Journal of Cancer Research and Clinical Oncology (2025) 151:187
https://doi.org/10.1007/s00432-025-06181-2

RESEARCH

Time to breast cancer recurrence and associated predictors in Public Hospitals of Addis Ababa, Central Ethiopia: a retrospective Cohort Study

Yadessa Chala[1] · Tesfaye Techane[2] · Bonsisa Bekele[2] · Tesfaye Girma[2] · Warati Fekede[3] · Chalchisa Abdeta[5] · Kibiru Mardasa[3] · Tolera Abdeta[3] · Bedada Teshome[4] · Gashaye Atinkut[3] · Abdinasir Wako[3] · Mohammed Adem[3] · Alem Deksisa[3]

Received: 18 January 2025 / Accepted: 24 March 2025

Abstract

Background Breast cancer recurrence is a significant concern when the disease returns following surgery. The time to recurrence and factors affecting it are not well studied in low-income countries. This study aimed to assess the time to recurrence and predictors of breast cancer among women treated in public hospitals of Addis Ababa, Ethiopia.

Methods Retrospective cohort study was conducted from April 30 to May 30, 2024, among randomly selected 322 recorded cases. The study covered from September 11, 2018, to September 12, 2023. Data were collected by the Kobo toolbox and analyzed by Stata Version 15. The Cox proportional hazard model was used to identify predictor variables, with assumptions checked using the Schoenfeld residual/global test (0.79). Multi-collinearity was checked using the variance inflation factor (3.72). Variables with a P-value < 0.25 in bivariable analysis were entered into the final multivariable analysis. Variables with a P-value < 0.05 at 95% confidence level were considered independent predictors of recurrence.

Result The recurrence-free survival (RFS) status at the median follow-up time was 87.5%. The incidence rate of breast cancer recurrence was 6.8 per 100 women years (95%CI = 5.34–8.13) follow-up. The 75%RFS time was 44 months (95CI% = 40–48). The proportion of RFS survival at 24, 36, 48, and 60 months was 91.93%, 83.3%, and 67.7%, 61% respectively. Women aged 40 & below (AHR = 3.32; 95%CI 1.80–5.88), Overweight (AHR = 1.95, 95%CI 1.06 -3.59), surgical margin positive (AHR = 2.1; 95%CI 1.20–4.02), axillary node-positive (AHR = 1.98; 95%CI 1.08–3.61) and comorbidity (AHR = 4.45, 95%CI 2.39–8.30) were independent predictors for increased hazard of recurrence.

Conclusion This study confirms a substantial incidence of breast cancer recurrence, with identifiable predictors including comorbidity, age, overweight, positive axillary node status, lymph node involvement, and deep surgical margin. Targeted interventions aimed at improving patient understanding of recurrence risk, promoting adherence to treatment protocols, and fostering healthy lifestyle modifications are crucial for reducing recurrence rates.

Keywords Breast · Cancer · Ethiopia · Predictors · Recurrence

Introduction

Breast cancer is a complex illness with many faces – different biological characteristics, a range of treatments, and varying outcomes for those diagnosed. At its core, it's about cells in the breast tissue that begin to grow and multiply uncontrollably, ultimately becoming cancerous (Wu et al. 2016). In 2020, breast cancer became the most commonly diagnosed cancer worldwide, surpassing lung cancer, with 2.3 million new cases—that's nearly 12% of all cancers diagnosed globally. Sadly, it's also the fifth leading cause of cancer-related deaths, claiming 685,000 lives each year (Sung et al. 2021). In Africa, and specifically in Ethiopia, breast cancer is the most prevalent cancer affecting people, both in terms of new diagnoses and deaths (Sharma et al. 2020).

Breast cancer represents a significant global health burden, impacting millions of women worldwide. It is the most commonly diagnosed cancer among women, and a leading cause of cancer-related mortality. This burden extends beyond mortality, encompassing substantial morbidity, including physical and psychological consequence from

Extended author information available on the last page of the article

Published online: 12 June 2025

diagnosis and treatment. The economic impact is also considerable, with costs associated with screening, diagnosis, treatment, and long-term care placing a strain on healthcare systems and individuals (Sung et al. 2021).

When someone is diagnosed with breast cancer, the treatment approach depends heavily on how far the cancer has progressed. For those with Stage I–III breast cancer, surgery is often the first step, either a mastectomy (removal of the breast) or breast-conserving surgery followed by radiation therapy (Trayes and Cokenakes 2021). Stage IV breast cancer, where the cancer has spread to other parts of the body, is generally considered more difficult to cure and is usually managed with systemic therapy, such as chemotherapy or targeted drugs, although sometimes surgery might be considered for comfort or symptom relief (Horani and Abdel-Razeq 2023). After initial treatment, therapies like radiation, hormone therapy, and chemotherapy can be used to help lower the chances of the cancer coming back and improve survival (Wangchinda and Ithimakin 2016).

Unfortunately, breast cancer can sometimes return after initial treatment—we call this recurrence (Cossetti et al. 2014). The risk is highest in the first couple of years after diagnosis, but it remains a possibility, albeit lower, for many years afterward, roughly between 2 and 5% annually from years five to twenty (Metzger-Filho et al. 2013). Where the cancer returns can also vary, depending on the specific type of breast cancer. It might come back in the breast or chest wall area (local recurrence), spread to the bones (distant metastasis), or appear in nearby lymph nodes (Wu et al. 2016). This lingering possibility of recurrence can understandably make people feel that breast cancer is never truly "gone." Even with the best treatments and close monitoring, some people (5–10%) are diagnosed with metastatic disease right away, and another 20% will experience a recurrence later on (DeSantis et al. 2011). Sadly, when the cancer does return, it often behaves more aggressively (Elsayed et al. 2016).

Looking at the numbers around the world, we see a significant difference in recurrence rates depending on where people live, reflecting differences in access to healthcare and resources. For example, studies have shown that within 5 years after surgery, recurrence rates were around 3.3% in Australia (Wangchinda and Ithimakin 2016), 11.7% in the Netherlands (Franken et al. 2012), and 5.9% in South Korea (Choi et al. 2016). In countries with fewer resources, like Egypt and Iran, the rates were 4.2% (Elsayed et al. 2016) and 20.2% (Kheradmand et al. 2010), respectively. We have very limited information from Africa, but one study in Ethiopia found a recurrence rate of 18.5% (Shiferaw et al. 2020). Breast cancer recurrence is a key clinical challenge, influenced by patient factors like age and BMI, and tumor characteristics. Positive lymph node status, lympho-vascular invasion, high tumor grade, and hormone receptor negativity increase recurrence risk. Inadequate surgical margins also elevate local recurrence (Ren et al. 2014; Lafourcade et al. 2018).

