RESEARCH COMMUNICATION

Risk Factors for Breast Cancer among Women in Bhopal Urban Agglomerate: A Case-Control Study

Rama S Lodha[1*], Sunil Nandeshwar[2], D K Pal[2], Atul Shrivastav[3], KM Lodha[4], Vimal K Bhagat[1], Vishal V Bankwar[1], Sunil Nandeshwar[2], DM Saxena[1]

Abstract

Background: Breast cancer is the most common cancer in females worldwide, and the second leading cause of cancer deaths in women. The incidence is on the rise in India, and breast cancer is the second most common malignancy in Indian women. Objective: To assess the risk factors for breast cancer patients living in Bhopal. Study Design and Method: This case-control study was conducted in Bhopal urban agglomerate for a period of a year from October 2008 to August 2009. Demographic data and reproductive risk factor related information was collected using a structured questionnaire with analyses by Epi-info and SPSS 16. Results: A history of oral contraceptive pill use (OR=2.77, 95% CI: 1.15-6.65), history of not having breastfeeding (OR=3.49, 95% CI:1.22-9.97), over weight (OR=0.11, 95%CI:0.02-0.49), obese women (OR=0.24, 95%CI: 0.06-0.88) and family history of breast cancer (OR=3.89, 95% CI: 1.01-14.92) were associated significantly with the occurrence of breast cancer on multivariate analysis. Conclusions: The findings of the present study suggests that positive family history of breast cancer and history of using OCP may be the epigenetic factors promoting the occurrence of breast cancer while breastfeeding reduces the possibility of acquiring breast cancer.

Keywords: Breast cancer - breast feeding - oral contraceptive pills - reproductive - AORs

Asian Pacific J Cancer Prev, **12**, 2111-2115

Introduction

Geographical variation in incidence and mortality rates of breast cancer (BC) suggest that the known risk factors for breast cancer may vary in different parts of the world and that environmental factors are of greater importance than genetic factors (McPhersonk et al., 2000). Worldwide more than one million new patients are detected annually who are suffering from breast cancer. In developed countries, breast cancer is the most common malignancy diagnosed in women, and in developing regions, it ranks second to cervical cancer.

Currently, in India, the incidence of breast cancer has steadily increased over the years and as many as 100,000 new patients are being detected every year (Zeleniuch, 2005). Trends in breast and cervical cancer in six population based cancer registries (Mumbai, Bangalore, Chennai, Delhi, Bhopal and Barshi) were evaluated over the last two decades. This approach showed a decreasing trend for cancer of the cervix and increasing trends for cancers of the breast throughout the entire period of observation in most of the registries (Yeole, 2008). Meshram et al. (2009) suggested that changes in menstrual and reproductive patterns among women i.e. early age at menarche and late age at first childbirth and some environmental factors in Central India may have contributed to the increase in breast cancer risk, particularly among younger women. Most large studies have found that women who are overweight or obese, especially those who gain weight throughout adulthood, are at an increased risk of BC after menopause (Friedenreich, 2002; Vainio and Bianchini, 2002; Carmichael and Bates, 2004). Urbanization, industrialization, changes in life style, population growth and ageing have all contributed for epidemiological transition in the country. The absolute number of new cancer cases is increasing rapidly, due to growth in the size of the population and increase in the proportion of elderly persons as a result of improved life expectancy following control of communicable diseases. Thus, study of risk factors for breast cancer in Bhopal women is important and might contribute to current knowledge on this important topic. The aim of the present study was to find out the relation between reproductive risk factors for breast cancer in Bhopal women.

