A CASE CONTROL STUDY OF RISK FACTORS ASSOCIATED WITH FEMALE BREAST CANCER

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ABSTRACT

Objective: To find the association of various risk factors with breast cancer.
Study Design: It was a case-control study.
Place and Duration of Study: The study was carried out in NORI Hospital Islamabad and Combined Military Hospital Rawalpindi between August, 2013 and February, 2014.
Material and Methods: Two hundred breast cancer patients and 200 control subjects were inducted. A short approved and planned questionnaire was used to collect data regarding basic demographic, menstrual and reproductive characteristics of participating females. Cases and controls were then interviewed after taking written consent.
Results: Breast cancer patients and control subjects did not differ regarding age (p = 0.15), early menarche (OR for menarche at <13 years vs. ≥13=1.3, 95% CI = 0.84 – 2.02), and history of breast cancer in 1st degree relatives did not increase breast cancer risk (OR = 1.0, 95% CI = 0.57 – 1.74). Nulliparous women had significantly higher risk than parous women (OR = 2.43, 95% CI = 1.22 – 4.84) and women with late menopause compared to women with early onset of menopause were also at higher risk for breast cancer (OR for menopause at ≥ 50 vs. < 50 = 5.16, 95% CI = 2.59 – 10.29).
Conclusion: Nulliparity and menopausal age of more than 50 years was associated with increased breast cancer risk. Breastfeeding and age less than 25 years at first live birth was not protective against breast cancer.

Keywords: Breast cancer, Nulliparity, Lactation, Risk factors.

INTRODUCTION

The incidence of breast cancer is on the rise in the developing countries. Breast cancer has become the most common cancer amongst women in Pakistan[1]. Pakistan has got the highest incidence rate across Asia. It kills about 40,000 women every year and one out of every nine women is at the risk of having breast cancer in her life[2]. What exactly is to be blamed for the development of breast cancer is still not known, however there are many risk factors for breast cancer which have been very well recognized. The incidence of breast cancer is continuously increasing in almost all over the world predominantly in the developing countries owing to urbanization and modernization of social and cultural life.

Age is an important risk for breast cancer, as the age progresses the risk of breast cancer increases[3]. Reproductive factors like more age at birth of first child, nulliparity and no lactation are very strongly associated with breast cancer in western world. Women with early age menarche, late menopause, use of oral contraceptives and hormone replacement therapy are considered to be at high risk[4]. Family history of breast cancer in first degree blood relation increases the risk to more than two fold[5]. Large studies have been carried out and proved that overweight and obese women who are used to unhealthy diet and physically inactive are at increased risk of developing breast cancer[6,3] . In our population parity, age at first birth and breast feeding practices are different as compared to the developed nations and therefore their contribution to the risk of developing breast cancer may well be different. So far quite a few case control studies on risk factors for breast cancer have been carried out in Pakistan with conflicting results. We conducted our study with an aim to elucidate the current confusion regarding the association of reproductive and various other factors with the risk of developing breast cancer in our population.

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MATERIAL AND METHODS

This case-control study was conducted from August 2013 to February 2014 at Nuclear Medicine, Oncology and Radiotherapy Institute (NORI) Hospital, Islamabad and Combined Military Hospital (CMH) Rawalpindi.

Cases: Females with histopathologically confirmed breast cancer who visited Nuclear Medicine, Oncology and Radiotherapy Institute (NORI) hospital, Islamabad and Combined Military Hospital (CMH) Rawalpindi, irrespective of their time of diagnosis, above > 25 years and were able to give an informed consent, were included. All those cases who did not show willingness were excluded from the study. Cases comprised of 200 confirmed breast cancer patients.

Controls: Healthy women, not having breast or any other cancer or gynaecological problem and were age matched and gave consent were enrolled from the general population, as controls. A total of 200 controls were recruited from the general population. However, proportion of controls in each age-specific stratum was fixed in advance based on the age distribution of cases. The pre-determined age-specific quotas for sampling of controls were: 20%, 35%, 30%, and 15% for age groups 25-35 year, 36-45 year, 46-55, and >56 years respectively. A written informed consent was taken from each of the participant of the study.

Table-1: Comparison of cases and controls regarding reproductive risk factors.

