



EXPOSURE TO SMOKELESS FORM OF TOBACCO AND RISK OF BREAST CANCER: A CASE CONTROL STUDY FROM RURAL MAHARASHTRA, INDIA

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ABSTRACT

Introduction: Tobacco exposure has been associated with development of a variety of cancers and breast cancer is one of them. The study objective was to determine the strength of association between smokeless form of tobacco and breast cancer risk among the women residing in rural area of western Maharashtra, India.

Methods: A case-control study was conducted in Satara district, India during year 2009-10 to 2010-11 among newly diagnosed cases of breast cancer and matched controls. Sample size includes a total of 434 participants enrolled from Krishna Hospital Karad. Descriptive and inferential statistics employed to determine the strength of association and statistical significance.

Results: Highest proportion of breast cancer cases, [31.80%] were in age group 40-49 yrs with lowest age at the diagnosis of the disease was 25 years. Maximum proportions of cases, [63.59%], [71.42%] and [56.68%] were housewives, literate and from upper economic class. Out of total 217 cases, [58.99%] were exposed to smokeless form of tobacco and significantly associated with breast cancer [Odd's -1.7, CI- 1- 2.1]. The frequency and duration of exposure to smokeless form of tobacco were significantly associated with breast cancer [Odd's- 2.5, CI- 1.4-4.4], [Odd's - 2.5, CI-1.4-4.6].

Conclusion: Study revealed smokeless form of tobacco is a risk factor for breast cancer among the women residing in rural Maharashtra

Keywords: Breast cancer, smokeless tobacco, risk, rural habitations, odd's ratio

INTRODUCTION

Breast cancer is the most common type of cancer in women worldwide. Since last two to three decades, it's reflected as an important public health problem for adult women residing in developing countries like India and stood the rank second amongst the all cancerous conditions in Indian women.¹ Exposure to smokeless form of tobacco like chewing tobacco and tobacco snuffs are most commonly practiced among Indian women residing in each and every part of country.² Tobacco use alone accounts for about 40% of all cancers in India and a point prevalence of smokeless form of tobacco in India is

about 275 million (35% of adult population and 14.1% of children aged 13-15 years) as said by Paul E. Goss of Harvard Medical School, Boston, and others.³ There are an estimated 100,000 to 125,000 new breast cancer cases detected in India every year and this number of breast cancer cases in India is estimated to double by 2025.⁴ Mumbai, the capital of Maharashtra state has highest incidence of breast cancer cases in country followed by Delhi, Nagpur, Bangalore, Kolkata and Chennai with age adjusted rates for breast cancer cases (female) as (33.1), (31.6), (29), (28.7), (27.8) and (27.5) respectively.^{5,6}

Satara is a huge sugar producing district from Maharashtra, India where approximately 68% population resides in rural areas. The maximum rural women using smokeless tobacco in the form of khaini, tobacco mishri, and snuff for teeth cleaning, pleasure, healing and as cultural and traditional practices etc. According to western literature, cigarette smoking has been associated with breast cancer^{7, 8, 9} however; the role of smokeless tobacco use has never been evaluated as a breast cancer risk factor. However, preliminary results suggested smokeless tobacco may dramatically increases the risk of breast cancer reported among tribal women from western North Carolina, America.¹⁰

The study designed to determine the strength of association between smokeless form of tobacco and breast cancer among the women residing in Satara district, western Maharashtra, India. The results of this study can contribute to formulate a public health policy for increasing the awareness among women.

