



Citation: Agodirin O, Olatoke S, Rahman G, Kolawole O, Oguntola S, Olasehinde O, et al. (2021) Determinants of late detection and advanced-stage diagnosis of breast cancer in Nigeria. PLoS ONE 16(11): e0256847. https://doi.org/10.1371/journal.pone.0256847

Editor: Shah Md Atiqul Haq, Shahjalal University of Science and Technology, BANGLADESH

Received: March 28, 2021

Accepted: August 17, 2021

Published: November 3, 2021

Peer Review History: PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: https://doi.org/10.1371/journal.pone.0256847

Copyright: © 2021 Agodirin et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All relevant data are within the manuscript and its <u>Supporting</u> information files.

RESEARCH ARTICLE

Determinants of late detection and advancedstage diagnosis of breast cancer in Nigeria

Olayide Agodirin 1,2*, Samuel Olatoke¹, Ganiyu Rahman^{1,3}, Oladapo Kolawole⁴, Saliu Oguntola⁵, Olalekan Olasehinde⁶, Omobolaji Ayandipo⁷, Julius Olaogun⁸, Aba Katung⁹, Amarachukwu Etonyeaku¹⁰, Olufemi Habeeb¹, Ademola Adeyeye¹¹, John Agboola 2, Halimat Akande¹², Olusola Akanbi⁵, Oluwafemi Fatudimu¹³, Anthony Ajiboye²

1 Department of Surgery, University of Ilorin and University of Ilorin Teaching Hospital, Ilorin, Nigeria,
2 Department of Surgery, General Hospital, Ilorin, Nigeria,
3 Department of Surgery, Cape Coast University and Cape Coast Teaching Hospital, Cape Coast, Ghana,
4 Department of Surgery, LAUTECH Teaching Hospital, Ogbomoso, Nigeria,
6 Department of Surgery, Obafemi Awolowo University and Obafemi Awolowo University Teaching Hospital, Ile-Ife, Nigeria,
7 Department of Surgery, University College Hospital, Ibadan, Nigeria,
8 Department of Surgery, Ekiti State University and Ekiti State University Teaching Hospital, Ado-Ekiti, Nigeria,
9 Department of Surgery, Federal Medical Center, Owo, Nigeria,
10 Department of Surgery, Obafemi Awolowo University Ile-Ife and Obafemi Awolowo Teaching Hospital Complex, Ilesha, Nigeria,
11 Department of Surgery, University of Ilorin Teaching Hospital, Ilorin, Nigeria,
12 Department of Radiology, University of Ilorin and University of Ilorin Teaching Hospital, Ilorin, Nigeria,
13 Department of Surgery, Federal Teaching Hospital, Ilorekiti, Nigeria
14 Department of Surgery, Federal Teaching Hospital, Ilorekiti, Nigeria
15 Department of Surgery, Federal Teaching Hospital, Ilorekiti, Nigeria
16 Department of Surgery, Federal Teaching Hospital, Ilorekiti, Nigeria
17 Department of Surgery, Federal Teaching Hospital, Ilorekiti, Nigeria
18 Department of Surgery, Federal Teaching Hospital, Ilorekiti, Nigeria

* cancer1992@yahoo.com

Abstract

Late detection of Breast cancer(BC) and progressing with advanced-stage diagnosis after early detection contribute differently to the challenges of managing BC in Africa. Understanding the difference may improve cancer education programs and their effectiveness.

Objective

To describe the risk factors for late detection and advanced-stage diagnosis among patients who detected their BC early.

Method

Using secondary data, we analyzed the impact of socio-demographic factors, premorbid experience, BC knowledge, and health-seeking pattern on the risk of late detection and advanced-stage diagnosis after early BC detection. Test of statistical significance in SPSS and EasyR was set at 5% using Sign-test, chi-square tests (of independence and goodness of fit), odds ratio, or risk ratio as appropriate.