This lack of data in Ethiopia shows us that we don't fully understand how often breast cancer comes back, or what factors might contribute to it. That's why this study is so important—we want to understand how long it takes for breast cancer to recur and identify any factors that might predict recurrence among women treated in public hospitals in Addis Ababa, Ethiopia.

Methods

Study design and setting

An institution-based retrospective cohort study was conducted at Saint Paul's Hospital Millennium Medical College (SPHMMC) and Tikur Anbessa Specialized Hospital (TASH) from April 30- May 30, 2024. The study was conducted at the largest tertiary care, specialized, referral, and teaching hospitals. There are 13 public hospitals in Addis Ababa, and four public hospitals have oncology treatment centers (Tikur Anbessa Specialized Hospital, St. Paul's Hospital Millennium Medical College, Ethiopian Public Health Institute, and Yekatit 12 Hospital Medical College). Tikur Anbessa Specialized Hospital and St. Paul's Hospital Millennium Medical College were selected by using simple random sampling.

The St. Paul's Hospital Millennium Medical College was established in Addis Ababa, the capital city of Ethiopia in 1968 by the late Emperor Haile Selassie. The college has more than 2800 clinical, academic administrative, and support staff that provide medical specialty services to patients who are referred from all over the country, teaching medicine and nursing students and doing basic and applied research. The College can accommodate more than 700 inpatient beds, but on a daily average, 1200 emergency and outpatient patients are seen. St. Pauls ' Hospital Millenium Medical College oncology unit was established on August 1, 2018. It was the second hospital offering cancer treatment in the country (Ren et al. 2014).

Tikur Anbessa Specialized Hospital is the largest tertiary care, specialized, referral, and teaching hospital in the country that is owned by the government and established in 1973. TASH has 51 specialty outpatient clinics, serving 500,000 patients annually (Shiferaw et al. 2020).

Sample size determination

As the study was a cohort study, the sample size needed for acquiring statistically significant results was determined using a two-population proportion formula. Therefore, the

sample size was calculated by taking into account the predictor variables and using open epiInfo version 7.2.6 statistical package (Colleoni et al. 2016). Among predictor variables, lymph node status is chosen as the main predictor variable of breast cancer recurrence during the 6 years of follow-up since it was considered to give the optimal sample size and most significant result. In this regard, with a 5% level of significance (two-sided), a power of 80%, and a ratio of unexposed to exposed of 1:1, the estimated proportion of recurrence in Ethiopia was taken at 10% for the non-exposed group (negative lymph node status) and 22.4% for the exposed group (positive lymph node status) (Shiferaw et al. 2020) (Table 1). However, in practice getting 153 patients their positive lymph nodes was difficult and the rest were from negative lymph nodes. Thus, the total sample size was 306. Finally, by adding 10% for incomplete data, the final sample size required was 337.

Subjects

All medical records with breast cancer who had breast surgery in a selected public hospital in Addis Ababa, from September 11st 2018 to September 12, 2023. All medical records of breast cancer patients who had breast surgery in the SPHMMC and TASH hospitals from September 11 2018 to September 12 2023 were included in the study.

Data collection

A data extraction tool was developed from related literature to collect information from patients' medical records. Socio-demographic, clinic-pathological, and treatment-related factors that are supposed to be predictors for breast cancer recurrence were extracted from the patient's medical records by using the Kobo toolbox. Data were collected by four BSc nurses and supervised by two MSc Oncology nurses.

Before the data was collected, 5% (Lowery et al. 2012) of the total sample size underwent a pretest to ensure that the questionnaires were clear and easy to access on the chart. After pre-testing the checklist, Cronbach's Alpha was calculated by using Stata version 15 to test the internal consistency (reliability) of the item and the result was 0.79. Study variables are identified based on similar studies and a data extraction tool was developed by the information available in the patient's medical record at the cancer treatment center. Training on how to collect data by the Kobo toolbox was given to data collectors and supervisors before one day of data collection. Senior experts in the area of study for content validity examined the data extraction tool. The entire data collection process was closely supervised by the supervisors and principal investigator. Supervisors checked the ID of the patient with the registry code whether clinically matched (at diagnosis stage I-III) or not.

Data analysis

Data were entered, checked, and arranged in Kobo toolbox software. After Coding, editing, and cleaning analysis were done in Stata Version15. To summarize the cohort's characteristics, descriptive statistics such as frequency tables, life tables, graphs, median, and Inter quartile range were used. The incidence density rate was computed throughout the study. The survival time was estimated using the Kaplan–Meier survival curve. Log-rank test was performed for the presence of any differences in time to recurrence among different categorical variables. Those variables that the test statistics & Kaplan–Meier analysis displayed as a significant difference in RFS function among categorical variables are considered as having significant evidence of differences in time to recurrence. The Cox proportional hazard model was used to identify the predictor variables. The Cox-proportional hazard model assumption was checked using the Schoenfeld residual/global test (0.79). Overall the fitness' of the proportional hazard model was assessed by using the Cox Snell residual graph. Multi-co linearity was checked using the variance inflation factor (3.72).

Table 1 Sample size calculation for time to recurrence and predictors of breast cancer recurrence among patients treated in a public hospital, Addis Ababa, Ethiopia 2024 by using open epi version 7.2.6 Software

Assumptions		Major predictors variable	Sample size by Fleiss with CC Formula	Total sample size
Two-sided significance level:	0.05	Lymph node status (positive exposed; negative unexposed)	Number of exposed = 153	306
Power:	80			
Ratio of sample size:	1:1			
% of Unexposed with Outcome	10		Number of unexposed = 153	
% of exposed with Outcome	22.4			
Hazard ratio	2.6			
Relative risk	2.24			

Variables with a P-value < 0.25 in the bivariable analysis were entered into the final multivariable analysis. Variables with a P-value < 0.05 at a 95% confidence level were considered independent predictors of recurrence.

Results

Socio-demographic traits of the respondents

Out of 337 study participants of this study, 322 complete record reviews were done. This makes the response rate of the study 96%. The median age at diagnosis was 43 years (Inter-quartile range: 34–51). Of the 322 study participants, 162(50.31%) were diagnosed at age 40 and above. One hundred sixty-two (81.37%) were married, and 195 (60.56%) were from rural areas (Table 2).

