

Socio-demographic Determinants for Distant Metastases of Breast Cancer

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Abstract

Original Research Article

Background: In Bangladesh, breast cancer continues to be the second-most common disease overall (12.5%) and the most prevalent cancer in women (27.4%). Patients with late-stage illness who present in low-income regions with distant metastases have a very poor prognosis. **Objective:** To determine the socio-demographic variables for breast cancer distant metastases in Bangladeshi women treated at a tertiary level hospital. **Materials and Methods:** This case control study was done from July 2017 to June, 2018 in National Institute of Cancer Research and Hospital (NICRH), Mohakhali, Dhaka. **Results:** A total number of 42 patients were taken as cases and another 84 patients without distant metastases were taken as controls. Mean age in case group was 42.67 ±9.27 years and in control group it was 45.13±9.60 years. The majority of the study participants in both the case (33.3%) and control (38.1%) groups had only completed kindergarten. In both the case group (71.5%) and the control group (85.7%), the majority of the women were found to be married. In both categories, the majority of the participants were sedentary workers. Additionally, Table 4 demonstrates that there is no statistically significant difference between the two groups with regard to co-morbidities, a positive family history, cigarette use, type of employment, and the existence of obesity ($P > 0.05$), stage of primary tumor ($p=0.002$, OR= 5.81; 95% CI: 1.85 – 18.15). **Conclusion:** Both the diagnosis and the course of treatment are delayed. Due to their lack of resources and lack of knowledge, many of them did not complete the course of treatment. Additionally, each of these factors contributes to the spread of breast cancer to distant areas.

Keywords: Breast cancer, Socio-demographic factors, Tumor, Resources.

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INTRODUCTION

The most common malignancy in women diagnosed worldwide is breast cancer [1]. Due to the recent implementation of early detection and multidisciplinary treatment approaches involving individualized surgery, chemotherapy, radiotherapy, hormonal therapy, and targeted therapy, the mortality rate of breast cancer is significantly declining, especially in high income countries [2]. However, case fatality rates are much higher in low- and middle-income countries (LMICs), including Indonesia [2, 3], than in high-income nations. The higher death rates in LMICs are attributed to a number of reasons, including demographic, socioeconomic, and healthcare system determinants [2-4]. Mortality from cancer is primarily brought on by distant metastases in the clinical course of the disease [5, 6]. Even those who are diagnosed in the early stages of breast cancer will later experience distant spread in about

one-third of cases [7]. Identification of hazards related to metastasis may help in breast cancer management.

Cancer is one of the most significant diseases, and the burden of non-communicable diseases is rising globally today [1, 2]. Breast cancer is one of them and is one of the cancers that is most prevalent worldwide [3]. It is the second most prevalent cancer, accounting for 1.7 million new cases each year and 25% of all malignancies [4]. From 19.4 per 100,000 people in East Africa to 89.7 per 100,000 in West Europe, breast cancer incidence rates fluctuate widely [5].

Although breast cancer is mostly a disease of postmenopausal women (>50 years) in developed nations, nearly half of all cases (45%) of breast cancer in developing countries in 2010 were detected in women of reproductive age (15–49 years) [6]. Breast cancer incidence peaks in Asia with premenopausal women in

their forties, whereas it does so in Western nations among postmenopausal women in their sixties [7]. In developing nations compared to high-income nations, breast cancer mortality is much higher. Nearly 62% of breast cancer-related deaths in 2012 took place in underdeveloped nations [4]. In Bangladesh, breast cancer continues to be the second most frequent disease overall (12.5%) and the most prevalent cancer in women (27.4%) [8]. It has turned into a secret burden that causes 69% of cancer deaths in women [9]. In Bangladesh, there were approximately 22.5 new cases of breast cancer for every 100,000 females [10]. According to reports, Bangladeshi women have the highest prevalence rate of breast cancer (19.3 per 100,000). Compared to other types of cancer, 3 occur between the ages of 15 and 44. In Bangladesh, there are more women than men (84.1 million to 79.5 million). Approximately 45 million women are of reproductive age, and 13.5 million are over 50 [11]. There isn't much information accessible in Bangladesh on breast cancer. The prevalence of breast cancer is comparable in West Bengal, India (which has a similar cultural and people makeup), to Bangladesh (ASR 25.2 per 100,000) [12]. The National Institute of Cancer Research and Hospital in Bangladesh maintains the only hospital-based cancer registry that systematically monitors newly diagnosed cancer cases (NICRH). According to a NICRH report, 1373 cases of breast cancer were completely detected there in 2014. The age range of the breast cancer patients was 15 to 94 years, with a mean age of 42.97 and an SD of 10.873 years. Only 7.2% of them were nulliparous, whereas 55% of them had multiple pregnancies [8].

