Survival and Predictors of Mortality among Breast Cancer Patients Diagnosed at Hawassa Comprehensive Specialized and Teaching Hospital and Private Oncology Clinic in Southern Ethiopia: A Retrospective Cohort Study

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Abstract

Background: Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death in over 100 countries. Despite the high burden of the problem, the survival status and the predictors for mortality are not yet determined well in Ethiopia. Therefore, we aimed to determine the survival and predictors of mortality among breast cancer patients diagnosed from 2013-2018 at Hawassa comprehensive specialized and teaching hospital and private oncology clinic in Southern Ethiopia.

Methods: Hospital-based retrospective cohort study of 302 patients was conducted. Data was collected on breast cancer patients diagnosed from January, 1st, 2013 to December, 30th, 2018 using a data extraction checklist and by telephone interview. The median survival was estimated by Kaplan- Meier. Log Rank test was used to compare survival among groups. Cox proportional hazards model was used to identify predictors. Results were repaired as hazard ratio (HR) along with the corresponding 95% CI. Sensitivity analysis was done with the assumption of loss to follow-ups (LTF) might die 3 months after the last hospital visit.

Results: Advanced stage diagnosis of breast cancer was found on 83.4 % of patients with breast cancer. The study participants were followed for a total of 4685.62 person-months. Their median survival was 50.61 months (IQR=18.38-50.80) which declined to 30.57 months in the worst-case analysis (WCA). The overall survival of patients at two years was 73.2% and it declines to 51.3 % in the worst-case analysis. Rural residence (AHR=2.71, 95% CI: 1.44, 5.09), travel time ≥7 hours (AHR=3.42, 95% CI: 1.05, 11.10), duration of symptom 7-23 months (AHR=2.63, 95% CI: 1.22, 5.64), > 23 months (AHR=2.37, 95% CI: 1.00, 5.59), advanced stage (AHR=3.01, 95% CI: 1.05, 8.59) and not taking chemotherapy (AHR=6.69, 95% CI: 2.20, 20.30) were independent predictors of death.

Conclusion: Above two-third of the patients have two years of overall survival in south Ethiopia. Rural residence, advanced stage, and poor adherence to chemotherapy were independent predictors of death. Thus, Improving early detection, diagnosis, and treatment capacity of breast cancer patients are an important way-outs to avert the problem with appropriate intervention means.

Background

Globally the newly diagnosed female breast cancer (BC) by 2018 was estimated to be 2.1 million accounting for almost 1 in 4 cancer cases among women. It is the most frequently diagnosed cancer in the vast majority of the countries and is also the leading cause of cancer death (1, 2).

Incidence rates vary greatly in transitioned compared with transitioning economies. It was 19.3 and 89.7 per 100,000 women in Eastern Africa and Western Europe respectively. However, the differences in mortality between these 2 regions are smaller because of a higher case fatality in low to middle-income countries (1).

In Ethiopia, the annual incidence of cancer is around 60,960 cases and its annual mortality is over 44,000 accounting for about 7 % of mortality (3). BC was the most prevalent cancer in Ethiopia among adults (30.2%), followed by cervical cancer (13.4%) and colorectal cancer (5.7%). The estimated prevalence of BC cases in 2015 was 13,987 with a crude incidence rate of 28.2 per 100,000. The trend of BC has significantly increased year to year among females than males (4, 5).

In many countries with advanced medical care, the five-year survival rate of early-stage breast cancers is 80–90 percent, while it falls to 24 percent for advanced stage(6). Five-year survival was 89% in Hawaii, 7.3% in Brazil, 67.6% in Iran, 63% in Mexico (7-10), and 51.8% in Uganda, 24% in Nigeria (11, 12). The only available studies in Ethiopia show that it is far below other developed and developing countries. The overall 5-year metastatic free survival (MFS) is 46% and the overall 2-year survival of patients with BC is 53% in rural Ethiopia(13, 14).

Scholars are warning, unless urgent action is taken, BC will compound Sub-Saharan Africa's disease burden, increase poverty and gender inequality as well as reverse the current global gains against maternal and neonatal mortality (15).

United nation had planned to reduce premature mortality from non-communicable diseases including cancer by one third by 2030 (16). In line with this, Ethiopia had drafted a national cancer control program (NCCP) in 2016(2). However, even if there is a focus to expand to the other six additional centers, there is only one radiation therapy center in Tikur Anbesa Specialized Hospital (TASH) in the capital and very limited chemotherapy centers at the national level (14). To achieve the goals of global and national programs, knowing the breast cancer patient's overall survival and its predictors will have paramount importance. Surveillance of cancer survival is also seen as vital by stakeholders. It is being used to formulate cancer control strategies, to prioritize cancer control measures, and to assess both the effectiveness and cost-effectiveness of those strategies (17). However, little is known about this issue in Ethiopia. As to the knowledge of the authors, there is only one study on the overall survival of BC in the country. Hence, this study could fill the information gap by estimating overall survival and identifying its predictors in settings that have adjuvant systemic therapies. Moreover, it will beused as a baseline for future comparison or evaluation of the progress in the quality of BC care and treatment, and it could be important for health programmers, health professionals and future researchers.