Materials and Methods

Study subjects

This case–control study was conducted at Bhopal urban agglomerate from October 2008 to August 2009. The case group was defined as the women suffering from breast cancer and registered between January 2006 and December 2008 at Population-Based Cancer Registry (PBCR), Department of Pathology, Gandhi Medical

*[1]Community Medicine, LN Medical College, [2]Community Medicine, [3]Population-based Cancer Registry, [4]Biochemistry, Gandhi Medical College, Bhopal, Madhya Pradesh, India *For correspondence: drramalodha@gmail.com*

College, Bhopal. The addresses of such 465 patients were taken from the registry office and the investigators then visited their home for interview. Out of these 465 cases, 226 cases could be traced and from these 226 cases, 215 cases gave consent for the interview. A few patients and residents refused to participate in our study. The control women were recruited from the same locality as of cancer patients but without any history of breast problem or neoplastic diseases reported earlier. Total 215 cases and 215 controls completed interview. The ratio of case to control was kept at 1:1. Case and control were individually matched with age (±2 year), religion and socioeconomic status. Socioeconomic status was determined by the modified Prasad classification which is based on per capita per month income of the family. (Parashar ss, 2009) Operationally cut-off limit to detect early menarche was set on 12 years based on a study done at Madhya Pradesh (that reports that the age of menarche varies from 12 to 15 years) and another study that reports the mean age of menarche 13.2±1.10 (to include the observations below 1SD as early menarche)(Biswas and Kapoor, 2004; Deo and Gattarji, 2004). Similarly late menopause was considered as age more than 50 years and women were stratified into three groups after adopting the reported mean age of menopause 44.7 years. (Sivkami and Syamala, 2005).The effect of age at first pregnancy on breast cancer was determined by dividing the patients and control into two group as per age more than or less than 25 years at the time of first conception based on previous study (Ahmad, 2003).

Data sollection and statistical analysis

Informed consent was taken from the study subjects before the interview. Information was collected in regards with demographic factors, socioeconomic status, height and weight, visual obesity, menstrual history and history of reproductive factor, history of use of oral contraceptive pills, age at first pregnancy and parity, reported abortions, positive history and duration of breast feeding, age at menopause and family history of breast cancer through personal interview of subjects. Height (without shoes in cm) and weight in light clothing (in kg) of each subject was measured using inched tap & weighing machine. Body mass index was calculated and visual obesity measured by pictogram. Body mass index (kg/m^2) was grouped into three categories, namely lean weight (BMI 25), overweight (25<BMI<30) and obese (BMI 30) (WHO, 1998) and visual obesity into nine different body sizes (Figure 1) (Mathew et al., 2008).

Data entry and data analysis were done with the help of Epi-info and SPSS 16 software. Both bivariate and multivariate analyses were performed and adjusted odds ratios (by logistic regression analysis) were calculated for potential confounders.

Table 1. Bivariate Analysis of the Selected Reproductive Factors, Obesity & Body Size Distributions Among Case and Control Group

	Cases (215) n (%)	Controls (215) n (%)	P value
Marital Status			
Unmarried	8 (3.72)	4 (1.86)	0.243
Married	207 (96.3)	211 (98.1)	
Age of Menarche (Year)			
<12	50 (23.2)	6 (2.7)	0.629
>12	165 (76.8)	209 (97.3)	
Status of Menarche			
Irregular	88 (41.0)	76 (35.3)	0.234
Regular	127 (59.1)	139 (64.7)	
History of Oral Contraceptive pills			
Yes	21 (10.1)	8 (3.8)	0.011*
No	186 (89.9)	203 (96.2)	
Age of Marriage (Year)			
>25	38 (18.4)	19 (9.00)	0.227
<25	169 (81.6)	192 (91.0)	
Age at first pregnancy (Year)			
>25	67 (33.2)	60 (28.7)	0.017
<25	135 (66.8)	149 (71.3)	
Parity			
No	5 (2.4)	2 (0.9)	0.220
1–2	90 (43.5)	80 (37.9)	
>3	112 (54.1)	129 (61.1)	
History of Abortion			
No	172 (86.0)	193 (91.5)	0.214
Induced	17 (8.5)	10 (4.7)	
Spontaneous	11 (5.5)	8 (3.8)	
History of Breastfeeding			
No	16 (7.9)	5 (2.4)	0.011*
Yes	186 (92.1)	206 (97.6)	
Duration of breastfeeding (Month)			
<12	159 (48.5)	169 (51.5)	0.478
>12	27 (43.5)	35 (56.5)	
Age of Menopause (Year)			
<45	45 (36.0)	24 (17.6)	0.107
45–50	30 (24.0)	83 (61.0)	
>50	50 (40.0)	29 (21.3)	
Family History of Breast Cancer			
Yes	14 (6.5)	3 (1.4)	0.006*
No	201 (93.5)	212 (98.6)	
Body mass index			
Normal	14(6.5)	34(15.8)	
Over weight	186 (86.5)	176(81.8)	0.000*
Obese (>30.00)	5(6.9)	3(1.4)	
Visual obesity			
>5	212(98.6)	201(93.5)	
<5	3(1.4)	14(6.5)	0.006*

