IJBPAS, August, 2018, 7(8): 1445-1453

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

SOCIO-ECONOMIC RISK FACTORS FOR BREAST CANCER INWOMEN AFTER MENOPAUSAL: A CASE-CONTROL STUDY

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Received 15th Nov. 2017; Revised 25th Jan. 2018; Accepted 29th March 2018; Available online 1st August 2018

https://doi.org/10.31032/IJBPAS/2018/7.8.4315

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ABSTRACT

The objective of the study was to investigate risk factors for breast cancer in women at least of age 50 years. A case-control study was conducted from December 2013 to March 2014 in Faisalabad and Lahore, Pakistan. Prognostic risk factors related information was collected using a structured questionnaire. Odds ratios (ORs), 95% confidence intervals (CIs) and P-values of estimate were derived from logistic regression context. In all, 547 women with breast cancer and 1020 control were interviewed. In statistical analysis, only family history (OR=2.386, 95% CI=1.549-3.676, P<0.001), BMI (OR=0.807, CI = 0.754-0.864, P<0.001), ethnicity (OR=1.168, CI=0.083-0.338, P<0.001), and breastfed (OR=0.698, CI = 0.648-0.753, P<0.001) were associated with significantly increased risk for breast cancer after menopausal. The findings of study suggest that family history of disease, breastfed, ethnicity and BMI may have an impact on the incidence of breast cancer in women after menopausal.

Keywords: Breast cancer, odds ratio, logistic regression

1. INTRODUCTION

A malignant benign is a group of cancer cells that can metastasize to distant areas of the body (American Cancer Society, 2016). Human being is unprotected to the risk of several diseases. A large fraction of our population is being hit by a number of diseases. Accounting for a quarter of all cancers in female is the

breast cancer (Ferlay et al., 2010).The incidence of suffering from different diseases and the associated death rates are increasing rapidly. Every year 40,000 young girls die of breast cancer (National Breast Cancer Awareness, 2016).There is approximately a four-fold variation of incidence rate across the globe, with rates ranging from 27 per 100,000 in middle Africa and Eastern Asia to 96 in western Europe (Ferlay et al.,2013). Efforts are being made to reduce the occurrence of diseases, the awareness of the public regarding the factors causing these diseases and to recommend various lines of treatment. It has become possible due to the knowledge of causality of the diseases. Breast cancer is one of the disastrous diseases and to a great part of our population a constant physical and mental anguish. For the better health of mankind, the oncologists, statisticians and medical research workers need to put their combined exertions in identifying and examining the causes of cancer and employing the suggestions.

Breast cancer is increasing in all regions of the world with majority of rise seen in developing countries (Butt et al., 2009). Pakistan is a developing country with poor literacy rate. This research will be helpful to create awareness in the society about the possible reasons of prevalence of breast cancer and consequences of ignoring it or taking it non-seriously. The outcome of this research will be identifying the potential risk factors of breast cancer, preventive measures to avoid this fatal disease and possible treatment and cure for the disease in our society. Inflammatory breast cancer is a rare but the most lethal type of breast cancer and has a poor prognosis Moonindranath et al., (2016). The cohort study by Brewer et al (2013) reviewed how medicin use and type used affected progression free survival and overall survival in723 patients diagnosed and treated.

The findings of this study will be a good contribution and addition in the medical research and will be a pathway for future Biostatisticians, medical researchers and epidemiologists.

2. MATERIALS AND METHODS

Design, Setting and Participants

A case-control study was conducted during the academic sessions Fall 2013 and Spring 2014 of GC University, Faisalabad. The hospitals remained the best option for the researchers to approach the cases. The data for breast cancer patients were collected from the four leading cancer hospitals Allied Hospital Faisalabad (AHF), Institute of Nuclear Medicines and Oncology Lahore (INMOL), Punjab Institute of Nuclear Medicine (PINUM) Hospital Faisalabad

and Mayo Hospital Lahore. The data set comprised of 547 breast cancer patients and 1020 controls in all with 1:2 ratio between cases and controls.

