



RESEARCH ARTICLE

BREAST FEEDING AND BREAST CARCINOMA – FINDINGS FROM A CASE CONTROL STUDY

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ABSTRACT

**Background:** The rising trend in breast cancer worldwide and in India has become a matter of great concern. The most common site-specific cancer is breast cancer and also it is the leading cause of death from cancer in women. Geographical variations in incidence and mortality rates of breast cancer 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. It is important to identify these factors in order to bring down the incidence, morbidity and mortality. One of the major modifiable risk factor associated with breast carcinoma is breast feeding. Hence this case control study mainly focuses to study practice of breast feeding and its risk with breast carcinoma

**Aim:** To study association of breastfeeding with breast carcinoma and to assess its strength of association.

**Methods:** This was a case control study carried out in Government Medical College, Nagpur from August 2010 to February 2011. 240 women were studied which included 120 histopathologically confirmed cases of breast carcinoma and 120 age ( $\pm 5$  years) and residence (rural / urban) matched controls. Data was gathered using predesigned and pretested proforma.

**Results:** The women who had never breastfed were 5.12 (1.60 – 21.34) times at a risk of breast carcinoma than those who have ever breastfed. No association was found between initiation of breastfeeding after delivery and breast carcinoma. Decreasing trend with increasing cumulative duration of breastfeeding was seen.

**Discussion:** Similar findings are seen from other authors.

**Conclusion:** Longer duration of breastfeeding is a protective factor for development of breast carcinoma.

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INTRODUCTION

Cancer... The dreaded "C" word. It has become such an epidemic that; "Today, there is no population around the world with a truly low risk of breast cancer and no woman in the world at a truly low risk of developing the disease."<sup>1</sup> With the growth and ageing of the world's population, considerable increases in life expectancy in people of lower-income countries and the increased tendency to adopt a westernized lifestyle, cancer is a rapidly growing global problem and majority of the world is not ready to cope with it.<sup>2</sup> Breast cancer is the commonest form of cancer in women worldwide; there were an estimated 1.4 million cases worldwide in 2008<sup>3</sup> and there is no part of the world where breast cancer is now a rare form of cancer<sup>4</sup>. Breast cancer ranks as the fifth cause of death from cancer overall. The situation of breast cancer in India is certainly typical of the situation in many countries of Asia and other regions where dramatic economic and social change is taking place.<sup>1</sup> Considering the various risk factors for breast cancer, including the aging and growth of the Indian population, there is increasing trend in breast cancer incidence. It is estimated that the breast cancer burden in India will grow from 80,000 in 2005, through 122,000 new cases in 2011, and attain a level of 141,000 cases by 2016.<sup>1</sup> Breast cancer is increasing in India with such a pace that we may face a serious burden of this disease in coming years.<sup>5</sup> Geographical variations in incidence and mortality rates of breast cancer suggest that the known risk factors for breast cancer may vary in different parts of the world and also environmental risk factors are more important than genetic factors<sup>6</sup> It is important to identify the environmental factors in order to bring down the incidence, morbidity and mortality due to this disease.

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One of the major modifiable risk factor associated with breast carcinoma is breast feeding. Hence this case control study mainly focuses to study practice of breast feeding and its risk with breast carcinoma.

METHODOLOGY

A retrospective case-control study was conducted to assess the relationships between some clinicosocial variables and breast cancer risk in Nagpur, India. Ethical approval from Government Medical College, Nagpur's institutional ethical committee was sought. Cases comprised 120 histologically confirmed female breast cancer patients who presented in the inpatients and outpatients departments of Oncology from August 2010 to February 2011. Control subjects were matched one for one with age (within 5 years) and place of residence (rural / urban). They were selected from the community. The controls for urban cases were selected from field practice area of urban health training centre of study institution. For rural cases, to obtain controls, the nearest Taluka was selected purposively. There are 4 PHCs in the selected Taluka. Out of that one PHC was selected by simple random sampling by lottery method. In the selected PHC, there are 7 subcentres. Out of that, one subcentre was selected by simple random sampling by lottery method. The eligible women were then examined clinically in their home ensuring privacy and those without lump in breast were selected as controls. Those with a palpable lump were referred to Government Medical College, Nagpur for further investigation and management. Exclusion criteria for controls were those with known malignant diseases, those who are pregnant or who are lactating their offsprings. A structured questionnaire was prepared in English and in-person interviews were conducted for both cases and controls. Verbal consent was taken from every patient. The