While breast cancer can spread to any part of the body, the most common sites for spread include the bone, lungs, local lymph nodes, liver, skin, adrenals, and brain [10]. Depending on where the metastatic tumors are, various therapies, including surgery, radiation, chemotherapy, biological treatment, and hormone therapy, are used to treat metastatic breast cancer. Breast cancer is a diverse illness that can come back either right away after the original diagnosis or four to ten years later. According to genomic and clinical risk factors, the likelihood of a recurrence changes with time [11]. After a brief amount of time, ER-negative tumors and HER2-positive tumors exhibit an increased annual risk of recurrences and mortality (1–3 years). In contrast, ER-positive (ER)/HER2-negative (HER2-) individuals have annual recurrence rates that are persistent after the first five years but are noticeably lower in the first years. 18 Despite the initial and ongoing benefits of tamoxifen treatment in ER/HER2- malignancies, more than two-thirds of fatalities and 45% of all relapses happen more than five years after diagnosis [12]. Depending on the subtypes, several tropisms can be seen in breast cancer. 20 Along with distant lymph nodes, bone, lung, liver, and the brain are frequently the targets of breast cancer metastasis. The best prognosis is for ER+ tumors, which

have a low incidence rate in the first five years. However, this rate gradually rises (up to 40%) as the time period beyond five years. The brain is significantly less impacted than bone, which is the primary metastatic location. The poorest prognosis is shown in TN breast tumors, which have an increased incidence rate within the first one to two years and almost no metastases before the age of five [11, 12]. The brain and lung are more frequently impacted with TN tumors than other visceral organs.

Additionally regarded as an aggressive condition are HER2+ tumors. 20 Anti-HER2 therapy has greatly improved the prognosis and dramatically extended the patients' lifetime. The treatment is quite efficient at reducing extracranial lesions, but brain metastasis is still a problem. Both local recurrences and distant metastases are time-dependent, partially independent occurrences, with variable occurrence rates for both. Women who experience local recurrences are more likely to develop distant metastases. Women who had initial peritumoral lymphatic invasion and local recurrence within 2 years and were 35 years of age or younger at first diagnosis are especially at risk for distant spread. Women are at decreased risk for recurrence in instances with a significant intraductal component or if the initial local surgery was perhaps insufficient [13]. Fewer women are now suffering distant metastases as a result of consistent advancements in the treatment of early breast cancer. Since 1991, when it peaked at 215.1 fatalities per 100,000 people, the overall cancer death rate has been steadily falling, reaching 171.8 deaths per 100,000 people in 2010. A total of 1,340,400 cancer deaths (952,700 in males and 387,700 in women) were prevented over this time due to the 20% drop. Age, ethnicity, and sex all significantly influenced the pace of drop in cancer death rates from 1991 to 2010, with white women 80 years and older experiencing the smallest decline [13].

OBJECTIVE

To find out the socio demographic factors for distant metastases of breast cancer among Bangladeshi women in a tertiary level hospital.

MATERIALS AND METHODOLOGY

Type of Study: This study was a case control study.

Place of Study: National Institute of Cancer Research and Hospital (NICRH), Dhaka.

Period of Study: This study was carried out from July 2017 to June 2018 for a period of 12 months.

Study Population: All diagnosed cases of breast cancer with distant metastases who were older than 18 and admitted to the NICRH's Department of Medical Oncology, Radiation Oncology, and Surgical Oncology were chosen as cases. And everyone who had breast cancer, received treatment for it, attended for follow-up,

but hadn't yet shown any additional signs of metastasis, was chosen as the control.

Sampling Method: The sample was collected by purposive sampling technique using inclusion and exclusion criteria.

Sample Size: Total sample size was 126. Among them 42 was selected as cases and 84 was selected as control.

Inclusion Criteria:

- Patients diagnosed with metastatic breast cancer will be selected as cases.
- Patient diagnosed with breast cancer and got treatment for breast carcinoma minimum 2 years before but had not yet developed any features of metastasis cancer will be selected as control
- Age above 18 years for both cases and control.
- Admitted patients for cases and patients coming for follow up clinic as control.