MATERIALS and METHODS:

Institutional ethics committee clearance, permissions from health institutions and informed consent from each study subject was obtained before starting the study. A hospital based case- control study was conducted in Satara district of the state Maharashtra, India. Conveniently, Krishna Hospital was selected for study as a premier institute provides diagnostic, therapeutic and whole range of cancer therapy for rural people residing in Satara district, Maharashtra. The study was conducted over the period of thirty six months [Jan 2009 - Dec 2011]. All newly diagnosed cases of breast cancer [clinically and histo-pathologically confirmed] and matched controls [confirmed by clinical breast examination by cancer surgeon] were selected from hospital as well as relatives, neighbourhood with respect to number, age, religion and residence fol-

lowing 1:1 ratio. A sample size consists of total 434 women include 217 cases and 217 controls were enrolled according to inclusion criteria of study. **Inclusion criteria:** Newly diagnosed cases of cancer breast within the period of one year of diagnosis, irrespective of stage of diagnosis of breast cancer, ready to participate in study and residents of Satara district. **Exclusion criteria:** Non cooperative cases.

A pre-tested structured questionnaire that include socio-demographic, economic characteristics of the women and tobacco exposure characteristics etc. utilized to collect the data from the cases and the controls through individual, personal interview method on schedule basis. Data was entered into Microsoft Excel 2007 and analyzed by using Statistical Packages for Social Sciences [SPSS] statistical software version 17. Descriptive statistics, exposure rate of risk factor in cases and controls, existence and strength of association was found out by using chi-square test and Odd's ratio at 95% confidence interval. Statistical significance was considered when *p value* was less than 0.05 at 95% confidence interval.

RESULTS:

In all, 217 women with breast cancer and 217 from the control group were interviewed. They were in the age group ranging from 25 to 70 years with the mean age of 48.59 and 48.43 years for the cases and the controls respectively. With respect to age, religion and residence, maximum 31.80 %, 88.02% and 67.28% of both cases and controls were in age group of 40-49 yrs, Hindu by religion and residing in rural area respectively [Table 1[A]].

The proportions of the cases and the controls with respect to occupation shows that maximum number of subjects were housewives, 63.59% and 61.75% with apparent differences in occupational groups.

Table 1[A]: Demographic distribution of cases [N=217] and controls [N=217]

Variables	Cases (%)	Controls (%)	Total (%)	Test of Significance	p- value
Age(yrs)					
≤ 30	7 (3.23)	7 (3.23)	14(3.22)	0.14	0.88
30 - 39	40 (18.43)	40 (18.43)	80(18.43)		
40 - 49	69 (31.80)	69 (31.80)	138(31.79)		
50 - 59	52 (23.96)	53 (24.42)	105(24.19)		
≥ 60	49 (22.58)	48 (22.12)	97(22.35)		
Religion:					
Hindu	191 (88.02)	191 (88.02)	382(88.01)	0.00	1.000
Muslim	19 (8.76)	19 (8.76)	38(8.75)		
Christian	7 (3.23)	7 (3.23)	14(3.22)		
Residence:					
Rural	146 (67.28)	146 (67.28)	292(67.28)	0.00	1.00
Urban	71 (32.72)	71 (32.72)	142(32.71)		

Table 1(B): Socio-Economic distribution of cases [N=217] and controls [N=217]

Variables	Cases (%)	Controls (%)	Total (%)	Test of Significance	p- value
Occupation					
House Wife	138 (63.59)	134 (61.75)	272(62.67)	7.756	0.100
Daily Wagers	36 (16.59)	48 (22.12)	84(19.35)		
Self Employed	35 (16.13)	23 (10.60)	58(13.36)		
Civil Servant	5 (2.30)	3 (1.38)	8(1.84)		
Private Sector employee	3 (1.38)	9 (4.15)	12(2.76)		
Education:					
Illiterate	62 (28.57)	66 (30.41)	128(29.49)	16.33	0.002*
Primary	68 (31.34)	39 (17.97)	107(24.65)		
Secondary	73 (33.64)	95 (43.78)	168(38.70)		
Higher Secondary	6 (2.76)	14 (6.45)	20(4.60)		
Degree/Diploma	8 (3.69)	3 (1.38)	11(2.53)		
Income:					
Low class	94 (43.32)	110 (50.69)	218(50.23)	2.3	0.12
Upper class	123 (56.68)	107 (49.31)	216(49.76)		