questionnaires were divided into several sections comprising socio-demography, reproductive history and established and potential risk factors for breast cancer. Religion, Education, Socio-economic status, Dietary habits, Age at marriage, Age at menarche, Parity, Age at 1<sup>st</sup> childbirth, Ever breastfed, Duration of breastfeeding, Duration of reproductive life, Initiation of breast feeding after delivery, Use of OC pills, H/O chest radiation, past H/O breast condition were the various potential risk factors included in study. The sample size was based on OR for age at first full term birth  $\geq 25$  years of 2.59 with case:control = 1:1. A sample size of 232 was calculated including 116 subjects in each group with 80% precision and 95% confidence. The actual sample studied was 240 (120 per each group).<sup>7</sup> All data entry and analyses were conducted using STATA 10.1, 2009. Means and standard deviations (SD) for continuous variables and frequencies and percentages for categorical variables were calculated. Differences of proportions between cases and controls for categorical variables were analysed by simple conditional logistic regression. The p-values of the likelihood-ratio (LR) test were used. Crude odds ratios (OR) for variables in the model were also drawn from simple conditional logistic regression. In the full model, because of colinearity between two risk factors for breast carcinoma i.e. nulliparity and no H/O breastfeeding were omitted. The level of significance was set at p less than 0.05 for all hypotheses tests in this study. The odds ratios were estimated with 95% confidence intervals (CI).

**Observations**

The study included 120 cases and 120 controls. The response rate was 100%. The ratio of urban: rural distribution in cases of breast carcinoma was 1.44:1. The urban cases were in the age group of 27 – 75 yrs with mean age of 46.27 yrs and SD was 9.65 yrs. While the rural cases were in the age group of 27 – 66 yrs with mean 45.59 yrs and SD was 9.62 yrs. Breastfeeding the offspring was a universal practice observed. Only those study subjects who were nulliparous or without viable offspring could not breastfed. Majority of the study subjects, 102 (85.00%) cases and 116 (96.67%) controls, had breastfed their child. Thus 18 cases and 4 controls had never breastfed. The reason for not breastfeeding was nulliparity in 17 cases and given birth to single stillborn in 1 case. 4 (03.33%) controls were also nulliparous. The women who had never breastfed were 5.12 (1.60 – 21.34) times at a risk of breast carcinoma than those who have ever breastfed. [Table 1].

**Table 1. Distribution of study subjects according H/O breast feeding**

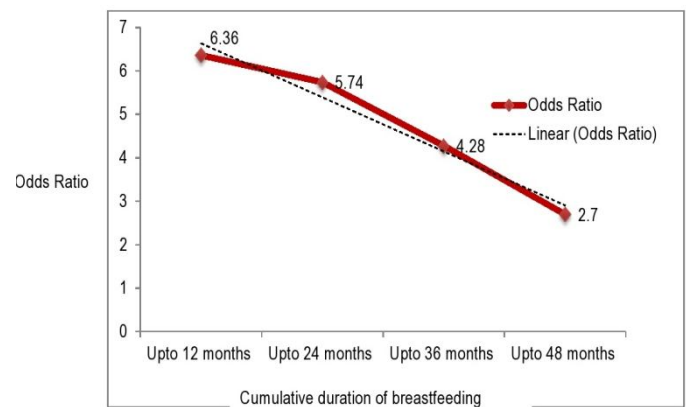
Parameter	Cases		Controls		Significance	
	Number	%	Number	%		
Ever breastfed	No	18	15.00	04	OR =5.12(1.60-21.34), p=0.0017, HS	
	Yes	102	85.00	116		96.67
Initiation of breast feeding	< 2 hours	52	50.98	69	$\chi^2= 1.59, df = 1,$ NS	
	2-48 hours	14	13.73	15		12.93
	> 48 hours	36	35.29	32		27.59
Cumulative duration of breastfeeding (months)	0	18	15.00	04	t = 5.06, df = 238, p= 0.0001, HS	
	$\leq 12$	08	06.67	01		00.83
	13-24	18	15.00	06		05.00
	25-36	18	15.00	13		10.83
	37-48	17	14.17	26		21.67
	49-60	17	14.17	21		17.50
	>60	24	20.00	49		40.83

Majority of the women, 52 (50.98%) cases and 69 (59.48%) controls had started breastfeeding within 2 hours of delivery. But a significant proportion of women initiated breastfeeding after 48 hours; 36 (35.29%) cases and 32 (27.59%) controls. No association was found between initiation of breastfeeding after delivery and breast carcinoma;  $\chi^2= 1.59, df = 1, p=0.2075$  [Table 1]. The mean duration of cumulative breastfeeding in cases (42.28 months) was significantly lower than that in controls (67.16 months); t = 5.06, df = 238, p= 0.0001. Majority of the cases, 24 (20%) and controls, 49 (40.83%) had breastfed cumulatively for a period of >60 months. But nearly half of the cases had breastfed cumulatively for  $\leq 36$  months and similar number of controls had done same for > 48 months. [Table 1]

The risk of breast carcinoma was calculated for different cutoffs of cumulative duration of breastfeeding. OR for breast carcinoma in women having cumulative duration of breastfeeding  $\leq 12$  months was 6.36 compared to >12 months. Similarly OR was 5.74 for cutoff of 24 months, 4.28 for cutoff of 36 months, 2.70 for cutoff of 48 months. The OR thus calculated at different cutoffs had a decreasing trend with increasing cumulative duration of breastfeeding. [Table 2 and Fig 1].