Methods

Study area and approach

A hospital-based retrospective cohort study was conducted at oncology units of Hawassa University Comprehensive Specialized Hospital (HUCSH) and Yanet Internal Medicine Specialized Center (YIMSC) which are found in Hawassa, SNNP Regional State of Ethiopia, 273km far from Addis Ababa. Both of the health facilities provide diagnostic, surgical, and chemotherapy treatment services for cancer patients including breast cancer. They are also used as referral centers for all cancer cases in the southern region

of the country. They referred cases to Tikur Anbesa specialized hospital (Addis Ababa) for radiotherapy for who can afford the service.

Sampling and data collection procedures

A total of 302 BC patient charts diagnosed from January, 1st, 2013 to Dec, 30th, 2018 was extracted and patients or their relatives are contacted by telephone. Out of 302 patients with BC, the phone number is not found on 13 patient cards. Among 289 cards that have a telephone number, a telephone interview was made with 206 patients or with their close relatives who are > 18 years of age. The rest of the phone call trials were not successful with three and more trials. There was a language barrier with two of them, 6 of them didn't respond for three call trials, 16 were mistaken phone numbers, and the remaining were not functional. (see fig. 1).

Variables and operational definitions

The dependent variable was time to death. Independent variables include 1) socio-demographic data: age, place of residence, marital status, level of education, religion, travel time to hospital and occupation 2) Clinical and pathological characteristics of the disease: duration of symptom, stage of BC at diagnosis, tumor size, histological type, nodal status, nuclear grade, and distant metastasis, 3) Type of BC therapy: Adherence to chemotherapy, surgical therapy and hormonal therapy 3) Co-morbidities: HIV, hypertension, diabetes mellitus, Asthma.

Event (failure): patient death regardless of its cause. In the worst-case analysis, LTF patients that are unavailable by telephone calls are considered as they developed events after 3 months of the last date of hospital visit (13, 14).

Lost to follow up (LTF): patients that are lost from follow up for > 6 months.

Good adherence to chemotherapy: when patients had completed all cycles of chemotherapy as per the guideline(18).

Poor adherence to chemotherapy: when patients didn't complete all cycles of chemotherapy as per the guideline(18).

Main analysis: analysis of LTF patients as left-censored and alive.

Worst-case analysis: analysis of LTF patients by assuming as they developed the event 3 months after the last date of hospital visit (13, 19)

Survival time: The total time the patient had survived without developing the outcome after diagnosis,

Censored: patients that are alive at the end of the study are right-censored, those who developed the event or LTF are left-censored.

Follow up time: time from date of entry to date of death or end date.

Measurements

The stage of BC was determined by the American Joint Committee on Cancer staging system AJCC (seventh edition) using the information on tumor size (T) and nodal status (N) and metastasis (M) (20). Two observations were used for this regard; TNM staging at the time of diagnosis and the last follow up to confirm the progression of the disease. Tumor size was primarily ascertained by clinical examination of the oncologist, if not available it was obtained from a biopsy. Histological type and nuclear grading were taken from biopsy results.

Patients with non-metastatic BC were treated with 8 cycles of adjuvant chemotherapy; 4 cycles of AC (Adriamycin + Cyclophosphamide) and four cycles of Taxol. Those with metastatic BC are treated with 6 cycles of AC. The current status of patients (alive or dead) was confirmed by telephone or taken from the chart or if the patient has a follow-up after the end date of the study, she was registered alive.

Data collection tools and procedure

A structured record review checklist was developed after a review of the literature and by assessing the availability of information from patients' cards. For a telephone interview, a questionnaire was prepared based on the required information in English and translated to local languages (Amharic, Sidama, and Affan Oromo) and then back to English to maintain consistency by experts.

Primarily, all cards of patients with BC were identified by their medical record number, reviewed for eligibility, and the information was extracted. A phone call to patients with BC was made to assure their current status, whether they are alive or dead.

Data analysis procedures

The data were analyzed by STATA V.14 software. The overall survival was estimated by the Kaplan- Meier curve. A log-rank test was used to compare survival among groups with a confidence interval of 95%. The assumptions of the Cox proportional hazard regression model are checked by Log (-log (St) plots, Schoenfeld residual test. Covariates that did not violate the assumption test and have 25 % ($p<0.25$) significant level on bivariate Cox regression were considered for multivariable analysis. Breslow test was used to handle tied failures. A P-value of < 0.05 was considered to denote statistical significance. Multi-collinearity and interaction for the main effect model were checked, and the variance inflation factor greater than 10 was considered to denote its existence. Finally, the goodness of fit of the model was assessed by the Cox-Snell residual plot.

Ethical consideration

Ethical clearance was obtained from Addis Ababa University, College of Health Sciences, School of Public Health, Research and Ethical Committee (REC). After an in-depth explanation of the aim of the study,

formal permission was obtained from HUCSH and YIMSC to review patient records and contact patients on a phone call. Verbal consent was obtained by telephone from patients and patients who are died of it were obtained from the patient's relatives (father, mother, husband, or children > 18 years).

