



RESEARCH ARTICLE

RISK FACTORS ASSOCIATED WITH BREAST CANCER AND BENIGN BREAST DISEASE AMONG  
WOMEN IN EASTERN INDIA: A HOSPITAL BASED STUDY

Ruma Roy, Dr. Diptendra Kumar Sarkar and \*Dr. Debarshi Jana

Institute of Post Graduate Medical Education and Research (IPGME&R) and Seth Sukhlal Karnani Memorial  
Hospital (SSKM), Kolkata – 700 020, India

ARTICLE INFO

Article History:

Received 24<sup>th</sup> May, 2017  
Received in revised form  
19<sup>th</sup> June, 2017  
Accepted 19<sup>th</sup> July, 2017  
Published online 31<sup>st</sup> August, 2017

Key words:

Breast cancer,  
Benign breast disease,  
Risk factors,  
Eastern India.

ABSTRACT

**Introduction:** Breast cancer (BC) is one of the most common cancers of women in India. This study aimed to identify the risks such as age, menopausal status, age at menopause, age at menarche, parity, lactation, age at first pregnancy, use of oral contraceptives, domicile status, literacy, occupation, duration of symptoms and BMI of breast cancer in comparison with benign breast diseases in females. **Methods:** In this study 522 BC patients and 522 women with benign breast diseases, who attended at Out Patient Door (OPD) of IPGME&R and SSKM Hospital, Kolkata, India during the period from January, 2005 to December, 2010 were included.

**Results:** Significant risk of BC was found 4.80 times more for higher age ( $\geq 35$  years), 1.34 times more for postmenopausal status, 3.57 times more for late menopause women, 2.47 times more for early menarche women, 1.59 times more with nulliparous patients, 1.66 times more for non-breastfeeding women, 5.73 times more for late age of first pregnancy, 3.58 times more for urban women, 8.34 times more for the illiterate women and 4.49 times for the women having breast lump for more than 06 months

**Discussion:** Several risk factors which had already been established by researchers. But the studies were based on different populations of different geographical areas. This study is based on the females of eastern India. Thus the risk factors established through this study may help for early detection and prevention of BC in this region.

Copyright©2017, Ruma Roy et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Citation: Ruma Roy, Dr. Diptendra Kumar Sarkar, Dr. Debarshi Jana, 2017. "Risk factors associated with Breast Cancer and Benign Breast Disease among women in Eastern India: A Hospital Based Study", *International Journal of Current Research*, 9, (08), 55887-55892.

INTRODUCTION

Breast cancer (BC) is the most common leading female cancer in the world (Debarshi Jana, 2012). In eastern India, BC is one of the most frequently reported cancers (22.7%) in females and the age-specific incidence rate is 25.1 per 100,000 females (Sen et al., 2002). Risk of BC depends on various factors such as reproductive factors, age, socio-economic status and others. Thus it becomes important to know about the risk factors of BC for prevention and early diagnosis. Also the cases of benign breast diseases are increasing in alarming way in eastern India. No comprehensive study has been conducted so far to assess the risk factors of BC and factors related to benign breast diseases in eastern India. Postmenopausal status, early menarche (<12 years), late menopause (>55 years), no full term pregnancy, late age at first pregnancy (>30 years), no breast feeding and others increase the hormonal profiles of breast tissue.

\*Corresponding author: Dr. Debarshi Jana

Institute of Post Graduate Medical Education and Research (IPGME&R) and Seth Sukhlal Karnani Memorial Hospital (SSKM), Kolkata – 700 020, India.

The risk factors of BC are also associated with other factors like age, use of OCP, education, socio-economic status, physical activity and obesity (American Cancer Society, 2011-2012). The degree of risk not only depends on single factor but also it depends on several factors. Control of high risk associated with malignancy is one of the proper preventions of BC and it also increases the overall survival and disease free survival of the BC patients (American Cancer Society, 2003-2004). KMcPherson et al demonstrated that risk for breast cancer depends on several factors such as geographical location, early menarche, late menopause, late age of full term pregnancy, family history, socioeconomic group, food habit, menopausal status, use of oral contraceptives and Body Mass Index (BMI) (McPherson et al., 2000). Various reproductive risk factors are directly associated with BC (Ewertz, 1988; Soumen Das et al., 2012). The risks of BC depend on some reproductive factors such as menarche, menopausal status, age of first pregnancy and parity (Gaurav Agarwal Pooja Ramakant, 2008; Eva Singletary, 2003). Early menarche and late menopause are vital risk factors for BC which are genetically mutated carriers (Jenny Chang-Claude et al., 2007).

Antonis C Antoniou et al suggested that nulliparous women are significantly higher risk of developing BC for BRCA1 and BRCA2 mutation (Antonis *et al.*, 2003). Dorothy R et al also found that multiparity is a protective risk factor for BC (Dorothy *et al.*, 1986). Parity is the independent risk factor for BC (Peter *et al.*, 1989; Kelsey *et al.*, 1993; Marianne Ewertz *et al.*, 1990). Risk of BC is independently associated with age at first full term pregnancy, parity and duration of lactation (Peter *et al.*, 1989; Nadine Andrieu *et al.*, 2006). Early age of first childbirth and long term duration of breast-feeding are reduced the risk of BC in BRCA1 and BRCA2 carrier in general population and regulates the normal cell differentiation (Nadine Andrieu *et al.*, 2007).