CI, Confidence level; *Significant at 5% level using Chi-square test

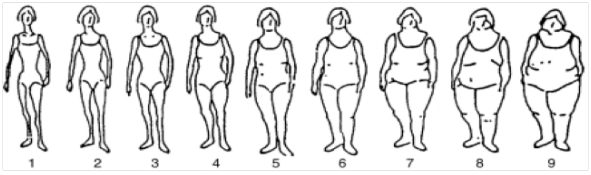

Figure 1. Subclassification into Body Sizes with Regard to Obesity

Results

Out of the 465 participants, we could trace the address of 226 (48.6%) breast cancer patients and 215 (46.2%) gave their consent for interview. The reasons for non-traceability were migration to other places (49/339, 20.5%), incomplete addresses (118/239, 49.4%), death (29/239, 12.13%), and non-specified reasons (43/239,

Table 2. Multinomial Logistic Regression for Variables Found Significant in Univariate Analysis Showing Adjusted Odd Ratios (ORs) with 95% Confidence Interval

	Adjusted OR(95%CI)	P value
History of oral contraceptive pills		
Yes	2.77(1.15-6.65)	0.023*
No	0[a]	
Age at first pregnancy (Year)		
>25	0.89(0.57-1.41)	0.645
<25	0[a]	
History of Breastfeeding		
No	3.49(1.22-9.97)	0.020*
Yes	0[a]	
Family History of Breast Cancer		
Yes	3.89(1.01-14.9)	0.048*
No	0[a]	
Body mass index		
Normal	0.11(0.02-0.49)	0.004*
Overweight	0.24(0.06-0.88)	0.032*
Obese (>30.00)	0[a]	
Visual obesity		
>5	2.13(0.52-8.71)	0.292
<5	0[a]	

CI, Confidence level; Significant at 5% level using Chi-square

18.0%).

Cases were 51.1±10.8 years old ranging from 28 to 78 years and controls were 51.0±10.7 years old ranging from 28 to 78 years. Tables 1 and 2 indicate the distribution of studied independent variables in case and control groups, adjusted odds ratios and related 95% confidence intervals.

Logistic regression showed that history of using OCP (p=0.023), history of not having breast feeding (p=0.020), family history of breast cancer (p=0.048), over weight (p=0.004) and obese women (p=0.032) were found to be significantly associated with breast cancer; similarly adjusted odds ratios (AOR) for history of OCP (OR=2.77, 95% CI: 1.15-6.65), history of not having breastfeeding (OR=3.49, 95% CI:1.22-9.97), over weight (OR=0.11, 95%CI:0.02-0.49), obese women (OR=0.24, 95%CI: 0.06-0.88) and family history of breast cancer (OR=3.89, 95% CI: 1.01-14.92), showed positive association with the occurrence of breast cancer.