Variables	Cases n=200 No (%)	Controls n=200 No (%)	OR	CI 95%	*p*-value
Parity					
Nulliparous	29 (14.5)	13 (6.5)	2.43	1.22 – 4.84	0.010*
Parous	171 (85.5)	187 (93.5)			
Age at first birth					
< 25 years	126 (74)	124 (66)	1.42	0.901– 2.244	0.129
≥ 25 years	45 (26)	63 (34)			
No of live births					
0	29 (14.5)	13 (6.5)	2.23	1.11 – 4.7	0.024*
1-2	37 (18.5)	53 (26.5)	0.70	0.43 – 1.13	0.145
≥ 3	134 (67)	134 (67)	1.0	Reference	Reference
Lactation					
Never	3 (1.75)	8 (4.28)	0.39	0.104 – 1.53	0.180
Ever	168 (98.25)	179 (95.72)			
Duration of lactation					
< 2 years	28 (14)	54 (27)	1.38	0.33 – 5.62	0.652
≥ 2years	140 (70)	125 (62.5)	2.98	0.77 – 11.5	0.111
No lactation	3 (1.5)	8 (4)		Reference	Reference

**p* value<0.05 significant

A well thought out and specially planned short questionnaire was used to collect information regarding risk factors for breast cancer from each participant. Cases and controls were interviewed after written informed consent. The questionnaire included details regarding socio demographic factors like age, height, weight, marital status, education, reproductive and menstrual factors like age at menarche, age at first child birth, parity, breast feeding, menopausal status, oral contraceptive intake and family history of breast cancer. The data had been analysed using Statistical Package for the Social Sciences (SPSS) version 17.0. Descriptive statistics were used to describe the results. Independent samples t-test was used to compare quantitative variables and to find significance of qualitative

Table-2: Characteristics of cases and controls regarding risk factors other than reproductive ones.

Variables	Cases n=200 n (%)	Controls n=200 n (%)	OR	CI 95%	*p*-value
Menopausal status					
premenopausal	120 (60)	120 (60)	1.00	0.67 – 1.4	1.00
Postmenopausal	80 (40)	80 (40)			
Age at Menopause			5.16	2.59 – 10.29	0.0001*
≥50years	48 (60)	18 (22.5)			
<50 years	32 (40)	62 (77.5)			
Marital status			1.34	0.45 – 3.95	0.587
Unmarried	8 (4)	6 (3)			
Married	192 (96)	94 (97)			
Age at Menarche					
< 13 years	63 (31.5)	52 (26)	1.30	0.84 – 2.02	0.224
≥ 13 years	37(68.5)	148 (74)			
Oral Contraceptive use			0.8	0.37 – 1.70	0.56
Ever	13 (6.5)	6 (8)			
Never	18 (93.5)	84 (92)			
Family history					
Present	29 (14.5)	29 (14.5)	1.00	0.57 – 1.74	1.00
Absent	171 (85.5)	71(85.5)			
Body Mass index					
≥ 28	92 (46)	7 (36.5)	1.48	0.99 – 2.21	0.054
< 28	108 (54)	12 (63.5)			

*p value<0.05 significant

variables Chi-square test was used. The risk factors and their association with breast cancer were estimated by using odds ratio (OR) and their 95% confidence interval. A *p* value of < 0.05 was considered as significant.

RESULTS

Controls and cases of breast cancer did not vary regarding age, with mean ages 45.23 and 46.25 years respectively ($p = 0.15$). Table-1 gives an evaluation of cases and controls as regards their reproductive risk factors. Nulliparous women according to our study demonstrated a higher risk for breast cancer compared to parous women (OR =2.23 95% CI = 1.11 – 4.7). Amongst the parous women never breastfeeding, compared to ever breastfeeding group, did not show any significant increase in breast cancer risk. Duration of lactation more than 2 years was found not to be protective. Table-2 shows the analysis for association of breast cancer and personal variables other than reproductive ones. More cases than controls were un-married but this was not statistically significant. Case and controls did not differ in age at menarche and menopausal status. Menopause at age ≥ 50 was associated with increased risk for breast cancer with OR 5.16 (95%CI = 2.59 – 10.29). Body mass index ≥ 28 did not show any significant association with increased risk of breast cancer. Family history of breast cancer in 1st degree relatives did not increase breast cancer risk. Use of oral contraceptives was also not associated with breast cancer.