Results

Patient's characteristics with breast cancer

There were 337 patients with BC diagnosed from 1st January- 2013 to 30, Dec 2018 in HUCSH and YIMSC. Out of 302 patients included in the study, a telephone interview was made with 206 patients or their relatives. The second review of patient charts was made after two months of the beginning of data collection and 29 patients that are unavailable by telephone call had visited the hospitals during the second review time and thus, they were confirmed alive. Therefore, out of 302 BC patients, the outcome of 235 (77.8%) patients was confirmed (168 were alive, 67 have died), 57 (18.8%) patients were LTF and the rest 10 patients have visited the hospital within 6 months before the end date of the study. Out of 141 alive patients contacted by telephone, 101 (71.6%) reported they were working their usual job, 35 (24.8%) were ambulatory, 5 (3.5%) were bedridden. All relatives of deceased patients with BC believe the cause of patients' death was BC.

Socio-demographic and clinical characteristics

Out of 263 patients, 189 (71.8%) of them were from urban areas. Their median travel time to Hawassa cancer treatment units is 2 hours (IQR=0.30-3.30 hours). Out of 302 women with BC recruited to this study, the majority of them, 177(58.6%) were within the age of 35-50 years, the median age being 39 (IQR=32-45) years, 79.1% of them were pre-menopause. Out of 208 patients, majorities 178 (85.6%) were married, 108 (51.9%) were house wife's and 78 (37.5%) can't read and write. Two hundred eleven (69.9%) of patients were diagnosed within the years 2016-2018 and the rest within 2013-2015. About one-third of BC patients, 208 (73.5%) came with complaints of a breast lump, and 171 (60.4%) were presented to the oncology unit within 7-23 months of a complaint. Out of 196 patients whose tumor grade is available 109 (56.2%) were grade II (moderately differentiated). Out of all 302 BC patients, 50 (16.6%) were early stage, 252 (83.4%) were presented with advanced stage at the first hospital visit, 161(53.3%) were stage III and 91(30.1%) were stage IV. About 173 patients (58.8%) had tumor size III/IV, 249 (83.4%) had ductal carcinoma, 240 (84.2%) had positive lymph node, and 56 (18.54%) had distance metastasis at the time of diagnosis. Thirty-five (11.5%) patients have comorbidity out of which, 23(7.6%) have hypertension, and 5 (1.6%) have HIV (Table 1).

Table 1: Socio-demographic and tumor characteristics of patients with breast cancer in HUCSH & YIMSC, 2013-2018.

Covariates	Frequency	Percentage
Resident		
Urban	189	71.86
Rural	74	28.14
Total	263	100
Travel time		
< 3 hours	197	74.9
3-6 hours	51	19.39
≥ 7 hours	15	5.7
Total	263	100
Age		
<35	82	27.15
35-50	177	58.61
>50	43	14.24
Total	302	100
Menopausal status		
Pre-menopause	239	79.1
Post-Menopause	63	20.86
Total	302	100
Breast complain at the first visit		
Breast lump	208	73.5
Breast ulcer	34	12.01
Other #	41	14.49
Total	283	100
Duration of symptom		
0 - 6 months	110	38.87
7 - 23 months	112	39.58
> 23 months	61	21.55
Total	283	100

Histological type		
Ductal	249	82.45
Lobular	24	7.95
Other*	24	8.08
Total	297	100
Stage of BC		
Early	50	16.55
Advanced	252	83.44
Tumor size		
TI/II	121	41.16
TIII/IV	173	58.84
Total	294	100
Distant -metastasis		
Yes	56	18.54
No	246	81.45
Total	302	100
Nodal status		
Positive	240	84.21
Negative	45	15.79
Total	285	100
Co-morbidities		
Yes	35	11.59
No	267	88.41
Total	302	100

NB: *#=shortness of breath, axillary swelling, nipple retraction, nipple discharge.* *******=Mixed ductal & lobular, mucinous*

The diagnosis and treatment given to the patients

One hundred twenty-eight (45.7%) patients had referral paper from another hospital and 69 (22.8%) are referred after they had surgery. A total of two hundred eight patients with BC were treated with breast

surgery. Out of 190 patients with BC whose type of surgery is available on their chart, 173(91.05%) of them underwent MRM. Chemotherapy was administered for 219 BC patients, out of this, 54(24.7%) had completed the treatment (good adherence) while 138 (63.0 %) had discontinued (poor adherence) and 27 (12.3 %) were on schedule at the time of data collection. Out of 100 patients with BC that took hormonal therapy, 65(65%) were treated with Tamoxifen. Eight patients with BC had taken radiation therapy at Tikur Anbesa Specialized Hospital (table 2).

Table 2: Breast cancer therapies and other characteristics of patients with breast cancer in HUCSH & YIMSC, 2013-2018.

