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RESEARCH PAPER

Smokeless Tobacco Consumption and Breast Cancer in Women: Findings of a Case-Control Study

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Abstract

Background: Breast cancer is the most commonly occurring cancer in women and the second most common cancer overall. Among the various risk factors of breast cancer, smokeless tobacco is the neglected potential one. Hence the study was conducted to assess the association between smokeless tobacco consumption & breast cancer risk among the women.

Objective: The objective of the study was to assess the association between smokeless tobacco consumption and breast cancer in women and to compare the pattern of smokeless tobacco consumption, relevant other factors of breast cancer and the socio-demographic characteristics between the cases and controls.

Methods: This case control study was conducted in 302 women of two tertiary hospitals of Dhaka city from January to December'2020. The study enrolled 151 breast cancer patients as cases and another 151 non cancer age-matched women as controls. Convenient technique was used for data collection. A pre-tested semi-structured questionnaire and a checklist were used for face to face interview and to review the medical record respectively. The data were analyzed by SPSS software. Quality control checks of the data were done at all stages of the study. All ethical issues were maintained strictly and informed written consent was taken from each case and control.

Results: The mean (±SD) age of cases and controls was 44.4(±10.56) &44.82(±10.2) years respectively (p=0.769). Maximum cases (90.1%) were married in comparison to controls (76.2%) and the association was significant (p=0.003). Majority of the cases (63.58%) had monthly income of 21000-50000tk compared to controls (51.66%) and this difference was significant (p=0.01).Among the cases, 36.4% were exposed to smokeless tobacco in comparison to 33.8% controls. Though this association was not significant (p=0.630) but maximum cases (70.9%) were found to be exposed for 16-30 years in comparison to controls (43.9%) and it was statistically significant (OR: 7.58, 95%CI: 0.865-66.404). Among the cases, who were exposed to zarda were 3.25 times more likely to have it >10 times in comparison to 2.6% controls (OR: 3.25, 95% CI: 1.05-9.99, p=0.040).

Conclusion: Increased frequency and duration of smokeless tobacco intake is found significantly associated with breast cancer so specific preventive intervention is required for prevention of smokeless tobacco consumption among women to alleviate breast cancer.

Keywords: Smokeless Tobacco, Breast Cancer, Women, Odd's ratio, Bangladesh.

Introduction

Breast cancer is the most common cancer in women worldwide. There were more than 2 million new cases every year. Breast cancer accounts for 25% of all cancer cases and 15% of all cancer deaths among females. In women the risk factors associated with breast cancer are obesity, a lack of physical exercise, alcoholism, hormone replacement therapy during menopause, ionizing radiation, an early age at first menstruation, late menopause, having children late in life or not at all, older age, having a prior history of breast cancer and a family history of breast cancer. Tobacco is the largest single preventable cause of death in the world and the tobacco epidemic is one of the biggest public health threats the world has ever confronted, which is believed to account for about 6 million deaths a year.[1] Smokeless tobacco (SLT) means the use of any unburned tobacco those intended to be sucked, chewed or inhaled by the user. The smokeless tobacco refers to more than 30 different products, broadly categorized as 'spit tobacco'.[2]

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Since last two to three decades, it's reflected as an important public health problem for adult women residing in developing countries. Almost 90% of the global burden of SLT use is estimated to be present in South East Asia.[3] The prevalence of SLT use in most of the South Asian countries is much higher than in sub-Saharan Africa, Central and Western Asia and other developed countries. South Asian countries are facing a hidden breast cancer epidemic and a significant proportion of the breast cancer cases occur in premenopausal women.[4]

In South and Southeast Asia SLT is used in diverse forms, particularly In Bangladesh the two major forms of SLT products are zarda (industrially processed tinned tobacco leaves containing lime, spice, vegetable dye and areca nut) and sadapatha (sun dried or cured whole tobacco leaves, mostly done at home), both of which are usually consumed with betel leaves.[5] Although the prevalence of smoking is high among males (26.4%) than females (1.5%), use of SLT is slightly higher among females (47.2%) than among males in Bangladesh.[6]

The increasing prevalence of breast cancer around the world is an important public health issue. Smoked tobacco has been associated with breast cancer but the effect of smokeless tobacco on breast cancer has not studied to that extent in global perspective and there is no study reported yet in this field in our country as well.