Baseline clinical, pathological, and treatment characteristics of the study participants

Eighty-six (26.71%) women had preexisting comorbidity at the time of diagnosis, 152 (47.20%) cases were in clinical stage III cancer; and 135(41.93%) were moderately differentiated (grade II) histologic cancer cases at a time of diagnosis. Out of a total of 151 (46.8%), women were overweight during diagnosis. Invasive carcinoma was a commonest histologic type; accounting for 256(79.50%) of all cases. One hundred seventy-one (53.11%) cases had positive lymph involvement of two or above, and 160 (39.69%) cases had tumor size of 2 to 5 cm at the time of diagnosis. Ninety-eight (30.43%) cases had involved surgical margin status. About 157 (48.76%) women had positive axillary node status. One hundred sixty-one (50%), and 147(45.65%) of study participants had positive estrogen and progesterone receptors respectively (Table 3).

According to this study, about 55.28% of women's surgery was done after 30 days from the date of diagnosis. Three hundred eight (95.56%) cases had undergone Modified Radical Mastectomy. Three hundred forty (81%) women were using adjuvant chemotherapy and out of these ACT is the most common chemotherapy used as an Adjuvant regimen 173(53.7%). About Two hundred fourteen (66.46%) were using hormone therapy. Out of 214, about 148 (69.16) women who were diagnosed with early-stage breast cancer used the Tamoxifen regimen of hormonal therapy during these follow-ups (Table 4).

Overall status of breast cancer patients

In this study, 322 women patients with breast cancer who underwent surgery were followed retrospectively. The median follow-up time was 33 months, with a minimum and maximum follow-up time of 5 and 60 months, respectively. The recurrence-free survival status at the median follow-up time was 85.73% (95%CI = 80.8–89.4%). In this study 63 (19.56%) patients developed recurrence (Fig. 1).

Incidence of breast cancer recurrence

The overall incidence rate of breast cancer recurrence in the cohort during the 919 person-years of observation was 6.8 per 100 person-years (95%CI = 5.35–8.14) follow-up. In this study, the 75% recurrence-free survival (RFS) time was 44 months (95%CI = 40- 48.00). The estimated overall RFS survival at 24, 36, 48, and 60 months was 91.93%, 83.3%, and 67.7%, 61% respectively (Fig. 4). There were 32(50.79%) distant recurrences & 31 (49.21%) loco regional recurrences; and regarding the site of recurrence, axillary and opposite breast recurrence for loco regional type, and lung & chest wall for the distant recurrence were the commonest sites (Fig. 2).

Comparison of time to breast cancer recurrence among categorical variables

Log-rank test was performed to determine the presence of a significant difference in recurrence rate among categorical variables such as;-Age of patients at diagnosis, Preexisting comorbidity status, Surgical margin status,

Table 2 Socio-demographic characteristics of breast cancer patients who had surgical treatment in a selected public hospital, Addis Ababa, Ethiopia, 2024 (n = 322)

Variables	Category	Frequency, (%)	Outcome	
			Recurrence N (%)	Censored N (%)
Age at dx	= > 40	190 (59.01)	31 (16.31)	159 (83.69)
	< 40	132 (40.99)	32(24.24)	100(75.76)
Marital status	Single	42 (13.04)	6(14.28)	36 (85.72)
	Married	162 (81.37)	57(35.18)	205(64.82)
	Widowed	11 (3.42)		11(100)
	Divorced	7 (2.17)		7(100)
Residence	Urban	195 (60.56)	35(17.94)	160(82.06)
	Rural	127 (39.44)	28(22.04)	99 (77.96)

Table 3 Clinical and pathological characteristics of breast cancer patients who had surgical treatment in a selected public hospital, Addis Ababa, Ethiopia, 2024 (n = 322)

Variables	Category	Frequency, (%)	Outcome status	
			Recurrence N (%)	Censored N (%)
Comorbidity	Yes	86 (26.71)	40 (46.51)	46 (53.49)
	No	236 (73.29)	23 (9.74)	213(90.26)
BMI at diagnosis	Normal weight	171 (53.11)	16 (9.35)	155 (90.65)
	Overweight	151 (46.89)	47 (31.12)	104 (68.98)
Laterality	Left	147 (45.65)	28 (19.05)	119 (80.95)
	Right	175 (54.35)	35 (20)	140 (80)
Cancer stage at diagnosis	I	30 (9.32)	2 (6.66)	28 (93.34)
	II	140 (43.48)	14 (10)	126 (90)
	III	152 (47.20)	47 (30.92)	105 (69.08)
Histological grade	Grade I	65 (20.19)	5 (7.70)	60 (92.30)
	Grade II	135 (41.93)	18 (13.33)	117 (86.67)
	Grade III	122 (37.89)	40 (37.78)	82 (62.22)
Histological type	Noninvasive	66 (20.50)	4 (6.06)	62 (93.94)
	Invasive	256 (79.50)	59 (23.04)	197 (86.96)
Surgical margin	Free	224 (69.57)	25 (11.16)	199 (88.84)
	Involved	98 (30.43)	38 (38.78)	60 (61.22)
Number of + lymph nodes involved	< 2	151 (43.89)	16 (10.60)	135 (89.40)
	> = 2	171 (53.11)	47 (27.48)	124(72.52)
Axillary node status	Negative	165 (51.24)	17 (10.30)	148 (89.70)
	Positive	157 (48.76)	46 (29.29)	111 (70.71)
Tumor size at diagnosis	< 2 cm	36 (11.18)	3 (8.33)	33(91.67)
	2–5 cm	160 (39.69)	24 (15.00)	136 (75.00)
	> 5 cm	126 (29.13)	36 (28.57)	90 (71.43)
Estrogen receptors	Positive	161 (50.00)	35 (21.74)	126 (78.26)
	Negative	129 40.06)	26 (20.16)	103 (79.84)
	Not determined	32 (9.94)	2 (6.25)	30 (93.75)
Progesterone receptor	Positive	147 (45.65)	25 (17.00)	122 (83.00)
	Negative	142 (44.10)	36 (25.35)	106 (74.65)
	Not determined	33 (10.25)	2 (6.06)	31 (93.94)

Table 4 Treatment characteristics of breast cancer patients who had surgical treatment in selected public hospitals Addis Ababa, Ethiopia, 2024 (n = 322)

