

## Original Research Article

# Factors affecting survival of women with breast cancer in King Fahad Medical City, Saudi Arabia

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**Received:** 16 February 2017

**Accepted:** 06 March 2017

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## ABSTRACT

**Background:** Breast cancer is the most frequently diagnosed cancer among women in 140 of 184 countries worldwide. The association between breast cancer survival and socio-demographic and pathologic factors has been widely studied in the developed countries. But scarce data is available from Saudi Arabia. We aimed to determine the overall observed one year and three years survival rate of female breast cancer patients and to investigate the factors affecting survival rate.

**Methods:** Retrospective data was collected from the cancer center registry at King Fahad Medical City (KFMC) that included all women diagnosed with breast cancer between 1<sup>st</sup> January 2011 till 31<sup>st</sup> December 2012 and were followed to 31<sup>st</sup> December 2015 (cut off point for follow-up). Kaplan-Meier analysis was done to assess overall survival. The factors affecting survival rate such as age, histological type, tumor grade at diagnosis, metastases and treatment options were investigated using log rank test and Cox regression analysis.

**Results:** The overall observed survival probability of the study population at 1, and 3 years was 95%, and 85%, respectively. The 3 year survivals for the younger ( $\leq 40$  years), 41-50 years and older (50+ years) patients were 83.9%, 90.6% and 80.6% respectively, the differences not reaching statistical significance. There were statistically significant associations between three year survival and histological type of tumour, laterality, metastases and type of treatment by the univariate analysis log rank test.

**Conclusions:** One and three-year survival rate of breast cancer at KFMC was 96% and 85% respectively. Investigating the factors affecting survival rate is one of the most essential means of improving cancer prognosis.

**Keywords:** Breast Cancer, Female, Survival, Prognosis

## INTRODUCTION

Breast cancer (BC) is a major health problem in both developed and developing countries. Around the World, nearly 1.7 million new breast cancer cases were diagnosed in 2012 and this figure represented about 12% of all new cancer cases and 25% of all cancers in women. Since 2008, worldwide breast cancer incidence has increased by more than 20% and mortality has increased by 14%.<sup>1</sup>

In Saudi Arabia, the number of women with BC increased steadily from 1990-2010. There were 1152 female BC cases in 2008 in comparison with 1308 in 2009, and 1473 in 2010. Breast cancer ranked first among females accounting for 27.4% of all newly diagnosed female cancers (1473/5378 cases) in the year 2010. The average age at the diagnosis of BC was 48; weighted average was 49.8, and range 43-52.<sup>2</sup>

The age specific rate (ASR) was 24.9/100,000 for Saudi female population while in the USA, it was 118.7/100,000 and in the UK, ASR was 129.4/100,000. In developing Arab countries, most of patients are below 50 and median age is 49-52 years as compared to 63 in developed nations.<sup>3</sup> Diagnosed women with breast cancer are mostly from developing countries, where they present at a younger age with advanced-stage disease and also have poor overall outcomes compared to women in developed countries. The advanced stage of presentation of breast cancer in developing countries is due to lack of mass education and screening programs, poverty, poor access to health care facilities, lack of expertise, and poor country resources.<sup>4</sup>

There is worldwide variation as well for cancer survival. 5-year relative survival for breast, colorectal, and prostate cancer was higher in North America, Australia, Japan, and northern, western, and southern Europe and lower in Algeria, Brazil, and Eastern Europe.<sup>5</sup> Further, the association between breast cancer survival and socio-demographic and pathologic factors has been widely studied in the developed countries. However, scarce data regarding the impact of different factors on female breast cancer survival were obtained from Saudi Arabia. Hence, the current study was conducted to determine the overall observed one year and three years survival rate of female breast cancer and to investigate the factors affecting survival rate such as age, histological type, tumor grade at diagnosis, metastases and treatment options.

### **Objective**

1. To determine the female breast cancer observed survival rate at 1-year and 3-year at KFMC.
2. To investigate the factors affecting the survival of women with breast cancer at KFMC.

### **METHODS**

In this retrospective study data was obtained from the cancer center registry at KFMC. The study subjects were all women diagnosed with breast cancer between 1<sup>st</sup> January 2011 till 31<sup>st</sup> December 2012 and who were followed-up for at least three years from the date of diagnosis. So, the cut-off point for follow-up was 31<sup>st</sup> December 2015.

#### **Inclusion criteria:**

1. Complete record of the patients and laboratory/radiological investigations.
2. Diagnosed at or referred to KFMC with breast cancer.