* indicate, p value is significant at 95% confidence interval

Table 2: Exposure to smokeless tobacco and risk of breast cancer

Exposure	Cases (%)	Controls (%)	Total (%)	Odd's	CI	x ²	P
Tobacco Use							
Yes	128 (58.99)	107 (49.31)	235(54.14)	1.7	1-2.1	4.093	0.043*
No	89 (41.01)	110 (50.69)	199(45.85)				
Total	217	217	434				
Freq. of Tobacco exposure/day							
1/day	23 (17.97)	47 (43.93)	70(29.78)	reference	0.7-2.1	20.56	0.0001**
2 - 4/day	46 (35.94)	27 (25.23)	73(33.61)	1.2			
≥ 5/day	59 (46.09)	33 (30.84)	92(36.59)	2.5			
Total	128	107	235				
Duration of Exposure (yrs)							
<5 yrs.	3 (2.34)	7 (6.54)	10(4.26)	reference	0.2-0.8	10.48	0.0001**
5-10 yrs.	21 (16.40)	33 (30.84)	54(22.98)	0.4			
>10 yrs.	104 (81.25)	67 (62.61)	171(72.77)	2.5			
Total	128	107	235				

** indicate, p value is highly significant at 95% confidence interval

Table 3: Multiple logistic regression analysis

Variables	aOR (95% CI)	P value
Exposure to tobacco		
No	1	0.0001*
Yes	2.35 (1.01-5.51)	
Frequency of exposure		
< 5/day	1	0.0001*
>5/day	10.13 (5.41-18.23)	
Duration of exposure		
<10 yrs	1	0.007*
>10yrs	31.13 (11.67-39.82)	

aOR=Adjusted odd's ratio; * indicate, p value is significant at 95% confidence interval

Maximum cases as well controls, 71.42% and 69.58% were literate i.e. able to read and write in own language and showed statistically significant difference with respect to educational level [p< 0.05]. The proportion of cases was higher in the Upper socio- economic class [According to modi-

fied BG Prasad classification class I and II] 56.68% as compared to the controls 49.30%. [Table 1[B]].

Out of 217 cases of breast cancer, 128 cases were exposed to smokeless form of tobacco viz. Tobacco mishri, tobacco powder, chewing tobacco. The rate of exposure to the tobacco was higher in cases (58.98%) as compared to the controls (49.30%) indicating exposure to tobacco to be a risk factor for cancer of breast. The strength of association between exposure to tobacco and breast cancer (odd's ratio) was 1.7 with a confidence interval of 1 to 2.1 and a significant association existed between tobacco exposure and breast cancer ($\chi^2= 4.09$, $p = 0.04$).

As the frequency of tobacco exposure increased to 5 and above, the odd's ratio was 2.5 with confidence interval of 1.4 to 4.4 indicating that such higher use of tobacco was a risk factor for occurrence of breast cancer. Overall, the proportions of frequency of use of tobacco among cases and controls varied significantly ($\chi^2= 20.56$, $p = 0.001$).

When the duration of exposure increased to 10 years and above, the odd's ratio was 2.5 with confidence interval of 1.4 to 4.6 indicating that higher the duration of exposure of tobacco was a risk factor for occurrence of breast cancer. Overall, the proportions of duration of exposure to tobacco among cases and controls are statistically significantly ($\chi^2=20.56$, $p=0.001$) (Table 2).

After multivariate logistic regression analysis [Enter method], it was observed that exposure to smokeless form of tobacco, frequency and duration of exposure to tobacco were strongly associated with occurrence of breast cancer ($p < 0.05$) (Table 3).

DISCUSSION:

The present study has revealed, lowest age at incidence of breast cancer to be 25 years as observed from a rural area of Western Maharashtra. The proportion of breast cancer cases has been maximum [74.19%] in the age group 30-60 years. Pakseresht S et al (2009)¹¹ have shown that the age incidence of breast cancer is maximum in the age group of 30-60 yrs with minimum age incidence has been 25 yrs. Similar findings also have been observed by Kamat R(2013).¹² The majority of breast cancer cases, 67.28% have been from rural area as compared to the urban area. However study conducted by Pakseresht S et al(2009) from urban area of Delhi¹¹ have shown maximum breast cancer cases to be from urban area and difference could be related to the placement of hospital and the population catered by it. The present study is conducted in Satara district where approximately 80 % population is residing in the rural area and the district is known to be from sugar belt of western Maharashtra.

