



Research article

The five-year survival rate of breast cancer at Radiation and Isotopes Centre Khartoum, Sudan

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ABSTRACT

Background: The Radiation and Isotopes Centre Khartoum (RICK) is the largest public cancer centre in Sudan. The most common cancer in Sudan (and RICK) is breast cancer. The study aims to determine the five year survival of breast cancer as well as factors influencing this survivorship.

Methods: This retrospective facility-based study was conducted on patients diagnosed as having breast cancer at RICK during the year 2013. At 305 patients, the population under study was totally covered. Data analysis was conducted using SPSS version 23. Kaplan-Meier method was used to estimate survival, and to further plot it against specific variables.

Results: The five-year survival was found to be 79%. Lymph nodes were involved in 70.5% of the cases. The mean time between patients' first discovery of symptoms and diagnosis at RICK was 13.03 months. Presence of comorbid diabetes and hypertension significantly increased breast cancer mortality.

Conclusions: Breast cancer in Sudan is characterized by younger age, delayed diagnosis and advanced staging at presentation, as well as lower five-year breast cancer survival in comparison to developed countries.

1. Introduction

Breast cancer is a major public health issue globally. It is the most common site-specific malignancy affecting women and the most common cause of cancer mortality amongst women [1]. While the mortality rates of breast cancer are declining in the developed countries, the opposite is true for developing countries. The remarkable improvement of breast cancer survival in the developed countries is attributed to advances in early detection and treatment modalities. This is in contrast to what is seen in Africa, where the disease is characterised by advanced staging at presentation, consequently leading to poorer prognosis [2].

In Sudan, the incidence of cancer in general has been increasing steadily. The number of cancer cases presenting at Radiation and Isotope Centre in Khartoum (RICK) has jumped from 250 in 1967–7500 in 2011 [3]. Like other countries in Africa, breast cancer patients in Sudan present quite late. Over 3 quarters (78%) of Sudanese breast cancer patients have stage 3 or 4 disease (TNM classification) at presentation. They also tend to present at a younger age. This however may be attributed to the overall younger population in Africa. In a study conducted by *Awadelkarim et al* [4] comparing Sudanese and Italian breast cancer patients, the Sudanese patients were younger and their tumours were larger, more

advanced in stage, and more frequently positive for nodal metastases. No significant differences were found for hormone receptors or breast cancer subtypes. This indicates that the differences between the Sudanese and Italian patient survival are due to the stage at diagnosis rather than intrinsic biological characteristics.

There are only two major public cancer centres in Sudan, the Radiation and isotope centre (RICK) and the National Cancer Institute of the University of Gezira (NCI -UG), with 80% of cases covered by RICK. Breast cancer is the most frequently seen malignancy at both centres. A study [5] conducted at the National Cancer Institute NCI-UG estimated that the 5 year survival rate of breast cancer patients in NCI was 38%. A study of similar nature has not been reported at RICK. With coverage of over three-quarters of cancer patients in Sudan, the necessity of investigating cancer survival at RICK is crucial for pinpointing key prognostic factors like the stage at diagnosis and the quality of care provided by the centre, which will later serve as guidance to the establishment of evidence-based health policies striving to improve the outcome for cancer patients in Sudan.

This study aims to determine the 5-year-survival of patients diagnosed at RICK during 2013, as well as the possible association of factors such as demographic data (sex, age, parity, birthplace and BMI), family

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history, certain comorbidities, tumor-specific factors, and different treatment regimens with patient survival.

2. Materials and methods

This is an analytical facility-based retrospective cross-sectional study implemented using medical records of the Department of Statistics of the Radiation and Isotopes Centre Khartoum (RICK).

The study population includes 305 all breast cancer patients representing all diagnosed in the Radiation and Isotopes Centre in Khartoum (RICK) from 1st of January 2013 to 31st of December 2013. Patients who underwent partial or complete cancer treatment in countries other than Sudan were excluded from the study, as one of the main objectives of the study is evaluation of the quality of care for cancer patients in Sudan.

Data was extracted from patients' files. Using a structure form, investigators obtained demographics data (sex, age, birthplace, parity and BMI), patient-specific data (family history, comorbid conditions and patient interval), tumor-specific data (laterality, lymph node involvement, lymphovascular/neural invasion, Estrogen receptor status, Progesterone receptor status, Her2/neu receptor status) and treatment regimens (surgery, chemotherapy, radiotherapy and hormonal therapy). The date of diagnosis was recorded, as well as the date of the last follow-up visit and the date of death (if documented). For patients who were lost to follow-up before the 60 months benchmark, listed contact numbers were contacted via phone calls to check the patients' survival status. For deceased patients, the date of death and cause of death were also inquired about.