#### **Exclusion criteria:**

Women who did not follow-up after initial diagnosis.

### **Data collection tool**

Data collection form was designed (Excel sheet) to collect data from the electronic patients' medical records.

The data collection form included the following variables:

- 1- Socio-demographic data including age, marital status, residency, nationality, education, and occupation.
- 2- Clinico-pathological data including tumor grade, tumor stage, tumor location, laterality, histological type, treatment modalities, and site of metastasis if present.

### **Data analysis procedure:**

Data analysis has been compiled using Statistical Package for Social Sciences (SPSS) software version 20. Frequencies and percentages of demographic and clinical characteristics of the patients were taken as categorical variables. The Kaplan Meier method has been used to determine survival probability over time where the effect of age, grade, stage and type of treatment on one and three -year survival of the patients was determined. Differences in survival effect were compared by the log-rank test. P-value less than 0.05 was taken as significant. Cox proportional hazard regression has used to assess the independent effect of different demographic and clinical variables on the survival rate.

### **RESULTS**

Socio-demographic characteristics of study sample (n=155) is depicted in Table 1. The median age at diagnosis was 47 years and the range was 64 years (from 19 to 83).

Most of the patients diagnosed were in grades II and III (42.5% and 45.2% respectively). The majority of the cases had duct carcinomas 142 (91.6%). About half of cases (50.3%) had localized tumor, nearly one third of them (32.1%) had lymph node involvement and (17.3%) had distant metastases. More than half of the cases (55.5%) had a combined treatment of surgery, chemotherapy and radiotherapy (Table 2).

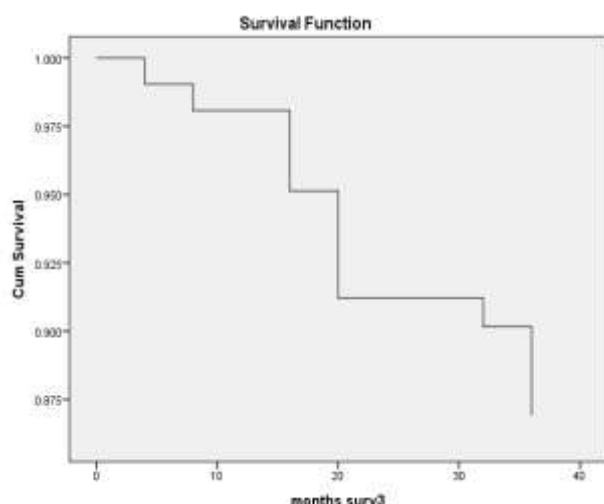
The overall observed survival probabilities for the entire study population at 1, 2 and 3 years were 95%, 91% and 85%, respectively (Figure 1).

The 3-year survival for the younger (< 40 years), 41-50 years and older (50+ years) patients were 83.9%, 94.6% and 80.6% respectively, the differences not reaching statistical significance. There was statistically significant association between three year survival and histological type of tumour (0.014), laterality (0.02), metastases (0.000) and type of treatment (0.001) by the univariate analysis log rank test (Table 3).

**Table 1: Socio-demographic characteristics of the study sample (n=155).**

Socio-demographic variables	N	(%)
<b>Age at diagnosis (years)</b>		
Mean ± S.D	47.7±11.2	
≤40	39	(25.2)
>40-50	60	(38.7)
>50	56	(36.1)
<b>Marital status</b>		
Single	7	(4.5)
Married	127	(81.9)
Divorced	5	(3.2)
Widowed	8	(5.2)
unknown	8	(5.2)
<b>Nationality</b>		
Saudi	135	(87.1)
Non Saudi	20	(12.9)
<b>Residence</b>		
Rural	9	(5.8)
Urban	146	(94.2)

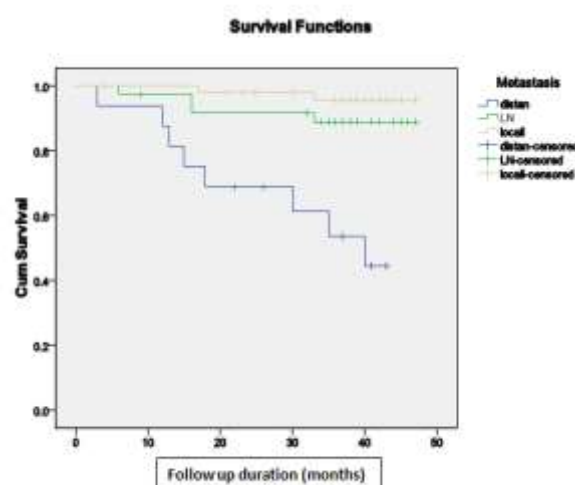
To identify the independent effects of prognostic factors on survival, the Cox proportional hazards ratio was estimated only for the following variables: age at diagnosis, histology and extent of disease. However, none of these variables had emerged as an independent predictor of breast cancer survival. Figure 2 shows that cases with localized breast tumours had better survival (98.1%) than cases with distant metastases (61.5%).