Materials and methods

Institutional ethics committee clearance, permissions from health institutions and informed consent from each study subject was obtained before starting the study. This case- control study was conducted at both the outpatient and inpatient department from purposively selected two cancer hospital i,e National Institute of Cancer Research And Hospital (NICRH) and Ahsania Mission Cancer and General Hospital, (AMCGH) from January to December'2020. All diagnosed cases of breast cancer [clinically and histo-pathologically (F.N.A.C) confirmed] and matched controls were selected from hospital as well as relatives, neighborhood with respect to age, following 1:1 ratio. A sample size of total 302 women include 151 cases and 151 controls were enrolled according to inclusion criteria of study.

Inclusion criteria: Diagnosed cases of CA breast where breast was the primary site of cancer irrespective of stage of diagnosis of breast cancer, ready to participate in the study. *Exclusion criteria:* Women with secondary neoplasm and non-cooperative cases.

A pre-tested semi-structured questionnaire that include socio-demographic characteristics, factors related to breast cancer and the detailed exposure history which was taken by using WHO STEP wise approach (STEPS Instrument) by face to face interview. Medical record review was done by checklist. Data was analyzed by Statistical Packages for Social Sciences [SPSS] statistical software. Descriptive statistics, exposure rate of risk factor in cases and controls, existence and strength of association was found out by using chi-square test, Odds ratio and their corresponding 95% confidence intervals (CI) were calculated by binary logistic regression. Statistical significance was considered when *p value* was less than 0.05 at 95% confidence interval.

Results

Among 151 women with breast cancer and 151 from the control group were interviewed. They were in the age group ranging from 18 to 77 years with the mean age of 44.4 and 44.8 years for the cases and the controls respectively. Majority (90.1%) of the cases were married in comparison to 76.2% controls. (p=<0.05). Maximum (53.6%) cases and 40.4% controls were illiterate. The proportions of the cases and the controls with respect to occupation shows that maximum number of subjects were homemaker and residing in rural area i.e 89.4%, 78.1% and 79.5%,68.2% with apparent differences in occupational groups and place of residence. The proportion of cases was higher (63.58%) in the group of monthly earning of 2100-5000bdt as compared to the controls 51.66%. (p=<0.05) (Table I).

Out of 151 cases, 55(36.4%) were exposed to SLT in comparison to 51(33.8%) controls. Chi-square test showed no significant association between smokeless tobacco exposure and type of participants (p=0.630). From the cases, 40(26.5%) were exposed to zarda in comparison to 38(25.1%) controls and which was a significant association (p<0.05). The number of the exposed cases increases to 22(55%) in comparison to control 1 (2.6%) as the frequency of tobacco exposure increased to 10 times and above per day and it also showed significant association (p<0.05) (Table II).

Majority i.e 53% of the cases had their menarche at the age group 13-15 years in comparison to 69.5%

Table I: Comparison of socio demographic characteristics between cases and controls

Variable	Case n(%)	Control n(%)	Significancep<0.05
Age group (Years) n=302			
18-29	3(2.0)	5(3.3)	Fisher's Exact Test:
30-49	26(17.2)	27(17.9)	0.585
50-59	59(39.1)	57(37.7)	df=3
60-77	63(41.7)	62(41.1)	p=0.905
Mean±SD	44.4±10.56	44.82±10.2	t=-0.294
			df=300
			p=0.769
Marital status			
Married	136(90.1)	115(76.2)	Fisher's Exact Test:
Unmarried	4(2.6)	2(1.3)	12.44
Divorced	1(0.7)	1(0.7)	df=4
Separated	0(0.0)	2(1.3)	p=0.003
Widow	10(6.6)	28(18.5)	
Educational qualification			
Illiterate	81(53.6)	61(40.4)	χ^2 =6.089
Primary	39 (25.8)	55(36.4)	df= 3
Secondary	24(15.9)	29(19.2)	p=0.107
Higher secondary and above	7(4.6)	6(4.0)	
Occupation			
Homemaker	135(89.4)	120(79.5)	Fisher's Exact Test:
Business	1(0.7)	3(2.0)	6.334
Service	13(8.6)	21(13.9)	df= 3
Unemployed	2(1.3)	7(4.6)	p=0.09
Place of residence			
Rural	118(78.1)	103(68.2)	χ^2 =3.796
Urban	33 (21.9)	48(31.8)	df= 1
			p=0.51
Family Income (BDT)			
5000-20000	55(36.42)	73(48.34)	χ^2 =18.528
21000-50000	96 (63.58)	78(51.66)	df= 3
		p=0.01	
Mean±SD	20311.3±9973	24827±11752	t= -3.60
		df=292	
		p=0.000	