DISCUSSION

Our study aimed at finding out the association of various risk factors with breast cancer. Breast cancer is a health problem with increasing incidence and identification of the risk factors may help in chalking out the future health policies for the prevention of breast cancer. Age is considered as one of the major risk factors for breast cancer. It is known that advancing age amplifies the risk of breast cancer[3]. After every ten years the risk for breast cancer doubles until menopause when it declines[7]. In western world the females over 60 years of age are at maximum risk. Breast cancer patients in our study were comparatively young. The most affected age group at diagnosis for cancer of the breast in our study was 36 to 45 years with median age 43 years which is in accordance with studies carried out in other Asian subgroups i.e., Iranian[8] and Indians[9]. The reason for the difference could be due to the various cultural, socio-demographic, geographical and life style factors which needs further exploration. Our study data showed that the breast cancer patients and the controls did not differ in age at menarche and menopausal status. There are conflicting findings in local and other neighboring countries regarding age at menarche and breast cancer risk. Early menarche was considered a risk factor that was not statistically significant in Asian studies[10,11]. This type of result for Asian studies may be due to the recall bias as most women are illiterate and poor who do not remember their age at menarche. Gajalakashmi et al[12] and Pakseresht et al[13] carried out studies on Indians and found no relationship between age at menarche and breast cancer risk. A study on Pakistani females by Gilani et al[14] demonstrated that early age menarche and menopause at late age are protective. We observed an association between age at menopause and breast cancer risk. In our study women with natural menopause at age more than 50 years compared to those having menopause at less than 50 years, were exposed to increased risk of breast cancer. Ewertz and Duffy[15] also showed an increased risk for women with late menopause. However early age at menopause has also been associated with breast cancer risk[16] which is not in agreement to our study. We did not find any association between breast cancer risk and family history of breast cancer in first degree relatives. This is in contrast to western and other local studies[5,17]. An increase in risk of breast cancer is associated with women who use oral contraceptives[7]. Pervaiz et al[18] also documented in another Pakistani study that oral contraceptive use is significantly associated with breast cancer. But our findings did not show any relationship between oral contraceptive use and breast cancer risk. Women with BMI ≥ 28 are at the risk of developing breast cancer as compared to women with BMI<28. These findings are

reported by some studies[19,20]. No statistical significance was established in our study with regard to increased risk of breast cancer with increased body mass index.

Breastfeeding is regarded to be protective against development of breast cancer as established by various studies[21,22]. Some Pakistani studies showed different results, in one breastfeeding was related with risk of developing breast cancer, while another established that breast cancer has no statistically significant relation with breastfeeding[23,18]. Longer duration of lactation reduces breast cancer risk. Authors of a meta analysis of 47 studies arrived at the conclusion that after every 12 months of breastfeeding the risk for breast cancer is reduced by 4.3%[24]. Most women breastfeed for longer durations in our country and this has led some professionals to conclude that breast feeding has no association with breast cancer risk[25]. Our study did not show any statistically significant association of breastfeeding and its duration with increased risk of breast cancer. Nulliparity as compared to parity increases lifetime risk of breast cancer[7]. In a meta-analysis carried out in Nordic countries nulliparity was related with 30% increase in breast cancer risk compared to parity[26]. Memon et al[27] in a Pakistani study noted that breast cancer was common in nulliparous women. Our study also is in agreement to these studies and showed nulliparous women had more risk of breast cancer as compared to parous women. Earlier local studies have established conflicting results contradictory to well-established protective effect of parity concerning breast cancer risk and parity[14,28]. Our females have more children than do western women, and this is one of the major causes of somewhat low incidence of breast cancer in our women as compared to women in west. First live birth at late age was associated with increased risk for breast cancer, our study did not find any statistically significant association with late age at first birth. Many western and local studies support the association of late age at first birth with breast cancer risk[14,28]. McPherson et al[7] in review article summarized that compared to women with first live birth below 20 years of age; women with first live birth at 30 years of age have two times more breast cancer risk.

CONCLUSION

In conclusion this study established the fact that nulliparous women and women with menopause at age more than 50 years are exposed to increased risk of breast cancer. Family history and late age at first live birth did not show increased risk and we could not explain this.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

