

# Breast cancer: patient characteristics and survival analysis at Salmaniya Medical Complex, Bahrain

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سرطان الثدي: خصائص المريضات وتحليل مدد البقاء على قيد الحياة في مجمع السلمانية الطبي، البحرين

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**خلاصة:** سرطان الثدي هو أكثر الأورام الخبيثة انتشاراً بين النساء في البحرين. ولقد قمنا بدراسة الخصائص الديموغرافية والصورة السريرية التي تتقدم بها المصابات بسرطان الثدي، وأجرينا تحليلاً لمدد البقاء على قيد الحياة، وذلك استناداً إلى عوامل مختلفة. تمت مراجعة البيانات المتاحة عن 117 مصابة بسرطان الثدي في مجمع السلمانية الطبي، كن قد صُرفن من المجمع في الفترة 1982-1994. وتبين أن 70% من المريضات كانت لديهن كتل محسوسة بالثدي يزيد قطرها عن سنتيمترين عندما فحصهن الطبيب أول مرة. وكانت 51.3% من المريضات حينذاك في الطور السريري الثاني، بينما كانت 21.4% في الطور السريري الثالث، و11.1% في الطور السريري الرابع. ولم تتقدم في الطور السريري الأول إلا 6.8% من المريضات. وتم حساب المعدلات التراكمية للبقاء على قيد الحياة بتطبيق طريقة كابلان ومايير فكانت 68.8% ثم 57.33% ثم 36.44% بعد مضي خمس سنوات ثم سبع ثم عشر سنين على التوالي. إن هذه الدراسة تبرز ضرورة زيادة التوعية بسرطان الثدي بين النساء في البحرين، وضرورة الاكتشاف المبكر لهذا السرطان من خلال التحري المنتظم.

**ABSTRACT** Breast cancer is the most common malignant neoplasm affecting women in Bahrain. We studied the demographic characteristics and clinical presentation of patients with breast cancer and conducted survival analyses based on various factors. Data on all the 117 breast cancer patients at the Salmaniya Medical Complex who had been discharged during the period 1982-94 were audited. When first seen by a physician 70% of the patients had a lump size > 2 cm, with 51.3% presenting in clinical stage II, 21.4% in clinical stage III and 11.1% in clinical stage IV. Only 6.8% of patients presented in clinical stage I. Cumulative survival rates calculated using the Kaplan-Meier method were 68.8%, 57.33% and 36.44% after 5, 7 and 10 years respectively. Our study highlights the need for increased awareness about breast cancer by women in Bahrain, and the need for early detection through regular screening.

## Cancer du sein: caractéristiques des patients et analyse de survie au Centre médical Salmaniya à Bahreïn

**RESUME** Le cancer du sein est le néoplasme malin le plus fréquent chez les femmes à Bahreïn. Nous avons étudié les caractéristiques démographiques des patientes atteintes d'un cancer du sein ainsi que la présentation clinique et effectué des analyses de survie basées sur divers facteurs. On a examiné les données concernant les 117 cas de cancer du sein admis au Centre médical Salmaniya qui sont sortis de ce Centre durant la période 1982-1994. Lors de leur premier examen par un médecin, 70% des patientes avaient une tumeur d'une taille supérieure à 2 cm; 51,3% présentaient un stade clinique II, 21,4% un stade clinique III et 11,1% un stade clinique IV. Seulement 6,8% des patientes présentaient un stade clinique I. Les taux cumulatifs de survie calculés au moyen de la méthode de Kaplan-Meier étaient de 68,8%, 57,33% et 36,44% après 5, 7 et 10 ans respectivement. Notre étude souligne la nécessité d'une sensibilisation des femmes à l'égard du cancer du sein à Bahreïn, et celle d'un dépistage précoce par des examens réguliers.