Discussion

Breast cancer incidence rates are increasing worldwide. In India, it is the most common cancer among women in many regions and has overtaken cervical cancer. The continuous rising breast cancer incidence has created an urgent need to develop strategies for prevention. Although the number of elderly women with breast cancer is increasing, knowledge regarding the characteristics and biology of this disease in old age is limited. Reduced availability of screening mammography is an example of the indifferent attitude towards the elderly. A lot of studies conducted about breast cancer with association, risk factors and etiology, particularly reproductive and physiological factors like age at menarche, marital status, OCP, age at menopause, age at first pregnancy and parity have been found to modify the risk of breast cancer (Oran et al., 2004; Anderson et al., 2007). In our study logistic regression analysis found that age at first pregnancy, history of OCP use, history of breast feeding, over weight women and a positive family history were associated with risk of breast cancer.

Association of reproductive factors and breast cancer is related to the effect of ovarian hormones, which start at the age of puberty, continue with monthly cycles and finish at menopause occurrence (Willett et al., 2000). In the present study, we did not find any differences in the various menstrual risk factors. Several studies have shown that the risk of breast cancer among women had been decreased with increasing parity (Russo et al., 2001; Yavari et al., 2005). Some studies have taken into consideration the role of full term delivery (Brinton et al., 1982). In the present study, the protective effect of parity and the number of full term delivery on the risk of breast malignancy were observed. This study did not measure hormonal replacement therapy for irregular menses and menopause.

Interesting findings were the absence of significant differences between cases and controls for marital status and age at first pregnancy. In many studies an excess of single women among the cases has been a predominant feature, they have observed statistically significant difference and associated high risk effect (Ebrahimi et al., 2002; Yavari et al., 2005; Iwasaki et al., 2007). Another study shows (ORs= 2.62, 95% C.I; 1.11–6.19) risk of breast cancer but was not statistically significant (Gajalakshmi et al., 1991).

There was significant association between the breastfeeding practices and breast cancer in this study. Several authors found protective effects of breast- feeding on breast cancer risk (Newcomb et al., 1999; Daud, 2004; Al-Saad et al., 2009). The failure of breastfeeding as a risk factor and to find no association with breast cancer in this study may be related to the prolonged breastfeeding practiced by most women as a tradition in India. Breast-feeding can prevent from breast cancer (Romieu et al.,1996; Gupta et al., 2002; Naieni et al., 2007). This point was also observed in the present study and by increasing the cumulative breastfeeding duration; the breast cancer proportion has decreased. One earlier study from Delhi reported the mean duration of the sum total breastfeeding for all children as 6.58 years in patients and 7.4 years in controls (OR=1.91; 95% CI, 1.17–3.13) (Pakseresht et al., 2009).

This study detected a significant association between OC use and breast cancer, consistent with another study which found association and was statistically significant (Jick et al., 1980; Daud et al., 2004; Norsa'adah et al., 2005; Beji and Reis, 2007). Several studies have found no significant association between history of oral contraceptive use and breast cancer (Brinton et al., 1982; Reid, 2007). This study could not measure the relationship of breast cancer with duration, type, dosage and pattern of OC usage because most of the subjects did not know or could not recall the details. The controversial effects of oral contraceptives on breast cancer have been studied extensively.

In this study there was no trend of increased risk with number of abortions, nor was there consistent evidence of an increased risk of breast cancer any particular subgroup. Another study also shows abortion was not related to breast cancer risk, OR being 0.92 for any spontaneous, 0.97 for any induced and 0.77 for 2 total abortions compared to none (Fioretti et al 1999). In some other studies spontaneous abortion was not associated with increased risk of breast cancer. There are estimating 1.3 OR (95 % CI = 0.9-1.9) for induced abortion (Palmer et al., 1997). We also observed about less odds of breast cancer risk in the menopausal women, which is concordant with earlier studies (Yavari et al., 2005). The present study did not find the number of abortion, age of first and last abortion.

