes No	13 (65%) 7 (35%)	39 (48.8%) 41 (51.2%)	0. 78

[Table/Fig-2]: Relationship of the Menstrual & Reproductive Health Factors between Cases and Controls
p < 0.05 - Significant *

Variables	Cases (n=20) Number (%)	Controls (n=80) Number (%)	p value
Family history of breast cancer Yes No	9 (45%) 11 (55%)	15 (18.8%) 65 (81.2%)	0.02*
Previous history of benign tumours Yes No	6 (30%) 14 (70%)	4 (5%) 76 (95%)	0.004*
Duration of breast feeding < 2 years ≥ 2 years	6 (30%) 14 (70%)	6 (7.5%) 74 (92.5%)	0.013*
History of OCP intake Yes No	2 (10%) 18 (90%)	1 (1.2%) 79 (98.8%)	0.084
Body mass index <25 ≥ 25	7 (35%) 13 (65%)	34 (42.8%) 46 (57.2%)	0. 78
Awareness about symptoms of breast cancer & breast self examination Yes No	5 (25%) 15 (75%)	42 (52.5%) 38 (47.5%)	0.04*

[Table/Fig-3]: Relationship of the Personal Variables between Cases and Controls
p < 0.05 - Significant *

Risk factor	OR	95 % CI	p value
Early menarche <13 years	3.22	1.17–8.83	0.03*
Marital status	19.75	1.85–497	0.001*
Family history of breast cancer	3.54	1.247–10.07	0.02*
Previous history of benign tumours	8.14	2.03–32.6	0.04*
Breast feeding < 2 years	2.28	1.48–18.87	0.013*
Poor awareness about breast cancer	11.61	1.2–12.8	0.03*
Socio economic status	14.47	1.28–98	0.03*
First child <30 years **	0.30	0.1–0.4	0.036*

[Table/Fig-4]: Risk Factors Associated with Breast Cancer
p < 0.05 - Significant *; Protective factor - **; OR – Odds ratio; CI – Confidence interval

having far advanced health indices among the states in India, the breast cancer is a public health problem in Kerala with increasing incidence. This study was carried out to identify the various risk factors associated with breast cancer in Arpookara Panchayat of Kottayam district in Kerala, as identifying the risk factors helps to plan the future course of action and framing the policies with regard to the prevention of the breast cancer.

Age is an important risk factor for breast cancer. The risk of breast cancer increases as the age progresses [7]. The median age at diagnosis for cancer of the breast in our study was 43 years, which is consistent with other studies done in India [8-10] and the median age at diagnosis for cancer breast was 61 years of age in the western world [11]. The reason for the above difference could be due to the various ethnic, socio-demographic, geographical and life style factors which needs further exploration.

We found that the early menarche before attaining 13 years was significantly associated with increased risk of breast cancer. Many studies have shown that breast cancer risk is more for women whose menarche occur at an early age, in India and other countries [12,13]. Early age at menarche is associated with increased risk of breast cancer and there appears to be a 20% decrease in breast cancer risk for each year if menarche is delayed [14,15]. Studies reported that women who began menstruating at an early age (before age 12) and those who reach menopause after age 55 years had an increased risk of breast cancer [16,17].

Marital status was found to be a significant risk factor for breast cancer in our study. The same finding that the single, unmarried women compared to married women had 4–5 fold higher risk for development of breast cancer in the age group of 40 years and above was noted in the studies done in India and outside India [17 ,18]. In most studies single and nulliparous married women were found to have a similar increased risk for cancer of the breast as

compared with parous women of the same age [19] and early first full-term pregnancy might attribute to this protective effect.

In our study, delivering the first child before 30 years was found to be a protective factor against the breast cancer. The increased risk for breast cancer in those women who were delivering their first child after 30 years has been found in many Indian and western studies [20, 21]. There is another study which found that each live birth reduced life time risk of breast cancer by 7% [22]. In present study both the study groups had average of two children and parity was not accounted to be a risk for breast cancer.

Breast feeding for less than two years or absence of breast feeding as in nulliparous women was significantly associated with the risk of breast cancer. The protective effect of prolonged duration of breast feeding reducing the risk of breast cancer is well established in studies conducted in India and abroad [17, 23, 24].