**Figure 1: Overall 3 -year survival rate of female breast cancer cases in KFMC calculated by the life table method.**

**Table 2: Distribution of female breast cancer cases registered from 2011 to 2012 in KFMC by clinic-pathological characteristics of the patients (n=155).**

Clinic-pathological variables	N	(%)
<b>Laterality</b>		
Right	79	(51)
Left	76	(49)
<b>Tumor grade</b>		
Stage 1	13	(8.4)
Stage 2	66	(42.5)
Stage 3	70	(45.2)
Stage 4	2	(1.3)
Unknown	4	(2.6)
<b>Histological type</b>		
Invasive Ductal Carcinoma (IDC)	142	(91.6)
Invasive Lobular Carcinoma (ILC)	9	(5.8)
Others	4	(2.6)
<b>Tumor location</b>		
Lateral	80	(51.6%)
Medial	24	(15.5%)
Central	21	(13.5%)
Overlapping/ Multiple	30	(19.4%)
<b>Metastases</b>		
Localized	78	(50.3)
Lymph Node	50	(32.3)
Distant	27	(17.4)
<b>Type of treatment</b>		
Surgery, Chemo. & Radio.	86	(55.5)
Surgery & Chemo.	23	(14.8)
Chemo. & Radio.	18	(11.6)
Surgery & Radio.	11	(7.1)
Chemotherapy	7	(4.5)



**Figure 2: Kaplan-Meier plot of survival by metastases for female breast cancer cases in KFMC.**

**Table 3: Overall survival rate of female breast cancer patients from 2011 to 2015 by age group, morphology, laterality, metastases and treatment.**

Variable	No. of cases	No. of deaths	Cumulative Survival rate	Log rank test
<b>Age at diagnosis</b>				
≤40	31	5	83.9	0.213
>40-50	37	2	94.6	
>50	36	7	80.6	
<b>Laterality</b>				
Right	51	3	94.1	0.02
Left	53	11	79.2	
<b>Histological type</b>				
IDC	97	12	87.6	0.014
ILC	4	0	100	
Others	3	2	33.3	
<b>Metastases</b>				
Localized	51	24	96.1	0.000
Lymph Node	37	4	89.2	
Distant	16	8	50	
<b>Type of treatment</b>				
Surgery, Chemo. & Radio.	64	5	92.2	0.001
Surgery & Chemo.	19	1	94.7	
Chemo. & Radio.	12	7	41.7	
Surgery & Radio.	4	0	100	
Chemotherapy	4	1	75	

## DISCUSSION

Breast cancer is the most common cause of cancer deaths among women (5, 22,000 deaths in 2012) and now represents one in four of all cancers in women.<sup>1</sup> Analysis of cancer survival data and related outcomes is necessary to assess cancer treatment programs and to monitor the progress of regional and national cancer control programs.<sup>6</sup> The present study was based on data obtained from the cancer registry at the Comprehensive Cancer Center, KFMC. Cancer Registry at KFMC is consistently recorded from 2011. It collects information about the cancer incidence, type, location, stage, and the kinds of treatment received. It Stages cancer records according to the American Joint Commission of Cancer TNM Staging System, as well as the Surveillance, Epidemiology, and End Results (SEER) Summary Staging System and maintain the components of the cancer-related data collection system consistent with all regulatory and procedural policies.

In the present study, the overall observed survival probability of the study subjects at 1 and 3 years was 95% and 85%, respectively compared with 93.9% and 79.2% reported from a previous population-based study conducted in Riyadh<sup>7</sup> and this difference might be explained by improved health care services and national breast cancer screening program in Saudi Arabia. Similar

findings to our results were reported by a cohort study conducted in Tabriz University hospital, Iran, between 1997 and 2008 and it was observed that the overall survival at one and three years was 96% and 86% respectively.<sup>8</sup> Also in Iran a recent meta-analysis and systemic review (included 24 studies, 22745 participants) was conducted to assess the survival rate of breast cancer and the findings revealed that the one, three, five, and ten-year survival rates were 0.956, 0.808, 0.695, 0.559 respectively.<sup>7</sup>