Norsa'Adah (2005) observed that high BMI had increased risk of breast cancer as well as overweight women (OR of 2.1; 95% CI of 1.1- 3.9). In addition, several studies have shown an association with body mass index (Must et al., 1999; Zhu et al, 2003), but in this study logistic regression shows no risk in over weight and obese women, but a statistically significant difference was observed between cases and controls. As visual obesity increased the risk of breast cancer also increased in two earlier reports (Mathew et al., 2008; Wilder Smith, 2009) but in this study any association with breast cancer showed no significant difference. Family history of breast cancer in different studies has shown the increase of breast cancer risk around 2-3 times (Gajalakshmi et al., 1991; Ebrahimi et al, 2002).

In conclusion, our study revealed roles for some modifiable determinants of breast cancer that can be focussed by public health intervention in Bhopal. Accordingly, the women who have one or more of the following risk factors should take the special attention to mitigate risk of breast cancer: According to this study, public awareness should be increased regarding the role of history of OCP use, over weight, family history of breast cancer and protective effect of full term pregnancy, longer duration of breast feeding and higher parity in developing breast cancer.

Because of case control nature of the study, certain bias arises in the study. Important is recall bias, which was minimized by including only incident cases. Medical records were checked to confirm past history of benign breast diseases. Genetic mutations, nutritional factors, obesity, radiation exposure and environmental exposure could not be ascertained because of lack of facility. Selection bias and confounding bias was minimized by selecting controls from similar age group and socioeconomic group. These clearly need to be recommended for consideration in future studies.

References

Ahmad M (2003). Risk factors for breast cancer among women attending breast clinic in University Malaya Medical Centre Kuala Lumpur. *NCD Malaysia*, **2**, 23-31.

Al-Saad S, Al-Shinnawi H, Shamsi NM (2009). Risk factors of breast cancer in Bahrain. *Bahrain Med Bull*, **31**, 1-11.

Anderson WF, Matsuno RK, Sherman ME (2007). Estimating age-specific breast cancer risk: A descriptive tool to identify age interactions. *Cancer Causes Control*, **18**, 439-47.

Beji NK, Reis N (2007). Risk factors for breast cancer in Turkish women: a hospital-based case–control study. *Eur J Cancer Care*, **16**, 178-84.

Brinton L, Hoover R, Fraumeni J (1982). Interaction of familial and hormonal risk factors for breast cancer. *J Natl Cancer Inst*, **69**, 817-22.

Biswas RK, Kapoor AK (2004). Age at menarche and menopause among Saharia women-A primitive tribe of Madhya Pradesh. *Anthroplogist*, **6**, 247-52.

Daud NA (2004). Risk factor of breast cancer. *NCD Malaysia*, **3**, 51-65

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

Carmichael AR, Bates T (2004). Obesity and breast cancer: a review of the literature. *Breast*, **13**, 85–92.

Deo DS, Gattarji CH (2004). Age at menarche and associated factors. *Indian J Pediatr*, **71**, 565-6.

Ebrahimi M, Vahdaninia M, Montazeri A (2002). Risk factors for breast cancer in Iran: a case-control study. *Breast Cancer Res*, **4**, 12-6.

Fioretti F, Tavani A, Bosetti C, et al (1999). Risk factors for breast cancer in nulliparous women. *Br J Cancer*, **79**, 1923-8.

Friedenreich CM (2002). Review of anthropometric factors and breast cancer risk. *Eur J Cancer Prev*, **10**, 15-32.

Gupta P, Sharma RG, Verma M (2002).Review of breast cancer cases in Jaipur region. *J Indian Med Assoc*, **100**, 282-3.

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

Jick H, Walker AM, Watkins RN, et al (1980). Oral contraceptive and breast cancer. *Am J Epidemiol*, **112**, 577-85.

McPhersonk, Steel CM, Dixon JM (2000). Breast cancer-epidemiology risk factors and genetics. *BMJ*, **321**,624-28.