In this study, majority of breast cancer cases, 88% are from Hindu religion and proportion of Muslim and Christians has been 8.7% and 3.2% respectively. The big gap in proportion of breast cancer cases with respect to religion could be due to the difference in the religion wise distributions in the populations groups in the India. Similar findings also have been reported by Badve RA (1990)¹³ as 82.4%, 7.3% and 2.7% respectively for the Hindus, Muslims and Christians and shows apparent difference when compared with our study and this difference could be due to time period of both the studies.

The majority of breast cancer cases [63.89%] in our study are housewives and similar findings are also observed by Pakseresht S et al (2009).¹¹ The proportion of illiterate to literate breast cancer cases are 28.57% and 71.43% respectively and this difference could be due to increase in women's literacy rate [82.9%] in Satara district. However, studies conducted by Parameshwari P (2013)¹⁴ have shown

maximum, 60% breast cancer cases among illiterate population from South Kerala. Even though in Kerala women have high literacy rate i.e. > 90% , majority of breast cancer cases were illiterate and difference in study results could be due to behavior of majority of literate Kerala women who prefer residence in abroad or in metros, however illiterate resides in local area.

In our study, the rate of occurrence of breast cancer cases is higher among women from upper economic class. A study is conducted in rural area but modern agriculture, cash crop of sugar cane associated with higher economic status, increased literacy and sound economic status could be responsible for high incidence of breast cancer among upper economic class rural population. Similar findings have been observed by Kelsey JL(1979)¹⁵ from developed country. The behavioral aspects of upper economic class may be related to occurrence of breast cancer like having less number of children, late marriage etc.

In the present study, out of 217 breast cancer cases 58.99 % were exposed to smokeless tobacco and risk of getting breast cancer has been 1.7 times higher in these women as compared to non tobacco users. Study carried out by Splanger JG¹⁰ from tribal lands in western North Carolina, America showed 8 times risk of developing breast cancer in women exposed to smokeless tobacco. The risk of developing breast has been reported as 5.8 times higher in tobacco smoking women as compared to non smoking women by Johnson KC.¹⁶ Similar findings have also reported by Khuder SA.¹⁷ The chemical compounds found in tobacco, such as polycyclic hydrocarbons, aromatic amines, and *N*-nitrosamines, may induce mammary tumors. These factors have an affinity towards specific DNA adducts and *p53* gene mutations in the breast and also support the biological plausibility of a positive association between tobacco and breast cancer.^{18,19}

When the frequency increased to 5 and above, the odd's ratio was 2.5 with confidence interval of 1.4 to 4.4 indicating that such higher use of tobacco was a risk factor for occurrence of breast cancer. The frequency trend was 2.9 times significantly higher in women exposure to tobacco identified by Dobson R.²⁰ Similar trend also reported by Johnson KC.¹⁶ The duration of exposure increased to 10 years and above, the odd's ratio was 2.5 with confidence interval of 1.4 to 4.6 indicating that higher the duration of tobacco exposure was a risk factor for occurrence of breast cancer. The duration trend was significantly associated with increased risk of breast cancer also reported by Johnson KC¹⁶ and Khuder SA.¹⁷ The production, distribution and sell of tobacco products are commonly practiced in rural area of India. Cultural practices, illiteracy, poor

rural health care infrastructure, poverty, ignorance leads to extensive exposure to smokeless form of Tobacco. Need proper enforcement of health legislations in context to tobacco.

CONCLUSION

Our study revealed that, maximum breast cancer cases were in age group 40-49 yrs. The smokeless form of tobacco is to be identified risk factor for breast cancer and at the same time risk of breast cancer is also increased as frequency and duration of exposure increases.

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