Variables	Category	Frequency,%	Recurrence(63) N (%)	Censored (259) N (%)
Duration from diagnosis to surgery	< = 30 days	144 (44.72)	23 (15.97)	121(84.03)
	> 30 days	178 (55.28)	40 (22.47)	138(77.53)
Neo-adjuvant chemotherapy use	Yes	38(11.80)	11 (28.94)	27(71.06)
	No	284(88.20)	52 (19.79)	232(80.21)
Adjuvant chemotherapy use	Yes	288 (89.44)	57(19.79)	231(80.21)
	No	34 (10.56)	6(17.65)	28(72.35)
Chemotherapy regimen used	ACT	173 (53.7)	36(20.80)	137(79.20)
	AC	75 (23.3)	12 (16.00)	63(84.00)
	Paclitaxel	40 (12.4)	9 (22.50)	31(77.50)
Use of hormonal therapy	Yes	214 (66.46)	43(20.09)	171(79.91)
	No	108 (33.54)	20(18.51)	88 (81.49)
A regimen of hormonal therapy	Tamoxifen	148 (69.16)	27(18.24)	121 (81.76)
	Anastrazole	66 (30.84)	16(24.24)	50 (75.76)

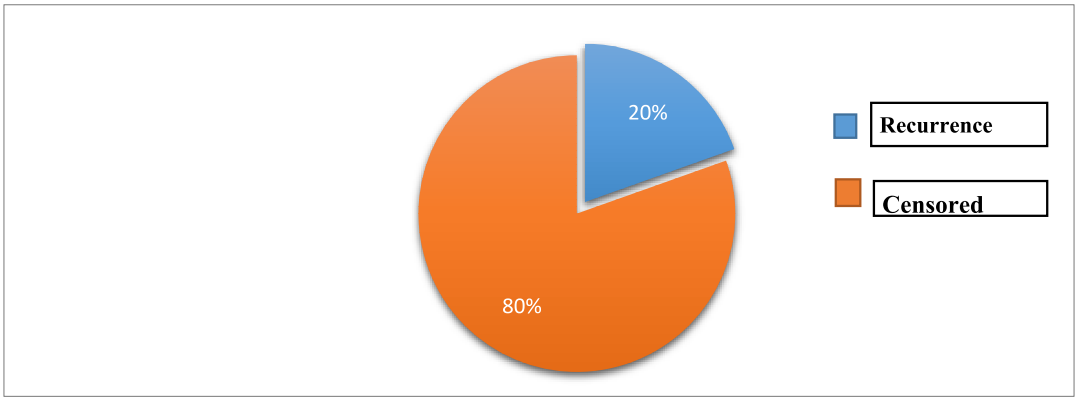


Fig. 1 Survival status of breast cancer patients who underwent surgery in selected public hospitals of Addis Ababa, Ethiopia, 2024

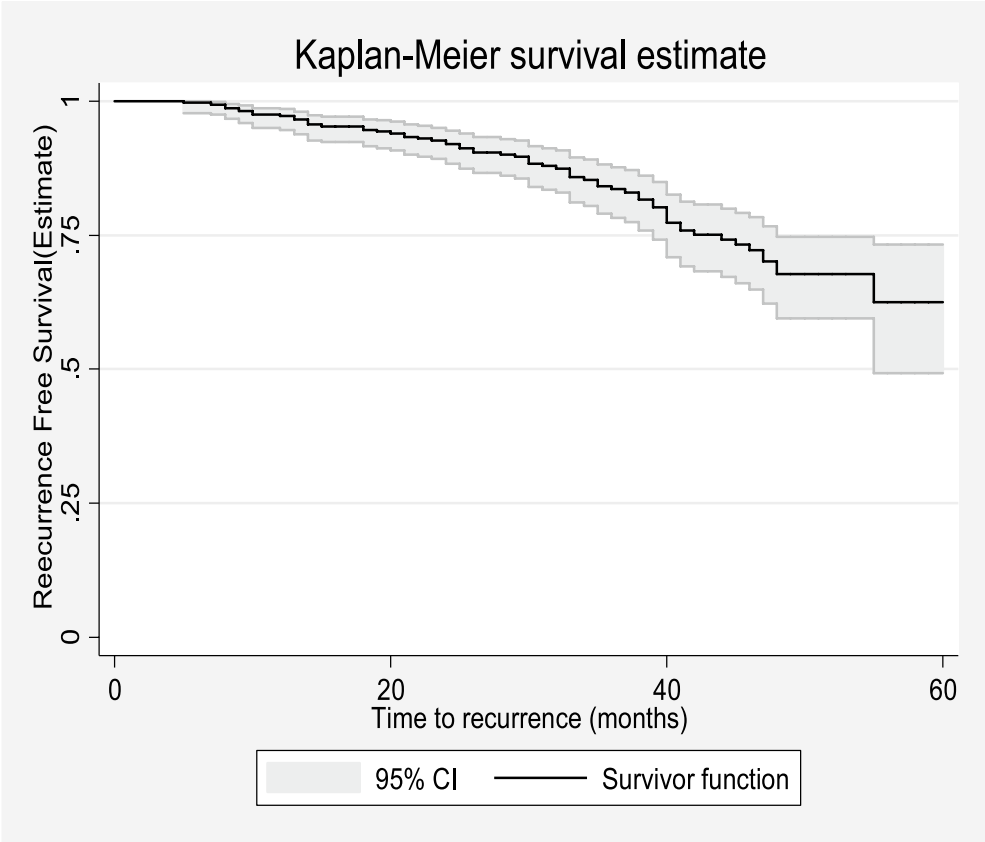


Fig. 2 An overall Kaplan–Meier analysis of recurrence-free survival of breast cancer patients who had surgery at a selected public hospital, Addis Ababa, Ethiopia, 2024

Clinical stage of cancer, and Axillary node status at 5% level of significance (Table 5). The Log-rank (LR) test has shown that women who were age 40 and below, and those above 40 years at diagnosis had differences in their time recurrence-free survival time (P value for LR test = 0.041). Also, the recurrence-free survival time was different among women who had preexisting comorbidity and those with no preexisting comorbidity at baseline (P value for LR test < 0.001). In addition, patients who were diagnosed with clinical stage III cancer have a shorter median time to recurrence compared to those who were presented with clinical stage I and II cancer (P value for LR < 0.001).