Exclusion Criteria:

- Aged below 18 years.
- Having any other clinical features not from metastatic breast cancer.
- Those who refused to give consent for this study.

Study Population: The study was conducted using a variety of parameters, such as the patient's age, tumor size, lymph node status, tumor grade, time between the patient's primary diagnosis and the onset of their first metastatic relapse, treatment factors, including loco-regional and adjuvant medical therapy, hormone receptor status, margin status, peritumoral vascular invasion, morphologic characteristics of the cancer, menopausal status, breastfeeding, delayed diagnosis, insufficient or incomplete treatment, etc.

Data Collection: Using a pre-tested data sheet, data were gathered through face-to-face interviews. All

additional necessary information was gathered from paperwork and medical records. Reports from the CT scan, ultrasonography, and histology were all recorded. Also performed and recorded was staging.

Data Analysis: Chi square test was done for analysis. For multivariate analysis, regression analysis was performed. Statistical analysis of the study was done by SPSS for windows version

22. The result is presented in tables, figures, charts and diagrams. Confidence interval was considered at 95% level.

Ethical Consideration: This study was carried out after gaining the approval of the research protocol from the respective authority (RRC & EC). All the patients included in this study were informed about the risk and benefit of the study. Proper written consent was taken from the patients for the study.

RESULTS

The purpose of this case control study was to determine the risk factors for breast cancer distant metastases. Cases were defined as those who experienced distant metastases following breast cancer treatment, while controls were those who did not experience any such distant metastases. We looked for and studied a variety of socio-demographic traits, behavioral factors, treatment factors, grading, staging, and clinical features.

According to this study's findings (Table I), the majority of the cases (35.7%) and controls (38.1%) were between the ages of 41 and 50. The mean age in the case group was 42.67 + 9.27 years, whereas it was slightly higher in the control group, at 45.13 + 9.60 years (Table – I). The age range in both groups was quite similar. The level of significance was determined using the chi-square test. Since the p-value was >0.05 (i.e., 0.172), the result of 2=6.38 was not significant.

Table I: Distribution of the study subjects according to age group

Age group In years	Case		Control		χ ² value	P value
	N	%	N	%		
20-30	06	14.3	04	4.7	6.38	0.172
31 – 40	13	30.9	28	33.3		
41 – 50	15	35.7	32	38.1		
51 – 60	8	19.0	14	16.7		
> 60	0	0	6	7.1		
Mean±SD	42.67±9.27		45.13±9.60			
Range(min – max)	28 – 60		27 – 65			

In this study, it was found that (Table II) highest percentage of the study subject both in case (33.3%) and control (38.1%) group had education only up to primary

level. Lowest education level was found in higher secondary level.

Table 2: Distribution of the education level of the patients

	Case		Control		χ^2 value	P value
	N	%	N	%		
Level of education						
Illiterate	14	33.3	32	38.1	5.7	0.22
Primary	12	28.6	23	27.4		
Secondary	6	14.3	21	25.0		
Higher secondary	4	9.5	4	4.7		
Graduation and above	6	14.3	4	4.7		

Figure 1 shows that Muslims were the majority in both group - 95.3% in case group and 86.9 % in control group.

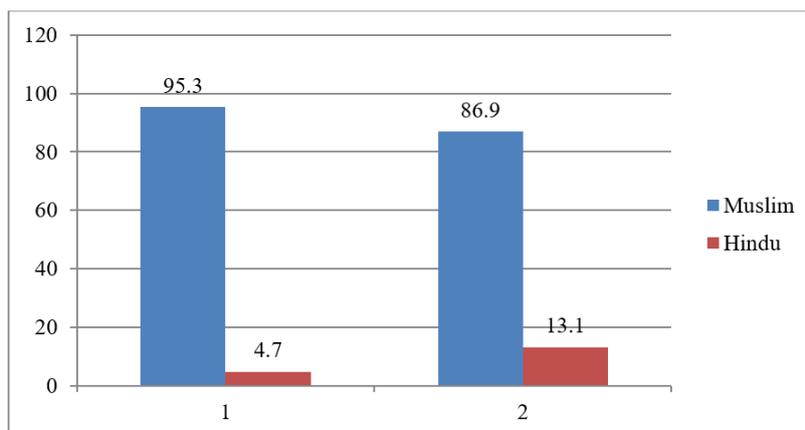


Figure 1: Religion status of the study subjects

Table 3 shows that most of the women were found married (71.5%) in case and

(85.7%) were found in control group. The lowest status found in unmarried in case and control group.