Pregnancy is the independent risk factor for BC (Kara Britt, 2007; Kalache and Maguire, 1993). BUTT Z et al found that lactation significantly reduces the risk of BC for female (Butt *et al.*, 2009). Long time breastfeeding is associated with a decreased risk of BC (Ma *et al.*, 2006; Collaborative Group on Hormonal Factors in Breast Cancer, 2002). Early age ( $\leq 30$  years) of first pregnancy have protected risk of developing BC (Ma *et al.*, 2006; Bernstein, 2002; Lord *et al.*, 2008).

The women with age more than 30 years, who give the first child birth, are at higher risk of BC (Kelsey *et al.*, 1993). Various studies have demonstrated that the risk of BC depends on increasing age, domicile status, family history of this disease and genetic factors such as BRCA-1 and BRCA-2 genes mutation (Antoniou *et al.*, 2005). Two rare genes, p53 and PTEN are associated with familial syndromes that enhance the degree of risk for BC (McPherson *et al.*, 2000; Dumitrescu and Shields, 2005). Oral contraceptives users are also more prone to be BC patient in their life time (Jick *et al.*, 1989). Risk of BC is significantly associated with illiterate female compare to literate women (Soumen Das *et al.*, 2012). Iraj Harirchi et al demonstrated that low risk of breast cancer is found in literate females due to the lack of cancer awareness (Iraj Harirchi *et al.*, 2012). Galen Joseph et al. suggested that low literacy women are at higher risk of breast cancer compared to illiterate women (Galen Joseph *et al.*, 2010). Illiteracy or inadequate education may influence the knowledge regarding BC (Thornton and Pillarisetti, 2008). Higher incidence of BC was observed among urban women compared to rural women (Doescher and Jackson, 2009; Daniel and Vorobiof, 2009). In India, occurrence of BC is higher in urban women than in rural population (Mathew *et al.*, 2008). BMI is one of the most important risks of BC in western population (Aiko Sueta *et al.*, 2012). Some of the studies concluded that BC patients having BMI  $\geq 25$  kg/m<sup>2</sup> are subjected to poor survival and which also enhances the tumor growth of BC (Rebecca *et al.*, 2007; Maura *et al.*, 2005; Masaaki *et al.*, 2012).

In India few studies are found related to assessment of risks of BC. Gajalakshmi et al suggested that late menarche, early menopause, early first child birth, multiparity, lactating women were found defensive factors for breast cancer in South India (Vendhan Gajalakshmi *et al.*, 2009). Illiterate women, poor socio-economic rural female with early menarche and menopause, late age of first child birth, non-lactating female, never use of oral contraceptives are at high risk for BC in Eastern India (Soumen *et al.*, 2012). This study aimed at identifying the risks of BC related to hormonal status, domicile status, literacy, age, occupation, use of oral contraceptives, duration of symptoms and BMI in comparison with women with benign breast diseases in Eastern India.

## MATERIALS AND METHODS

### Patient Selection

In this study 522 BC patients and 522 women with benign breast diseases who attended at Out Patient Door (OPD) of IPGME&R and SSKM Hospital, Kolkata, India during the period from January, 2005 to December, 2010 were included. Information related to demography of the patients was obtained by direct interview with the patients. After clinical examination all patients were subjected to true-cut biopsy or FNAC for the confirmation of their diagnosis. After the diagnosis information related to stage of the carcinoma, histological grade, tumor size, lymph node involvement, ER, PR, HER-2/neu and type of histopathology were also obtained.

### Histology and Immunohistochemistry

Breast carcinoma tumors were fixed in 10% neutral-buffered formalin for 24 h, measured the tumor size, nodal status, grade, type of carcinoma and embedded in paraffin, and sectioned. For immunohistochemistry, paraffin sections of tumors were deparaffinized and hydrated by successive washes with xylene, 100% ethanol, and a phosphate buffer [10 mM], (pH 7.4) and 0.138 M saline containing 2.7 mM KCl). Antigen retrieval was accomplished with diluted antigen retrieval buffer (DAKO Corp.) Endogenous peroxidase was blocked with 3% hydrogen peroxide. Subsequently, slides were washed in PBS/KCl, incubated with 10% normal horse serum followed by the primary antibody (rabbit anti-ER antibody or rabbit anti-PR antibody rabbit anti-c-erbB2; HER-2/neu) and incubated overnight at 4°C. The slides were then incubated with biotinylated secondary antibody for 45 min, followed by ABC reagent and diaminobenzidine. Counterstaining was done with hematoxylin. Sections were dehydrated by washing sequentially with 95% ethanol, 100% ethanol, and xylene. Coverslips were mounted on slides using Paramount. Digital images of stained and unstained cells were obtained using an Olympus microscope equipped with a SPOT digital camera.

