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RESEARCH ARTICLE

Patient delay impact on breast cancer survival at Khartoum Referral Hospital: a retrospective study [version 1; peer review: awaiting peer review]

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Abstract

Background: Breast cancer can be invasive and advanced at diagnosis causing enormous suffering and premature death. Delay to stage diagnosis and treatment is related to survival evaluation and several factors determine delay. The aim of the study was to examine predictor covariates associated with breast cancer delay and its impact on patient prognosis and survival.

Methods: This retrospective cross-sectional hospital-based study was carried out at Khartoum Oncology Hospital. Participants were 411 breast cancer patients diagnosed and treated during the period 2016. Patients' pathological and socio-demographic data were extracted from their medical files and delay data from telephone questionnaire survey and survival times calculated from follow-up. Fisher exact test, Cox and Logistic regression models were used to examine relationships between demographic, clinical and delay variables and survival outcome.

Results: The mean age of the study subjects was 50.07 years old and the majority were ≥ 45 years. Cancer delay analysis showed that there were different reasons for different types of delay but the majority of participants (86.2%) claimed fear of the disease and treatment and lack of information were real drivers of delay. The study confirmed the majority of participants expressed long delay estimated at 28.3 weeks and patient delay had a significant association with the advanced stage (P -value <0.05). The hazard ratio was four times for risk of dying from cancer for long delay compared to the short one.

Conclusion: The results of the study suggest delays at diagnosis and treatment are more common steps leading to advanced stage at diagnosis and poor survival. Early detection of the disease provides tremendous opportunities for early diagnosis, effective treatment and high chances of survival.

Keywords

Breast, cancer, stage, delay, survival, Sudan

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Introduction

Cancer is a major public health problem worldwide, particularly in low- and middle-income countries due to the aging population as well as wider social and environmental factors such as infectious disease, education and ethnicity.¹ There are observed variations in world cancer prognosis as mortality is higher among developing countries due to a lack of comprehensive early diagnosis, screening and effective medical treatment.² Cancer is a leading cause of death among women in both low- and middle-income and developed countries and the rate is rising.³ In Sudan, cancer can be described as of advanced stage at diagnosis and there is a noticeable delay at Khartoum Oncology Hospital (KOH), Khartoum, and National Cancer Institute (NCI), Wad Medani, central of Sudan, because patients come from all over the country, travelling long distance (hundreds of miles) looking for medical care.⁴ Some reports suggested that cancer mortality became the third highest cause of death.⁵

Breast cancer is an extensive cause of death among women in low- and middle-income countries even though it is potentially curable if detected early and treated effectively. In Sudan, according to KOH annual statistics, breast cancer represents more than 36% of all cancers in women in 2016 and is increasing steadily and remains the most important type of cancer. This alarming increase in breast cancer was attributed to changes in demography, economic and social factors, other disease factors and disease awareness.⁶ Breast cancer patients peak at an age less than 50 years old (premenopausal) and the majority are diagnosed at an advanced stage with invasive ductal carcinoma leading to poor survival.⁷

Previous related studies linked late diagnosis with the advanced stage at presentation.⁸ Though late stage at diagnosis is considered the main cause of poor survival, it has been explained by other risk factors, especially by delay at diagnosis and treatment.⁹ Delay is observed in all steps taken by women cancer patients along the journey from recognition of disease symptoms to completion of medical care.⁹ Cancer is a progressive disease and delays in disease progression overtime can lead to unfavourable opportunities of successful treatment of the more difficult to cure cancers at late stages. Delays to stage at diagnosis could lead to exasperating of the disease state and treatment complications.¹⁰

Early diagnosis improves breast cancer patient survival outcome by providing greater chances of effective treatment, at low cost and with optimal intervention.¹¹ It has been suggested that delay in starting diagnosis and treatment could reduce survival significantly.¹² The consequences of delays in diagnosis and treatment make the likelihood of dying from the disease increase by a large extent. Several studies have attempted to explain the relationship between patient survival and stage at diagnosis and delay.⁹ These studies came to different conclusions about the strength and the shape of these relationships and their impact. Socio-demographic attributes such as age, gender, education and ethnicity have also shown significant relationships with stage and delay.⁹