REFERENCES

1. Bhurgari Y. Karachi cancer registry data- implications for the national cancer control program of Pakistan. Asian Pacific J Cancer Prev 2004; 5: 77-82.
2. Sohail S and Alam SN. Breast cancer in Pakistan: awareness and early detection. J Coll Physicians Surg Pak 2007; 17: 711-2.
3. Goodarz D, Stephen , Hoorn, A.D, Lopez CJ, Murray L. Ezzati M 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.
4. Kumar V, Abbas AK and Fausto N. Robbins and Cotran Pathologic Basis of Disease, New Delhi: Elsevier 2004; 7th edition: 1131-35.
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. Int J Cancer 1997; 71(5): 800-09.
6. Carmichael AR and Bates T. Obesity and breast cancer: a review of the literature. Breast 2004; 13: 85–92.
7. McPherson K, Steel CM. and Dixon, JM. ABC of breast diseases: breast cancer epidemiology, risk factors, and genetics. BMJ 2000; 309: 1003-6.
8. Ebrahimi M, Vahdaninia M and Montazeri A. Risk factors for breast cancer in Iran: a case-control study. Breast Cancer Res 2002; 4(5) : R 10.
9. Gupta P, Sharma RG and Verma M. Review of breast cancer cases in Jaipur region. J Ind Med Assoc 2002; 100: 282-84.
10. Ng EH, Gao F, Ji CY, Ho JH and Soo, KC. Risk factors for breast carcinoma in Singaporean Chinese women. Cancer 1997; 80: 725-31.
11. Rao DN, Ganesh B. and Desai PB. Role of reproductive factors in breast cancer in a low-risk area: a case-control study, Br J Cancer 1994; 70: 129-32.
12. Gajalakshmi CK and Shanta V. Risk factors for female breast cancer. A hospital-based case-control study in Madras, India. Acta Oncol 1991; 30 (5): 569-74.
13. Pakseresht S, Ingle GK, Bahadur AK. et al. Risk factors with breast cancer among women in Delhi. Indian J Cancer 2009; 46 (2): 132.
14. Gilani GM. Statistical aspects of epidemiology of breast cancer in Punjab, Pakistan, in Institute of Statistics. University of the Punjab Lahore: 2003; 231.
15. Ewertz M and Duffy SW. Risk of breast cancer in relation to reproductive factors in Denmark. Br J Cancer 1988; 58: 99-10.
16. Talamini R, Franceschi S, La Vecchia C, Negri E, Borsa L, Montella M. et al. The role of reproductive and menstrual factors in cancer of the breast before and after menopause. Eur J Cancer: 1996; 32A:303-10
17. Familial breast cancer: collaborative reanalysis of individual data from 52 epidemiological studies includ-ing 58,209 women with breast cancer and 101, 986 women without the disease. Lancet 2001; 358 (9291): 1389-99.
18. Parvez T, Anwar MS, Sheikh AM. Study of risk factors for carcinoma breast in adult female general population in Lahore. J Coll Physicians Surg Pak 2001; 11: 291-3.
19. Gilani GM. and Kamal S. Risk Factors for Breast Cancer in Pakistani Women aged less than 45 years. Annals of Human Biology: 2004; 31(4): 398-407.

20. Huang Z, Hankinson SE, Colditz GA, Stampfer MJ, Hunter, DJ, Manson JE, et al. Dual effects of weight and weight gain on breast cancer risk. JAMA 1997; 278:1407-11.
21. Newcomb PA, Storer BE, Longnecker MP, Mittendorf R, Greenberg ER, Clapp RW. et al. Lactation and a reduced risk of premenopausal breast cancer. New Eng J Med 1994; 330: 81-7.
22. Wrensch M, Chew T, Farren G, Barlow J, Belli F, Clarke C et al. Risk factors for breast cancer in a population with high incidence rates. Breast Cancer Res 2003; 5: R88-102.
23. Ahmad A, Naz F, Khawaja MA, Haq AU, Malik SN and Khan, SA. Presentation of carcinoma breast in Pakistan a study of 60 cases. Ann King Edward Med Coll 2000; 6-4: 424-6.
24. Collaborativ Group on Harmonal Factors in 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.
25. Bhurgri Y, Bhurgri A, Nishter S, Ahmad A, Usman A, et al. Pakistan - Country Profile of Cancer and Cancer Control. JPMA 2006; 56(3): 124-130.
26. Ewertz M, Duffy SW, Adami HO, Kvale G, Lund E, Meirik O, et al. Age at first birth, parity and risk of breast cancer: a meta-analysis of 8 studies from the Nordic countries. Int J Cancer 1990; 46: 597-603.
27. Memon, GA, Solangi RA, Dahri AM. and Chandio AM. An experience with breast cancer at P.M.C.H, Nawabshah. Med Channel 1999; 5: 7-14.
28. Mahmood S, Rana TF and Ahmad M. Common deterninants of CA breast- A case control study in Lahore. Annals of KEMU 2006; 12 (2): 227-228.