

## Role of Breast Feeding and Parity in Prevalence of Breast Cancer and Bone Metastasis

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### Authors' contributions

*This work was carried out in collaboration between all authors. Author HF designed the study, wrote the protocol and most of the manuscript. Author MS managed the literature searches and performed the analyses of the study. Author AA managed the experimental process. Author AM was the clinical supervisor. All authors read and approved the final manuscript.*

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### ABSTRACT

Our aim was to evaluate the role of breast feeding and parity (alive and abortion) in prevalence of breast cancer and secondary bone metastasis. For The study purpose 100 diagnosed females of breast cancer were selected. Proper history, especially about parity and lactation was sought. Consent and questionnaire forms were filled. Bone scan is done to rule out bone spread. In Pakistan per annum prevalence rate is 90,000. The frequency of breast cancer in Karachi was 69.1 per 100,000 according to 1998-2002 data. 1.7 million cases and 521,900 deaths were reported in year of 2012. Breast cancer as single cause of death accounts for 25% of diagnosed cancer cases and 15% of all cancer deaths. Major risk factors are primary infertility, long exposure of contraceptive pills and estrogen due to late menopause. Upper and outer quadrant of left breast is

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commonest site for breast cancer. Breast feeding exerts beneficial effect on both mother and infant health. During and after several years of lactation low estrogen levels may be directly responsible for decline in breast cancer cases. Delayed ovulation is another indirect safe effect for reduction in breast cancer cases. Bone scanning is the first choice to pick bone metastasis secondary to breast cancer. Recommended sensitivity is 95%.

This study evaluates the role of parity and breast feeding in patients of breast cancer with and without bone metastasis. No statistically significant difference was found in parity (alive children and abortion) among bone scan positive and negative case. Breast feeding practices were significantly less in bone scanning positive (76%) cases as compared to negative (87%) cases ( $p < 0.05$ ). Breast feeding of any duration has a significant role in protection from breast cancer. Parity does not directly impact the prevalence of breast cancer, but may exert an indirect beneficial role.

*Keywords: Breast cancer; prevalence; breast feeding; bone metastasis; bone scan; parity.*

## 1. INTRODUCTION

During the life span every 1 out of 9 woman is at risk of breast cancer [1]. In Pakistan per annum prevalence rate is 90,000. The frequency of breast cancer in Karachi was 69.1 per 100,000 according to 1998-2002 data [2]. Oral cavity and ovarian cancers are predominant but breast cancer is contributing among all cancers in significant ratio [3]. Breast cancer is account for highest mortality rate and diagnostic ratio among females worldwide, approximately 1.7 million cases and 521,900 deaths accounts in year of 2012. Breast cancer as single cause of death accounts 25% of diagnosed cancer cases and 15% of all cancer deaths. Advanced countries have about half of total cases of breast cancers and 38% of deaths. Greater number of cases belong to northern America, Australia/New Zealand, and northern and western Europe; average number of cases in central and eastern Europe, Latin America, and the Caribbean; and least in Africa and Asia. Difference in prevalence rate of breast cancer at international scale shows the differences in diagnostic facilities and risk factors. Major risk factors are primary infertility, long exposure of contraceptive pills and estrogen due to late menopause. Increase fertility along with sufficient breast feeding declines the risk of breast cancer [4]. 12. Use of menopausal and combine hormone therapy, obesity, alcohol addiction, sedentary life style are dynamic risk factors among nations [4,5]. 1980 and the late 1990s, was the era when breast cancer incidence came under considerable rates which was about 30% in western countries, the risk factors like common use of hormonal therapy, short family size or might be due to increased availability of diagnostic facilities [6]. In first of 2000s the prevalence suddenly became lowered because of less use of menopausal hormone

therapy in countries like United States, the United Kingdom, France, and Australia [7-12]. Mammographic screening was another attributed factor for decline in breast cancer incidence rates [13]. Mammography and improved treatment, were also proved help full tool in decreasing rate of breast cancer [6]. 14. However more work is needed to make the respective contributions clear [14-16].