More recent research has demonstrated clearly the complexity of determining the shape of these relationships. Many variables have been suggested in explaining these relationships, however, there is no complete agreement on potential predictor covariates that gave overall explanations. Thus, it becomes of great importance to examine and evaluate barriers to early diagnosis and treatment. One can conclude that stage at diagnosis and delay are related to survival evaluation and assessment. Several factors determine stage at diagnosis and delay including socio-demographic factors, clinical features, availability and accessibility of adequate diagnostic and treatment facilities.¹³ Stage at diagnosis is critical to disease treatment since treatment plans are normally based on stage of the disease at diagnosis.¹⁴ The aim of the study was to examine barriers to early diagnosis and treatment and whether delays in diagnosis and treatment could negatively impact cancer patient prognosis and survival.

Material and methods

Ethical approval

The research has received ethical approval of concerned parties and Sudan Federal Ministry of Health (number: 3-10-2015, dated: 15/12/2015) on strict adherence to procedures of confidentiality, debriefing, counselling and additional information. The health ministry waived the consent of the study participants to use their clinical and personal information from their respective medical files due to the utmost urgency to ascertain the reasons behind the unprecedented surge in these most devastating killer diseases of women. No written consent was obtained from the participants during the telephone interview survey due to the fact that the majority of them were illiterate. The study does not require any form of medical procedures or sample taking.

Study design, setting and population

This is a retrospective cross-sectional hospital-based study. It was carried out at Khartoum Oncology Hospital, Sudan, which is the only referral hospital that provides a complete diagnostic and cancer treatment service where more than 80% of all Sudan cancer patients are registered.¹⁵ Available patient data was collected from the hospital's medical records during the study period of 2016.

The target population of the study was patients with breast cancer at the hospital. To be included in the study, patients had to be between 14 and 99 years old, be registered at the hospital, have complete medical records, histopathologically confirmed cancer and had received available treatment. Patients with incomplete medical records, unclear diagnosis and not treated at the hospital were excluded from the analysis. Written consent was obtained from the hospital to use participants' data. No direct contact was made with patients during this data collection level. However, the telephone questionnaire survey interview aimed at collecting data describing seeking medical care behaviour and delay was carried out by the researcher. Before carrying out the telephone interview, a piloted pre-test was conducted to ensure validity and reliability of the survey as a tool for collecting accurate information. Consent was obtained verbally from patients and/or next of kin after explaining the reasons behind the interview.

The total number of patients at the hospital during the study period who met the inclusion criteria and included in the analysis was 411. This sample size of randomly selected participants was calculated from the number of cancer patients of this hospital as follows:

The formula $n = 3.84 p(1-p) / (\text{precision})^2$

For breast cancer, proportion = 0.484 (report of Federal Ministry of Health 2015), precision = 0.0483 with 95% CI

$n = 3.84 * 0.484(1-0.484) / (0.0483)^2 = 411$

Data collection and sources

The study data collected from patients' medical records were checked and rechecked for accuracy, completion, duplication and consistency by the researcher with continuous assistance from the hospital medical staff. Active follow-up was carried out during the period of 2017 by the researcher through contacting patients and/or next of kin to ensure collection of needed information concerning patients' survival status data (dead or alive) and delay at first medical consultation, diagnosis and initiation of treatment. Moreover, a checklist was prepared by the researcher from the literature of cancer patients' survival and delay times concerning socio-demographic and clinical factors affecting survival to assist in needed data collection.¹⁶ Data collected from patients' medical files and telephone interview was arranged according to TNM staging system which describes the extent of cancer based on morphological attributes numerically into four basic stages (I, II, III, IV). The T stands for the size and extent of the primary tumor, N for regional lymph involvement and M for the presence or absence of distant metastasis.¹⁷

Variables

Data routinely collected concerning socio-demographic characteristics and clinical status of patients and delay data included age, education, occupation, marital status, urban/rural residential area, tribe, menopause status, stage at diagnosis, tumor grade, histological subtype, treatment modalities, residence state and close family relation with previous cancer disease history. Date of birth, death, loss of follow-up, diagnosis, first medical consultation, initiation of treatment, survival times and reasons for patient-related delay were checked by other information provided by hospital medical and statistical staff. This information was clearly defined in medical terms concerning certificate of death, confirmation of diagnosis and calculation of survival and delay times.