In England, as an example of a well developed country, 96% of women survive breast cancer for at least one year, and this is predicted to fall to 87% surviving for five years or more, 78% of women are predicted to survive their disease for ten years or more, as calculated by age-standardized net survival for patients diagnosed with breast cancer during 2010-2011.<sup>9</sup> However, the figure in developing countries is different. In China, a survival analysis was conducted by Zhu et al. in 2014 for female breast cancer patients diagnosed during 1972–2011 to assess the long-term trends for the prognosis of this cancer. Results showed that the one-, three-, five-, ten-, fifteen-, twenty-, and forty- year observed survival rates were 83.61%, 67.53%, 58.75%, 48.56%, 42.57%, 38.30%, 29.19%, and 19.35%, respectively.<sup>10</sup> In a recent review study in India, 16 publications from the PUBMED database were reviewed and the results showed that the five-year overall survival rate of breast cancer ranged

from 40-62% and this wide variation in survival rate depends on many factors like age, stage at diagnosis, marital status, level of education, clinical extent of the disease, hormonal profile, and treatment received.<sup>11</sup>

Many studies have documented that the survival of breast cancer patients depends on factors such as genetics, age at diagnosis, stage of the cancer, access to care, weight, physical activity status, alcohol consumption, disease comorbidities, social, economic, environmental factors, and ethnicity.<sup>12-17</sup> Screening guidelines have also evolved based on the research findings correlating breast cancer-screening and survival times.<sup>18</sup> Consistent with other studies our study showed differences in overall survival rates among the different age groups.<sup>19,8,10</sup> Lower three year survival rate was noted from the group of age less than 40 years compared to the group of age >40-50 years. In agreement with two studies conducted in the Middle East area (Saudi Arabia and Jordan) the best survival was in the age group 41-50 years and the poorer observed survival for the 50+ cases.<sup>19,7</sup>

Similar findings were reported from Sweden where a recent study evaluated age at diagnosis as a prognostic factor for breast cancer. This study revealed that compared to women aged 40 to 49 years, those who were aged under 40 and 80 + years had a statistically significant higher 10-year mortality rate. When adjusted for confounders like stage at diagnosis, the associations remained statistically significant only for women aged 80 years or more.<sup>20</sup>

Another retrospective study assessed more than 200,000 women in the SEER database, who were diagnosed with breast cancer between the years of 1988-2003, showed that those under the age of 40 were 39% more likely to die when compared to those age 40 or older (hazard ratio = 1.39; 95% CI, 1.34-1.45). Moreover, the highest mortality disparity between younger (<40 years) and older women ( $\geq$ 40 years) was present in early stage, rather than later stage of disease.<sup>21,22</sup>

In agreement with other regional and global studies, our results revealed that the histological type of cancer and metastases are associated with survival differences.<sup>19,8,23</sup> In our study, the three-year survival rate for localized tumor was 96.1% and this figure is consistent with another Saudi study as the authors documented that the localized cancer had a clearly better prognosis (Five-year survival rate = 67.5%).<sup>7</sup>

Breast cancer is commonly treated by various combinations of surgery, radiotherapy, chemotherapy, and hormone therapy. Prognosis and selection of therapy may be influenced by many clinical and pathology features<sup>24</sup> such as: menopausal status of the patient, stage of the disease, grade of the primary tumor, estrogen receptor (ER) and progesterone receptor (PR) status of the tumor, human epidermal growth factor type 2 receptor (HER2/neu) over expression and/or

amplification, and histological type.<sup>25-27</sup> In our study, the best three year survival rate (100%) was achieved when Surgery and Radiotherapy was deployed rather than a combination of surgery and chemotherapy (94.7%), whereas in a Jordanian study, the highest five year survival rate (70%) was reported for cases treated by radiotherapy.<sup>19</sup>

## ACKNOWLEDGEMENTS

The authors are thankful to the Research Center, King Fahad Medical City for providing the research grant and appreciate their support.

*Funding:* This study was funded by the Research Center at King Fahad Medical City

*Conflict of interest:* None declared

*Ethical approval:* Approval of the study was taken by the King Fahad Medical City institutional review board (IRB no 16-057)

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**Cite this article as:** Abu Zaid LZ, Nuzhat A, Rafiqe M. Factors affecting survival of women with breast cancer in King Fahad Medical City, Saudi Arabia. *Int J Community Med Public Health* 2017;4:910-5.