Result

Most socio-demographic factors did not affect detection size or risk of disease progression in the 405 records analyzed. High BC knowledge, p-value = 0.001, and practicing breast self-examination (BSE) increased early detection, p-value = 0.04, with a higher probability (OR 1.6 (95% CI 1.1–2.5) of detecting <2cm lesions. Visiting alternative care (RR 1.5(95% CI 1.2–1.9), low BC knowledge (RR 1.3(95% CI 1.1–1.9), and registering concerns for

Funding: The African Research Group for Oncology (ARGO) sponsored the data-generating primary research with a pilot grant award to AO. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests: The authors have declared no competing interests exist.

hospital care increased the risk of advanced-stage diagnosis after early detection (64% (95% CI 55–72)). Adhering to the monthly BSE schedule reduced the risk of advanced-stage diagnosis by -25% (95% CI -49, -1.1) in the presence of socioeconomic barriers.

Conclusion

Strategies to increase BC knowledge and BSE may help BC downstaging, especially among women with common barriers to early diagnosis.

Introduction

Downstaging symptomatic breast cancer (BC) through early detection and diagnosis is a topical issue in sub-Saharan Africa (SSA) because socioeconomic barriers and lack of infrastructure make asymptomatic population-based screening impractical. The patient demographic and presentation patterns also make mammography an ineffective screening tool [1, 2].

Promoting early detection practices and following through with early diagnosis and timely treatment will improve BC outcomes in Africa [1]. Most breast cancers are incidental self-detection in Africa, and up to 80% are diagnosed at stage III or IV, with most patients delaying treatment for more than six months.

There are reports on the risk factors for late presentations in SSA [3–6]. However, direct reports on determinants of late detection among BC patients are rare. The few reports on early detection practices identified in a Black et al. [1] review were in healthcare providers and non-afflicted laywomen. Furthermore, reports on advanced-stage diagnosis failed to distinguish tumors already advanced at the time of detection or recognition from those progressing after early detection. Yet, our previous research showed that late detection and progressing to advanced disease after an early detection contributed differently to advanced-stage diagnosis and challenges of managing BC. In that research, 10% of tumors detected inadvertently were already advanced, while 30–70% of those detected early progressed to advanced-stage before diagnosis [7].

Late detection and progressing after early detection may have different determinants, and understanding the difference might improve cancer education programs' effectiveness in SSA. This study aimed to describe risk factors for late-stage detection and advanced-stage diagnosis among a subpopulation of BC patients who detected their cancers early.

Materials and method

This research was a secondary data analysis using de-identified data from a study sponsored by the African Research Group for Oncology (ARGO). The original research was a cross-sectional multicentered survey in referral centers in Northcentral and Southwestern Nigeria, including convenience sampling of newly diagnosed BC patients between June 2017 and May 2018 after obtaining ethical approval from all institutions and written consent from participants. The ethical review committee gave additional approval for the current study [UITH ERC PAN/2021/01/0170].

Trained personnel collected the data using specially designed pilot-tested proforma and entered it into a specially designed Microsoft Access database. The primary research instituted mechanisms to minimize recall bias and ensure data reliability. Details of the design and original data collection are available elsewhere [7].

Data of interest in the present research were the demographics and socioeconomic variables, including age, sex, employment status, religion, and marital status. The premorbid experience including the source of BC information, awareness, prior knowledge of BC treatment and outcomes, concern about hospital treatment of BC, and health-seeking pattern: premorbid help-seeking preferences, breast self-examination/ clinical breast examination, number of hospitals, and health care providers (HCP) visited to treat current disease, the initial symptom, tumor size at detection and diagnosis, and reason for referral. The tumor size at detection was a retrospective record, while the size at diagnosis was prospective in the original research.

Statistical analysis

In this analysis, clinical tumor size (T-size) was the surrogate for disease stage using the T1-3 according to the 7^{th} edition of the American Joint Committee on Cancer (AJCC) staging for BC, where T1 was \leq 2cm, T2 was 2.1-5cm, and T3 was >5cm. We defined early detection and early diagnosis as size \leq 5cm and small tumor as size \leq 2cm. To evaluate each risk factor, we analyzed its impact on the T-size distribution, the odds of detecting small tumors (\leq 2cm), and the probability of being diagnosed early after early detection.