Meshram I.I, Hiwarkar, P.A. and Kulkarni P.N (2009). Reproductive risk factors for breast cancer: a case control study. Online Journal of Health and Allied Sciences, 8(3), 5.

Mathew A, Gajalakshmi V, Rajan B, Kanimozhi V (2008). Anthropometric factors and breast cancer risk among urban and rural women in South India: a multicentric case-control study. Br J Cancer, 99,207-13.

Must A, Spadano J, Coakley EH, Field AE, Colditz G, Diezt WH (1999). The disease burden associated with overweight and obesity. JAMA, 282,1523-29.

Newcomb PA, Egan KM, Titus-Ernstoff L, et al (1999). Lactation in relation to post menopausal breast cancer. *Am J Epidemiol*, **150**, 174-82.

Oran B, Celik I, Erman M, et al (2004). Analysis of menstrual, reproductive and life-style factors for breast cancer risk in Turkish women: a case-control study. *Med Oncol*, **21**, 31-40.

Naieni KH, Ardalan A Moahmoodi M, et al (2007). Risk of breast cancer in north of Iran: A case-control in Mazandaran Province. *Asian Pac J Cancer Prev*, **8**, 395-8.

Norsa'adah B, Rusli BN, Imran AK, Naing I, Winn T (2005). Risk factors of breast cancer in women in Kelantan, Malaysia. *Singapore Med J*, **46**, 698-705.

Palmer JR, Rosenberg L, Rao RS, et al (1997). Induced and spontaneous abortion in relation to risk of breast cancer (United States). *Cancer Causes Control*, **8**, 841-9.

Parashar SS (2009). Principle of Sociology in Health Care. In: Rajvir B, Vaidya R, Tilak R, editors. Text Book of Public Health and Community Medicine. 1st ed. Pune: Department of Community Medicine.

Pakseresht S, Ingle GK, Bahadur AK, et al (2009). Risk factors with breast cancer among women in Delhi. *Indian J Cancer*,

46, 132-8.
Russo J, Lynch H, Russo IH (2001). Mammary gland architecture as a determining factor in the susceptibility of the human breast to cancer. *Breast J*, **7**, 278-91.
Romieu I, Hemandez-Avila M, Lazcano E, et al (1996). Breast cancer and lactation history in Mexican women. *Am J Epidemiology*, **132**, 17-26.
Reid RL (2007). Hormonal contraception and breast cancer: Keeping perspective. *J Obstet Gynaecol Can*, **29**, 207-13.
Sivkami M, Syamala TS (2005). Menopause: An emerging issue in India. *Econ Polit Wkly*, **40**, 282-9.
Vainio H, Kaaks R, Bianchini F (2002). Weight control and physical activity in cancer prevention: international evaluation of the evidence. *Eur J Cancer Prev*, **2**, 94-100.
Wilder-Smith A, Chang S (2009). Body size and breast cancer risk: Findings from the European Prospective Investigation into Cancer and Nutrition (EPIC). ?????
Willett WC, Rockhill B, Hankinson SE, et al (2000). Epidemiology, assessing and managing risk. In: Harris JR. Diseases of Breast. 2nd ed. Lippincott Williams and Wilkins Ch 15.
Yeole BB (2008). Trends in cancer incidence in female breast, cervix uteri, corpus uteri, and ovary in India. *Asian Pac J Cancer Prev*, **9**, 119-22.
Yavari P, Mousavizadeh M, Sadrol-Hefazi B, et al (2005). Reproductive characteristics and the risk of breast cancer: A case-control study in Iran. *Asian Pac J Cancer Prev*, **6**, 370-5.
Zeleniuch JA, Roy ES (2005). Epidemiology of breast cancer. In: Roses FD editors. Breast Cancer. 2nd ed. Philadelphia: Elsevier, 3-14.
Zhu K, Caulfield J, Hunter S, et al (2003). Body mass index and breast cancer risk in African American women. *Ann Epidemiol*, **15**, 123-8.