Covariates	Frequency	Percent
Surgical therapy		
Yes	208	68.87
No	94	31.13
Total	302	100
Type of surgery		
MRM	173	57.28
Toilet mastectomy	17	5.63
No surgery	112	37.09
Total	302	100
ACT		
Good adherence	54	19.64
Poor adherence	138	50.18
No chemotherapy	83	30.18
Total	275	100
Hormonal therapy		
Yes	100	33.12
No	202	66.89
Total	302	100
Hormonal therapy type		
Tamoxifen	65	21.52
Anastrazole	35	11.59
No hormonal therapy	202	66.89
Total	302	100
Recurrence		
Yes	22	7.28
No	280	92.72
Total	302	100
Progression		

Yes	40	13.25
No	262	86.75
Total	302	100

NB: ACT: *Adherence to chemotherapy*

Out of 57 LTF patients, 55 (96.4%) have an advanced-stage of BC. Among these, 28 (49.1%) of them have stage IV disease, and 21 (36.8%) have distant metastasis at the time of diagnosis. The majority of them, 39 (68.4%) had breast surgery, even if 35 (61.4%) of them started chemotherapy, only 6 (10.5%) have had good adherence, only 9 (15.8%) were started hormonal therapy. For 84.2 % of them, their last date of contact was before the end of 2017.

Survival status of the patients with breast cancer

A total of 302 BC patients had followed for 4685.61person-months or at-risk time. There were 67 confirmed deaths during the follow-up period which is 72 months. The median follow-up time was 50.61 (IQR=18.38-50.80) months. The overall survival of BC patients at the end of one, two, and three years is 83%, 73.2 %, and 63.1%, respectively. The overall survival for the early and advanced stages of BC at the end of 2 years was 89.9 % and 63.8 %, while it is 73.4% and 44.3% for stage III and IV respectively (see table 3).

Table 3: Log-rank test for equality of survival function of patients with breast cancer diagnosed in HUCSH and YIMSC from 2013-2018 in Southern Ethiopia, 2020

Covariates	Survival time		Observed death	Expected death	X^2 (df)	Log-rank test ($Pr > X^2$)
	2 years	3 years				
Overall survival	73.2 (65.8, 79.3)	63.0 (53.3, 71.2)				
Residence						
Urban	80.1 (71.6, 86.3)	71.4 (80.0, 60.1)	36	52.13	24.5 (1)	**<0.001**
Rural	50.5 (34.2, 64.7)	27.5 (07.4, 52.6)	30	13.87		
Age in years						
<35	61.5 (43.9, 75.0)	56.7 (38.2, 71.6)	23	14.06	7.93 (2)	**0.019**
35-50	76.0(66.5, 83.1)	70.2 (58.9, 78.9)	34	43.65		
>50	81.5 (63.0, 91.3)	48.8 (21.1, 71.8)	10	9.28		
Stage of BC						
Early	95.1 (81.9, 98.7)	89.8 (69.3, 96.9)	5	17.52	12.76 (1)	**<0.001**
Advanced	67.4 (58.5, 74.8)	55.6 (44.1, 65.6)	62	49.48		
Nodal status						
Positive	70.9 (62.3, 77.8)	58.9 (47.4, 68.7)	57	48.74	7.75 (1)	**0.005**
Negative	95.0 (69.4, 99.2)	87.6 (58.1, 96.8)	3	11.26		
Surgical therapy						
Yes	78.7 (70.3, 85.0)	70.5 (59.6, 78.9)	37	53.07	23.81 (1)	**<0.001**
No	58.0 (41.8, 71.1)	42.0 (22.9, 60.1)	30	13.93		
ACT						
Good adherence	94.4 (79.0, 98.6)	82.2(55.7, 93.6)	6	15.79		
Poor	75.6 (65.0,	66.1(52.7,	31	35.27	19.33	**<0.001**

adherence	83.4)	76.5)			(2)	
No chemotherapy	43.7 (27.6, 58.7)	36.6 (21.1, 52.3)	30	15.95		
Hormonal therapy						
Yes	94.2 (86.5, 97.5)	85.2 (72.0, 92.4)	13	35.64	32.36 (1)	**<0.001**
No	52.6 (40.5, 63.4)	41.3 (27.6, 54.5)	54	31.36		

ACT: *Adherence to chemotherapy*

In the worst-case analysis, a total of 124 patients were considered as they developed an event. The median survival of BC patients is 30.57 (IQR=7.23-64.23) months. The overall survival of patients at the end of one, two, and three years is 67.03 %, 51.3 %, and 44.6 % respectively. The overall survival for the early and advanced stage of BC at the end of 2 years is 85.1 % and 44.1 % and for stage III and IV, it is 55.1% and 23.7% respectively. (see fig. 2 and 3).