**Table 2. Trend in risk of breast carcinoma in relation to cumulative duration of breast feeding**

Cumulative exposure (Duration of breastfeeding)	OR	95% CI	P value
Upto 12 months	6.36	2.27-21.90	0.0001
Upto 24 months	5.74	2.68-13.04	0.0001
Upto 36 months	4.28	2.33-7.94	0.0001
Upto 48 months	2.70	1.55-4.71	0.0002



**Fig. 1. Declining trend in risk of breast carcinoma in relation to cumulative duration of breast feeding**

After adjusting with known risk factors, for cumulative duration of breastfeeding  $\leq 36$  months AOR = 2.60 (1.34 – 5.04) was calculated.

**DISCUSSION**

The incidence of breast cancer is increasing worldwide, a situation that challenges more stable health systems of developed countries. Several studies have determined the association between various risk factors and breast cancer, among which are the hormonal, genetic, environmental and benign breast disease.<sup>(8,9)</sup> Limited resources and treatment modalities, profound financial liabilities to both provider and patients and inequitable distribution of treatment center provide the prevention strategies (educational awareness about the risk factors and screening at risk population); an upper hand overtreatment as a key intervention against breast cancer.<sup>(10)</sup> Thus

determining the risk factors especially modifiable ones is important in terms of prevention and early detection of breast cancer. Breastfeeding is one of the major modifiable risk factors for development of breast carcinoma. In present study, it was observed that, the women who had never breastfed were 5.12 (1.60 – 21.34) times at a risk of breast carcinoma than those who have ever breastfed. Declining trend in risk of breast carcinoma in relation to cumulative duration of breast feeding was also observed. Meshram *et al.* (2009)<sup>11</sup> also found a significant protective effect of breastfeeding with breast feeding for 3 or more years. Daud (2004)<sup>12</sup> noted that those with no breast feeding had risk of 3.87 (1.71- 8.75) than those who had breastfed. Hadjisavvas *et al.* (2010)<sup>13</sup>, Pakseresht *et al.* (2009)<sup>14</sup>, Gajalakshmi *et al.* (2009)<sup>15</sup>, Butt *et al.* (2009)<sup>16</sup>, Yavari *et al.* (2005)<sup>17</sup> also have found protective effect of breast feeding for breast cancer. However several other authors McCormack *et al.* (2004)<sup>18</sup>, Michel *et al.* (1996)<sup>19</sup>, MacMohan *et al.* (1970)<sup>20</sup> did not find protective effect of breastfeeding on breast cancer. The pregnancy–lactation cycle (PLC) is a period in which the breast is transformed from a less-developed, nonfunctional organ into a mature, milk-producing gland that has evolved to meet the nutritional, developmental, and immune protection needs of the newborn. Cessation of lactation initiates a process whereby the breast reverts to a resting state until the next pregnancy. Changes during this period permanently alter the morphology and molecular characteristics of the breast (molecular histology) and produce important, yet poorly understood, effects on breast cancer risk.<sup>21</sup>

Various physiopathological mechanisms are involved in the protective effect of breastfeeding: anovulation, cellular differentiation of the mammary cells and excretion in the milk of breast carcinogens.<sup>22</sup> Lactation may reduce the risk of breast cancer simply by interrupting ovulation or by modifying pituitary or ovarian hormone secretion.<sup>23,24</sup> Estrogens stimulate the production of growth factors by normal breast epithelial cells and by cancer cells. It is hypothesized that the estrogen and progesterone receptors normally present in breast epithelium, and often present in breast cancer cells, may interact with growth promoters, such as transforming growth factor  $\alpha$ , platelet-derived growth factor, and fibroblast growth factor elaborated by human breast cancer cells, to create an autocrine mechanism of tumor development. Endogenous estrogen excess, or more accurately, hormonal imbalance, clearly has a significant role. Many of the risk factors mentioned (long duration of reproductive life, nulliparity, and late age at birth of first child) imply increased exposure to estrogen peaks during the menstrual cycle.<sup>25</sup> No association was found between initiation of breastfeeding after delivery and breast carcinoma in our study. It has been suggested that an alkaline milieu surrounding epithelial cells plays an important role in carcinogenesis of epithelial surfaces<sup>26</sup>. Literature states that the milk from the unsuckled breasts had a slightly higher pH<sup>27</sup>. An alkaline milieu surrounding epithelial cells causes hyperplasia, cell atypia and a marked increase in mitotic activity, changes which are a prelude to neoplasia. Our study revealed the role of very important modifiable risk factor for breast carcinoma that can be focused by public health intervention in local set up. Thus women who have lesser duration of breastfeeding should have special attention towards development of breast cancer.

### Conclusion and recommendation

Longer duration of breastfeeding is a protective factor for development of breast carcinoma, hence breastfeeding for a longer duration should be promoted.

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