Table 3: Distribution of the marital status of the women

Marital status						
Unmarried	3	7.1	2	2.4	3.99	0.136
Married	30	71.5	72	85.7		
Widow	9	21.4	10	11.9		

Figure 2 shows that homemaker women were mostly found in case (73.8%) and control (73.8%) group in this study. The lowest percentages were found in

service working women in both case (14.3%) and control (8.4%) group.

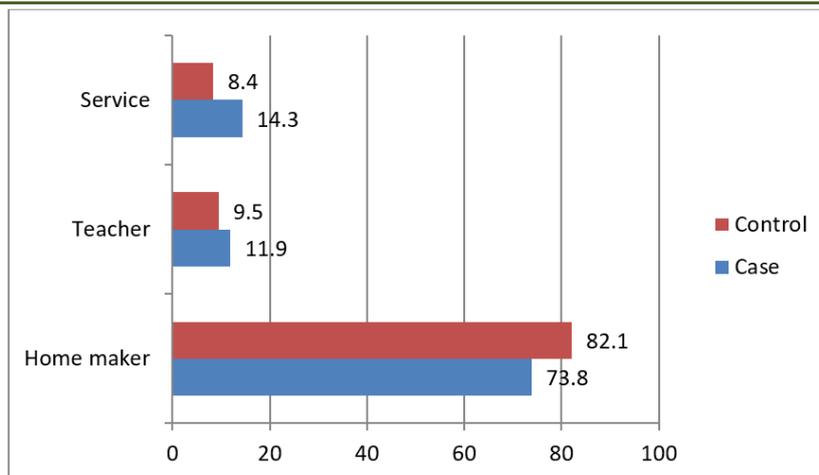


Figure 2: Occupational status of the study subjects

Behavioral Factors:

Positive family history of cancer was present in 23.8 % in case group and 22.6% in control group. Most of the participant was sedentary worker in both groups.

Table 4 also shows there is no significant statistical difference in the two groups regarding co-morbidities, positive family history, use of tobacco, work type and presence of obesity (P >0.05).

Table 4: Behavioral factors of the study subjects

Risk factors	Case	Control	χ^2 value	P value
	N	N		
Positive Family history				
Yes	10	19	0.60	0.43
No	32	65		
Type of work				
Sedentary	40	77	0.53	0.46
Heavy	2	7		
Use of Tobacco, alcohol, Pan Jorda				
Tobacco	4	9	0.18	0.91
Pan jorda	14	25		
No	24	50		
Obesity according to BMI				
Obese	14	36	1.06	0.30
Not Obese	28	48		

Table 5 shows that Infertility, very early or late age of conception or prolonged use of hormonal

contraceptive use was also analyzed but none of these was found to have significant difference in both groups.

Table 5: Factors related to pregnancy, hormonal use of drugs of the study subjects

Risk factors	Case	Control	χ^2 value	P value
	N	N		
Infertility				
Yes	2	3	0.11	0.74
No	40	81		
Age at conception				
Extreme age	12	21	0.18	0.66
Normal age	30	63		
Prolong use of hormonal contraceptive				
Prolonged use	25	39	1.92	0.66
Not use	17	45		
Exclusive breast feeding				
Yes	31	68	0.84	0.35

Not breast feeding	11	16		
State of menopause				
Pre menopause	13	18	1.36	0.24
Post menopause	29	66		

Factors Associated with Treatment of Primary Tumor:

Various factors regarding treatment of the initial treatment – as type of surgery, use of radiotherapy,

chemotherapy or hormonal therapy, use of local or foreign medicine, delay in the treatment was analyzed.