Table II: Comparison of smokeless tobacco consumption between cases and controls

Variable	Case f (%)	Control f (%)	Significance p<0.05
Ever use of SLT			
Yes	55(36.4)	51(33.8)	$\div^2$ =0.223
No	96(63.6)	100(66.2)	df= 1
			p=0.630
Type of SLT consumption (n=106)			
Zarda	40(26.5)	38 (25.1)	Fisher's Exact Test:
Gul	8(5.3)	7(4.6)	6.829
Sadapata	7(4.6)	6(3.9)	df= 8, p=0.431
Duration of SLT consumption (in years) n= 106			
1-15 years	10(18.2)	18(35.3)	$\div^2$ =8.355
16-30 years	39(70.9)	22(43.1)	df= 2
31-45 years	6(10.9)	11(21.6)	p=0.015
Total	55(100.0)	51(100.0)	
Mean±SD	1.4±0.68	1.8±0.78	t= -2.698
			df=104, p=0.008
Zarda intake Frequency per day (n=78)			
1-5	0(0.0)	28(73.68)	Fisher's Exact Test:
6-10	18(45.0)	9(23.68)	12.989
>10	22(55.0)	1(2.6)	df= 15, p=0.00
Total	40(100.0)	38(100.0)	
Mean± SD	13.3±5	8.7±3.5	t= -2.209
			df=64, p=0.000

controls. Chi-square test showed the association was significant (p<0.05).Among the cases, 64.2% had menopause at the age >40 years in comparison to 84.5% controls. This association was significant as well (p<0.05).Maximum cases; 65(45.5%) had 1-2 children in comparison to 44(30.1%) control's. About 85.4% of the cases had family history of breast cancer in comparison to 148 (98%) control's and 65.98% had history of OCP intake in compared to 51.68% controls and these associations were significant respectively (Table III)

After binary logistic regression analysis, it was observed that, married women had 3.2 times, women from affluent society had 4.9 times higher chance to develop breast cancer in comparison to controls. SLT exposure history showed women with exposure for ≥15 years, had 3.3 times and frequency of ≥10 times/ day intake, had 7.6 times higher chance of developing breast cancer. The breast cancer associated factor revealed women with late menarche had 2 times, with early menopause had 3 times , having <2 child had 6.3 times, positive family history had 8.4 times and history of OCP intake, had 1.7 times higher chance of developing breast cancer, in comparison to controls (Table-IV).

Table III: Comparison of other factors associated with breast cancer between cases and controls

Age at menarche (in years)	Type of participants		Significance
	Case	Control	$p<0.05$
	f (%)	f (%)	
10-12	80(53.0)	105(69.5)	χ^2 =8.720
13-15	71(47.0)	46(30.5)	df= 1
			p=0.003
Mean±SD	12.7±1.2	12.9±1.1	t=-2.127
			df=300
			p=0.034
Age at menopause (in years)			χ^2 =8.048
≤40	29(35.8)	11(15.5)	df= 1
>40	52(64.2)	60(84.5)	p=0.005
Mean±SD	42.7±4.3	43.9±2.6	t=-2.090
			df=132
			p=0.039
No of children			
1-2	65(45.5)	44(30.1)	χ^2 =20.141
3-5	70(49)	68(46.6)	df= 2
6-9	8(5.6)	34(23.3)	p=0.00
Mean±SD	2.9±1.3	3.8±2	t=4.954
			df=287
			p=0.00
Family history of breast cancer			
Yes	129(85.4)	148(98)	χ^2 =15.743
No	22(14.6)	3(2.0)	df= 1
			p=0.000
History of OCP intake			
Yes	97(65.9)	77(51.7)	fisher's exact test=
No	54(36.7)	74(49.7)	12.192
			df= 3
			p=0.004

Table IV: Binary logistic regression between type of participants and selective variables.

Attributes	Co-efficient (B)	OR	95% C.I for OR		Significance
			Lower	Upper	
Marital status					
Married	1.172	3.227	1.505	6.921	0.003
Unmarried			Reference		
Family income (In Taka)					
< 20000			Reference		
≥ 20000	1.200	4.901	1.526	7.226	0.002
Duration of SLT consumption(In years)					
<15			Reference		
≥ 15	1.179	3.250	1.057	9.997	0.040
Frequency of Zarda intake (Daily)					
<10			Reference		
≥ 10	2.025	7.579	0.865	66.404	0.057
Age at menarche (In years)					
10-12	.706	2.026	1.264	3.246	0.003
13-15			Reference		
Age at menopause (In years)					
≤40			Reference		
>40	1.113	3.042	1.385	6.683	0.006
No. of children					
<2	1.837	6.278	2.657	14.837	0.000
>2			Reference		
Family history					
Yes	2.130	8.413	2.461	28.760	0.001
No			Reference		
Exposure to OCP					
Yes	0.535	1.708	1.072	2.724	0.024
No			Reference		