A statistically significant association was found in those women having a family history of breast cancer and the risk of acquiring the same in our study and similar results were seen in other studies also [17, 25]. Also in the study, it was found that there existed a significant association between the risk of breast cancer and those who had history of benign breast tumours and this is in accordance with other studies [26].

Women in higher socio–economic status have an increased risk of breast cancer compared to those belonging to the low socio-economic status. Socio–economic status per se does not increase the risk but other factors like delayed age at marriage and first child birth after 30 years may play a significant role [24, 27]. In our study almost 60% of cases belong to lower socio–economic status and this could also be due to the various socio-demographic, geographical and life style factors and needs further studies.

Despite high literacy status among women, our study revealed a statistically significant poor awareness regarding breast self examination and the symptoms of breast cancer.

There are studies suggesting increased risk of breast cancer with increased body mass index [28] but no statistical significance was observed in our study with regard to overweight and breast cancer. Similarly history of oral contraceptive pills intake, history of abortions and menopause showed no significant association with the breast cancer in the study subjects.

LIMITATIONS
The study being a case control, the question of bias always arises. Though the selection bias was minimized with appropriate matching of the cases and controls, recall bias remained a challenge particularly when remembering the past events viz. Age at menarche, history of oral contraceptive pills intake, which might have influenced the outcome of these study variables.

Another point which has to be pondered is that the woman starts living in the husband's place after the marriage. So the geographical area, diet pattern and radiation exposure if any, before marriage when she was residing in her matriarchal residence have to be kept in mind before arriving at a conclusion.

CONCLUSIONS
Higher incidence of breast cancer particularly in Kerala among the Indian states which is accompanied by poor awareness regarding self examination of the breast and symptoms of breast cancer brings forth the need for the following possible remedial actions.

Active steps should be taken to train and sensitize the medical and paramedical personnel about identifying symptoms of breast cancer in the primary care settings itself and periodical follow up should be given.

Vulnerable groups must be identified and appropriate preventive measures like awareness creation with regard to breast self examin-

ation and symptoms of breast cancer. Suitable IEC (Information, Education and Communication) activities must be formulated to sensitize the vulnerable population for seeking immediate health care as and when the symptoms arise.

Policy makers can consider encouraging community participation by involving the Non-Governmental Organizations, Women Self Help Groups and Public Private Partnerships with the support of the grass root level health workers in spreading the awareness of breast cancer.

REFERENCES

[1] The World Health Organization; The global burden of disease: 2004 update - page no 29 & 30.

[2] Indian Council of Medical Research, BULLETIN, Vol 40, No: 2, February, 2010, page 11.

[3] Mathew. A Cancer Registration with emphasis on Indian Scenario In Basic Information For cancer registry documentation, RCC,Trivandrum,2003,pp 11-17

[4] PARK'S Text book of Preventive and Social Medicine. 21-th Edition, 2011. Concept of health and disease, page 23.

[5] Pharoah PD, Day NE, Duffy S, Easton DF, Ponder BA. Family history and the risk of breast cancer: a systematic review and meta-analysis. *International Journal of cancer*; 1997 May 29; 71(5):800-09.

[6] IARC (2008). World cancer report 2008. Lyon, *International Agency for Research on Cancer.* page no *72*.

[7] Goodarz Danaei, Stephen Vander Hoorn, Alan D Lopez, Christopher J L Murray, Majid Ezzati and the Comparative Risk Assessment collaborating group (Cancers)* Causes of cancer in the world: comparative risk assessment of nine behavioural and environmental risk factors. *Lancet* 2005; 366: 1784–93.

[8] National Cancer registry Program: Ten year consolidated report of the Hospital Based Cancer Registries, 1984–1993: An assessment of the burden and care of cancer patients. Indian Council of Medical Research. New Delhi; 2001.

[9] Gupta P, Sharma RG, Verma M. Review of breast cancer cases in Jaipur region. *J Ind. Med Assoc.* 2002; 100:282-84.

[10] Goel AK, Seenu V, Shukla NK, Raina V. Breast cancer presentation at a regional cancer center. *Natl. Med. J. Ind.* 1995;8:6-9.