### Statistical analysis

Statistical Analysis was performed with help of Epi Info (TM) 3.5.3. EPI INFO is a trademark of the Centers for Disease Control and Prevention (CDC). Both univariate and multivariate analysis had been done to find the Odds Ratio with 95% confidence interval and corresponding p-values. Under univariate analysis bivariate frequency tables were used to find the Odds Ratio with their 95% confidence interval and under multivariate analysis Multiple Logistic Regression has been used to find the Odds Ratio with their 95% confidence interval after adjusting the confounding factors. Also descriptive statistical analysis was performed to prepare different frequency tables and to calculate the means with corresponding standard errors. Chi-square test was applied as the measures of associations. Test of proportion was used to find the Standard Normal deviate (Z-values) and corresponding p-values for the test of differences between different proportions.

## RESULTS

The mean age at diagnosis for cases was 50.69 $\pm$ 7.79 years in BC females and 47.48 $\pm$ 10.25 years in benign breast disease females. The median age of both groups was 51 years. As per

table-1, Out of the 522 BC patients 500(95.8%) were higher having age ( $\geq 35$  years), ( $p < 0.01$ ), 370(70.9%) were having postmenopausal status ( $p < 0.01$ ), 392(75.1%) were in advance stage of their disease (stage-III, stage-IV), ( $p < 0.01$ ), 478(91.6%) were having large size tumor ( $> 2$  cm), ( $p < 0.01$ ), 448(85.8%) were having high grade tumor (Grade-III), ( $p < 0.01$ ), 471(90.2%) were having node positive tumor ( $p < 0.01$ ), 407(78.0%) were having ER negative tumor ( $p < 0.01$ ), 410(78.5%) were having PR negative tumor ( $p < 0.01$ ) and 431(82.6%) were having HER-2/neu negative tumor ( $p < 0.01$ ). According to histopathological type of BC patients, 456(87.4%) were invasive ductal carcinoma, 17(3.3%) were ductal carcinoma in situ, 43(8.2%) were lobular carcinoma and 6(1.1%) were medullary breast carcinoma.

**Table 1. Different parameters of Breast Cancer patients**

		Number(n)	Percentage (%)	p- value
Age (Years)	<35	22	4.2	<0.01*
	$\geq 35$	500	95.8	
Menopausal Status	Pre	152	29.1	<0.01*
	Post	370	70.9	
Stage	0	12	2.3	<0.01*
	I	17	3.3	
	II	101	19.3	
	III	360	69.0	
	IV	32	6.1	
Tumor Size (Cm)	T1(<2)	44	8.4	<0.01*
	T2(2 - < 5)	290	55.6	
	T3(> 5)	188	36.0	
Grade	I	16	3.1	<0.01*
	II	58	11.1	
	III	448	85.8	
Node	Negative	51	9.8	<0.01*
	Positive	471	90.2	
ER	Negative	407	78.0	<0.01*
	Positive	115	22.0	
PR	Negative	410	78.5	<0.01*
	Positive	112	21.5	
HER-2/neu	Negative	431	82.6	<0.01*
	Positive	91	17.4	
Type	DCIS	17	3.3	<0.01*
	IDC	456	87.4	
	LC	43	8.2	
	MC	6	1.1	

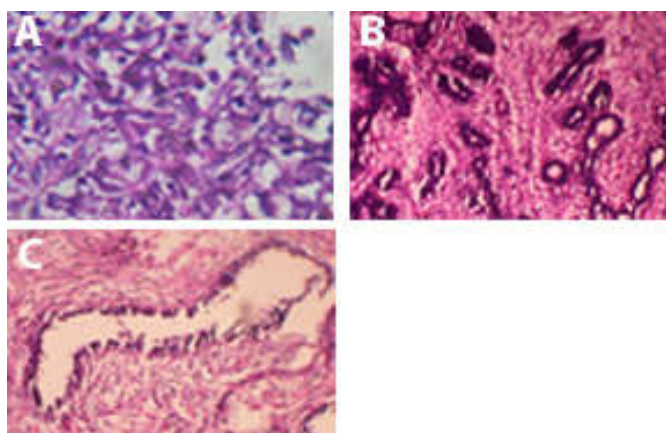
\*Statistically significant, DCIS - Ductal Carcinoma In Situ, IDC - Invasive Ductal Carcinoma, LC - Lobular Carcinoma, MC - Medullary Breast Carcinoma

However, invasive ductal carcinoma was significantly higher than other histopathological type of carcinoma ( $p < 0.01$ ). As per table-2, Out of the 522 control patients 431(82.6%) were having higher age ( $\geq 35$  years), 377(64.6%) were having postmenopausal status, 361(69.1%) were having large size tumor ( $> 2$  cm), According to histopathological type of benign breast disease patients, 259(49.6%) were fibroadenoma, 119(22.8%) were epithelial hyperplasia, 135(25.9%) were fibroadenosis and 9(1.7%) were phyllodes. As per table-3, in BC patients 71(19.2%) were having late menopause ( $> 55$  years), 458(87.7%) were having early menarche ( $< 12$  years), 127(24.3%) were having nulliparous women, 47(11.9%) were having late age of 1st pregnancy ( $> 30$  years), 155(29.7%) were having non-lactating women, 56(10.7%) were having intake oral contraceptives, 421(80.7%) were live in urban area, 442(84.7%) were illiterate women, 407(78.0%) were house wife, 389(74.5%) were having long duration of symptoms ( $\geq 6$  months), 8(1.5%) were having high BMI ( $\geq 25$  kg/m<sup>2</sup>). In benign breast disease patients 21(6.2%) were having late menopause, 388(74.3%) were having early menarche, 88(16.8%) were having nulliparous, 10(2.3%) were having late age of first pregnancy, 106(20.3%) were having non-lactating