According to one study breast cancer appear during thirties and fourtees age groups which are comparatively younger age group. That is supported by another study [17]. Breast cancer appearance in younger age is itself associated with worst outcome especially in hormone positive case [18]. The fifth and sixth decades are more vulnerable for breast cancer development in west [19]. Upper and outer quadrant of left breast is commonest site for breast cancer [20]. An opposite relation between breast-feeding reduced incidence of breast cancer is may be due to estrogen related changes in mammary gland differentiation. The mammary gland matures at puberty, developmental changes occur with each successive pregnancy [21-23]. During and after several years of lactation low estrogen levels may be directly responsible for decline in breast cancer cases [23]. Delayed ovulation is another indirect safe effect for reduction in breast cancer cases [24]. Lifetime ovulations has been proved a risk factor for the breast cancer and it suppresses during lactation especially first six months up to 1% - 5% [25]. Breast feeding has established role in declining number of breast cancer case. Educational programs and promotional activities for breast feeding are much essential and needs enthusiastic struggle to give awareness about this disease [26]. Women with BRCA1 mutated genes are advised to breast-

feed for more than 1 year showed a statistically significantly lower incidence of breast cancer [27]. International agency for research on cancer, predicted that at the end of 2015 India had to encounter about 250,000 new cases [28]. Breast feeding exerts beneficial effect on both mother and infant health. Fertility was not proved as protective factor from breast cancer, but full term pregnancies as compare to abortive cases were associated with a statistically significant reduction in number of breast cancer cases. Risk was reduced by 14% for every new birth. Among BRCA1 or BRCA 2 gene mutated females, child birth before 20 years (20–24) years, was appear a positive factor against protection from breast cancer (20–24 years) [29]. Hormonal change during full term pregnancy provides the better protection to hormone sensitive tissues like breast against cancer development especially in younger age. During successful pregnancies breast tissue become more mature and differentiated as compare to virgin breast tissues, the same exhibited by altered gene expression profiles. Unique hormonal changes during pregnancy influences the permanent differentiation especially the raised levels of Prolactin and Growth hormone in multiparous woman [30]. Every birth lowers the risk of breast cancer up to 11%. Two studies did not support that parity associated with protection against the development of ERC/PRC breast cancer [31-34]. Bone scanning is the first choice to pick bone metastasis secondary to breast cancer. 95% sensitivity is recommended. Bone scan may come positive in 10%-22% non malignant cases and rate for false negative cases is only 10%. [35,36]. In pathologically diagnosed stage ii tumors, a bone scan after surgical removal of malignant part is strongly recommended [37]. Bone scan is also recommended to detect primary bone disease like Paget disease and avascular necrosis even the radiographs is negative. There is a scope of radionuclide bone imaging in future as well [38]. Bone scan is the first imaging technique for detection of bone diseases. Radionuclide bone imaging is fast, cheaper and easy to avail for most patients as well as sensitive for various pathologic conditions. The dye for the procedure is technetium-99m–labeled with diphosphonates. These compounds take 2–6 hours for deposition after injection, 50% of injected compound dose deposit in skeletal system. A gamma camera equipped with a low-energy, high-resolution collimator yield the highest-resolution radiographs. Additional anterior and posterior whole-body images are often obtained as

needed [39]. Every successive birth lowers the risk of breast cancer up to 11%. The protective effect was maintained within the ERC/PRC group, are responsible for protection even when the analyses were stratified by age. Women in the oldest age at risk of 27% more for developing ERC/PRC positive breast cancers as compared with the young age. Although two studies presented that parity does not gives the protection against the REC/PRC positive breast cancer [31-34]. The aim of the study was to evaluate the role of parity and breast feeding in patients of breast cancer with and without bone metastasis.

## 2. METHODS

### 2.1 Participants

Data were collected by trained medical physician, nurses and laboratory persons. General information from each subject was collected through a standard questionnaire including participant's name, age, education, monthly income and living style, ethnicity, gravidity, para, abortions, clinical sign and symptoms, material status, family history, etc. We explained the objectives and important features of the study to all patients prior to the start of study and their consent was taken.

### 2.2 Blood Collection

Before interviewing and blood collection a verbal consent was taken from each respondent. Venous blood was withdrawn for the investigation. First the skin was cleaned thoroughly with sterilized with 70% Isopropyl Alcohol swab and dried before puncturing. Then 2 ml of blood taken from the antecubital vein with a 5 cc disposable syringe (Becton Dickinson, Pak pvt Ltd). The blood sample was transferred to labeled test tube. And then tubes were marked with codes and immediately taken to the lab.

Only histopathological diagnosed cases of breast cancer were selected for study. Study was done in Karachi Institute of Nuclear Medicine. They were of any age group premenopausal, perimenopausal, postmenopausal, passing through any stage of cancer, married, unmarried both, lactating, non- lactating. Bone scan was done to check the metastatic involvement of bones. During the study chemo therapy and radiotherapy was allowed accordingly and most of patients have passed through the first three cycles of chemotherapy and radiotherapy.