Predictors of survival of patients

After adjusting for age, histological type, surgery, and nodal status, the hazard of death among rural patients with breast cancer were 2.71 times higher as compared to urban dwellers (AHR=2.71, 95% CI: 1.44, 5.09). Patients with BC that travel >7 hours to Hawassa for cancer treatment had 3.42 times increased risk of death as compared to those traveled less than 3 hours

(AHR=3.42, 95% CI; 1.05, 11.10). Patients that present to the oncology unit within the range of 7 to 23 months after the beginning of sign and symptoms of BC had 2.63 times increased risk of death (AHR=2.63, 95% CI; 1.22, 5.64) and those who came >23 months had 2.37 times increased risk of death (AHR=2.37, 95% CI; 1.00, 5.59) as compared to those patients presented within 6 months. Those who have advanced stage of disease had 3.01 times increased risk of death as compared to early-stage (AHR=3.01, 95% CI; 1.05, 8.59). The hazard of death for patients that took no chemotherapy was 6.69 times (AHR=6.69, 95% CI; 2.20, 20.30) higher than those patients that have good adherence to chemotherapy.

Table 4: Multivariable cox regression analysis model for survival of patients with breast cancer diagnosed in HUCSH & YIMSC 2013-2018

Covariates	Category	Main analysis		
		CHR (95%CI)	AHR (95%CI)	p-value
Residence	Urban	1	1	
	Rural	3.29 (2.00, 5.42)	**2.71 (1.44, 5.09)**	**0.002**
Travel time	<3 hours	1	1	
	3-6 hours	1.40 (0.73, 2.66)	1.11 (0.52, 2.38)	0.773
	> 7 hours	2.22 (0.94, 5.20)	**3.42 (1.05, 11.10)**	**0.041**
Duration of symptom	0- 6 months	1	1	
	7-23 months	1.50 (0.84, 2.67)	**2.63 (1.22, 5.64)**	**0.013**
	> 23 months	1.71 (0.87, 3.39)	**2.37 (1.00, 5.59)**	**0.048**
Stage of BC	Early	1	1	
	Advanced	4.67 (1.85, 11.76)	**3.01 (1.05, 8.59)**	**0.040**
ATC	Good adherence	1	1	
	Poor adherence	3.37 (1.19, 9.54)	2.87 (0.96, 8.58)	0.032
	No CT	8.66 (3.03, 24.73)	**6.69 (2.20, 20.30)**	**0.001**
Global test			**0.8358**	

*NB: CHR: Crude hazard ratio, AHR: Adjusted hazard ratio, ACT: Adherence to chemotherapy, BC: breast cancer, *=Mixed ductal & lobular, mucinous, No CT: no chemotherapy.*

Discussion

This study identified predictors of survival and estimated overall survival of patients with BC, most of them treated with adjuvant chemotherapy and surgery in the Southern part of the country.

Our study found that the overall survival of patients with BC was 83%, 73.2%, and 63.0%, at one, two, and three years respectively.

Residence, travel time, duration of symptom, and adherence to chemotherapy were significant predictors of survival.

The two years OS in this study (73.2%) is higher than the result of Iran's systematic review which is 67.6% (9), it is higher than the finding of a study in rural Ethiopia which revealed 2-year survival is 53% (14). The difference with these studies could be due to a higher number of losses to follow-up in this study (18%) and or, due to the availability of adjuvant chemotherapy and hormonal therapy in our study setting.

In contrast to our study, better survival is observed in South Africa and Iran. Survival after two years is 80% in Sawoto South Africa (21) and 86% in Iran Yazd (22). This discrepancy could be due to methodological difference as a study in Sawoto relied on existed records and excluded loss to follow-ups which can lead to underestimation of the number of deaths and overestimation of survival (21), and due to the availability of BC care and treatment evidenced by 67% of patients with BC had received combined treatments of surgery, chemotherapy, and radiation in Iranian study (22) compared to only 50.7% in our study received surgery and chemotherapy but not radiation therapy.

In most studies of developed nations, even the five-year survival was better than the two-year survival of our study. The five-year survival in Idaho (rural state of US) is 89% and 83% for women linked and were not linked to women's health check programs respectively (23).

Increased survival in developed countries could be due to earlier presentation to cancer treatment, adequate screening service, and quality of care. A study in the US shows an association between increased breast cancer incidence and mammographic screening which in turn brings a shift in breast cancer stage distribution towards the earlier stage and finally brings a better survival (24).

In our study, most patients with BC (83.4%) presented at an advanced stage. This result is in line with the finding of a systematic review that compares BC patients' survival in developing and developed countries. Only 20%-50% of patients with BC present in early-stage in LMIC. The reason for diagnosis at an advanced stage in LMICs could be due to the patient's very long delay for consultation, access barriers and quality deficiencies in cancer care and treatment, negative symptom interpretation, fear, belief in alternative medicine, social relations, and networks(25, 26). A delayed presentation and diagnosis are also observed in Africa, especially in Sub-Saharan Africa (27). This is also evidenced by most studies in the developed world, an association between an advanced clinical stage of BC and delays greater than three months (25). In contrast to this study, 70% of patients with BC in most high-income countries are diagnosed in stages I and II (25).