Statistical analysis

The statistical analysis is divided into two parts, descriptive and analytical using several statistical techniques and tools including the most widely used software packages such as SPSS, SAS and Stata. The study selected Stata version 11 (StataCorp, College Station, Texas) software for use in the analysis for its appropriateness in observational studies. In the descriptive analysis, visual presentation of data in tables given provides socio-demographic and clinical data in numbers, percentage, Fisher exact test and p-values as a clear indication of the study population data distribution, relationships and associations. Then, important statistical conclusions were drawn. Statistical methods such as Fisher exact test, logistic and Cox regression were, also, used to find out most prognostic factors associated with cancer disease stage and delay. Socio-demographic variables, stage and reasons for delay were tested by Fisher exact test. Delay, stage, age, socio-demographic variables and treatment modalities were tested using univariate and multivariate models. Delays in relation to stage at diagnosis in terms of overall survival were tested by Cox regression. The analysis focuses on stage at diagnosis as the most crucial prognostic predictor of breast cancer patient survival.

Results

Descriptive statistics

The mean age of participants was 50.07 years (SD = 13.35 at 95%CI = 48.77-51.36) with the majority (67.9%) of these patients being ≥ 45 years old. In total, (83.7%) of participants were married, (85.4%) were unemployed and (87.1%) were

Table 1. Reasons related to patient delay and association with all factors.

Factors	Total no. N(%)	Fear N(%)	Lack of information N(%)	Misdiagnosis N(%)	competing life priorities N(%)	Distance/Financial constraints N(%)	Fisher test, P-value
Patient time							
Short delay	164(39.9)	71(43.3)	70(42.7)	8(4.9)	10(6.1)	5(3.0)	3.45, 0.490
Long delay	247(60.1)	120(48.6)	93(37.7)	18(7.3)	9(3.6)	7(2.8)	
Stage ^a							
Early	150(36.5)	70(46.7)	58(38.7)	14(9.3)	3(2.0)	5(3.3)	7.109, 0.127
Advanced	261(63.5)	121(46.4)	105(40.2)	12(4.6)	16(6.1)	7(2.7)	
Age mean±SD	50.07±13.3	47.5±11.1	54.2±14.6	52.2±11.8	40.2±13.9	46.4±13.6	9.41 ^b , 0.000**
Tribe							
Non-Arab decent	183(44.5)	72(39.3)	89(48.6)	7(3.8)	6(3.3)	9(5.0)	21.87, 0.002*
Arab decent	219(53.3)	116(53.0)	69(31.5)	18(8.2)	13(5.9)	3(1.4)	
Others	9(2.2)	3(33.3)	5(55.6)	1(11.1)	0	0	
Occupation							
Non-employed	351(85.4)	148(42.2)	152(43.3)	22(6.3)	18(5.1)	11(3.1)	19.04, 0.001*
Employed	60(14.6)	43(71.7)	11(18.3)	4(6.7)	1(1.7)	1(1.7)	
Marital status							
Unmarried	67(16.3)	37(55.2)	22(32.8)	6(9.0)	1(1.5)	1(1.5)	4.92, 0.278
Married	344(83.7)	154(44.8)	141(41.0)	20(5.8)	18(5.2)	11(3.2)	
Education							
Illiterate	207(50.4)	48(23.2)	140(67.6)	8(3.9)	6(2.9)	5(2.4)	154.25, 0.000**
Low education	151(36.7)	106(70.2)	19(12.6)	14(9.3)	6(4.0)	6(4.0)	
High education	53(12.9)	37(69.8)	4(7.5)	4(7.5)	7(13.2)	1(2.0)	
Urban/Rural status							
Rural	47(11.4)	19(40.4)	23(48.9)	1(2.1)	2(4.3)	2(4.3)	3.39, 0.467
Urban	364(88.6)	172(47.2)	140(38.5)	25(6.9)	17(4.7)	10(2.7)	
Resident state							
Khartoum	99(24.1)	52(52.5)	31(31.3)	5(5.1)	8(8.1)	3(3.0)	28.17 0.059
Central	77(18.7)	34(44.1)	32(41.6)	7(9.1)	2(2.6)	2(2.6)	
Northern	68(16.5)	36(53.0)	23(33.8)	6(8.8)	3(4.4)	0	
Eastern	25(6.1)	16(64.0)	6(24.0)	3(12.0)	0	0	
Western	119(29.0)	43(36.1)	61(51.3)	5(4.2)	4(3.4)	6(5.0)	
Southern	23(5.6)	10(43.5)	10(43.5)	0	2(8.7)	1(4.3)	
Parent relationship							
First degree relation	296(72.0)	136(46.0)	112(37.8)	25(8.4)	16(5.4)	7(2.4)	12.16, 0.120
Relatives	56(13.6)	28(50.0)	24(42.9)	0	1(1.8)	3(5.3)	
Non relatives	59(14.4)	27(45.8)	27(45.8)	1(1.6)	2(3.4)	2(3.4)	
Total	411	191(46.5)	163(39.7)	26(6.3)	19(4.6)	12(2.9)	