Data Collection Tools/Instruments

A structured questionnaire prepared in English and Urdu as well used to interview the cases and controls. Some information related to the patients' history also collected from the records (history sheet) of the hospitals. The questionnaire was designed after consulting doctors/specialists in the relevant field and on basis of their recommendations. For a person of weight W(kg) and height *H*(meters) it is simply:

$BMI = W / H^2$

In addition to basic demographic details, the questionnaire sought the information from cases and controls about the variables like present age, family history of cancer (first-degree relative), information about first full term pregnancy, age at menarche, ethnicity, breastfed, education, job status, consanguineous marriage (first cousin marriage), BMI (body mass index) etc. Women were classified as menopausal if they had not menstruated during the 6 months before the date of data collection. A full-term pregnancy was a pregnancy lasting 8 months or longer. The data were restricted to married women only because there was a very small population of unmarried women having breast cancer problem.

Data Analysis

The software SPSS version 20.0 is used to analyze the collected data. The odds ratios and confidence intervals in logistic regression context are calculated for different risk factors. $P<0.001$ was considered statistically significant. Those risk factors that were significantly associated with breast cancer were entered into a forward selection multivariate logistic regression analysis

The dependent variable is presence of breast cancer. All the data were coded and entered into computer. As and when needed editing of the data was done. For advanced analysis all the data were scrutinized. The outcome variable for this study was binary. The data were collected for 547 cases and 1020 control for different possible risk factors of breast cancer.

The risk factor age was divided in to four classes i.e., below 40, 40-49, 50-59, 60 & above. The total number of women of age below 40 years was 488 which was also maximum count with percentage 31.1. The number of women suffering from breast cancer of the same group was 129 with percentage 23.6. The total number of women of age of age class 40-49 was 359 with percentage 22.9, out of which 179 were cases and 216 was

control. Similarly, the total number of cases and control for other classes i.e., 50-59 and 60 & above was 350 and 344 respectively. The total number of women of family history of breast cancer having positive was 314 and having negative was 1253. Their percentages were 20.0 and 79.9. The number of women suffering from breast cancer with family history of breast cancer having positive was 228 and having negative was 319, , where the rest number of women falls in control. The age of early menarche was divided in to two categories i.e., below 13 and above 13. The total number of women having early menarche before 13 was 65 and the total number of women having early menarche above\after 13 was 1146. Therefore, The total number of women having early menarche before 13 was 3 and the total number of women having early menarche above\after 13 is 405. The age at menarche was given for age of 13 years or less and above 13 years. This may be because of the effect of age at menarche on breast cancer risk may be mediated simply by the prolonged exposure of breast epithelium to estrogen produced by regular ovulatory cycle. As far as age at first full term pregnancy FTP concerned, it was divided into two categories i.e., below 25 and 25 & above. The total number of women among 1567 of age at first full term pregnancy below 25 is 119 and the total number of women among 1567 of age at first full term pregnancy at 25 &above 25 is 436. Therefore, the number of women among 547 below 25 is 44 and the number of women among 547 below 25 was 202. Where the ultimate mechanism through which early pregnancy protects the breast from cancer development remains largely unknown.

After then the data is coded for statistical analysis. The positive category was coded as 1 and negative as 0. Similarly ever was coded as 1 and never is 0 before analysis. The age at menarche below 13 age was coded 1 and above 13 age 0. As age at menarche below 13 was a prognostic risk factor for our study population. The age at first full term pregnancy 25 and above was risk factor coded as 1. Similarly the remaining variables were coded before analysis.

The parameter estimates for logistic regression model of age less than 50 and greater than 50 are given in Table 1.The Table2 represents odds ratio of women before age of 50 years for the comparison between two mutually exclusive groups i.e. women of age group <50 and ≥ 50.

Table 1: Variables in logistic regression fit for married women with at least 50 years.