The effect of age was analyzed by comparing three subgroups; <40, 41–60, and >60. Marital status was analyzed as married vs. unmarried (with unmarried comprising single, widows, separated, or divorced). The level of education was analyzed as secondary/tertiary vs. no education/ primary level. Three subgroups of BC Knowledge were compared; no, low and high knowledge. [We defined none as the lack of BC awareness, low as BC awareness only, and high as BC awareness plus any additional information such as knowing screening modalities, types of breast lumps, BC treatment, or outcome of someone who had BC]. Being employed was compared to being unemployed. Living close to the study center (<30 minutes drive) was compared to living remotely (31–60 minutes and >60 minutes). Consulting an orthodox health care provider first was compared to consulting alternative medicine first. Visiting only one healthcare provider (HCP) was compared to visiting more than one HCP, and visiting a single hospital was compared to visiting multiple hospitals before diagnosis.

The inferential statistic for single proportion used the binomial test, comparison of two or more proportions used the chi-square test of independence/ Fisher's exact or goodness of fit. The risks (probabilities of events) were compared using either the binary logistic regression for the odds ratio or the risk ratio. We presented the results using descriptive statistics, including the 95% confidence intervals (95% CI). We set the test of statistical significance at 5% for all analysis. The analysis was conducted in SPSS v20 and EasyR.

Results

This research included 405 records of patients aged 24-95 (mean 49.3 ± 16 , median 49). The majority were middle age (176,43.4%), married (274, 79%), and educated (175, 43.2%). The younger age groups were more educated (p-value = 0.001). The majority (294, 73%) were aware of BC, 162 (55%) of which had low knowledge, and 132 (45%) had high knowledge. The most common source of BC information was a radio program. The younger patients had more BC information (p-value = 0.02) despite similar information sources across all age groups. Many patients obtaining information from non-medics (person-to-person social contacts and media outlets) had high BC knowledge. Fifty-five percent (95% CI 50–60) of the patients reported practicing breast self-examination (BSE), with only 17% (95% CI 12–23) maintaining the standard monthly schedule (Table 1).

Table 1. The patient demographics, distribution of information source, the comparison of level of eduction, practice of breast self-examination and information across age groups, comparison of breast cancer knowledge based on information source and education and distribution of BC knowledge across age groups.

The patient demographics						
		N(%)				N(%)
Age	40 & below	103(25)		Marital	Married	274(68)
	41 to 60	176(43)			Divorced	7(2)
	Above 60	70(17)			Widow	43(11)
	NS	56(15)			Single	21(5)
					NS	57(14)
Education	None	44(11)		Religion	Christian	283(70)
	Primary	48(12)			Muslim	108(27)
	Secondary	57(14)			NS	11(3)
	Tertiary	118(29)		Side	left	147(37)
	NS	138(34)			Right	143(36)
	'				NS	112(27)
Distribution of information source			'		'	, , , ,
Social contact/person-to-person	Church	13(3.1)				
. 1	Facebook	9(2.2)				
	Relations/Friends	41(10)				
	School	11(3.0)				
Media	Flier	2(0.5)				
	Newsprint	3(0.7)				
	Radio	76(19)				
	Television	21(5.1)				
Health talk	Hospital/NGO	49(12)				
Trouver team	NS NS	180(44.4)				
Comparison of the level of education		100(11.1)				
Comparison of the level of education		Age distribution (yea	urs)	p-value		
	40	41-60	>60	p varue		
Low education	11	43	39	0.001		
High education	98	168	47	0.001		
Comparison of the practice of Breast			17			
Practice BSE	49	106	28	0.01		
Not practice	45	73	45	0.01		
Comparison of the source of information		13	13			<u> </u>
Person-to-person	6	35	10	0.26		
media	20	58	23	0.20		
healthtalk	13	24	7			
		24	/			
Comparison of BC knowledge based		M. J.	TT141- 4 -11-			
I DC ll. l.	Person to person	Media	Healthtalk	0.01		
Low BC knowledge	30	57	33	0.01		
High BC knowledge	32	48	11			
Distribution of BC knowledge in low			•			
		reast cancer knowle				
	None	Low	High			
	36	36	22	0.02		
Low education High education	76	127	109			