*P-value <0.05 statistically significant relationship. **P-value < 0.001 highly statistically significant relationship.

^a% of invasive ductal carcinoma (74.8%). ^bOne way ANOVA test.

illiterate or had no formal education. Most of the participants resided in Western, Khartoum and Central states of Sudan (Table 1). The distribution frequency of breast cancer cases, according to TNM staging classification demonstrated that the majority (63.5%) of participants were at the advanced stage (III&IV), invasive ductal carcinoma (74.8%), with a high probability of spreading to distant organs (Table 2). Most of these tumors were of high-grade and moderately to poorly differentiated cells. Furthermore, most of these patients had first-degree relations with previous disease experience. Regarding different treatment modalities, (92.9%) of these participants received chemotherapy, (36.0%) surgery, (26.0%) hormone and (17.0%) radiotherapy, alone or in combination with other therapies. The analysis showed the reasons behind different types of delays such as fear of the disease and treatment, embarrassment, lack of information about the disease, competing life priorities, distance and financial constraints. The majority (86.2%) of these participants who were mainly patient-related delayed, claimed that fear and lack of information of the disease were the main reasons for delay. When these reasons claimed for delay were compared according to socio-demographic factors showed significant association with ethnicity, occupation, education and age group but not for the others (Table 1).

Regression analysis

The overall mean survival time interval after 12 months follow-up from time of diagnosis to the end of the study period, was 10.89 months at 95%CI (10.57 to 11.20) and the survival probability estimate was (30.0%). The median duration of delay time of the study participants was 12 weeks and 44.0 interquartile range (IQR) for patient delay, 3.29 weeks and 4.99 (IQR) for diagnostic delay, 0.43 weeks and 1.57 (IQR) for treatment delay and 23.0 weeks and 40.28 (IQR) for total delay. There was no significant association between short and long delays for different types of delays with the exception of diagnostic delay (Table 2).

Table 2. Association between delay and stage in relation to overall survival.

Factor	No. of subjects	Median of delay time (IQR)	HR(95%CI)	P-value
Patient-related delay				
Short delay	164	8.0(4.0)	1(reference)	-
Long delay	247	32.0(62.0)	1.45(0.77 to 2.70)	0.248
Total patient delay	411	12.0(44.0)		
Early stage	150	12.0(30.0)	1(reference)	
Advanced stage	261	12.0(44.0)	3.80(1.69 to 8.56)	0.001**
Diagnostic-related delay				
Short delay	358	3.0(3.71)	1(reference)	-
Long delay	53	19.29(15.36)	0.34(0.13 to 0.89)	0.028*
Total diagnostic delay	411	3.29(4.99)		
Early stage	150	3.86(4.62)	1(reference)	-
Advanced stage	261	3.14(5.06)	4.13(1.82 to 9.33)	0.001**
Treatment-related delay				
Short delay	401	0.45(1.22)	1(reference)	-
Long delay	10	16.93(15.86)	0.66(0.09 to 4.84)	0.684
Total treatment delay	411	0.43(1.57)		
Early stage	150	0.43(1.61)	1(reference)	-
Advanced stage	261	0.57(1.57)	3.72(1.65 to 8.36)	0.001**
Total-related delay				
Short delay	75	9.14(4.40)	1(reference)	-
Long delay	336	28.36(42.43)	0.67(0.33 to 1.35)	0.261
Total delay	411	23.0(40.28)		
Early stage	150	19.72(40.04)	1(reference)	-
Advanced stage	261	24.71(4.01)	3.76(1.67 to 8.46)	0.001*

HR: Hazard ratio, CI: confident interval, IQR: Interquartile range.