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## Introduction

Breast cancer is a major public health problem in many countries, with incidence and mortality high in Western industrialized nations, although relatively low in developing ones. In the United States of America (USA) breast cancer is the most commonly diagnosed nondermatologic cancer and the second most frequent cause of cancer-related deaths among women. It accounts for 32% of all newly diagnosed cancers. US data indicate that the incidence of breast cancer increases directly with age until 75–80 years. In 1996, a woman in the USA had a 1-in-8 chance of developing breast cancer and a 1-in-28 chance of succumbing to the disease over her lifetime [1,2].

Being born in North America or northern Europe increases the risk of developing breast cancer, while Hispanic-American women develop the disease at a younger age than white women. Other demographic characteristics associated with increased risk of developing breast cancer include increasing age, high socioeconomic status, never having been married, and for breast cancer diagnosed after 45 years of age, Caucasian origin. Early menarche, late menopause, late-age first full-term pregnancy and low parity all increase risk. Removal of the ovaries at an early age is protective [3,4].

In the Czech Republic, breast cancer is the most commonly diagnosed cancer and a leading cause of malignant neoplasm death in women, with approximately half of all new breast cancer cases diagnosed in the early stages [5]. In Japan, the age-adjusted mortality rate from breast cancer has been increasing gradually from 4.1 per 100 000 population in 1950 to 6.6 in 1991, with age-specific mortality rates increasing particularly in the 40–79-year-old age range [6,7]. In Madras (southern India), breast cancer is

the second most common cancer among women [8].

Breast cancer mortality rates have remained relatively steady over the past 20 years even though the number of new cases has grown [9]. Survival rates for women aged  $\leq 30$  years have improved in the USA with the use of less extensive surgical resections and the introduction of cytotoxic chemotherapy. Rates of survival after breast-conserving surgery have been at least as good as those for patients undergoing total mastectomy. With current treatment, primary operable breast cancer in young women appears to have a similar prognosis to that for breast cancer in older women [10,11].

Tumour size, lymph node involvement, tumour grade and other prognostic factors are important predictors of whether a tumour is localized, and therefore amenable to local treatment. Smaller tumours are more likely to be localized. Adequate effective irradiation of localized disease, including appropriate treatment of all nodal areas when needed, and limited radiation to sensitive organs, can significantly improve survival. In high-risk patients, it enhances the effect of systemic treatment in improving survival [12].

The decrease in the diagnosis of regional disease in the late 1980s in women over 40 years of age most likely reflects the increased use of mammography earlier in the decade. The increase in survival rates, particularly for regional disease, is probably a result of improvements in systemic adjuvant therapy [13].

In Bahrain, there are an estimated 40 new cases of breast cancer and approximately 12–15 deaths resulting from the disease each year. It is the most common type of malignancy affecting women. In the early 1990s, mortality from breast cancer represented approximately 6% of deaths from

all types of neoplasm in Bahrain [14]. The present study aimed to identify patient characteristics, and to compute survival rates among patients diagnosed with breast cancer who had been discharged from Bahrain's Salmaniya Medical Complex (SMC) during the period 1982-94.

## Patients and methods

Our study examined the demographic characteristics, clinical presentation and survival analyses of all cases in the SMC computerized database who had been discharged with a breast cancer diagnosis during the period 1982-94. SMC is the main Ministry of Health hospital and the largest referral centre in Bahrain. The study is a retrospective review of data obtained through chart audit of patients in the sample.

A questionnaire was used to collect data from patients' medical files. Cancer-related mortality events were also obtained and confirmed through Bahrain's Central Statistics Bureau. Data were analysed using *SigmaStat SigmaPlot*® statistical analysis software.