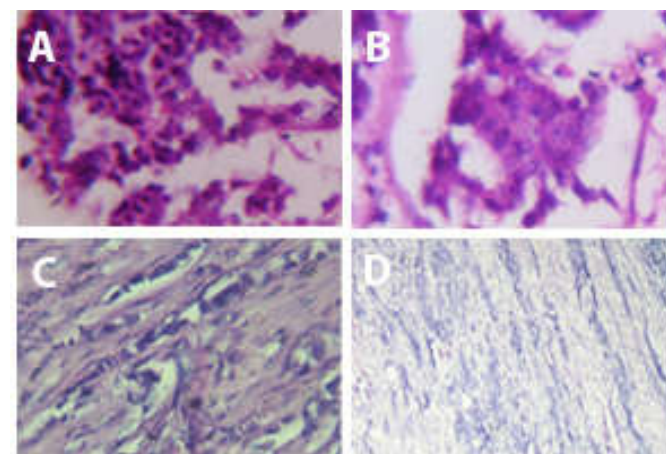
women, 71(13.6%) were having intake oral contraceptives, 281(53.8%) were live in urban area, 208(39.8%) were illiterate women, 428(82.0%) were house wife, 206(39.5%) were having long duration of symptoms, 24(4.6%) were having high BMI.

**Table 2. Different parameters of benign breast disease patients**

		Number (n)	Percentage (%)
Age (Years)	<35	91	17.4
	$\geq 35$	431	82.6
Menopausal Status	Pre	185	35.4
	Post	337	64.6
Tumor Size	T1	161	30.8
	T2	350	67.0
	T3	11	2.1
Type	Epithelial hyperplasia	119	22.8
	Fibroadenoma	259	49.6
	Fibroadenosis	135	25.9
	Phyllodes	9	1.7



**Figure 1. Histopathological breast lesion of benign breast disease (A) Epithelial hyperplasia of breast tissue, (B) Fibro adenoma of breast tissue, (C) Phyllodes of breast tissue**



**Figure 2. Histopathological breast lesion of breast cancer tissue (A) Ductal carcinoma in situ, (B) Invasive ductal carcinoma, (C) Lobular carcinoma, (D) Medullary carcinoma**

Under univariate analysis significant risk of BC was found 4.80[OR-4.80(2.96, 7.78);  $p < 0.01$ ] times more for higher age, 1.34[OR-1.34(1.03, 1.73);  $p < 0.03$ ] times more for postmenopausal status, 3.57[OR-3.57(2.14, 5.96);  $p < 0.01$ ] times more for late menopause women, 2.47[OR-2.47(1.78, 3.43);  $p < 0.01$ ] times more for early menarche women, 1.59 [OR-1.59 (1.17, 2.15);  $p < 0.01$ ] times more with nulliparous patients, 1.66 [OR-1.66(1.25, 2.20);  $p < 0.01$ ] times more for non-lactating women, 5.73 [OR-5.73(2.85, 11.50);  $p < 0.01$ ]