Data was consequently analysed using Software Package for Statistical Analysis (SPSS) version 23. The Kaplan-Meier method was used to draw up the survival curve and compare the survival periods for different variables. In Kaplan-Meier, variable 'survival length' was set as Time, variable 'survival' was set as Status, and death was chosen as the Event.

This was standardized for all independent variables which were, respectively, set as Factor to obtain the survival analysis output.

Ethical approval was obtained from Khartoum State Ministry of Health (Sudan). Informed consent was taken from patients or the closest relatives in cases of deceased patients when appropriate.

Table 1. Frequencies of overall tumour- and patient characteristics.

	<40 years	40–50 years	≥50 years	Unknown	Total
SITE					
Left	25	45	55	4	129
Right	36	46	71	0	153
Bilateral	0	1	1	0	2
Unknown	2	8	7	4	21
PARITY					
Nulliparous	18	14	7	1	40
Primiparous	9	7	9	0	25
Multiparous	25	61	72	1	159
Unknown	11	18	46	6	81
NODE INVOLVMENT					
Yes	22	38	41	2	103
No	5	16	22	0	43
Unknown	36	46	71	6	159
BMI					
Underweight	11	10	9	1	31
Normal	22	33	30	1	86
Overweight	13	26	33	0	72
Obese	7	18	21	2	48
Unknown	10	13	41	4	68

3. Results

3.1. Descriptive analysis

The population characteristics are summarised in Table 1. Of the 305 breast cancer patients, 302 were female (99%) and three were male (1%). One fifth (21.2%) were less than 40 years old, 33.7% were 40–50 years old, and 45.1% were 50 or more years old. Most of the patients were born in Khartoum (16.3%) and Aljazirah (15.9%), followed by River Nile (9.9%), White Nile (9.9%), North Kordofan (9.9%) and Northern state (9.5%). The least number of patients came from Central Darfur, East Darfur and Blue Nile (each at 0.4%).

Regarding the patients specific data, 24.3% have family history of similar condition, 10.7% had diabetes mellitus, 14.7% had hypertension and 4% had both diabetes and hypertension. The mean time between first discovery of symptoms by a patient and the diagnosis at RICK was 13.03 months (SD = 15.79).

At presentation, the site of tumour was right in 53.9% and left in 45.4% of patients. Two patients (0.7%) had bilateral tumours at presentation. Lymph nodes were involved in 70.5% of the cases, while 40% had lymphovascular/perineural invasion. As to the receptor status, 62.9% were ER+, 44.6% were PR+ and 54.1% were HER-2 +

In patients who underwent surgery, 83.8% had clear margins, while the rest had margins infiltrated with tumour. Patients usually undergo radiotherapy following surgery. In this study, the median of radiotherapy were 15 rounds. Different combinations of chemotherapeutic agents are used in RICK. The most common single regimen in this study was the FAC regimen (21.5%), followed by FEC (10.3%) and FMC (9.5%). Most of the patients, however, were treated with a combination of different chemotherapeutic regimens (36.0%)

While Different hormonal drugs are also used, the most common is Tamoxifen (54.6%) followed by Letrozole (25%). Other drugs are implemented separately or concomitantly with these mentioned.

Around 40.3% of patients completed the 5-year follow up period in the hospital, the rest were lost to follow-up and communication was attempted via registered phone numbers of patients and/or co-patients. Of them, 29.5% were lost to follow-up within the first year. The mean follow-up duration in this study was 36.35 months (SD = 25.21). The total number of confirmed deaths was 45.

3.2. Survival analysis

The mean survival time of the studied sample was 53.14 months (SD = 1.04), with a cumulative survival probability of 79% [Figure 1].

3.2.1. Patient-specific factors

Patients younger than 40 years old showed higher survival in both mean survival time (56.14 months; SD = 1.82) and cumulative survival probability (88%) compared to 40 to 50- and 50 or above year olds, who had a mean survival time of 52.90 months (SD = 1.82) and 52.05 months (SD = 1.65) respectively. In terms of parity, the mean survival time was lowest for nulliparous women (47.83 months; SD = 3.73). Underweight patients had the lowest cumulative survival (69%) and the lowest mean survival period. (47.99 months; SD = 4.19). Patients with concomitant chronic illnesses like diabetes and hypertension had poorer prognosis, and patients with both diabetes and hypertension carried the worst prognosis [Figure 2].

3.2.2. Tumour-specific factors

Negative ER, PR, and HER2 receptor status all had lower survival in terms of mean and cumulative survival probability when compared to parallel positive status cases. Patients with invaded lymph nodes had lower survival than patients with uninvaded lymph nodes (56.51 months and 57.68 months, respectively). Survival of people with lymphovascular/perineural invasion was higher than those without (57.71 months and 56.18 months respectively). The mean survival periods for patients

with certain patient- and tumor-specific factors are summarized in Table 2.