*P-value < 0.05 statistical significant association.

**P-value < 0.001 highly statistical significant association.

The median of patient-related delay time interval was eight weeks (range 0.70-10.0) and 4.0 (IQR) for short delays, 32 weeks (range 12.0-260.0) and 62.0 (IQR) for long delays and 12 weeks (range 0.70-260.0) and 44.0 (IQR) for total delay (Table 2). The patient delay had a strong significant association with the advanced stage at diagnosis (p-value < 0.001) in relation to overall survival. The hazard ratio which measures the risk of dying from cancer was approximately four times at the advanced stage at diagnosis for long delay compared to the short one. In a univariate single predictor regression, the advanced stage at diagnosed indicated strong association with patient delay, but not in a multivariate logistic regression analysis (Table 3). Patient delay can be described mainly as long since 60% of all these patients experienced long delay and most likely related to the advanced stage at presentation.

Table 3. Univariate and multivariate regression models for association between patient delay and all factors.

Factor	Univariate model		Multivariate model	
	OR(95%CI)	P-value	OR(95%CI)	P-value
Age	1.01(0.99 to 1.02)	0.407	1.004(0.99 to 1.02)	0.703
Stage				
Early	1(reference)		1 (reference)	
Advanced	0.64(0.42 to 0.98)	0.040*	0.65(0.40 to 1.05)	0.076
Treatment				
Surgery	1.05(0.69 to 1.58)	0.825	0.93(0.59 to 1.46)	0.739
Chemotherapy	1.07(0.49 to 2.29)	0.866	1.82 (0.71 to 4.65)	0.214
Radiotherapy	1.33(0.78 to 2.29)	0.293	1.53(0.86 to 2.72)	0.147
Hormonal	1.49(0.94 to 2.36)	0.088	1.59(0.91 to 2.80)	0.101
Residence state				
Khartoum	1(reference)		1(reference)	
Central	0.90(0.49 to 1.65)	0.743	0.91(0.48 to 1.72)	0.778
Northern	0.81(0.43 to 1.51)	0.506	1.16(0.58 to 2.36)	0.671
Eastern	0.63(0.26 to 1.51)	0.297	0.66(0.26 to 1.65)	0.371
Western	1.29(0.74 to 2.23)	0.366	1.37(0.71 to 2.66)	0.348
Southern	1.92 (0.69 to 5.29)	0.207	2.03(0.67 to 6.12)	0.211
Urban/Rural status				
Rural	1(reference)		1(reference)	
Urban	1.84(0.99 to 3.39)	0.050	1.99(1.001 to 3.95)	0.050
Education				
Illiterate	1(reference)		1(reference)	
Low education	0.77(0.50 to 1.18)	0.226	0.69(0.42 to 1.13)	0.141
High education	0.76(0.41 to 1.39)	0.372	0.56(0.26 to 1.22)	0.145
Marital status				
Unmarried	1(reference)		1(reference)	
Married	1.02(0.59 to 1.74)	0.942	0.94 (0.53 to 1.68)	0.844
Tribe				
Non Arab decent African	1(reference)		1(reference)	
Arab decent African	0.71(0.47 to 1.06)	0.091	0.80(0.47 to 1.38)	0.429
Others	1.10 (0.27 to 4.55)	0.894	1.08 (0.25 to 4.71)	0.922
Occupation				
Non employed	1(reference)		1(reference)	
Employed	1.66(0.092)	0.092	1.87(0.96 to 3.65)	0.066

*P-value < 0.05 statistical significant association, OR: Odds Ratio, CI: confident interval.

Both diagnostic- and treatment-related delays showed no significant associations with all factors, with the exception of diagnostic-related delay with chemotherapy treatment (Tables 4 and 5). They also revealed short delay estimated at (86.6%) and (97.5%) of patients experience, respectively. In contrast total delay demonstrated significant association only with Western state and high education in a univariate analysis and Southern state in a multivariate analysis. These results mean that there was a considerable amount of delay among breast cancer patients, since long delay was observed among (81.7%) of all these patients estimated at 28.36 weeks (198 days).