**Table 3. Risk factors of Breast Cancer (Under Univariate and Multivariate analysis)**

		Breast Cancer	Benign Breast Disease	Univariate Odds Ratio (OR) with 95% CI, p-value	Multivariate Odds Ratio (OR) with 95% CI, p-value
		Number (%)	Number (%)		
Age (Years)	≥35	500(53.7)	431(46.3)	4.80(2.96, 7.78); p<0.01*	12.83(6.74, 24.45); p<0.01*
	<35	22(19.5)	91(80.5)		
Menopausal Status	Post	370(52.3)	337(47.7)	1.34(1.03, 1.73); p<0.03*	0.77(0.52, 1.13); p=0.18
	Pre	152(45.1)	185(54.9)		
Menopause (Years)	>55	71(77.2)	21(22.8)	3.57(2.14, 5.96); p<0.01*	3.57(2.14, 5.96); p<0.01*
	≤55	299(48.6)	316(51.4)		
Menarche (Years)	<12	458(54.1)	388(45.9)	2.47(1.78, 3.43); p<0.01*	2.73(1.80, 4.14); p<0.01*
	≥12	64(32.3)	134(67.7)		
Parity	Nulliparous	127(59.1)	88(40.9)	1.59(1.17, 2.15); p<0.01*	0.88(0.41, 1.87); p=0.74
	Parous	395(47.6)	434(52.4)		
Lactation	No	155(59.4)	106(40.6)	1.66(1.25, 2.20); p<0.01*	1.54(0.75, 3.13); p=0.24
	Yes	367(46.9)	416(53.1)		
Age of first Pregnancy (years)	>30	47(82.5)	10(17.5)	5.73(2.85, 11.50); p<0.01*	5.73(2.85, 11.50); p<0.01*
	≤30	348(45.1)	424(54.9)		
OCP	Yes	56(44.1)	71(55.9)	0.76(0.53, 1.11); p<0.15	0.46(0.28, 0.73); p<0.01*
	No	466(50.8)	451(49.2)		
Domicile Status	Urban	421(60.0)	281(40.0)	3.58(2.71, 4.72); p<0.01*	2.30(1.62, 3.27); p<0.01*
	Rural	101(29.5)	241(70.5)		
Education	Illiterate	442(68.0)	208(32.0)	8.34(6.21, 11.21); p<0.01*	7.59(5.39, 10.69); p<0.01*
	literate	80(20.3)	314(79.7)		
Occupation	House-wife	407(48.7)	428(51.3)	0.78(0.57, 1.05); p<0.10	0.54(0.36, 0.81); p<0.01*
	Working Lady	115(55.0)	94(45.0)		
Duration of Symptoms	≥6 months	389(65.4)	206(34.6)	4.49(3.45, 5.84); p<0.01*	4.22(3.01, 5.93); p<0.01*
	< 6 months	133(29.6)	316(70.4)		
BMI (kg/m <sup>2</sup> )	≥25	8(25.0)	24(75.0)	0.32(0.14, 0.73); p<0.01*	0.58(0.22, 1.49); p=0.26
	<25	514(50.8)	498(49.2)		

\*Statistically significant

times more for late age of first pregnancy, 3.58 [OR-3.58(2.71, 4.72); p<0.01] times more for urban women, 8.34 [OR-8.34(6.21, 11.21); p<0.01] times more for the illiterate women, 4.49 [OR-4.49(3.45, 5.84); p<0.01] times for the women having breast lump for more than 06 months and 0.32[OR-0.32(0.14, 0.73); p=0.004] times more for the patients having high BMI. No risk was found for 0.76 [OR-0.76 (0.53, 1.11); p=0.15] OCP users and 0.78 [OR-0.78 (0.57, 1.05); p=0.10] for house-wife women and the risk was not statistically significant. Under multivariate analysis after taken into consideration of the confounding factors significant risk of BC was found 12.83[OR-12.83 (6.74,24.45); p<0.01] times more for higher age, 3.57 [OR-3.57(2.14, 5.96); p<0.01] times more late menopause females, 2.73[OR-2.73(1.80, 4.14); p<0.01] times more for early menarche, 5.73 [OR-5.73(2.85, 11.50); p<0.01] times more for late age of first pregnancy, 0.46 [OR-0.46(0.28, 0.73); p<0.01] times more for OCP users, 2.30 [OR-2.30(1.62, 3.27); p<0.01] times more for urban women, 7.59[OR-7.59(5.39, 10.69); p<0.01] time more for illiterate women, 0.54[OR-0.54(0.36, 0.81); p<0.01] times more for house wives, 4.22 [OR-4.22(3.01, 5.93); p<0.01] times for the women having breast lump for more than 06 months. Also risk of BC was found 0.77[OR-0.77(0.52, 1.13); p=0.18] times more for postmenopausal status, 0.88 [OR-0.88(0.41,1.87); p=0.74] times more for nulliparous women, 1.54 [OR-1.54(0.75, 3.13); p=0.24] times more for non-lactating women and 0.58[OR-0.58(0.22, 1.49); p=0.26] times more for the patients having high BMI but the risks were not significant.

## DISCUSSION

In our study we have established some risk factors associated with BC among women of eastern India and it also examined different aspects related to benign breast diseases. Different risk factors have been found to be good predictors for the risk of BC. Hypotheses to explain its etiology must take into account not only the carcinogenic agents to which a woman is exposed throughout her life, but also the action of these

carcinogens within the context of a breast cancer-susceptible and breast cancer-resistant host (Liyange *et al.*, 2002). Risk factors are broadly classified into those useful in clinical practice, that is significantly influencing the odds of contracting BC in individual woman, and those are very significant in large public health trends in population (American Cancer Society, 2011-2012). Under univariate analysis significant risk of BC was found 4.80 folds more for higher age group patients (>35years) and 1.34 folds more for postmenopausal patients. Among the risk factors which are important in population – hormonal factors are of important value. Early age of menarche, late age of menopause, late age at first childbirth, nulliparity and short duration of breast feeding are the common hormonal risk factors which has been discussed thoroughly in western data (American Cancer Society, 2011-2012; Marianne Ewertz *et al.*, 1990; Kara Britt, 2007; Disis *et al.*, 1994; American Cancer Society, 2009-2010; Furberg *et al.*, 1999). Parity, age of first pregnancy and lactation are the major role for BC protection (Ursin *et al.*, 2004). Peter M. Layde et al suggested that multiparity is the strong defensive factor of BC for female. The epidemiological study demonstrated that lactation and age at menarche may proceed through different hormonal activities (Ma *et al.*, 2006). Many research works support the hypothesis that full term pregnancy and breast feeding are associated with a condensed danger of BC in genetic mutation carriers, but they also raise the prospect that extent and pattern of this association may be different from that experimental in general population (Antonis *et al.*, 2006; Nadine Andrieu *et al.*, 2006). We found that significant risk of BC was found 3.57 folds more for late menopause women, 2.47 folds more for early menarche women, 1.59 folds more with nulliparous patients, 1.66 folds more for non-lactating women, 5.73 folds more for late age of first pregnancy. Gaurav Agarwal et al. demonstrated that incidence of BC is rising in urban Indian women compare to rural Indian woman (Gaurav Agarwal, 2008). Our data suggested that incidence of BC is higher in urban women than in rural women and 3.58 folds greater risk