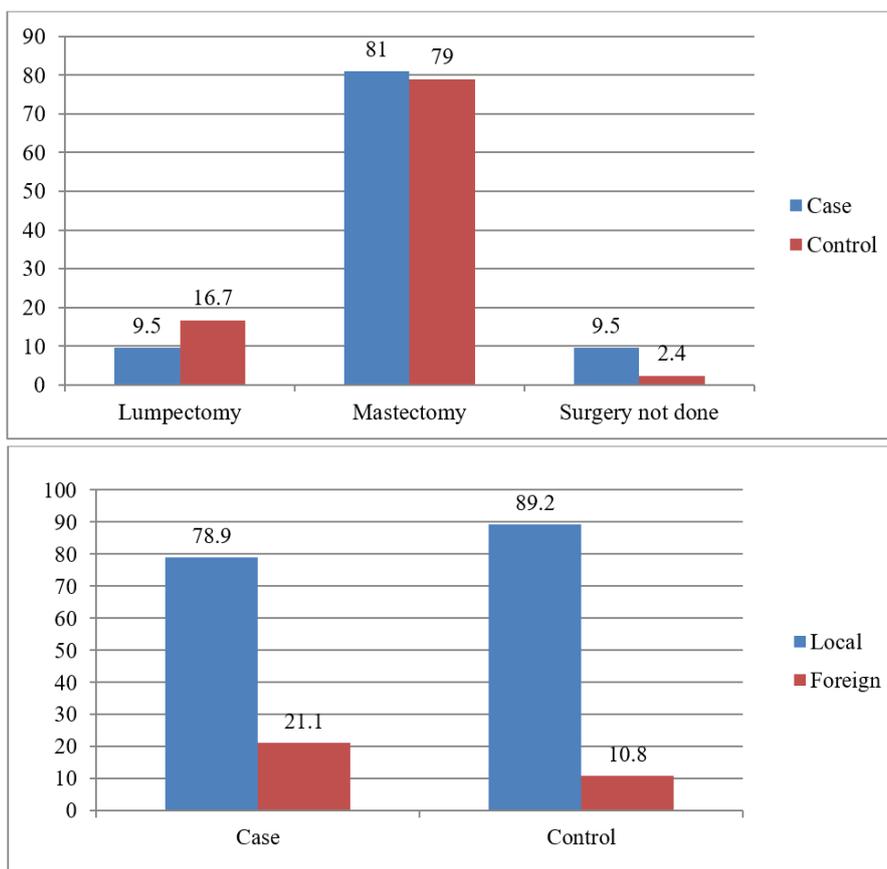


Figure 6(a-b): Factors associated with treatment of primary tumor

DISCUSSION

Among the cancers that affect women, breast cancer is very prevalent. About 90% of breast cancer-related deaths are attributable to distant metastases [14]. Several factors can influence whether a breast cancer survivor experiences a recurrence, including age at initial diagnosis, genetic background, and cancer stage at diagnosis, receptor type, histologic grade, and treatment of the initial tumor [15]. In the current study, the mean age in the case group was 42.67 + 9.27 years, whereas it was slightly higher in the control group, at 45.13 + 9.60 years. The average age of breast cancer cases, according to similar hospital-based studies conducted in Delhi and Jaipur, was 46.8 and 47 years [16, 17]. The average age at which breast cancer develops in Bangladeshi women is 61.0 years, which is a decade younger than the average age for white females in the US [18]. Even with

advancements in therapy, patients who are diagnosed at a younger age have a higher risk of recurrence [21]. Although statistically insignificant, we discovered that the mean age was lower in the control group in this trial as well. In our study, ductal carcinoma was the most prevalent form in both the case (95.5%) and control groups (77.4%). Nearly all of the findings published in India match those of the current study [19]. Infiltrating ductal breast cancer was discovered to be the most prevalent histological type in the US population as well [20]. While breast cancer is common in women of middle age, young patients frequently have local recurrence [21]. In an early radical mastectomy series, Lewis and Reinhoff reported crude local recurrence rates of 67% for patients aged 20 to 29 years and 41% for patients aged 30 to 39 years, whereas local failure rates were 21% to 25% for women aged > 40 years [22]. The stage of the tumor at the time of the initial diagnosis was also a

significant determinant in local recurrence. Advanced stage was a component in the multivariate analysis that was linked to lower survival and a bad prognosis. The chance of a recurrence increased with the stage of the tumor at the time of initial presentation [23, 25].

CONCLUSION

We can infer from this study that there are numerous risk factors for the distant metastases of breast cancer. The majority of patients with distant metastases are young, illiterate, or only minimally literate. Patients are unaware of the condition, its prognosis, and methods of therapy. As a result, there is a delay in both diagnosis and treatment. Many of them did not finish the course of treatment due to their poverty and ignorance. All of these elements also have a role in the spread of breast cancer to distant sites.

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