Table 4. Univariate and Multivariate regression models for association between diagnostic delay and all factors.

Factor	Univariate model		Multivariate model	
	OR(95%CI)	P-value	OR(95%CI)	P-value
Age	0.99(0.97 to 1.01)	0.381	0.98(0.96 to 1.01)	0.187
Stage				
Early	1(reference)		1(reference)	
Advanced	1.25(0.68 to 2.32)	0.474	1.51(0.73 to 2.99)	0.269
Treatment				
Surgery	1.19(0.66 to 2.16)	0.557	1.33(0.69 to 2.56)	0.386
Chemotherapy	0.35(0.15 to 0.84)	0.018*	0.13(0.04 to 0.45)	0.001*
Radiotherapy	1.33(0.65 to 2.73)	0.441	1.09(0.51 to 2.37)	0.817
Hormonal	0.99(0.52 to 1.91)	0.985	0.59(0.25 to 1.42)	0.237
Residence state				
Khartoum	1(reference)		1(reference)	
Central	0.84(0.33 to 2.17)	0.720	0.96(0.35 to 2.59)	0.932
Northern	1.11(0.44 to 2.79)	0.831	0.91(0.32 to 2.59)	0.862
Eastern	1.38(0.40 to 4.71)	0.606	1.59(0.43 to 5.95)	0.483
Western	1.29(0.59 to 2.83)	0.522	2.06(0.79 to 5.41)	0.142
Southern	0.69(0.14 to 3.32)	0.644	1.23(0.22 to 6.83)	0.812
Urban/Rural status				
Rural	1(reference)		1(reference)	
Urban	0.69(0.30 to 1.56)	0.372	0.73(0.29 to 1.86)	0.513
Education				
Illiterate	1(reference)		1(reference)	
Low education	1.09(0.58 to 2.09)	0.776	1.11(0.53 to 2.33)	0.788
High education	1.77(0.79 to 3.98)	0.165	2.06(0.71 to 6.01)	0.184
Marital status				
Unmarried	1(reference)		1(reference)	
Married	0.95(0.44 to 2.04)	0.886	0.86(0.37 to 2.00)	0.736
Tribe				
Non Arab decent African	1(reference)		1(reference)	
Arab decent African	1.39(0.77 to 2.53)	0.275	1.93(0.87 to 4.31)	0.108
Others	1.02(0.12 to 8.57)	0.986	1.79(0.19 to 16.45)	0.608
Occupation				
Non employed	1(reference)		1(reference)	
Employed	0.88(0.38 to 2.04)	0.759	0.79(0.30 to 2.08)	0.634

*P-value < 0.05 statistically significant association.

Table 5. Univariate and Multivariate regression models for association between treatment delay and all factors.

Factor	Univariate model		Multivariate model	
	OR(95%CI)	P-value	OR(95%CI)	P-value
Age	1.02(0.97 to 1.06)	0.467	0.99(0.93 to 1.05)	0.709
Stage				
Early	1(reference)		1(reference)	
Advanced	0.37(0.10 to 1.35)	0.132	0.32(0.07 to 1.53)	0.154
Treatment				
Surgery	1.19 (0.33 to 4.29)	0.790	0.75(0.17 to 3.29)	0.702
Chemotherapy	0.29(0.06 to 1.43)	0.128	0.10(0.01 to 1.45)	0.091
Radiotherapy	2.14(0.54 to 8.47)	0.280	3.64(0.69 to 19.16)	0.127
Hormonal	0.69(0.14 to 3.29)	0.638	0.15(0.01 to 1.90)	0.142
Residence state ^a				
Khartoum	1(reference)		1(reference)	
Central	3.97(0.41 to 38.97)	0.236	3.53(0.31 to 39.55)	0.307
Northern	6.13(0.67 to 56.05)	0.109	5.44(0.51 to 58.34)	0.161
Eastern	-		-	
Western	1.68(0.15 to 18.75)	0.675	5.33(0.36 to 79.43)	0.224
Southern	-		-	
Urban/Rural status				
Rural	1(reference)		1(reference)	
Urban	1.17(0.14 to 9.42)	0.885	1.56(0.16 to 14.90)	0.701
Education				
Illiterate	1(reference)		1(reference)	
Low education	1.09(0.29 to 4.16)	0.889	1.08(0.22 to 5.20)	0.928
High education	0.78(0.09 to 6.79)	0.820	0.79(0.05 to 13.85)	0.875
Marital status ^b				
Unmarried	1(reference)		1(reference)	
Married	-		-	
Tribe ^c				
Non Arab decent Arican	1(reference)		1(reference)	
Arab decent African	7.80(0.98 to 62.15)	0.052	6.95(0.55 to 87.53)	0.134
Others	-		-	
Occupation				
Non employed	1(reference)		1(reference)	
Employed	0.64(0.80 to 5.18)	0.679	0.72(0.06 to 8.87)	0.801