Variables	Estimate	OR (95% CI)	P-value
present age	-0.054	0.948(0.910-0.987)	0.009
age at first full term pregnancy	0.041	1.042(0.976-1.112)	0.221
age at menarche	-0.218	0.804(0.625-1.034)	0.090
Breastfed	-0.359	0.698(0.648-0.753)	<0.001
suffering benign condition	1.069	2.912(1.035-8.195)	0.043
chest radiation	0.345	1.412(0.445-4.476)	0.558
history of breast cancer in family	0.870	2.386(1.549-3.676)	<0.001
Education	-0.180	0.835(0.663-1.051)	0.124
intake oral contraceptive	0.161	1.175(0.687-2.010)	0.556
job status	-0.026	0.974(0.303-3.136)	0.965
physical activity	-1.244	0.288(0.075-1.114)	0.071
BMI	-0.215	0.807(0.754-0.864)	<0.001
consanguineous marriage	0.307	0.807(0.754-0.864)	0.043
Ethnicity	-1.786	0.168(0.083-0.3380)	<0.001

Chi-square =10.77 Cox and Snell R Square= 0.481 Nagelkerke R Square= 0.653

Table 2:Variables in logistic regression fit for married women less than 50 years of age.

Variable	Estimate	OR (95% CI)	P-value
present age	0.035	1.035(1.023-1.048)	<0.001
age at marriage	0.039	1.040(0.990-1.092)	0.120
no. of child and stillbirth	-0.076	0.927(0.842-1.020)	0.119
age at menarche	-0.211	0.810(0.664-0.988)	0.037
suffering benign condition	-0.150	0.860(0.431-1.718)	0.670
chest radiation	0.599	1.821(0.838-3.954)	0.130
history of breast cancer in family	0.977	2.657(1.975-3.575)	<0.001
Education	-0.401	0.669(0.567-0.790)	<0.001
intake oral contraceptive	0.119	1.127(0.860-1.476)	0.387
job status	0.218	1.244(0.511-3.028)	0.631
physical activity	0.168	1.183(0.377-3.711)	0.773
BMI	-0.219	0.804(0.766-0.843)	<0.001
Ethnicity	-1.478	0.228(0.144-0.361)	<0.001
consanguineous marriage	0.426	1.531(1.247-1.880)	<0.001

Chi-square =8.092 Cox and Snell R Square= 0.310 Nagelkerke R Square= 0.420

3. RESULTS AND DISCUSSION

The data presented in Table 1 shows that the value of odds ratio of variable present age is 0.948. It implies that odds ratio of present age is 5% or 0.05 less than odds ratio of breast cancer. In other words the breast cancer risk decreases by 5% as the age advances. The odds ratio 1.042 interprets that risk of breast cancer increases by 4% as age at FTP increases. Similarly the interpretation of 0.804 is that risk of breast cancer decreases by 19% as age at menarche advances from age of 13. The odds ratio of chest radiation is 0.412 more than odds ratio of breast cancer. It increases risk of breast cancer by 58. The odds ratio is 2.386, which means the odds ratio of having

history of breast cancer in family is 1.38 more than to the odds ratio of presence of breast cancer. The variable education has the odds ratio 0.835 interprets that the risk of breast cancer decreases as awareness of the disease rises by 16%. The OR=1.175 implies that there is 17% more chances/risk of breast cancer in case of in taking the oral contraceptive. The job status of working has odds ratio 2% less than odds ratio of breast cancer. The physical activity positive class decreases the risk of breast cancer by 71%. The women living in urban areas have less risk than women living in rural areas by 83% as OR= 0.168. Similarly, the variable breastfed has the odds ratio 0.698, which means increasing number of years of lactation among mothers reduces the risk of breast cancer by 30%. The risk factors or variables of this analysis suffering from benign condition and getting marriage in family also increase the risk of breast cancer by 191% and 36% respectively.

The Hosmer and Lameshow test is representing the p-value equal to 0.215 which is greater than 0.05. It concludes that model is good fit. The other tests as Cox and Snell R Square and Nagelkerke R Square are also in agreement.