(Continued)

Table 1. (Continued)

≤ 40	42	41	38	0.02	
41-60	48	85	78		
>60	25	45	20		

BSE- Breast Self Examination, Divorced = Divorced or separated, NGO- Nongovernmental, NS- Not specified Organization, Person-to-person = social and person-to-person contact.

https://doi.org/10.1371/journal.pone.0256847.t001

Determinants of tumor size distribution at detection

Common social and demographic factors such as age, level of education, marital status, education level, and employment status did not significantly affect tumor size distribution at detection. The premorbid health-seeking behavior, BC information source, and tumor laterality did not significantly affect tumor size distribution at detection (Table 2). More Christians detected earlier (\leq 5cm) tumors than Muslims (p-value = 0.001). Women with higher knowledge of BC detected earlier (\leq 5cm) tumor (p-value = 0.001), and women practicing BSE also detected earlier (\leq 5cm) tumors (p-value = 0.04) (Table 2). The odds of detecting small tumors (\leq 2cm) were also significantly higher among women practicing BSE (OR 1.6 (95%CI 1.1–2.5)). However, being educated (low education OR 0.9 (95% CI 0.6–1.1), high education OR 1.4 (95% CI 0.8–2.2) did not significantly affect the odds of detecting small tumors ((\leq 2cm) compared to being uneducated. Also, being a Christian (OR 1.2 (95% CI 0.8–2.0) did not significantly affect the odds of detecting small tumors women with high BC knowledge practiced BSE and adhered to the regular monthly schedule. Tumor laterality did not affect BSE's impact on the probability of detecting small tumors.

Risk factors for tumor progression after early detection

Age, level of education, employment, marital status, and place of residence did not significantly affect the risk of tumor progression after early detection. The pattern of symptomatology, learning about BC from non-medical personnel, and visiting multiple hospitals or multiple health care providers did not significantly affect the risk of tumor progression. First visiting an alternative to orthodox medical care, low BC knowledge, and not practicing BSE were associated with significant risk of progression (Table 3 and Fig 1). Among 79 patients who visited alternative care first, the majority resided close to the referral center (89% (95% CI 80–95). In the same population, 70% of those residing <60 minutes away experienced disease progression whereas a smaller proportion (44% (4 of 9)) of those living remotely experienced disease progression. The difference was not statistically significant (p-value = 0.14). Familiarity with BC patients and knowing poor BC outcomes were not significant deterrents to early-stage diagnosis (Table 3).

Risk of disease progression after early detection in patients with barriers to early presentation

Subgroup exploratory analysis showed significant risk of disease progression among women expressing any concern (64%(95% CI 55–72). The risk of progression was also significant among those expressing cost concern (67% (95% CI 53–79), whereas the risk was high but not statistically significant among those expressing concern about having a mastectomy (62% (95%CI 42–71) (Table 4 and Fig 2).

Table 2. The effect of the demographics, premorbid treatment preferences, level of knowledge, and practice of breast-self examination on tumor size distribution at detection. Also, showing the regularity of Breast Self-Examination based on breast cancer knowledge.