## Results

### Demographic and social characteristics of patients

There were 169 consecutive discharge events for the 117 patients registered in SMC's computerized database who had attended and been discharged from the hospital during 1982-94. The study sample comprised 93 Bahrainis (79.5% of the total) and 24 non-Bahrainis (20.5%). All cases were women. Mean age for all cases was 50.1 years (50.7 years for Bahrainis, 47.6 years for non-Bahrainis). Data analysis

**Table 1 Distribution of breast cancer cases by nationality and age group, Salmaniya Medical Complex, 1982-94**

Age group (years)	Bahraini	Non-Bahraini	Total cases	
			No.	%
30-39	17	4	21	17.9
40-49	28	11	39	33.3
50-59	15	6	21	17.9
60-69	16	3	19	16.2
≥ 70	12	0	12	10.3
Total	93	24	117	

showed 55.6% of the women to be < 50 years of age. The largest number of cases, 33.3% of the total, were aged 40-49 years. Table 1 illustrates the distribution of cases by nationality and age group.

The data also showed that 69.2% of all the women were married, 18.8% were widowed, 8.5% single and 3.4% were divorced. There was a history of breastfeeding in 48.7% of cases and of no breastfeeding in 10.3%. In 41% of cases no data on breastfeeding were available.

### Tumour characteristics

The site of the tumour on presentation was the left breast in 52.1% of cases, the right breast in 44.4% and bilateral involvement in 3.4% of cases.

Lump size on presentation (revealed by ultrasound, mammography and/or clinical palpation) in 61 women (52.1%) was 2-5 cm on first diagnosis, in 18 women (15.4%) it was < 2 cm and in 23 (19.7%) it was > 5 cm on diagnosis. Data relating to lump size in the remaining 15 women (12.8%) were incomplete. Figure 1 illustrates these findings.

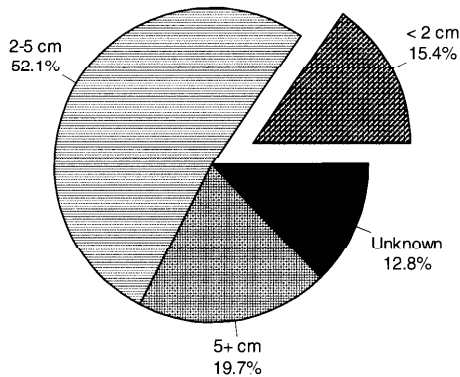


Figure 1 Frequency distribution of breast cancer cases by lump size, Salmaniya Medical Complex, 1982-94

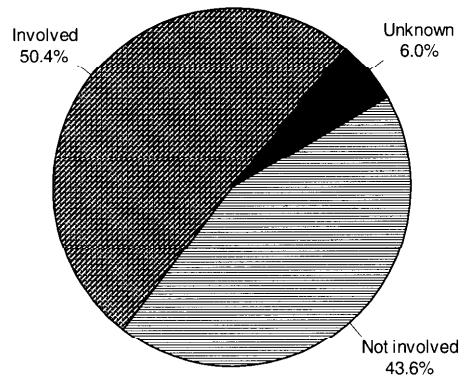


Figure 2 Frequency distribution of breast cancer cases by axillary lymph node involvement on first diagnosis, Salmaniya Medical Complex, 1982-94

Skin changes were present in 25.6% of cases. Nipple retraction was evident in 12.0%, nipple eczema in 8.5% and nipple discharge in 11.1% of cases. In 42.8% of cases no documentation regarding skin or nipple changes was available.

Axillary lymph node involvement was found in 59 women (50.4%) when first seen by a physician; 51 (43.6%) had clear axillary lymph nodes. In 7 women (6%) data relating to lymph node involvement were incomplete. Contralateral lymph nodes were involved in 2.6% of cases and supraclavicular lymph nodes in 1.7%. Figure 2 illustrates these findings. Distant metastases were identified in 11.1% of cases on first presentation.

### Clinical staging

Data relating to the clinical stages of breast cancer on first diagnosis [15] (see Figure 3) showed that 8 women (6.8%) presented in stage I, 60 (51.3%) presented in stage II, 25 (21.4%) in stage III and 13 (11.1%) in stage IV. There were no data for 11 (9.4%) women.