We found that patients with BC that have advanced stages of the disease have 3.01 times increased risk of death as compared to early stages. This finding is similar to findings in Mexico, Hawaii, the US, Nigeria, and Uganda (8, 10, 12, 28, 29). This implies that earlier presentation or downstaging of BC at the time of diagnosis will have a paramount effect on the survival of BC patients.

In our study, rural residents are more likely to die from BC than their counterparts. This is supported by a meta-analysis conducted in developed nations of the US and Europe that revealed rural-dwellers are 5% less likely to survive from cancer (3). Similarly, a study in Utah revealed that rural residents had a 10% increased risk of death(30). This variation between urban and rural residents could be due to decreased health care seeking behavior in rural residents (31) and decreased awareness of BC in rural parts of Sub-Saharan Africa (32). Another reason for the urban-rural difference in survival can be explained by comparing urban-rural discrepancies in this study evidenced by, advanced-stage presentation (87.8 % versus 79.7%), time to presentation after 23 months (28.4%. versus 18.6 %), no chemotherapy (48.6%

versus 31.6%) and good adherence to chemotherapy (35.1% versus 47.1%) for rural and urban respectively. This result implies that awareness creation in the rural parts will be beneficial.

BC patients that present to cancer treatment centers within 7-23 months after the onset of breast complaint had 2.2 times increased risk of death as compared to those who had presented within six months. This finding is supported by a study in Rwanda that explored patient delays of 6–12 months and ≥12 months increased the odds of more advanced-stage disease when compared with patients presented within 3 months after the onset of symptoms (33). And this, in turn, can bring decreased survival.

In our study, patients that travel > 7hours have an increased risk of death as compared to those who travel < 3 hours to get cancer treatment. This association is not found significant in another reviewed study. This could be due to differences in awareness of the public and the facility in Wolega Ira might have good community sensitization about BC and this can increase early diagnosis (14).

Limitation of the study

Our study has certain limitations We used all available data which can minimize sampling error and it is the most up to date and the first for the study area. We also did a sensitivity analysis. On the other hand, due to a retrospective nature of the study, missing data was the challenge: Socio-economic variables and other tumor characteristics are not well addressed due to large missing, Study participants might die from causes other than BC, and these rates don't take that into account. Besides, the outcome of 57 (18.9%) patients is unknown and they are considered as left-censored and alive, this overestimates the survival time in the main analysis.

Conclusion

Near to three fourth of the breast cancer women had two years of overall survival. Living in a rural area, travel time > 7hours, duration of symptom > 6 months, advanced stage of cancer, poor adherence to adjuvant chemotherapy are independent predictors of poor survival. Thus there should be a focus on improving early detection, diagnosis, and treatment capacity at the lower health facilities with early referral procedures to facilitate timely diagnosis and treatment for those who need specific attention. There should be appropriate patients documentation with detailed information in the follow-up and helps for monitoring the quality of care, treatments, outcomes, and further research works.

Declarations

Ethics approval and consent to participate

Ethical clearance was obtained from Addis Ababa University, College of Health Sciences, School of Public Health, Research and Ethical Committee (REC) (Project number 0054/2019). Only a verbal consent was obtained from each of the participant and family caregivers in the study. And this procedure was approved by the REC. Permission was obtained from the selected hospitals before data collection. The

objectives and importance of the study were explained to the participants and caregivers before the data collection. All methods were performed in accordance with the relevant guidelines and regulations of declaration of Helsinki.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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None

Authors' contributions

AS, SG, and AW conceptualized the study. AS analyzed and wrote the first draft of the manuscript. All authors commented on the design of the study and reviewed each draft of the manuscript. All authors read and approved the final manuscript.