is found for urban BC patients in eastern India. The western data suggested that females who use any kind of oral contraceptives have a slightly increased risk of BC; whereas females who never used oral contraceptives have reduced risk of BC (Collaborative Group on Hormonal Factors in Breast Cancer, 2012; Polly *et al.*, 2002; Joanna Kruk, 2007) but use of oral contraceptives in Indian women is not significant risk of BC (Soumen Das *et al.*, 2012). No risk was found in oral contraceptives users of BC patients in our population. The inverse relationship of educational level with BC risk observed in western countries due lack of knowledge and practice of breast cancer screening (Iraj Harirchi *et al.*, 2012; Galen Joseph *et al.*, 2010). Our result suggested that risk of BC is 8.34 folds higher for illiterate women compare to literate women in eastern India. Thus the finding from this study suggests that illiterate women are in high risk of BC due to lack of negligence of symptoms of BC, breast self examination and clinical breast examination. Knowledge might play a major role in simple preventive way of BC. Our data supported that late presentation of tumor symptom is 4.49 folds higher risk for the women having breast lump for more than 6 months of BC patients. No risk was found for high BMI and for housewife. We examined that under multivariate analysis after taken into consideration of the confounding factors significant risk of BC was found 12.83 folds more for higher age, 3.57 folds more late menopause females, 2.73 folds more for early menarche, 5.73 folds more for late age of first pregnancy, 0.46 fold more for OCP users, 2.30 folds more for urban women, 7.59 folds more for illiterate women, 0.54 folds more for housewives, 4.22 folds for the women having breast lump for more than 06 months. Our result suggested that the association was found of the period of ovarian activity with risk for breast cancer. This result supported that the protective effect was found in early age of first child, multiparity, and breast feeding on BC in eastern Indian Women. So hormonal function like age of menarche, age of menopause, parity, age first child, breast feeding are the important predictors of BC in Eastern Indian female.

## CONCLUSION

Being one of the pioneer studies on risk factors of BC of eastern India this study provided some idea of pattern of risk factors of BC in this region. From this study it may demonstrated that early start of ovarian function, late first childbirth, late menopause, nulliparous, non-lactating women are the important predictors of BC, whereas use of oral contraceptives and occupation are the poor predictors of BC among eastern Indian women. Also some factors such illiteracy, duration of symptoms and domicile status which are directly or indirectly related to awareness of BC, are found to be potential risk factors of BC. Thus it may be concluded that creating awareness regarding these risks among the women of eastern India may help for early detection and prevention of BC in this region. In conclusion, this is one of the largest case-control studies on BC in Eastern India; it revealed a strongly protected risk of breast cancer females with early age, premenopausal females, late menarche, early menopause, porous females, lactating women, early age of first pregnancy, rural women, literate women and long duration symptoms. In conclusion the findings from this study suggest that illiterate women are high risk of BC due to lack of negligence, BSE and CBE. In our country with significant rate of illiterate females can influence breast cancer screening due to lack of education. In our good clinical practice to identify the high risk factors

such as postmenopausal status, early menarche, late menopause, late age of first child birth, less duration of breast feeding, nulliparous women, urban females, illiteracy and ignorance of symptoms for the prevention of BC, where as no risk is found in oral contraceptives users, daily physical activity and high BMI in Indian scenario.