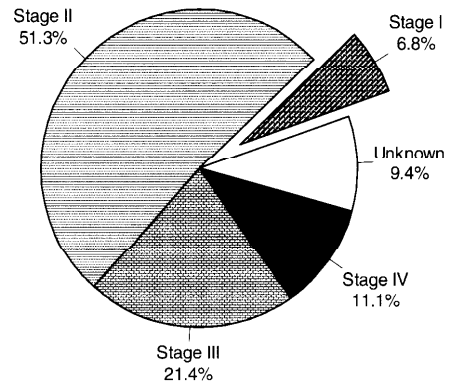


Figure 3 Frequency distribution of breast cancer cases by clinical staging of the tumour on first diagnosis, Salmaniya Medical Complex, 1982-94

### Line of management

Data indicated that 6.8% of cases were managed by surgery only, and 93.2% by surgery and other adjuvant therapy. Of this latter group, 45.3% had surgery, chemotherapy and/or hormone replacement thera-

py and radiotherapy; 36.8% had surgery and chemotherapy and/or hormone replacement therapy; 2.6% had surgery and radiotherapy; 8.5% had surgery and unknown post-operative care. Data concerning the type and extent of surgical intervention could not be used in the study because a significant number of files were incomplete.

## Survival analysis

### Kaplan–Meier method

Survival analysis using the Kaplan–Meier method showed 38 cancer-related deaths (32.5%) among the 117 subjects in the study. Mean survival time was 8 years, with 95% confidence interval (95% CI) between 7 and 9 years. Cumulative survival for all subjects was 68.68%, 57.33% and 39.31% after 5, 7 and 10 years respectively. Cumulative survival rates for Bahraini patients after 5, 7 and 10 years were 64.31%, 54.67% and 36.44%.

In the following survival analysis data, unless otherwise stated, the percentage given refers to the cumulative survival rate after 5 years. Where this first percentage is followed by a second (bracketed) percent-

age, the cumulative survival rate after 7 years is indicated.

### By lump size

Cumulative survival for cases diagnosed with lump size < 2 cm was 70.16% (unchanged). For cases with lump size 2–5 cm, cumulative survival was 75.00% (64.39%). For cases with lump size > 5 cm, the rate was 72.11% (not computed as the remaining cases had a follow-up period of < 7 years). Among cases where the tumour size was not available, cumulative survival was 35.56% (26.67%). Table 2 illustrates these findings.

### By lymph node involvement

Of the 59 cases with local lymph node involvement, cumulative survival was 66.64% (61.51%). Among 51 cases with no local lymph node involvement at diagnosis, cumulative survival was 81.59% (61.19%). Among the 7 cases with unknown involvement of local lymph nodes, cumulative survival was 14.29%. Table 3 illustrates these findings.

### By clinical stage

Among 8 cases diagnosed in stage I, cumulative survival was 87.50% and for the 60

Table 2 Survival estimate (Kaplan–Meier method) according to lump size at diagnosis, Salmaniya Medical Complex, 1982–94

Lump size (cm)	No. of cases	Deaths		Censored cases		Mean survival time in years (95% CI)	Cumulative 5-year survival (%)
		No.	%	No.	%		
< 2	18	4	22.2	14	77.8	6 (4–7)	70.16
2–5	61	17	27.9	44	72.1	9 (7–10)	75.00
≥ 5	23	6	26.1	17	73.9	5 (4–6)	72.11
Unknown	15	11	73.3	4	26.7	5 (2–7)	35.65
All cases	117	38	32.5	79	67.5	8 (7–9)	68.80

CI = confidence interval

**Table 3 Survival estimate (Kaplan–Meier) according to axillary lymph node involvement, Salmaniya Medical Complex, 1982–94**

Axillary lymph node status	No. of cases	Deaths		Censored cases		Mean survival time in years (95% CI)	Cumulative 5-year survival (%)
		No.	%	No.	%		
Involved	59	18	29.51	41	69.49	7 (6–8)	66.64
Not involved	51	14	27.45	37	72.55	8 (7–10)	81.59
Unknown	7	6	85.71	1	14.29	2 (1–3)	14.29
All cases	117	38	32.50	79	67.50	8 (7–9)	68.80