Discussion

This present study has revealed, mean age for the cases and controls was 44.4±10.56 and 44.82±10.2 years respectively. This value explained that case and control groups were almost matched on the basis of age as no significant association (p>0.05) between them was seen. A similar case control study was conducted in Maharashtra, India which showed maximum breast cancer (74.19%) was in the age group of 30-60 years.[7]

Regarding marital status of the women, majority i.e. 90.1% of the cases were married in comparison to 76.2% control's and this association was significant (p<0.05). The married women had 3.227 times higher chance of developing breast cancer in comparison to controls (OR: 3.2,95% CI: 1.505-6.921,p=0.003). Similar finding was seen by Bhaduria A.S. He stated 94% of the patients were married and other study also showed, being married can have a positive effect on the early diagnosis, treatment, and survival of breast cancer.[9]

Regarding educational qualification, 53.6% cases were illiterate in comparison to 40.4% control's and no association was noticed (p=>0.05).This is may be due to women literacy rate in Bangladesh. However studies conducted by parameshwari have shown maximum 60% breast cancer cases among illiterate population from South Kerala even though in kerala women have high literacy rate >90% .[10]

Considering monthly family income, among cases majority i.e. 36.4% had monthly income ranging from

(21000-50000) tk compared to 52.3% controls. Women belong to higher socio-economic status has got 4.9 times higher chance of developing breast cancer in comparison to controls (OR:4.901,95% CI: 02.301-10.439) (*p*=0.01). Same finding has been observed by Mohite, where the rate of occurrence of breast cancer cases is higher among women from upper economic class.[7]

In the present study, 36.4% cases were exposed to SLT in her entire life in compare to 33.8% controls and the association was not significant (p=0.630) but study by Splanger JG from tribal lands in western North Carolina, showed 8 times risk of developing breast cancer and study by Mohite revealed, 1.7 times higher chance to develop breast cancer in smoker than nonsmokers.[7,11]

Regarding duration of smokeless tobacco exposure, 70.9% cases were exposed for 16-30 years in comparison to 43.1% controls and the association was significant (p=0.015). Women who were exposed for more time, had 3.250 times higher chance of developing breast cancer, in comparison to controls (OR: 3.250,95% CI: 1.057-9.997,0.040). Similar findings were revealed by Johnson KC i,e long duration of exposure is 2.5 times higher in breast cancer patients and also reported by Khuder S.[12,13]

Present study showed, 53% cases had their menarche at 13-15 years in comparison to 69.5% control's and it revealed, women having early menarche had 2 times higher chance of developing breast cancer, in comparison to controls (OR:2.03,95%CI:1.264-3.246,p=0.003). Similar finding were seen by Bhaduria where mean age at menarche in cases was 13.20 ± 1.33 years.[9]

Regarding age at menopause, maximum (64.2%) of the cases had late menopause (after 40 years) and had 3times higher chance of developing breast cancer, in comparison to controls (OR:3.04,95% CI: 1.385-6.683,p=0.003). Similar findings were seen where 85.8% of breast cancer cases had their menopause after 40 years.[14]

Considering number of the children, 45.5% cases had less than 2 children or no children and they had 6.3 times higher chance of developing breast cancer than controls (OR: 6.3, 95% CI: 2.657-14.837,p=0.000). Similar findings were seen, where 41% women had up to two pregnancies and 50% had at least two childbirths. In this regard, it has been shown that multiparity has a preventive effect against breast cancer and nulliparity increases the risk of it.[15]

Regarding family history, 14.6% cases had family history of breast cancer and they have 8.4 times higher chance of developing breast cancer, in comparison to controls (OR: 8.4, 95% CI:2.461-28.760,p=0.001). Similar findings seen in other study by Akbari M, where 18% of patients had first or second-degree family member(s) with breast cancer.[15] Another study also revealed positive family history had 2 times more chance to develop breast cancer. (OR = 2.07, 95% CI = 1–4.4).[14]

Conclusion

The study revealed, the risk of breast cancer is increased as frequency and duration of exposure increases though significant association between smokeless tobacco consumption and breast cancer is not observed. The result of the present overview provides valuable insights and viewpoints toward breast cancer prevention in Bangladesh. This study directly doesn't suggests smokeless tobacco as the risk factor of breast cancer but as other factors related to SLT consumption is associated with increased breast cancer cases, hopefully very soon it would be recognized as one of the important risk factors as well. As increased frequency and duration of smokeless tobacco intake is found significantly associated with breast cancer so specific preventive intervention is required for prevention of smokeless tobacco consumption among women to alleviate breast cancer.

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