[11] Surveillance, Epidemiology and End Results (SEER) Stat Fact Sheets: Breast cancer, National cancer Institute, U.S. http://seer.cancer.gov/.

[12] Iwasaki M, Otani T, Inoue M, et al: Role and impact of menstrual and reproductive factors on breast cancer risk in Japan. *Eur J Cancer Prev.* 2007; 16 (2): 116-23.

[13] Shantakumar S, Terry MB, Teitelbaum SL, et al. *Reproductive factors and breast cancer risk among older women.* Breast Cancer Res Treat 2007; 102 (3): 365-74.

[14] Kelsey JL, Gammon MD, John EM. Reproductive factors and breast cancer. *Epidemiol Rev.* 1993; 15:36-47.

[15] Hassey ED, Dow K. Pocket Guide to breast cancer. Boston: *Jones and Bartlett.* 2005; p. 3-12.

[16] Rookus MA, van Leeuwen Fe; Netherlands Oral Contraceptives and Breast Cancer Study Group. Oral contraceptives and risk of breast cancer in women aged 20-54 years. *Lancet.* 1994;24:844-51.

[17] Gajalakshmi CK, Shanta V: Risk factors for female breast cancer. A hospital-based case-control study in Madras, India. *Acta Oncol.* 1991; 30 (5): 569-74.

[18] Chen, J, D Pee, R Ayyagari, B Graubard and C Schairer et al., 2006. Projecting absolute invasive breast cancer risk in white women with model that includes mammographic density. *J. Nat.Cancer Institute*. 98: 1215-26.

[19] Rosner, B, G A Colditz and W C Willett, 1994. Reproductive risk factors in a prospective study of breast cancer: The nurses' health study. *Am. J. Epidemiology*.139: 819-35.

[20] Rao DN, Ganesh B, Desai PB. Role of reproductive factors in breast cancer in low risk area: case control study. *Brit. J. Cancer* 1994; 70:129-32.

[21] Familial breast cancer: collaborative reanalysis of individual data from 52 epidemiological studies including 58, 209 women with breast cancer and 101, 986 women without the disease. *Lancet.* 2001; 358 (9291): 1389-99.

[22] Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50302 women with breast cancer and 96973 women without the disease. *Lancet.* 2002; 360 (9328): 187-95.

[23] Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50302 women with breast cancer and 96973 women without the disease. Lancet 2002; 360 (9328): 187-95.

[24] Pakseresht S, Ingle GK, Bahadur AK, et al: Risk factors with breast cancer among women in Delhi. *Indian Journal of Cancer*. Vol. 46, No. 2, April-June, 2009, pp. 132-38.

[25] http://www.cancer.net/cancer-types/breast-cancer/risk-factors.

[26] Lynn C, Hartmann M D et al. Benign Breast Diseases and the Risk of Breast Cancer. *The New England Journal of Medicine.* 2005; 353:229-37.

[27] Jeyalakshmi, Gangadharan P, Mani KS, *Cancer in women in Kerala Asian pacific J cancer* 2007; 16:186-90.

[28] Mathew A, Gajalakshmi V, Rajan B, Kanimozhi V, Brennan P, Mathew BS, et al. Anthropometric factors and breast cancer risk among urban and rural women in South India: A multicentric case-control study. *Br J Cancer*. 2008; 99(1):207-13.

PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Community Medicine, Karpaga Vinayaga Institute of Medical Sciences & Research Centre, Maduranthagam, Kanchipuram – 603308, Tamil Nadu, India.
2. Associate Professor, Department of Community Medicine, Karpaga Vinayaga Institute of Medical Sciences & Research Centre, Maduranthagam, Kanchipuram – 603308, Tamil Nadu, India.
3. Assistant Professor in Biostatistics, Department of Community Medicine, Karpaga Vinayaga Institute of Medical Sciences & Research Centre, Maduranthagam, Kanchipuram – 603308, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. P. Parameshwari,
Assistant Professor, Department of Community Medicine, Karpaga Vinayaga Institute of Medical Sciences & Research Centre, Maduranthagam, Kanchipuram – 603308, Tamil Nadu, India.
Phone: 9894167357, E-mail: paramesh1584@gmail com

FINANCIAL OR OTHER COMPETING INTERESTS: None.