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Figures

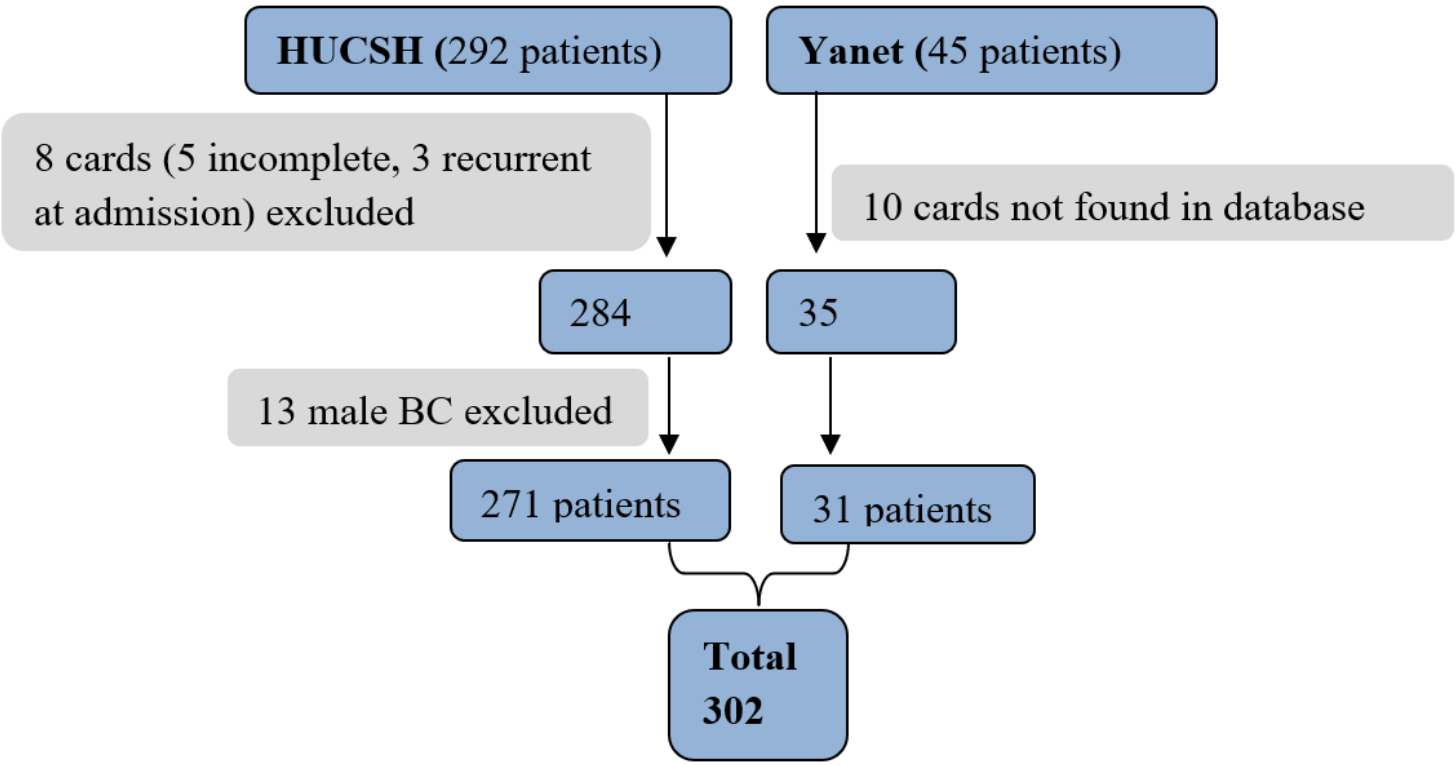

Figure 1

Sampling procedure to obtain study participants from HUCSH & YIMSC, 2018

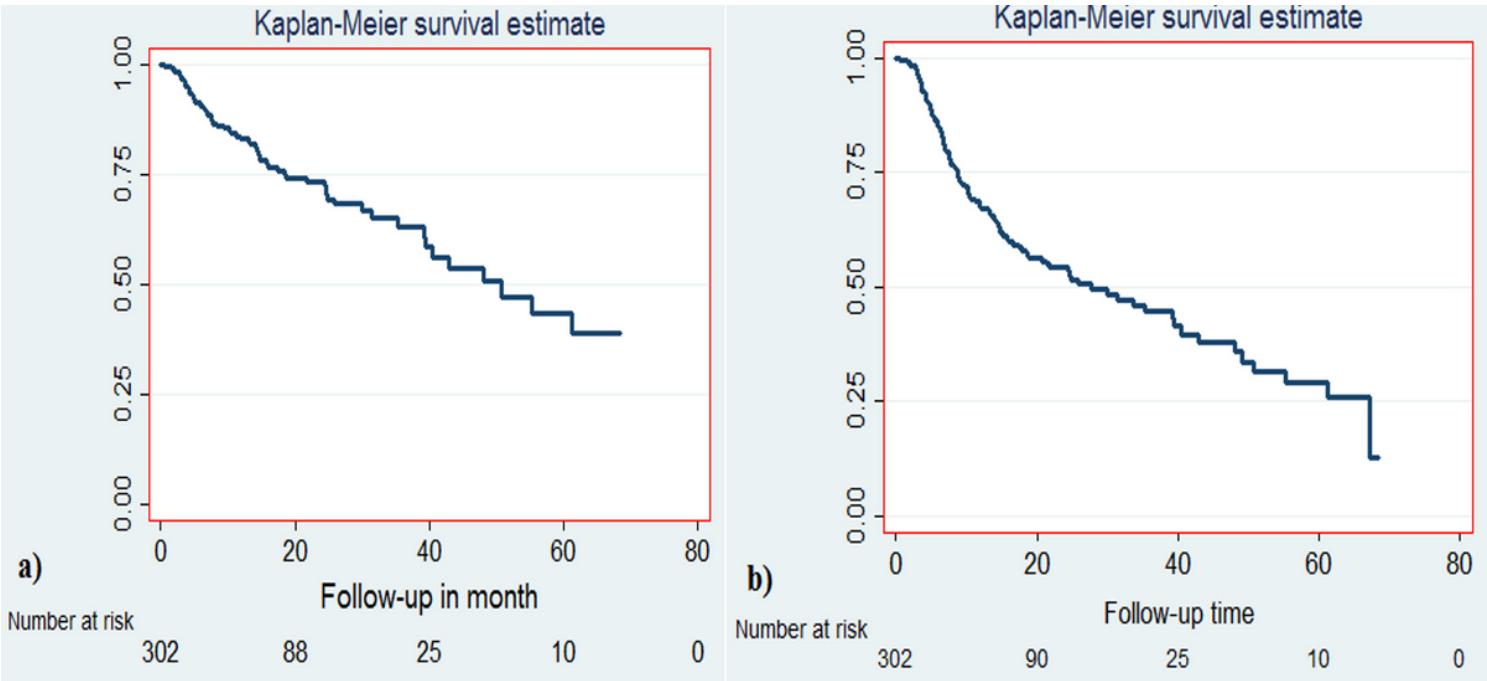

Figure 2

Kaplan-Meir curve showing time to death of patients with BC among patients of HUCSH & YIMSC, 2013-2018 a) Main analysis b) Worst-case analysis