### 2.3 Bone Scan

Bone scan was done on Siemen e cam scanner with accessories. Intravenous dye technetium 99 mdp has been used. This test helps to see if a cancer has metastasized to bones and is useful because it provides a picture of the entire skeleton. For this purpose, 20/mci (dose] of radioactive material (technetium 99) was injected into a vein (intravenously or IV). The substance settles in areas of damaged bone throughout the entire skeleton over the course of a couple of hours. (Six hours to twenty four hours). Patient lied on a table for about 30 minutes while a special camera detected the radioactivity and created a picture of the skeleton.

### 2.4 Statistical Analysis

The data feeding and analysis was on computer package SPSS (statistical packages of social sciences) version 11.0. Clinical characteristics will be summarized in terms of frequencies, means ± standard deviation and percentages for qualitative/categorical variables (parity, breast feeding practices).

## 3. RESULTS

During the study it was observed that in nulliparous women the bone metastasis was frequent, while mothers with small, average and large parity showed comparatively lesser bone metastasis. On the other side abortions are not proved as protective factor for bone metastasis in breast cancer patients and women with more abortions showed more cases of bone metastasis. Breast feeding practices were significantly less in bone scanning positive (76%) cases as compared to negative (87%) cases ( $p < 0.05$ ). Prevalence of breast cancer and frequency of bone metastasis were found both in mother who never breast fed their children as shown in Table 1.

During our study it also determined the frequency of breast cancer cases. In this study we found that the breast cancer was high in those mothers who never fed their children. We also came across the metastasis of bones was common in these mothers as shown in Fig. 1.

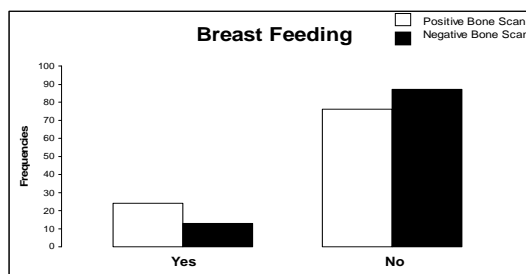
In this study it was also observed that nulliparous and mothers showed high parity which was 7 and above with low prevalence of breast cancer as well as less bone metastasis. In some cases mothers with average parity, having 4-6 children

shows highest prevalence and bone metastasis, whereas in those mothers with small parity having 1-3 children showed higher prevalence and bone metastasis. Frequency distribution as per abortions shows highest prevalence and bone metastasis in women with no abortion and least in women with more abortions 7 and above as shown in Fig. 2.

**Table 1. It shows no statistically significant difference in parity (alive children and abortion) among bone scan positive and negative cases**

Parity	Bone scan		P- value
	Positive (N= 100)	Negative (N= 100)	
<b>Alive children</b>			
None	14	7	0.209
1-3	23	27	
4-6	40	49	
7 & above	23	17	
<b>Abortion</b>			
None	59	59	0.320
1	21	29	
2	15	11	
3	5	1	
<b>Breast feeding</b>			
No	24	13	0.045
Yes	76	87	

\* Statistically significant  $P < 0.05$

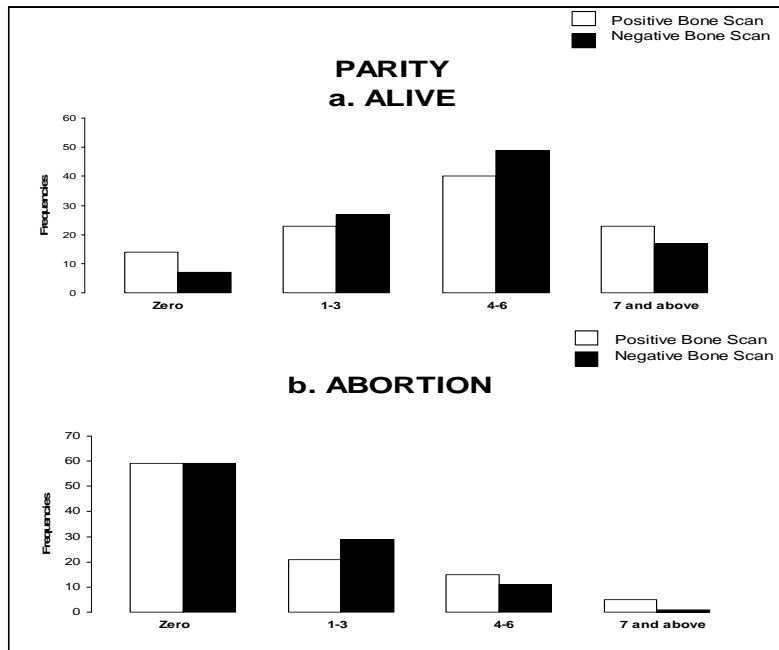


**Fig. 1. Distribution of the subjects as per breast feeding, having positive- and negative bone scan values are presented as frequencies of breast feeding in bone scan negative and positive patients**