^aAll patient from Eastern and Southern states have short delay only and predicted probability of long delay would have to be zero.

^bOmitted because of collinearity.

^cAll patient from other tribe have short delay only and predicted probability of long delay would have to be zero.

These different delays results confirmed strong evidence of the association between long delay and advanced stage at diagnosis. This long delay was most likely related to patient delay. Though there was no clear association between long delay and survival outcome, the association between long delay and advanced stage was strong in relation to overall survival. The progression of the disease to the advanced stage due to long delay could lead to poor prognosis, outcome, limited and complicated treatment options.

Table 6. Univariate and Multivariate regression models for association between total delay and all factors.

Factor	Univariate model		Multivariate model	
	OR(95%CI)	P-value	OR(95%CI)	P-value
Age	1.02(0.99 to 1.04)	0.054	1.02(0.99 to 1.04)	0.179
Stage				
Early	1(reference)		1(reference)	
Advanced	1.12(0.67 to 1.88)	0.666	1.19(0.66 to 2.14)	0.573
Treatment				
Surgery	0.71(0.43 to 1.18)	0.185	0.71(0.39 to 1.25)	0.233
Chemotherapy	0.49(0.15 to 1.69)	0.262	0.65(0.16 to 2.58)	0.537
Radiotherapy	0.97(0.50 to 1.89)	0.939	1.08(0.53 to 2.19)	0.833
Hormonal	1.29(0.71 to 2.32)	0.404	1.47(0.74 to 2.93)	0.274
Residence state				
Khartoum	1(reference)		1(reference)	
Central	1.52(0.73 to 3.17)	0.264	1.51(0.69 to 3.25)	0.294
Northern	1.58(0.73 to 3.41)	0.247	1.80(0.75 to 4.35)	0.189
Eastern	1.07(0.38 to 2.98)	0.897	1.01(0.34 to 2.96)	0.985
Western	2.03(1.02 to 4.02)	0.043*	2.09(0.91 to 4.77)	0.081
Southern	7.43(0.95 to 58.0)	0.056	8.63(1.03 to 72.26)	0.047*
Urban/Rural status				
Rural	1(reference)		1(reference)	
Urban	1.24(0.59 to 2.62)	0.568	1.68(0.71 to 3.97)	0.235
Education				
Illiterate	1(reference)		1(reference)	
Low education	0.62(0.38 to 1.14)	0.135	0.77(0.41 to 1.46)	0.430
High education	0.47(0.23 to 0.97)	0.042*	0.73(0.29 to 1.83)	0.501
Marital status				
Unmarried	1(reference)		1(reference)	
Married	0.75(0.37 to 1.55)	0.443	0.59(0.27 to 1.26)	0.169
Tribe				
Non Arab decent African	1(reference)		1(reference)	
Arab decent African	0.73(0.44 to 1.22)	0.227	0.92(0.48 to 1.78)	0.808
Others	1.51(0.18 to 12.51)	0.704	1.94(0.21 to 17.85)	0.559
Occupation				
Non employed	1(reference)		1(reference)	
Employed	0.78(0.59 to 1.52)	0.459	0.94(0.43 to 2.03)	0.870

*P-value < 0.05 statistically significant association.