Effect of age on the distribution of tu	mor size at detection				
		T1 n(%)	T2 n(%)	T3 n(%)	p-value
Age	40 and below	52(46)	51(45)	11(9)	0.42
	41-60	80(39)	102(49)	24(11)	
	Above 60	30(34)	45(51)	14(15)	
Effect of Premorbid treatment prefer	ence on the distribution of tum-	or size at detection			
	Alternative	8(27)	14(49)	7(24)	0.17
	Self-medicate	61(46)	60(44)	15(10)	
	Visit hospital	71(39)	92(50)	20(11)	
Effect of religion on the distribution					I
	Muslim	39(19)	57(26)	111(55)	0.001
	Christian	116(40)	137(46)	35(14)	
Effect of breast cancer knowledge on	the distribution of tumor size a	t detection	I		
	No knowledge	42(38)	60(54)	10(8)	0.001
	Low knowledge	61(36)	79(49)	25(15)	
	High knowledge	60(45)	59(44)	15(11)	
Effect of level of education on the dis					1
	Low education	32(33)	51(53)	12(12)	0.38
	High education	131(44)	147(47)	38(9)	
Effect of employment status on the d					
	Unemployed	5(31)	6(38)	5(31)	0.14
	Employed	81(38)	103(49)	28(13)	
	Unmarried	25(35)	34(49)	12(16)	0.24
	Married	114(45)	135(49)	28(6)	
Effect of practice of Breast Self-Exam					
Practice BSE	No	58(36)	92(57)	12(7)	0.04
	Yes	93(47)	82(41)	25(12)	
BSE schedule	Daily	27(54)	19(38)	4(8)	0.03
	Weekly	4(20)	9(45)	7(35)	
	Monthly	14(42)	16(47)	4(11)	
	Occasionally	48(47)	38(42)	10(11)	
Effect of tumor laterality on the distr					
	left	51(34)	81(53)	19(13)	0.21
	right	60(41)	63(43)	22(16)	
Effect of information source on the d			<u> </u>		
	Person to person	20(32)	31(49)	12(19)	0.42
	Media	46(42)	52(47)	12(11)	
0	Healthtalk	21(47)	20(43)	5(10)	
Comparison of the distribution of tu	mor size based on the laterality		FF0 (21)	FIQ. (21)	
	1.6	Tln (%)	T2n (%)	T3n (%)	p-value
Among those performing BSE	left	25(42)	27(45)	8(13)	0.33
	Right	35(47)	24(32)	14(21)	
Among those on regular BSE	Left	4(29)	8(57)	2(14)	0.32
Among those on regular BSE	Right	6(55)	3(27)	2(18)	
		,			
Among those on regular BSE Regularity of Breast Self-Examination				771.1.1	
Regularity of Breast Self-Examination	n based on breast cancer knowle	No know	Low know	High know	0.000
			Low know 16 (18) 43(57)	High know 64(72) 6(8)	0.001

https://doi.org/10.1371/journal.pone.0256847.t002

Table 3. The effect of the demographics and socioeconomic factors, symptomatology, premorbid preferences, and level of breast cancer information on the risk of disease progression after early detection and the probability of disease progression in the presence of barriers to early presentation.

	Progression	No(n)	Yes(n)	p-value	Risk Ratio (95%CI)
Age					
	<40	33	70	0.43	1
	41-60	66	110		0.9(0.8–1.1)
	>60		41		0.9(0.7-1.1)
Level of Education		1			
	Educated	105	167	0.16	1
	Uneducated		56	0.10	1.2(1.0–1.4)
Religion	Chedicaled	25	130		1.2(1.0 1.1)
Kengion	Christian	02	162	0.44	1
	Muslim		56	0.44	0.9(0.9–1.1)
D:	·	30	30		0.9(0.9–1.1)
Distance (Drive to stud	<u> </u>		T_0	1	1.
	0-30		79	0.74	1
	31-60		40		1.1(0.9–1.4)
	>60	11	13		1.0(0.6–1.4)
Marital Status	1				
	Married	85	159	1.0	1
	Unmarried	20	38		1(0.8–1.2)
Employment Status					
	Employed	61	20	0.47	1
	Unemployed	7	4		1.4(0.6–3.5)
Tumor Laterality					
,	Right	42	48	0.64	1
	Left		79		1.1(0.9–1.3)
Γumor size	Lett	01	177		1.1(0.2 1.3)
i umor size	<2cm	6E	95		1
	>2cm		123		
2 , , 1	>2CIII	03	123		1.1(0.9–1.3)
Symptomatology	1		T_0	1	Ι.
	lump		70	0.97	1
	No lump	84	171		1.0(0.9–1.2)
Health seeking prefere	T. Control of the con	1			
	Visit hospital		89	0.007	1
	Self-medicate	36	83		1.2(1-1.5)
	Alternative care	3	18		1.5(1.2–1.9)
Number of Hospital or	r HCP visited				
	1hospital	48	70	0.33	1
	>1hospital		35		1.1(0.9–1.5
НСР	-		61	0.37	1
	>1HCP		118		1.1 (0.9–1.3)
Breast Self Examinatio		**	1	1	1 - ()
BSE		77	83	0.0003	1
DSE	Not Perform			0.0003	
n 1			107	0.70	1.4(1.2–1.7)
Regularity	·		13	0.78	1
	Weekly		6		1.0(0.5-2)
	Daily		21		1.2(0.7–2)
	Occasionally	35	43		1.2(0.8–2)