\* $p > 0.05$  from patients with positive bone scan following student t- test

## 4. DISCUSSION

Cancer is a leading cause of death in both more and less economically developed countries. The burden is expected to grow worldwide due to the growth and aging of the population, particularly in less developed countries where about 82% of the world's population resides. The adoption of



**Fig. 2. This figure shows the frequencies of parity both alive and abortion in bone scan positive and negative patients**

lifestyle behaviors that are known to increase cancer risk, such as smoking, Poor diet, physical inactivity, and reproductive changes (including lower parity and later age at first birth), have further increased the cancer burden in less economically developed countries [40]. Breast cancer incidence rate is being rising. Estimated number of new cancer cases in 21 world regional areas do not estimates the sum due to different calculation methods (2012) [41]. According to the presenting study, on the bases of breast feeding 87% cases were breast fed in negative bone scan as compared to 76% cases positive bone scan  $p < 0.05$  were found. Which is statistically significant and reflecting the importance of breast feeding in protection from breast cancer and decrease morbidity due to bone metastasis. Frequency of breast cancer and bone metastasis in breast feed mothers found lower than non-lactating mothers. Nulliparous women are at more risk to develop bone metastasis. No statistically significant role of parity found in decreasing the prevalence of breast cancer and secondary bone metastasis. Parity especially 4-6, either alive or abortions, showed higher frequency and are at greater risk to develop breast cancer and secondary bone metastasis. Abortive pregnancies may play same protective role as alive parity. Breast feeding as known risk factors for the development of cancer but protective effect of lactation against the cancer

according to different research is controversial except the impact of parity and age at first birth. Many research papers show the inverse association, and the estimated risk is between 0.4 and 0.9, not dependent on age group, or for women developed breast cancer at different ages of life. Some research papers show the opposite relation between duration of breastfeeding and development of cancer. While some papers support the protective effect when compares the lactating and non-lactating cases. Most of statistically insignificant case-control studies support an inverse relationship. Although some studies, shows no relationship. Two cohort studies did not indicate any relation between breast feeding and prevalence of breast cancer. There is evidence in some papers regarding the beneficial effect of lactation from breast cancer if detected under the age of 40, but provide some protection for older patients. Even though breast cancer is relatively rare in young women but it is a serious problem. Preventive measures are lacking both for women with an inherited tendency to develop breast cancer and for other women. Breastfeeding has various beneficial effects in addition to those reported here [42]. Minimum two studies [43,44] showed lesser risk of breast cancer in women who breast-fed their babies and it is more effective and active for premenopausal women than postmenopausal women 43. According to a big international

research, 44, the risk of breast cancer decline up to 4.3% with a total duration of 12 months of breast-feeding and up to 27% for women with a total duration of breast-feeding of 55 months or more. The only factor known to consistently decrease lifetime breast cancer risk regardless of ethnicity is early childbirth. Women who have undergone a first full-term pregnancy/birth before 20 years of age have a 50% reduced life time risk of developing breast cancer when compared with nulliparous women, whereas first full-term births over 35 years of age lead to an increased risk of developing breast cancer. However, the protective effect of pregnancy is not immediate. When compared with nulliparous women, uniparous women have an elevated risk of breast cancer soon after delivery, which only declines some years later. This increased risk is most pronounced in women who are aged 30 years or older at the time of their first delivery. On average, the transient increase lasts 10 years but is also dependent on age, being postpone an additional 10 years in women with first full term birth after 30 years of age [45].

## 5. CONCLUSIONS

Breast feeding has a significant role in protection from breast cancer development and secondary bone metastasis as well. If the breast fed mother develops breast cancer any how the related morbidity is less.

Duration of breast feeding is not important factor.

Parity does not directly affect the prevalence of breast cancer, but multiparity may lower the rate of bone metastasis. Females with average parity are at more risk of breast cancer and bone metastasis.

## ETHICAL APPROVAL

It is confirmed that all the authors have obtained all necessary ethical approval from ethical committee of Board of Advance Studies, University of Karachi.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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