Discussion

Various factors contribute to the differences in breast cancer survival rates at the global and regional levels. Determining drivers of these disparities is complicated and no comprehensive studies looking at this to date. However, stage, clinical features, quality of treatment and delay are the most likely accepted explanation for these differences.⁹ Breast cancer survival depends mainly on early detection and effective treatment modalities.^{10–12,18,19} Thus, by examining this survival through the eyes of prevention and control of the disease at diagnosis, one can make assessment and evaluation of the potential covariates which have the most effect on patient survival. This study focused on stage at diagnosis and delays as the most important potential predictor covariates of survival. The results showed that these breast cancer patients were

relatively young, married, unemployed, illiterate and belonged to non-Arab decent African groups. Breast cancer, in Sudan, is described as advanced at presentation and grade, aggressive and invasive ductal carcinoma and moderately to poorly differentiated cells leading to poor survival. Several previous studies reached the same conclusion of the disease as being invasive, advanced at presentation and delayed at diagnosis.^{5,15,20–25} The stage at diagnosis and delay are much related to survival and cancer survival and delay analysis measure these relationships and the effectiveness of the medical care system.

This study showed clearly that advanced stage presentation at diagnosis and long delay had a significant effect on survival outcome compared to the early stage. This conclusion agrees with previous studies in different parts of developed and low- and middle-income countries.^{12,18,26–28} The study provided an adequate explanation for the significant association between the advanced stage at diagnosis and long delay and expected poor survival. The consequences of breast cancer delay are most likely would lead to greater risks of death as the disease progresses overtime. In this sense, delay could affect prognosis and survival outcome.

Patient-related delay was observed to be mostly long and related to the advanced stage at diagnosis. This clear conclusion is in concert with several previous studies.^{29–31} Reasons for this patient-related delay were clearly explained in terms of fear of disease and treatment and lack of disease awareness. Many other studies showed similar reasons for patient-related delay.^{25,31–34} The study explained factors associated with patient delay reasons for delay as education, employment, ethnicity, and age group.^{35–39} One Sudanese breast cancer study revealed no such association between delay and several socio-demographic factors.^{40,41} However, there are other studies that showed an association between delay and socio-demographic and other variables such as distance, lack of medical care and early detection.^{18,42–44} Though there was no consensus on the exact shape and strength of the relationship between delay and prognosis and survival, more than three months delay was accepted as the major cause of the advanced stage at diagnosis. For breast cancer, effective control measures are generally available and affordable. This disease can be, to a large extent, prevented by screening and treating pre-cancerous lesions. Other than this, early detection of breast cancer is imperative to improve treatment outcomes. Assessment of the study conclusion should be interpreted with relative caution since the study was based on retrospectively collected data from a referral hospital with the largest registration of cancer patients in the country. It does not include all data of breast cancer patients and is limited by the type and quality of available data. Due to differences in setting between countries, one would expect the outcome not to be similar.

Conclusions

The results of the study suggest that stage at diagnosis and delay are important covariates affecting survival and prognosis. The evidence presented has shown the complexity of determining exactly what drives variations in cancer outcome. It is most likely all steps the cancer patient takes when looking for medical care contribute to some degree or another to differences in breast cancer survival rates.

Delay at diagnosis can affect the disease level of stage classification, negatively. Long patient delay has significant association with the advanced stage at diagnosis. Breast cancer current bleak situation can be reversed by early detection and prompt treatment. Early detection of cancer provides tremendous opportunities for early diagnosis, screening, more effective treatment and better chances of survival outcome.

Government intervention to reduce the suffering of breast cancer patients is of vital importance by providing diagnostic and oncological services in all general public hospitals and the introduction of oncology units in all states capital's public hospitals. Early detection of breast cancer should be the core of a proposed woman cancer strategy through providing intensive and comprehensive breast cancer screening and raising disease awareness among female patients.

Data availability

Underlying data

Zenodo: Elgoraish, Amanda, & Alnory, Ahmed. (2021). breast cancer dataset. <https://doi.org/10.5281/zenodo.5150469>.⁴⁵

This project contains the following underlying data:

- breast cancer2016 1.xlsx

Extended data

Zenodo: Elgoraish, Amanda, & Alnory, Ahmed. (2021). breast cancer questionnaire. <https://doi.org/10.5281/zenodo.5150476>.⁴⁶

This project contains the following extended data:

- Questionnaire.docx

Data are available under the terms of the [Creative Commons Attribution 4.0 International license](#) (CC-BY 4.0).

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