CI = confidence interval

**Table 4 Survival estimate (Kaplan–Meier) according to clinical staging, Salmaniya Medical Complex, 1982–94**

Clinical stage	No. of cases	Deaths		Censored cases		Mean survival time in years (95% CI)	Cumulative 5-year survival (%)
		No.	%	No.	%		
Stage I	8	1	12.50	7	87.50	4 (3–4)	87.50
Stage II	60	19	30.00	42	70.00	8 (7–10)	74.48
Stage III	25	5	20.00	20	80.00	7 (6–9)	73.46
Stage IV	13	6	46.15	7	53.85	6 (4–9)	48.00
Unknown	11	9	72.73	3	27.27	5 (3–8)	45.36
All cases	117	38	32.50	79	67.50	8 (7–9)	68.80

CI = confidence interval

cases diagnosed in stage II, 74.48% (58.65%). The 25 stage III cases had a rate of 73.46% (63.30%) and for the 13 stage IV cases, 48.00% (unchanged). For 11 cases that were not classified, cumulative survival was 45.36% (36.36%). Table 4 shows these findings.

### By management

Our study included 8 cases managed by surgery only and 3 cases managed by surgery and radiotherapy. A survival estimate was not computed in these two categories as all cases were censored. Among the 43 cases that had surgery and chemotherapy, cumu-

lative survival was 70.34% (63.30%). Among 53 cases that had surgery, chemotherapy and radiotherapy, cumulative survival was 61.73% (unchanged). Of the 10 cases treated by surgery and unknown supportive measures, cumulative survival was 64.00% (unchanged).

### By age group

For 5 cases in age group 20–29 years, the cumulative survival rate was 75.00%. For the 21 cases in age group 30–39 years, the cumulative survival rate was 64.00% (51.20%); for the 39 cases in age group 40–49 years, 67.35% (unchanged); for 21 cases

Table 5 Survival estimate (Kaplan–Meier) according to age group, Salmaniya Medical Complex, 1982–94

Age group (years)	No. of cases	Deaths		Censored cases		Mean survival time in years (95% CI)	Cumulative 5-year survival %
		No.	%	No.	%		
20–29	5	1	20.00	4	80.00	4 (3–6)	75.00
30–39	21	7	33.33	14	66.67	7 (5–9)	64.00
40–49	39	10	25.64	29	74.36	8 (6–9)	67.35
50–59	21	8	40.10	13	61.90	9 (7–11)	84.82
60–69	19	10	52.63	9	47.37	4 (3–5)	43.86
≥ 70	12	2	16.67	10	83.33	6 (4–7)	73.33
All cases	117	38	32.50	79	67.50	8 (7–9)	68.80

CI = confidence interval

in age group 50–59 years, 84.82% (72.70%); for 19 cases in age group 60–69 years, 43.86% (29.24%). For 12 cases in the age group ≥ 70 years, the cumulative survival rate was 73.33% (not computed as cases in this age group had been entered into the study roster for less than 7 years). Table 5 illustrates these findings.

## Discussion

The study examined 117 non-randomized cases managed and discharged from Salmaniya Medical Complex, Bahrain between 1982 and 1994. Although nearly 40 cases of breast cancer were being reported annually, the Salmaniya database included only a portion of them, as many patients were being managed abroad, particularly during the 1980s. The ratio of Bahraini to non-Bahraini cases in our study mirrored that of Bahrain's total population (approximately 62% Bahraini, 38% non-Bahraini). The proportion of females and males in the non-Bahraini population is 29.2% and 71.8% respectively [16].

The literature from industrialized countries indicates increased risk of breast cancer with advancement of age. Our study showed the largest proportion of cases (33.3%) occurring in the age group 40–49 years, with over half (55.6%) < 50 years of age. Further population-based studies are needed to identify more precisely the probability, by age group, of developing breast cancer in Bahrain.