The interpretations of odds ratio in Table 2 is considered now. The value of odds ratio of variable age at marriage is 1.040. It implies that odds ratio of age at marriage is 4% or 0.04 more than odds ratio of breast cancer. In other words the breast cancer risk increases by 4% as the age at marriage advances. The odds ratio 0.810 interprets that risk of breast cancer decreases by 81% as age at menarche increases. Similarly the interpretation of 0.860 is that risk of breast cancer decreases by 86% as women suffer from benign condition increases. The interpretation of OR=1.821 is that risk of breast cancer increases by 82% as if the women facing the chest radiation increases. The odds ratio of history of disease in family is 1.657 more than odds ratio of breast cancer. It increases risk of breast cancer by 165%. It is also highest odds ratio in Table 2. The variable education has the odds ratio 0.669 interprets that the risk of breast cancer decreases as awareness of the disease rises. The OR=1.127 implies that there is 12% more chances/risk of breast cancer in case of in taking the oral contraceptive. Similarly, the values of odds ratio of getting married in family increases the risk of breast cancer by 53%. The job status of working has odds ratio 24% more than odds ratio of breast cancer. The physical activity decreases the risk of breast cancer by 18%.The women living in urban areas have less risk than women

living in rural areas by 77% as OR= 0.228.

The goodness of fit tests for analysis of married women of age less than 50 out of cases 547 and control 1020 against the hypothesis that model is good fit, is tested. The significance value of Hosmer and Lameshow test is 0.425 greater than 0.05. It concludes that model is good fit.

Age is an important risk factor. The breast cancer risk increases by 3% as the age advances (OR=1.035, CI = 1.023-1.048, P<0.001) [Table-2] for the group of women less than 50 years but breast cancer decrease by 5% as age advances (OR=0.948, CI=0.910-.987, P=0.009) [Table-1] for the women of age at least 50 years. The age at menarche (OR=0.804, CI = 0.625-1.034, P=0.090) [Table-1] and age at first full term pregnancy (OR=1.042, CI = 0.976-1.112, P=0.221) [Table-1] are independent of breast cancer for women at and after 50 years of age. The risk factor as suffering from benign condition (OR=2.912, CI = 1.035-8.195, P=0.043) [Table-1] and consanguineous marriage (OR=1.360, CI = 1.010-1.832, P=0.043) [Table-1] are not statistically significant at P <0.001 for aged women. The risk factors education, intake oral contraceptive, job status, physical activity is insignificant for population of study at least of 50 years old. The family history of disease (OR=2.386, CI = 1.549-3.676, P<0.001) [Table-3], BMI (OR=0.807, CI = 0.754-0.864, P<0.001) [Table-3], and ethnicity (OR=1.168, CI = 0.083-0.338, P<0.001) [Table-3], and breastfed (OR=0.698, CI = 0.648-0.753, P<0.001) [Table-3] are statistically significant.

Table 3: Odd ratio (OR) and 95% CI between < 50 and ≥ 50 age groups.

Variable	Age less than 50		Age at least 50	
	P-value	OR(95% CI)	P-value	OR(95% CI)
age at menarche	0.037	0.810(0.664 - 0.988)	0.090	0.804(0.625 - 1.034)
suffering benign condition	0.670	0.860(0.431 - 1.718)	0.043	2.912(1.035 -8.195)
chest radiation	0.130	1.821(0.838 -3.954)	0.558	1.412(0.445 - 4.476)
history of breast cancer in family	<0.001	2.657(1.975 -3.575)	<0.001	2.386(1.549 , 3.676)
Education	<0.001	0.669(0.567 -0.790)	0.124	0.835(0.663 - 1.051)
intake oral contraceptive	0.387	1.127(0.860 -1.476)	0.0056	1.175(0.687 - 2.010)
BMI	<0.001	0.804(0.766 - 0.843)	<0.001	0.807(0.754 -0.864)
Ethnicity	<0.001	0.228(0.144 - 0.361)	<0.001	1.168(0.083 -0.338)
consanguineous marriage	<0.001	1.531(1.247 - 1.880)	0.043	1.360(1.010 - 1.832)

4. CONCLUSION

In statistical analysis, family history (positive family history of first degree relatives of breast cancer with OR=2.368, 95% CI=1.549-3.676, P=0.001),), BMI (OR=0.807, CI = 0.754-0.864, P<0.001), ethnicity (OR=1.168, CI = 0.083-0.338, P<0.001), and breastfed(OR=0.698, CI =

0.648-0.753, P<0.001) were associated with significantly increased risk for breast cancer after menopausal. The findings of study suggest that family of disease, breastfed, ethnicity, BMI may have an impact on the incidence of breast cancer in women throughout the life even after menopausal.

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