## REFERENCES

- Aiko Sueta, Hidemi Ito, Tania Islam, Satoyo Hosono, Miki Watanabe, Kaoru Hirose et al. Differential impact of body mass index and its change on the risk of breast cancer by molecular subtype: A case-control study in Japanese women. Springer Plus, 2012; 39: 1-10.
- American Cancer Society. Breast Cancer Facts & Figures 2009-2010. Atlanta: Inc.
- American Cancer Society; Breast Cancer Facts & Figures 2011-2012. Atlanta, Georgia, USA
- American Cancer Society; Breast Cancer Facts and Figures, 2003-2004. Atlanta GA, USA.
- Antoniou AC, Pharoah PD, Narod S, et al. Breast and ovarian cancer risk to carriers of the BRCA1 5382 insC and 185 delAG and BRCA2 6174 delT mutations: a combined analysis of 22 population based studies. *J Med Genet.*, 2005; 42: 602-3.
- Antonis C Antoniou, Andrew Shenton, Eamonn R Maher, Emma Watson, Emma Woodward, Fiona Lalloo et al. Parity and breast cancer risk among BRCA1 and BRCA2 mutation carriers. *Breast Cancer Research*, 2006; 8:1-6.
- Bernstein L. Epidemiology of endocrine-related risk factors for breast cancer. *Journal of Mammary Gland Biology and Neoplasia*, 2002; 7: 3-15.
- Butt Z., Shahbaz U., Naseem T., Ashfaq U., Khan U. A., Khan M. R., Hashmim A. T., Bukhari M. H. Reproductive Risk Factors for Female Breast Cancer: A Case – Control Study, *ANNALS* 2009; 15: 206-10.
- Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50,302 women with breast cancer and 96,973 women without the disease. *The Lancet*, 2002; 360:187-95.
- Collaborative Group on Hormonal Factors in Breast Cancer. Menarche, menopause, and breast cancer risk: individual participant meta-analysis, including 118 964 women with breast cancer from 117 epidemiological studies. *Lancet Oncol*, 2012; 13: 1141-51.
- Daniel A. Vorobiof, Freddy Sitas, and Gabriel Vorobiof. Breast Cancer Incidence in South Africa. *Clin Oncol.*, 2001; 19:125s-127s.
- Debarshi Jana, Syamsundar Mandal, Madhumita Mukhopadhyay, Debabrata Mitra, Sunit K Mukhopadhyay, Diptendra Kumar Sarkar. Prognostic Significance of HER-2/neu and Survival of Breast Cancer Patients Attending a Specialized Breast Clinic in Kolkata, Eastern India. *Asian Pacific J Cancer Prev.*, 2012;13: 3851-55.
- Disis ML, Calenoff E, McLaughlin G, Murphy AE, Chen, W et al. Existent T-cell and antibody immunity to HER-2/neu protein in patients with breast cancer. *Cancer Research*, 1994; 54: 16-20.
- Doescher MP, Jackson JE. Trends in cervical and breast cancer screening practices among women in rural and urban areas of the United States. *J Public Health Manag Pract*, 2009; 15: 200-9.