Data from various countries indicate that increased breast cancer incidence coincides with the increased use of mammography in asymptomatic women in the 1980s [17]. In Bahrain, a mammography screening programme aimed at early detection of breast cancer has recently been initiated. Results to date have yet to reveal any change in the incidence of the disease.

Our data indicate that breast cancer patients in Bahrain visit the physician late in the progression of the disease. Our findings showed 51.3% of cases had tumour size 2–5 cm and about 70.0% had a tumour of size > 2 cm when first seen by the physician. In terms of clinical staging, 51.3% presented in stage II, 21.4% in stage III and 11.1% in

stage IV. Only 6.8% were diagnosed in stage I. There were 50.4% of patients in our sample with axillary lymph node involvement on first diagnosis, with 11.1% of cases having distant metastases.

The findings are alarming. They suggest an urgent need to improve women's awareness of breast cancer, and a need for increased emphasis on early detection by clinical and mammographic methods. Various studies on the efficacy of screening have demonstrated significant reductions in mortality among women  $\geq 50$  years of age [18,19]. Other studies claim that regular mammographic screening of women of age  $> 65$  years can reduce breast cancer mortality by approximately 45% [20].

Parity, contraceptives and hormone replacement therapy have been extensively researched in the Nordic countries. Studies have shown an increased breast cancer risk in women of low parity, those who have their first child late, and those who had used oral contraceptives and hormone replacement therapy for prolonged periods [21].

In Norway it has been found that high parity is associated with an overall reduced risk of breast cancer. Among women 20–29 years of age, however, the results suggested increased risk with increasing parity. The protective effect of high parity was particularly strong among women with first birth before the age of 20 years, and rather weak among those with first birth at the age of 30 years or more [22]. Data relating to these variables were absent from the medical charts of the patients in our study. We recommend their inclusion for future breast cancer studies.

In reviewing the line of management, our study showed 6.8% of cases were managed by surgery alone, 93.2% by surgery and other adjuvant measures, and 45.3% by surgery, chemotherapy, hormone replacement and radiotherapy. We believe that this

finding accords with the accepted breast cancer management regimens.

We conducted survival analyses (employing the Kaplan–Meier method) in relation to the following factors: tumour size, lymph node involvement, clinical stage, line of management and age group. Survivability increased dramatically with early diagnosis and aggressiveness of clinical management. Cumulative survival for all cases was 68.80% after 5 years, 57.33% after 7 years and 36.44% after 10 years.

Survival analyses by clinical stage showed an 87.5% cumulative survival rate after 5 years for stage I, 74.48% for stage II, 73.46% for stage III and 48.0% for stage IV. These findings are similar to other studies which identified clinical stage at diagnosis as an important determinant of survival [23]. We also found that the age group 60–69 years had the lowest survival rate after 5 years (43.86%), despite the lack of any significant difference in distribution of cases by clinical stage among the age groups.

By comparison, the cumulative survival for all women with breast cancer in Sweden after 7 years has been reported to be 88.00% [24]. In Florence (Italy) the observed 5-year survival rate has been found to be 68.40% [25] and in Madras, 48.00% [8].

## Conclusion

The study found that over 93.2% of cases were first seen by the attending physician with disease progression beyond clinical stage I, including 21.4% in clinical stage III and 11.1% in clinical stage IV. Axillary lymph node involvement was noted in 50.4% of the patients when first seen. Survival analyses indicate better survivability



with early detection of the disease and aggressive management.

The study reinforces the urgent need for improved screening techniques for early detection, and for an aggressive health education campaign to increase the awareness of women in Bahrain about the potential risk of breast cancer and early detection by regular testing. Further population-based studies are required to identify the incidence and probability of developing breast

cancer in relation to specific demographic variables in Bahrain.

Many of the cases in our study had incomplete data related to clinical staging, tumour characteristics and surgical procedures, one result of which was our inability to study the efficacy of different surgical procedures. There is clearly a need to improve documentation of clinical data in patients' medical records.

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