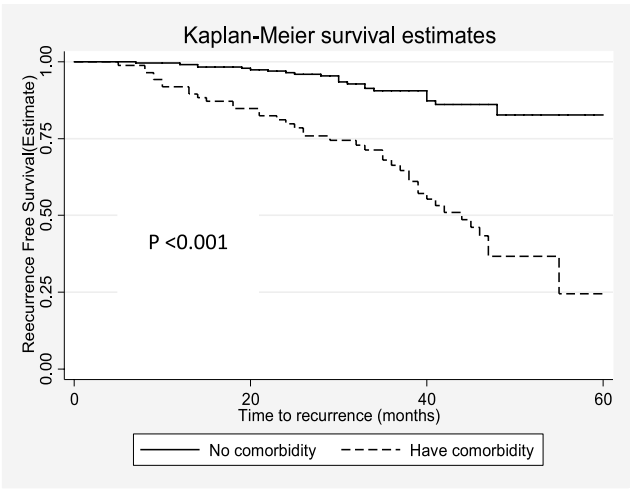
Table 5 Log-rank test for categorical independent variables among breast cancer recurrence patients who had surgical treatment in Addis Ababa, Ethiopia, 2024

Variables	Chi-square	Df	p-value
Age	4.15	1	0.0417
Stage of cancer	24.82	2	< 0.001
Comorbidity	49.11	1	< 0.001
Histological grade	24.91	2	< 0.001
Body mass index	18.98	1	0.001
Surgical margin	47.38	1	< 0.001
Lymph node	10.58	1	0.0012
Tumor size	12.15	1	0.0023
Axillary node status	19.54	1	< 0.001

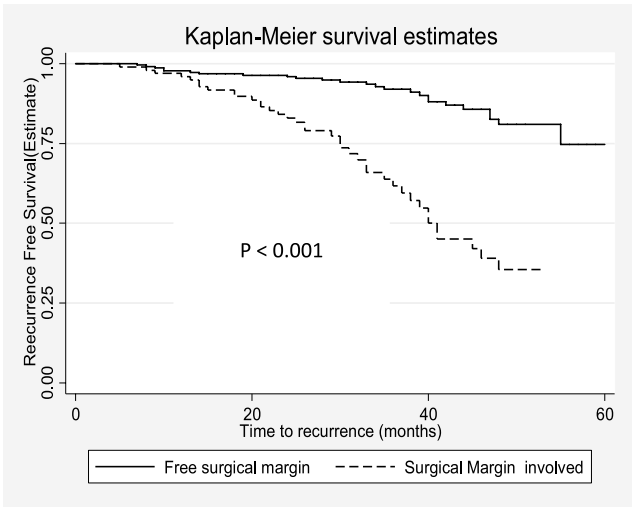
The graph of the log displayed that there was a difference in recurrence-free survival time among women presented with histologic grades I & II, and those with grade III. The median time to recurrence is longer in grades I and II than in histological grade III, and this difference was significant at a log-rank test P value of < 0.001. Additionally, the median time to recurrence was shorter in women who had two or more lymph node involvement than those with less than two lymph node involvement (P value for LR-test = 0.0012) (Fig. 3).

Cox proportional hazard assumption

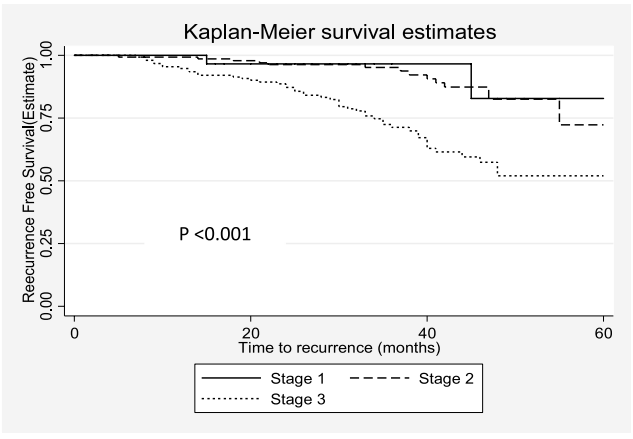
The Cox proportional hazard assumptions were checked statistically using a global test. All the covariates met the



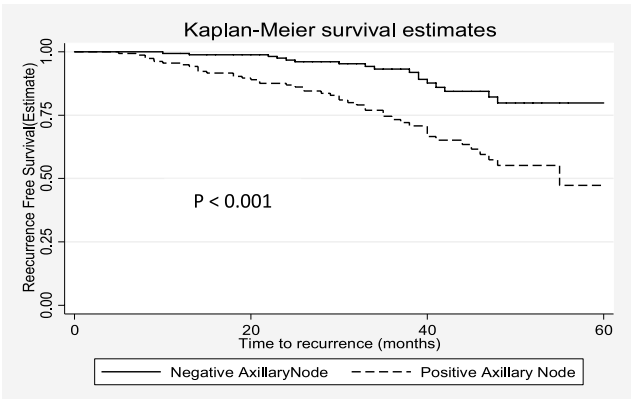
A



B



C



D

Fig. 3 Kaplan–Meier recurrence-free survival function among different groups of breast cancer patients with log-rank test P-value by Preexisting comorbidity status (P < 0.001) (**A**), Surgical margin status (P < 0.001) (**B**), Clinical stage of cancer (P < 0.001) (**C**), and Axillary node status (P < 0.001) (**D**) at selected public hospital Addis Ababa Ethiopia, 2024

Table 6 Proportional Hazard assumption model of the Cox model for breast cancer patients who had surgical treatment in selected public hospitals in Addis Ababa, Ethiopia, 2024

Variables	Rho	Chi-square	Df	Pro > chi2
Age	-0.05794	0.24	1	0.6262
Comorbidity	-0.06379	0.30	1	0.5861
Cancer stage	-0.12249	1.05	1	0.3066
BMI	0.06916	0.34	1	0.5587
Histological type of cancer	-0.12654	1.06	1	0.3023
Histological grade	0.16340	2.12	1	0.1453
surgical margin status	0.12185	1.20	1	0.2742
Lymph node involvement	0.00868	0.00	1	0.9474
Axillary node status	-0.17863	1.65	1	0.1993
Tumor size	-0.04265	0.13	1	0.7220
Global test		**6.26**	**10**	**0.7933**

proportional hazard assumption, and the p-value over all Schoenfeld global tests was 0.7933 (Table 6).

Model goodness-of-fit

After fitting a multivariable Cox Proportional Hazard Model, the adequacy of the fitted model was evaluated using Cox Snell residuals. The hazard function follows the 45°-line, which approximately, indicates that the model fits the data well (Fig. 4).