(Continued)

Tabla 2	(Continued)
i anie 5.	Commuea

e	Health talk	21	20	0.31	1
	Others	99	141		1.2(0.9–1.7)
Level of Breast Cancer	Knowledge				
	High knowledge	56	60	0.0002	1
	No knowledge	21	79		1.5(1.2–1.9)
	Low knowledge	51	84		1.3(1.1–1.5)
Previous Interaction W	7ith BC Patients				
Interaction	No patient known	5	2	0.23	1
	Knows BC patient	13	19		2.0(0.6–7.0)
Outcome known	Alive	4	5	1.0	1
	Died	9	12		1.0(0.5-2.0)
Prompt for Visiting Spe	ecialist				
Reason	referred	42	73	0.57	1
	self	11	27		1.1(0.9–1.4)
	advice	14	33		1.0(0.8-1.3
The probability of disea	ase progression in the presence of barriers to early pro	esentation			
	Subgroups with Barrier (Concerns)	No(n)	Yes(n)		Risk of Progression in subgroup% (95% CI)
	Concern for mastectomy	21	34	0.11	62 (48–75)
	Mastectomy concern in forty years and below	7	15	0.13	68 (45–86)
	Mastectomy concern above 40 years	14	19	0.48	58 (39–75)
	Cost concern	21	41	0.015	66 (53–78)
	Other concerns	11	15	0.56	58 (37–77)

HCP- Health Care Provider.

Other concerns: The attitude of personnel, chemotherapy/fertility, conflicting statements, delay/bureaucracy/stress, death.

https://doi.org/10.1371/journal.pone.0256847.t003

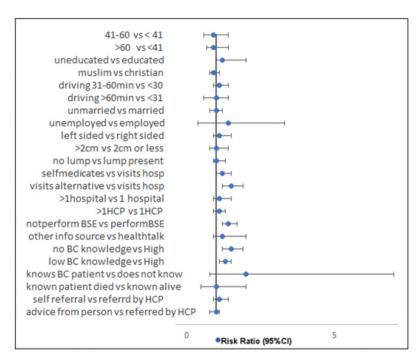


Fig 1. Forest plot of risk ratio for disease progression. Showing the Risk Ratio for disease progression based on demographic, socioeconomic factors, symptomatology premorbid preferences, and knowledge. BC- Breast Cancer, BSE-Breast Self-Examination, HCP-Healthcare Provider, vs = 'compared to'.

https://doi.org/10.1371/journal.pone.0256847.g001

Table 4. Showing interaction between practice of BSE and incidence of progression.

Risk of progression amo	ong patients with barrier			
Concern (N)	No progression	Progression	Risk of Progression (95%CI)	p-value
Any (141)	51	90	64(55–72)	0.001
Mastectomy (49)	21	28	57(42-71)	0.39
Cost (57)	19	38	67(53–79)	0.016
Others (35)	11	24	69(51-83)	0.041
Among those practicing	g any BSE			
Any concern (74)	33	41	54(43-67)	0.42
Mastectomy (27)	14	13	49(29–68)	1.0
Cost (28)	13	15	53(34-75)	0.85
Others (19)	6	13	68(43–87)	0.17
Among those practicing	g monthly BSE			
Any concern (18)	11	7	39(17-64)	0.48
Mastectomy (7)	6	1	14(0.4–58)	0.13
Cost (60	3	3	50(12-88)	1.0
Others (5)	2	3	60(15–95)	1.0
Comparison between th	ose practicing BSE and those not pr	acticing		
	No BSE N(progession)	Practice BSE N(progression)	Risk Ratio for progression	
Any	67(49)	74(41)	1.32(1.0-1.7)	0.04
Mastectomy	22(15)	27(13)	1.4(0.9-2.3)	0.25
Cost	29(23)	28(15)	1.5(1.0-2.2)	0.05
Others	16(11)	19(13)	1.0(0.6-1.6)	1.0

BSE- Breast Self Examination.