3.2.3. Treatment factors

A surgery with a clear resection margin has higher mean survival period (56.52 months; SD = 1.01) than those with margins infiltrated with cancerous cells (54.08 months; SD = 3.50). Radiotherapy also significantly impacts survival, those who underwent radiotherapy had better prognosis and mean survival (56.91 months; SD = 0.90) compared to those with undocumented radiotherapy (49.46 months; SD = 0.48).

Kaplan-Meier analysis showed that the presence of comorbidities and the treatment with radiotherapy were the only statistically significant variables. The non-significance of the rest of the factors may be explained by the small sample size, the relatively large number of data missing from the files and/or the percentage of patients lost to follow-up. A summary of the data collected as well as the outcomes of survival analysis are supplemented as “Data in Brief” and “Survival Statistics and Graphs”, respectively.

4. Discussion

Both the clinical and epidemiological pictures of the disease are different between developed and developing countries like Sudan. If the results of this study (and similar studies conducted in likewise developing countries) are compared with those of developed countries, it is seen that the breast cancer patients present at a younger age with more advanced disease. The male to female ratio in this study is similar to that reported in high income countries [6]. It is worth noting that the distribution of breast cancer in Sudan documented in this study does not correlate well with population density in each state. While the River Nile and the Northern state account for 6% of the total population in Sudan, nearly one fifth of the breast cancer patients in this study were born in these states. This correlates with the findings of the most recent National Cancer Registry (NCR) of Sudan, which reported that the aforementioned regions had the highest prevalence of cancer in Sudan. An investigation of radioactive activity in soil and air elements was accordingly issued. Upon investigation, no abnormal activity was reported in water or air samples [7]. As such, alternative explanations to the apparent disparity

should be explored, such as inequitable access to health care and poor data availability.

Another chief finding is the length of the time period between the first discovery of breast cancer symptoms by a patient and their diagnosis at RICK. The mean period reported by this study (13 months) is among the longest to be reported, both in high- and low-income countries [8]. The delay in diagnosis and treatment initiation has been associated with advanced staging at diagnosis and higher breast cancer mortality. It is suggested that factors leading to such picture, including both patient delay and health system delay, be further scrutinized.

The cumulative survival probability reported by this study is lower than that seen in developed countries, denoting a room for improvement in Sudan. Underweight patients have been found to have the poorest outcomes, this may be due to the general association between advanced malignancy and cachexia. Comorbidities, negative receptor status and lymph node invasion were also associated with increased mortality, all in accordance with the existing body of knowledge [8, 9, 10, 11, 12, 13]. However, unlike what is commonly reported in the literature, younger patients carried better prognosis in this study than their older counterparts [14]. This may be also be attributed to the association between older age and comorbidities which can have a magnified effect on Sudanese patients, due to socioeconomic factors, defective healthcare system and poorer compliance.

The treatment plan in Sudan was found to be generally similar as to what is found in guidelines [15], with few exceptions that will be addressed below. Surgery is the mainstay of curable management. 84.8% of the patients underwent surgery and had histologically tumor-free margins, a positive prognostic feature. Radiotherapy is used to double-check this procedure. Patients who underwent radiotherapy had higher five-year survival rate than those who were not reported to have undergone radiotherapy. Chemotherapy is done by giving different combinations of chemotherapeutic drugs. The FAC regimen is by far the most commonly used in RICK. Other regimens like TAC, which have been reported to have higher efficacy and better survival outcome [16], are also used but to a lesser extent. This may be due to their higher cost. Hormonal therapy, given for five years, improved the prognosis in this study. However, the drug must be taken for an average of five years and compliance is seen to be an issue.