Predictors of breast cancer recurrence

Covariates selected for the final model were age at diagnosis, preexisting comorbidity, BMI at diagnosis, histologic grade, histological type of cancer, stage of cancer, surgical margin, axillary node status, number of positive lymph nodes involved, and histological type of cancer. According to the results of multivariate Cox proportional hazard analysis, women aged 40 & below were nearly 3 times more at risk of increased time to breast cancer recurrence than those with age above 40 years (AHR = 3.32; 95%CI 1.8–5.88). Similarly, women who were presented with body mass index ≥ 25 mg/m^2 at diagnosis had nearly 2 times higher risk of developing recurrence than those who had body mass index < 25 mg/m^2 (AHR = 1.95;95%CI 1.06–3.59). On the other hand, women who were surgical margin positive at diagnosis had 2 times higher risk of developing recurrence than those who were surgical margin negative (AHR = 2.1;95%CI 1.20–4.02). In addition, women who had axillary node status positive were nearly 1.9 times at higher risk of developing recurrence than those with axillary nodes negative (AHR = 1.98;95%CI 1.08–3.61). Similarly, the presence of preexisting comorbidity (AHR = 4.45; 95%CI 2.39–8.30) was 4 times more at risk for recurrence than its counterpart (Table 7).

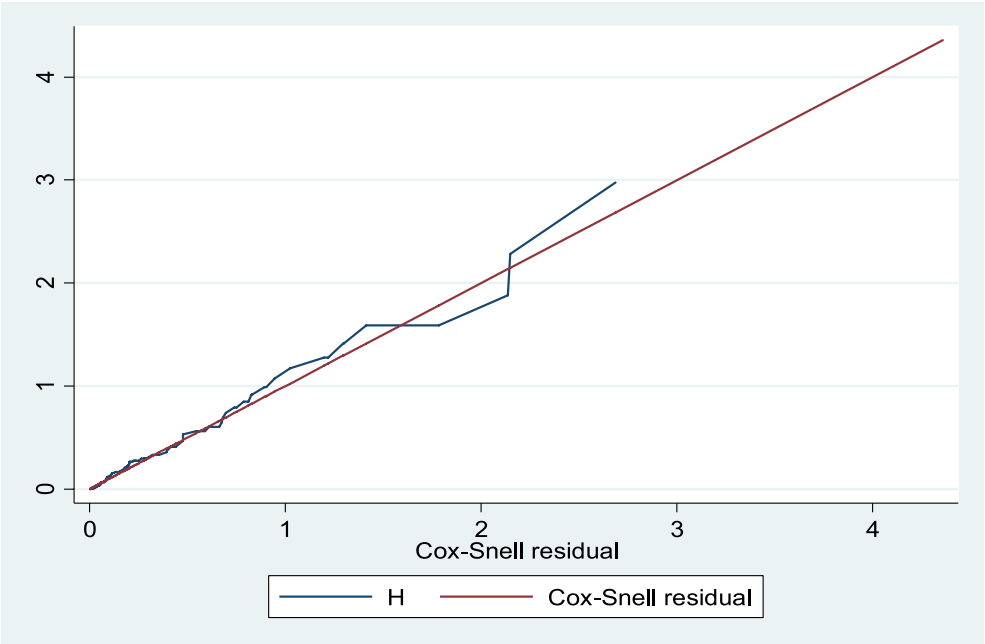


Fig. 4 Cox Snell residual test for the model's overall fitness

Table 7 Bivariable and multivariable Proportional Cox Hazard regression analysis of predictors associated with breast cancer recurrence in patients who had surgical treatment in Addis Ababa, Ethiopia, 2024

Variables	Category	Outcome		CHR with 95% CI	AHR with 95%CI	P-value
		Recurrence	Cen-Sored			
Age at dx	≥40	31	159	1	1	<0.001***
	<40	32	100	1.66(1.01–2.72)	3.35(1.8–5.8)	
Comorbidity	Yes	40	46	5.16(3.09–8.6)	4.77(2.39–8.30)	<0.001***
	No	23	213	1	1	
BMI at diagnosis	Normal weight	16	155	1	1	0.032*
	Overweight	47	104	3.2 (1.8–5.7)	3.33(1.06–3.59)	
Cancer stage at diagnosis	I	2	28	1	1	0.851
	II	14	126	1.18(0.26–5.21)	1.16(0.24–5.58)	0.302
	III	47	105	4.43 (1.07–18.2)	2.26(0.47–10.75)	
Histological grade	Grade I	5	62	1	1	0.859
	Grade II	18	116	1.7(0.60–4.6)	0.93 (0.31–2.49)	0.949
	Grade III	40	81	5 (1.9–12.6)	0.96(0.31–2.76)	
Histological type	Noninvasive	4	62	1	1	0.303
	Invasive	59	197	4.77(1.72–13.21)	1.8(0.58–5.71)	
Surgical margin	Free	25	199	1	1	0.011*
	Involved	38	60	5.08(3.0–8.5)	3.47(1.20–4.02)	
Number of + lymph nodes involved	<2	16	135	1	1	0.339
	≥2	47	124	2.48(1.40–4.37)	1.4(0.72–2.61)	
Axillary node status	Negative	17	148	1	1	0.025*
	Positive	46	111	3.26(1.86–5.69)	2.84 (1.09–3.60)	
Tumor size at diagnosis	<2 cm	3	33	1	1	0.306
	2–5 cm	24	136	1.44(0.433–4.79)	0.5(0.13–1.83)	0.635
	>5 cm	36	90	3.2(0.98–10.12)	0.7(0.19–2.5)	

NB: *significant, *p < 0.05, **p < 0.01 and ***p < 0.001.

CHR crude hazard ratio, *AHR* adjusted hazard ratio, *BMI* body mass index, **1** = references

Discussion

This study investigated time to recurrence and predictors among women with breast cancer treated in selected public hospitals in Addis Ababa, Ethiopia. Our findings discovered a breast cancer recurrence incidence rate of 6.8 (95% CI 5.35–8.14) per 100 person-years, with a median recurrence-free survival (RFS) of 85.73%. The 75% RFS time was 44 months, with estimated RFS proportions of 91.9%, 83%, 67%, and 61% at 24, 36, 48, and 60 months, respectively. Independent predictors of recurrence included age ≤ 40 years, BMI (overweight), positive surgical margins, positive axillary node status, and pre-existing comorbidities.

The observed incidence rate is comparable with to findings from Addis Ababa (6.5%) (Shiferaw et al. 2020) and South Korea (5.9%) (Choi et al. 2016), but higher than those reported in Australia (3.3%) (Lowery et al. 2012) and Egypt (4.2%) (Elsayed et al. 2016), and lower than that reported in the Netherlands (11.9%) (Franken et al. 2012). These variations may be attributed to differences in patient populations, including stage at diagnosis. Our study population likely included a higher proportion of patients diagnosed at later stages, which is strongly associated with increased recurrence risk (Shiferaw et al. 2020; Lafourcade et al. 2018).