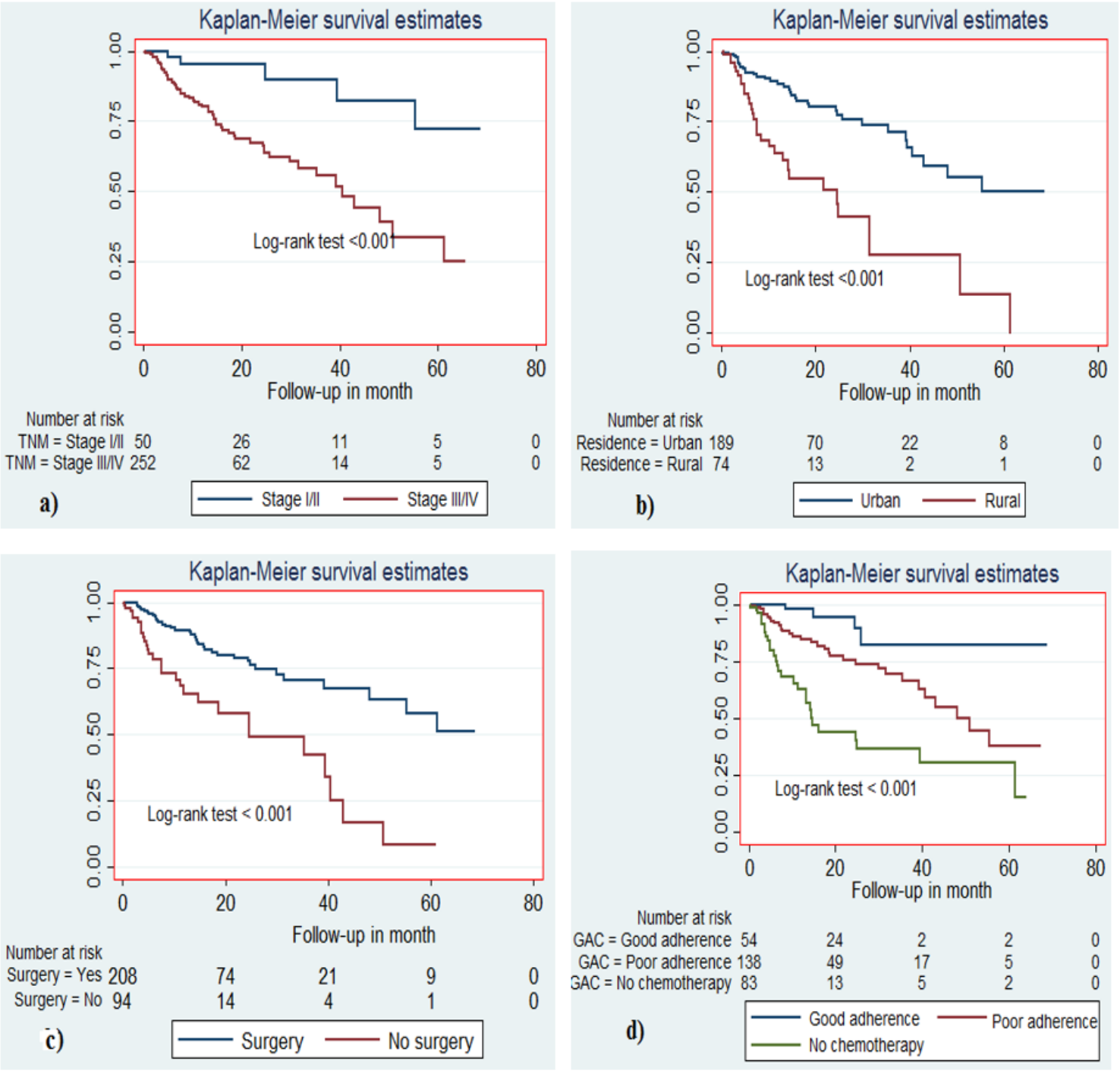

Figure 3

Kaplan-Meier survival estimates of patients with BC diagnosed in HUCSH and YIMSC 2013-2018 for significant covariates on Log-rank test, a) for the stage of breast cancer b) for residence c) for surgical therapy d) for adherence to chemotherapy