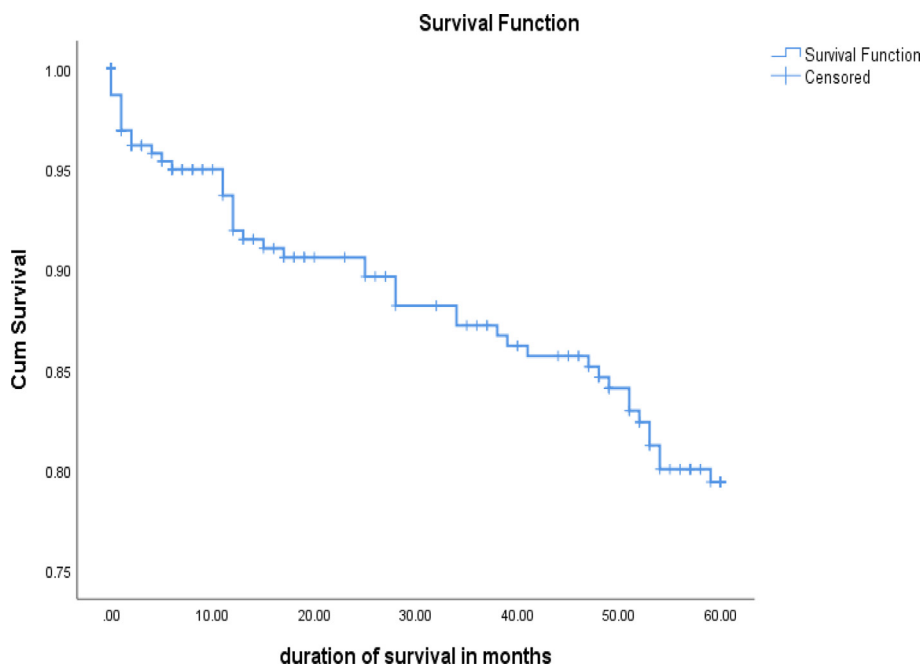


Figure 1. Overall survival of the study population.

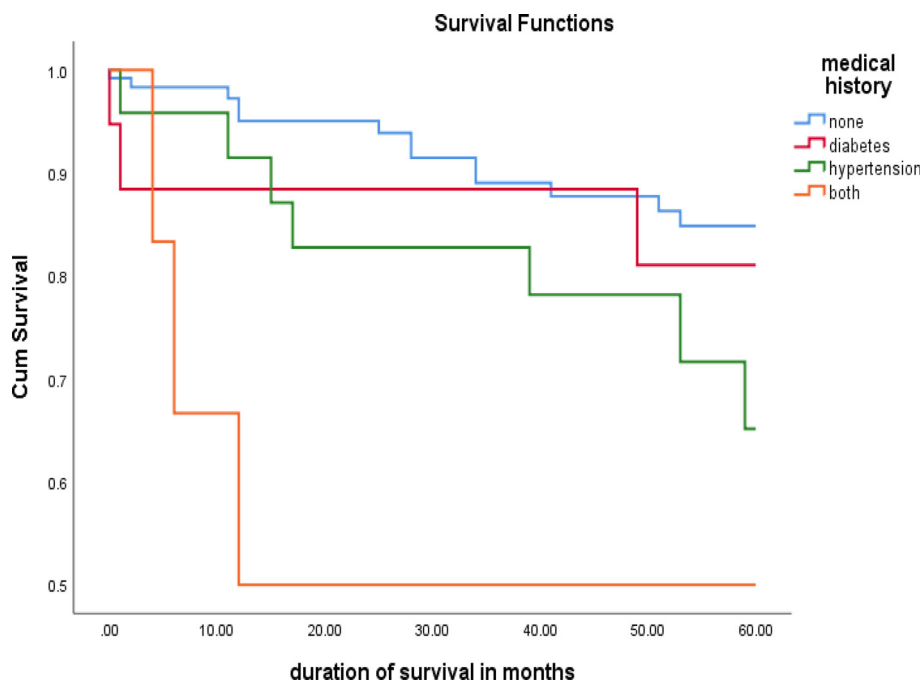


Figure 2. Survival rates for the study population according to presence and type of comorbidities.

A major limitation of this study is lack of proper documentation and relatively large number patients lost to follow-up. Inability to determine the survival status of some patients in the study population negatively impacts the internal and external validity of the study's main result - the cumulative survival probability -as well as the capacity to correlate the study's independent variables to patient survival.

A template or a format may be used to improve the quality of documentation in the future. At least two phone numbers should be requested from the patient to ensure adequate communication. It is also recommended that similar researches be conducted routinely for breast cancer for continuous assessment and improvement of healthcare.

Table 2. Mean survival period in months, cumulative survival probability and log rank significance test for the study population according to different characteristics.

Characteristic	Mean Survival	Overall Survival (%)	Significance test
AGE (in years)			
<40	56	88	
40–50	53	79	0.255
≥50	52	75	
PARITY			
Nulliparous	48	68	
Primiparous	57	95	0.069
Multiparous	54	82	
BMI			
underweight	48	69	
Normal	52	79	0.602
overweight	54	78	
obese	54	81	
LYMPH NODE STATUS			
Positive	56	84	0.232
Negative	58	94	
COMORBIDITY			
None	55	85	
Diabetes	52	81	0.028
Hypertension	50	65	
Both	34	50	

5. Conclusion

This study was done to improve understanding about the breast cancer situation in Sudan. The cumulative survival probability was found to be 79%. Diabetes and hypertension were found to negatively impact the survival of breast cancer patients, while undergoing radiotherapy improved survival. Late presentation is seen to be a problem in Sudan, and is hypothesized to be a cause of much of the disparity in survival between Sudan and countries of the developed world. This may be addressed by improving community awareness about the disease, introduction of self-examination concepts and provision of screening services.

Declarations

Author contribution statement

S. Elhassan: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

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Competing interest statement

The authors declare no conflict of interest.

Additional information

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