The 75% RFS time of 44 months is consistent with findings from the USA (48 months) (He and Zou 2017), Thailand (45.43 months) (6), and South Korea (47 months) (Choi et al. 2016), but higher than reports from France (Crozier et al. 2013) and Addis Ababa (Shiferaw et al. 2020). This difference might be related to the high proportion (98%) of our participants undergoing modified radical mastectomy, a surgical approach proven effective in recurrence prevention (Crozier et al. 2013).

Our study demonstrated estimated RFS rates of 97.19%, 91.7%, 83.3%, 67.07%, and 61.24% at 1, 2, 3, 4, and 5 years, respectively. The RFS rates for the first three years are comparable with those reported in Iran (2.5-year RFS: 86%) (Kheradmand et al. 2010) and Addis Ababa (2-year RFS: 91.5%; 3-year RFS: 82.4%) (Shiferaw et al. 2020). However, our 5-year RFS rate is higher than that reported in Addis

Ababa (50.5% at 5 years and 28.5% at 6 years) (Shiferaw et al. 2020) and more in line with findings from Iran (82.5% at 5 years) (Kheradmand et al. 2010) and the Netherlands (88.4% at 4 years) (Franken et al. 2012). This seemingly paradoxical finding of higher long-term survival despite likely later-stage diagnoses in our population warrants further investigation. It may be partially explained by the high prevalence of two or more lymph node involvements in our cohort, as this has been associated with poorer RFS in other studies (Elsayed et al. 2016; Lafourcade et al. 2018; Tonellotto et al. 2019).

Consistent with previous research (Zhao et al. 2021; Bundred et al. 2020), our analysis identified age ≤ 40 years as a significant predictor of recurrence, with these women having a three times higher risk compared to those over 40. The 5-year RFS was 63% for younger women and 60% for older women. This increased risk in younger women may be linked to more aggressive tumor biology, including a higher prevalence of estrogen receptor/progesterone receptor-negative, HER2-positive, and triple-negative tumors (American Cancer Society 2019), and presentation at more advanced stages, as observed in our study where a higher proportion of women ≤ 40 years presented with stage III disease.

Preexisting comorbidity were also associated with a fourfold increased recurrence risk, potentially due to metabolic impairments interfering with treatment response (21, 43). Overweight at diagnosis nearly doubled the risk of recurrence, consistent with the established link between overweight, chronic inflammation, and breast cancer progression (Teferi et al. 2024).

As expected, positive surgical margins and positive axillary node status were also significant predictors of recurrence, aligning with findings from other studies (Elsayed et al. 2016; Tonellotto et al. 2019; Sh Mutlak et al. 2012; Teferi et al. 2024). Lymph node involvement is a strong indicator of potential disease spread and future recurrence. The association of these factors with recurrence highlights the importance of achieving negative surgical margins and thorough axillary staging.

While histologic grade and clinical stage were not independently analyzed in this study, previous research, including studies conducted in Ethiopia (Shiferaw et al. 2020; Lafourcade et al. 2018), has consistently identified poorly differentiated histologic grade (grade III) and advanced clinical stage (stage III) as predictors of recurrence. These findings are likely related to delayed tumor detection and diagnosis.

Limitation and strength of the study

We couldn't include some behavioral factors in our study because the patient charts didn't have all the necessary information. Also, because we had to exclude incomplete charts, our data might not fully represent the whole population we were studying.

However, it's important to note that this study employed a large sample size from a major referral hospital, providing valuable insights into breast cancer recurrence patterns within this specific population.

Conclusions

Overall the incidence rate of breast cancer recurrence was high. Comorbidity, Age less than 40 years, overweight, axillary node status positive, more number of lymph nodes involved and deep surgical margin were predictors variables with higher recurrence rates. These findings underline the need for targeted interventions and improved post-treatment surveillance.

Acknowledgements We acknowledge St. Paul's Hospital Millennium Medical College, Oromia Regional Health Bureau, Madda Walabu University Goba referral hospital, and Adama Hospital Medical College.

Authors contributions Design and conception of the study: Y.C., T.T., T.G., W.F., and A.D.; Performed the study: W.F., A.D., Y.C., T.G., T.T., G.A., C.A., and B.T.; Data analysis and interpretation: A.D., W.F., K.M., B.B., A.W., M.A., and T.A.; Writing of the manuscript: A.D., Y.C.; All authors have read and approved the final manuscript.

Funding No funding was obtained for this study.

Availability of data and materials No datasets were generated or analysed during the current study.

Declarations

Competing interests The authors declare no competing interests.

Ethical approval and consent to participate The ethical clearance was obtained from SPHMMC the institutional review board (IRB) (Ref. No;-Pm 23/1138). Then a support letter was submitted to the respective hospital authorities and permission was granted. Finally, the questionnaire was kept locked after the data entry.

Consent for publishing 'Not Applicable'.

References

American Cancer Society (2019) Breast Cancer: Treating Breast Cancer. Am Cancer Soc 1–120. Available from: https://www.cancer.org/cancer/breast-cancer/treatment.html

Bundred J, Michael S, Bowers S, Barnes N, Jauhari Y, Plant D et al (2020) Do surgical margins matter after mastectomy? A systematic review. Eur J Surg Oncol 46(12):2185–94. https://doi.org/10.1016/j.ejso.2020.08.015

Choi YJ, Shin YD, Song YJ (2016) Comparison of ipsilateral breast tumor recurrence after breast-conserving surgery between ductal carcinoma in situ and invasive breast cancer. World J Surg Oncol. https://doi.org/10.1186/s12957-016-0885-6

Colleoni M, Sun Z, Price KN, Karlsson P, Forbes JF, Thürlimann B et al (2016) Annual hazard rates of recurrence for breast cancer during 24 years of follow-up: results from the international breast cancer study group trials I to V. J Clin Oncol 34(9):927–935

Cossetti RJD, Tyldesley SK, Speers CH, Zheng Y, Gelmon KA (2014) Comparison of breast cancer recurrence and outcome patterns between patients treated from 1986 to 1992 and from 2004 to 2008. J Clin Oncol 33(1):65–73

Crozier JA, Moreno-Aspitia A, Ballman KV, Dueck AC, Pockaj BA, Perez EA (2013) Effect of body mass index on tumor characteristics and disease-free survival in patients from the HER2-positive adjuvant trastuzumab trial N9831. Cancer 119(13):2447–2454