- Dorothy R. Pathak, Frank E. Speizer, Walter C. Willett, Bernard Rosner, Robert J. Lipnick. Parity and breast cancer risk: Possible effect on age at diagnosis. *Int J of Cancer*, 1986; 37: 21–25.
- Dumitrescu RG, Shields PG. The etiology of alcohol- induced breast cancer. *Alcohol*, 2005; 35: 213-25.
- Ewertz, M. and S. W. Duffy. Risk of breast cancer in relation to reproductive factors in Denmark. *Br J Cancer*, 1988; 58: 99–104.
- Galen Joseph, Mary S. Beattie, Robin Lee, Dejana Braithwaite, Carolina Wilcox, Maya Metrikin et al. Pre-counseling Education for Low Literacy Women at Risk of Hereditary Breast and Ovarian Cancer (HBOC): Patient Experiences Using the Cancer Risk Education Intervention Tool (CREdIT). *J Genet Couns*, 2010; 19: 447–62.
- Gaurav Agarwal Pooja Ramakant. Breast Cancer Care in India: The Current Scenario and the Challenges for the Future. *Breast Care*, 2008; 3:21–27.
- H Furberg, B Newman, P Moorman and R Millikam. Lactation and breast cancer risk. *Int J of Epidemiology*, 1999; 28: 396-402.
- Iraj Harirchi, Saeedeh Azary, Ali Montazeri, Seyed Mohsen Mousavi, Zahra Sedighi, Gelavizh Keshtmand, Zahra Zarinkolah, S M Amin KhalifehSoltani. Literacy and Breast Cancer Prevention: a Population-Based Study from Iran. *Asian Pacific J Cancer Prev.*, 2012; 13: 3927-30.
- Jenny Chang-Claude, Nadine Andrieu, Matti Rookus, Richard Brohet, Antonis C. Antoniou, Susan Peock et al., Age at Menarche and Menopause and Breast Cancer Risk in the International BRCA1/2 Carrier Cohort Study. *Cancer Epidemiol Biomarkers Prev.*, 2007; 16: 740-46.
- Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. *Br J Cancer*, 1989; 59: 618-21.
- Joanna Kruk. Association of Lifestyle and Other Risk Factors with Breast Cancer According to Menopausal Status: A Case-Control Study in the Region of Western Pomerania (Poland). *Asian Pacific J Cancer Prev.*, 2007; 8: 513-24.
- Kalache, A., A. Maguire, S.G. Thompson. Age at last full-term pregnancy and risk of breast cancer. *The Lancet*, 1993; 341: 33 – 36.
- Kara Britt, Alan Ashworth and Matthew Smalley. Pregnancy and the risk of breast cancer. *Endocrine-Related Cancer* 2007; 14: 907–933.
- Kelsey JL, Gammon MD, John EM. Reproductive factors and breast cancer. *Epidemiol Rev.*, 1993; 15: 36-47.
- Lai FM, Chen P, Ku HC, Lee MS, Chang SC, Chang TM, Liou SH. A case-control study of parity, age at first full-term pregnancy, breast feeding and breast cancer in Taiwanese women. *Proc Natl Sci Coun Repub China B* 1996; 20: 71-7.
- Liyange UK, Moore TT, Joo H-G, Tanaka Y, Herrmann V, Doherty G et al. Prevalence of regulatory T cells is increased in peripheral blood and tumor microenvironment of patients with pancreas or breast adenocarcinomas. *J of Immunology*, 2002; 169: 2756–61.
- Lord SJ, Bernstein L, Johnson KA, et al. Breast cancer risk and hormone receptor status in older women by parity, age of first birth, and breastfeeding: a case-control study. *Cancer Epidemiology, Biomarkers, and Prevention*, 2008; 17: 1723–30.
- Ma H, Bernstein L, Pike MC, Ursin G. Reproductive factors and breast cancer risk according to joint estrogen and progesterone receptor status: a meta-analysis of epidemiological studies. *Breast Cancer Research*, 2006; 8: R43.
- Marianne Ewertz, Stephen W. Duffy, Hans-Olov Adami, Gunnar Kvåle, Eiliv Lund, Olav Meirik et al., Age at first birth, parity and risk of breast cancer: A meta-analysis of 8 studies from the nordic countries. *Int J of Cancer*, 1990; 46: 597–603.
- Masaaki Kawai, Yuko Minami, Yoshikazu Nishino, Kayoko Fukamachi, Noriaki Ohuchi, and Yoichiro Kakugawa. Body mass index and survival after breast cancer diagnosis in Japanese women. *BMC Cancer*, 2012; 12: 1-9.
- Mathew A, V Gajalakshmi, B Rajan, V Kanimozhi, P Brennan, BS Mathew and P Boffetta. Anthropometric factors and breast cancer risk among urban and rural women in South India: a multicentric case-control study. *Br J of Cancer*, 2008; 99: 207 – 13.
- Maura K. Whiteman, Susan D. Hillis, Kathryn M. Curtis, Jill A. McDonald, Phyllis A. Wingo, and Polly A. Marchbanks. Body Mass and Mortality After Breast Cancer Diagnosis. *Cancer Epidemiol Biomarkers Prev.*, 2005; 14: 2009-14.
- McPherson, K, C M Steel, J M Dixon. Breast cancer—epidemiology, risk factors, and genetics. *BMJ*, 2000; 321: 624-28.
- Nadine Andrieu, David E. Goldgar, Douglas F. Easton, Matti Rookus, Richard Brohet, Antonis C. Antoniou et al., Pregnancies, Breast-Feeding, and Breast Cancer Risk in the International BRCA1/2 Carrier Cohort Study (IBCCS). *Journal of the National Cancer Institute*, 2006; 98: 535-44.
- Peter M. Layde, Linda A. Webster, Andrew L. Baughman, Phyllis A. Wingo, George L. Rubin, Howard W. Ory. The independent associations of parity, age at first full term pregnancy, and duration of breastfeeding with the risk of breast cancer. *J of Clinical Epidemiology*, 1989; 42: 963–73.
- Polly A. Marchbanks, Jill A. McDonald, Hoyt G. Wilson, Suzanne G. Folger, Michele G. Mandel, Janet R. Daling et al. Oral contraceptives and the risk of breast cancer. *N Engl J Med.*, 2002; 346: 2025-32.
- Rebecca J. Cleveland, Sybil M. Eng, Page E. Abrahamson, Julie A. Britton, Susan L. Teitelbaum, Alfred I. Neugut et al. Weight Gain Prior to Diagnosis and Survival from Breast Cancer. *Cancer Epidemiol Biomarkers Prev.*, 2007; 16: 1803-11.
- S.Eva Singletary. Rating the risk factors for breast cancer. *Annual of Surgery*, 2003; 237: 474-82.
- Sen U, Sankaranarayanan R, Mandal S, Ramanakumar AV, Parkin DM, Siddiqi M. Cancer patterns in eastern India: The first report of the Kolkata Cancer Registry. *Int J Cancer*, 2002; 100: 86–91.
- Soumen Das, Santanu Sen, Anindya Mukherjee, Debadatta Chakraborty, Pankaj Kumar Mondal. Risk Factors of Breast Cancer among Women in Eastern India: A Tertiary Hospital Based Case Control Study. *Asian Pacific J Cancer Prev.*, 2012; 13: 4979-81.
- Thornton H, Pillarisetti RR. ‘Breast awareness’ and ‘breast self examination’ are not the same. What do these terms mean? Why are they confused?. *Eur J Cancer*, 2008; 44: 2118-21.
- Ursin G, Bernstein L, Wang Y, Lord SJ, Deapen D, Liff JM et al. Reproductive factors and risk of breast carcinoma in a study of white and African-American women. *Cancer*, 2004; 3–362.
- Vendhan Gajalakshmi, Aleyamma Mathew, Paul Brennan, Balakrishnan Rajan, Vendhan C. Kanimozhi, Anitha Mathews et al. Breastfeeding and breast cancer risk in India: A multicenter case-control study. *Int J of Cancer*, 2009; 125: 662–65.