DeSantis C, Siegel R, Bandi P, Jemal A (2011) Breast cancer statistics, 2011. CA Cancer J Clin 61(6):408–418

Elsayed M, Alhussini M, Basha A, Awad AT (2016) Analysis of loco-regional and distant recurrences in breast cancer after conservative surgery. World J Surg Oncol. https://doi.org/10.1186/s12957-016-0881-x

Franken B, de Groot MR, Mastboom WJB, Vermes I, van der Palen J, Tibbe AGJ et al (2012) Circulating tumor cells, disease recurrence and survival in newly diagnosed breast cancer. Breast Cancer Res 22:14

He XM, Zou DH (2017) The association of young age with local recurrence in women with early-stage breast cancer after breast-conserving therapy: a meta-analysis. Sci Rep. https://doi.org/10.1038/s41598-017-10729-9

Horani M, Abdel-Razeq H (2023) Treatment options for patients with hormone receptor-positive, HER2-negative advanced-stage breast cancer: maintaining cyclin-dependent kinase 4/6 inhibitors beyond progression. Front Oncol 13:1–8

Kheradmand AA, Ranjbarnovin N, Khazaeipour Z (2010) Postmastectomy locoregional recurrence and recurrence-free survival in breast cancer patients. World J Surg Oncol 17:8

Lafourcade A, His M, Baglietto L, Boutron-Ruault MC, Dossus L, Rondeau V (2018) Factors associated with breast cancer recurrences or mortality and dynamic prediction of death using history of cancer recurrences: the French E3N cohort. BMC Cancer. https://doi.org/10.1186/s12885-018-4076-4

Lowery AJ, Kell MR, Glynn RW, Kerin MJ, Sweeney KJ (2012) Locoregional recurrence after breast cancer surgery: a systematic review by receptor phenotype. Breast Cancer Res Treat. https://doi.org/10.1007/s10549-011-1891-6

Metzger-Filho O, Sun Z, Viale G, Price KN, Crivellari D, Snyder RD et al (2013) Patterns of recurrence and outcome according to breast cancer subtypes in lymph node-negative disease: Results from international breast cancer study group trials VIII and IX. J Clin Oncol 31(25):3083–3090

Ren Z, Li Y, Hameed O, Siegal GP, Wei S (2014) Prognostic factors in patients with metastatic breast cancer at the time of diagnosis. Pathol Res Pract 210(5):301–6. https://doi.org/10.1016/j.prp.2014.01.008

Sh Mutlak N, Ramiz Al-Mukhtar F, Nabeel Al-Dawoodi FS, Tharwat Sulaiman CI (2012) Recurrent breast cancer following modified radical mastectomy and risk factors. J Fac Med Baghdad Baghdad. 54:198–203

Sharma R, Nanda M, Fronterre C, Sewagudde P, Ssentongo AE et al (2022) Mapping Cancer in Africa: a comprehensive and comparable characterization of 34 Cancer types using estimates from GLOBOCAN 2020. Front Public Heal. https://doi.org/10.3389/fpubh.2022.839835

Shiferaw WS, Aynalem YA, Yirga Akalu T, Demelew TM (2020) Incidence and Predictors of Recurrence among Breast Cancer Patients in Black Lion Specialized Hospital Adult Oncology Unit, Addis Ababa, Ethiopia: Retrospective Follow-up Study with Survival Analysis. J Cancer Prev 25(2):111–8. https://doi.org/10.15430/JCP.2020

Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A et al (2021) Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 71(3):209–249

Teferi D, Dadi D, Hassen I, Teklemariam B, Yesufe A (2024) Empowering catchment health center to deliver comprehensive and safe obstetric care near clients' home: an Institutional experience in Ethiopia. Clin Audit 16:29–37

Tonellotto F, Bergmann A, de Souza AK, de Aguiar SS, Bello MA, Thuler LCS (2019) Impact of number of positive lymph nodes and lymph node ratio on survival of women with node-positive breast cancer. Eur J Breast Heal 15(2):76–84

Trayes KP, Cokenakes SE (2021) Treatment cancer breast. Am Fam Physician 104(2):171–178

Wangchinda P, Ithimakin S (2016) Factors that predict recurrence later than 5 years after initial treatment in operable breast cancer. World J Surg Oncol. https://doi.org/10.1186/s12957-016-0988-0

Wu X, Baig A, Kasymjanova G, Kafi K, Holcroft C, Mekouar H et al (2016) Pattern of local recurrence and distant metastasis in breast cancer by molecular subtype. Cureus. https://doi.org/10.7759/cureus.924

Zhao C, Hu W, Xu Y, Wang D, Wang Y, Lv W et al (2021) Current landscape: the mechanism and therapeutic impact of obesity for breast cancer. Front Oncol 11(July):1–20

Authors and Affiliations

Yadessa Chala[1] · Tesfaye Techane[2] · Bonsisa Bekele[2] · Tesfaye Girma[2] · Warati Fekede[3] · Chalchisa Abdeta[5] · Kibiru Mardasa[3] · Tolera Abdeta[3] · Bedada Teshome[4] · Gashaye Atinkut[3] · Abdinasir Wako[3] · Mohammed Adem[3] · Alem Deksisa[3]

✉ Alem Deksisa
alexdugna@gmail.com

Yadessa Chala
yadessachala403@gmail.com

Tesfaye Techane
tesfaye.techane@sphmmc.edu.et

Bonsisa Bekele
bonsisaoro@gmail.com

Tesfaye Girma
girmanet12@gmail.com

Warati Fekede
warati2016@gmail.com

Chalchisa Abdeta
chali4pa@gmail.com

Kibiru Mardasa
kibirumardasa5@gmail.com

Tolera Abdeta
tolera2011@gmail.com

Bedada Teshome
bedadateshome2@gmail.com

Gashaye Atinkut
gashayeatinkut40@gmail.com

Abdinasir Wako
wakoabdinasir@yahoo.com

Mohammed Adem
muhesalim@gmail.com

[1] Madda Walabu University Goba Referral Hospital, Goba, Ethiopia

[2] Department of Oncology, Saint Paul Hospital Millennium Medical College, Addis Ababa, Ethiopia

[3] Department of Public Health, General Surgery, and Internal Medicine, Adama Hospital Medical College, Adama, Ethiopia

[4] Adama Public Health Research and Referral Laboratory Center, Adama, Ethiopia

[5] Early Start, School of Education, University of Wollongong, Wollongong, Australia