Progression = number progressing from early to an advanced stage before diagnosis.

Risk of progression = number progressing divided by the total number (N).

https://doi.org/10.1371/journal.pone.0256847.t004

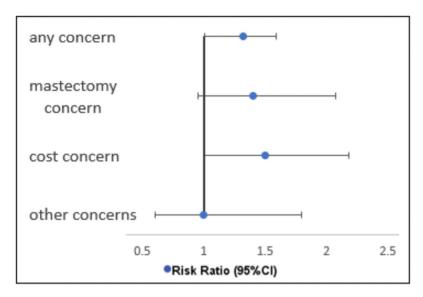


Fig 2. Forest plot of risk ratio of disease progression among those performing BSE. Showing Risk Ratio of disease progression among patients not performing Breast Self-Examination compared to those performing Breast Self-Examination.

https://doi.org/10.1371/journal.pone.0256847.g002

In patients expressing any concern for hospital care, the risk of disease progression was lower among those practicing BSE (-8.5% (95% CI -22, 5.4) compared to not practicing BSE and more so among those adhering to a monthly routine, with a significantly reduced risk of -25% (95% CI -49, -1.1).

Discussion

Breast cancer causes significant morbidity and mortality in SSA, and much-needed information on late detection and factors associated with advanced-stage diagnosis to improve BC outcomes in SSA is scarce. We researched the risk factors for late detection and advanced stage diagnosis of the disease after early detection. We found that high BC knowledge and practicing BSE were associated with detecting smaller tumors and lowered the risk of progressing to advanced stages before diagnosis. Visiting alternatives to orthodox care and concerns about healthcare costs were associated with disease progression.

The initial breast lump detection mode has prognostic implications; lesions detected by mammography are often smaller with a better prognosis than those seen by BSE [8]. Our finding here suggests that women practicing BSE detected small lumps. BSE's role is controversial as studies in developed countries [9, 10] showed that it increased the frequency of breast complaints, prompted more visits to physicians, and led to more biopsies without significant benefits in tumor size at detection or survival [11]. Nonetheless, the evidence supporting BSE/clinical breast examination (CBE) is mounting, especially in centers where BC is detected inadvertently and diagnosed at the late stages [12–15].

Significant gaps exist in our knowledge of how best to improve early presentation and acceptance of BC treatment in SSA. Since population-based screening is not feasible [16] due to economic, infrastructural, and personnel deficiencies, Africa must explore innovative low-cost, and sustainable means of downstaging the disease. A program [12] in Sudan's rural communities used volunteers in door-to-door breast examination to increase early BC detection. Another research to integrate breast health services into clinical practice in Ghana [17] proposed a model grounded in human interaction and based on the experience of BC patient and their relations whereby trained personnel offered breast cancer information, the teaching of BSE, and CBE to the relations and micro-communities of breast cancer patients [17].

Given that most breast cancer in Africa is self-detected, understanding the BSE barriers and determinants is essential. Factors reported to affect BSE performance are years of college education, knowledge of BSE and its method, perception of the benefit of associating BSE with a likelihood of detecting smaller lesions, longer breastfeeding duration, the pressure of responsibilities, and forgetfulness [18–20].

Strategies to downsize Breast cancer rely on widespread patient-level education, personnel training, and an organized healthcare system [13] to retain patients and complete treatment. Unfortunately, ensuring timely diagnosis and adhering to medical care after disease detection is still a challenge in Nigeria and Africa. Encouragingly, we found that practicing BSE increased the chances of early diagnosis despite known barriers, even among those registering concern for mastectomy and cost of hospital treatment. This suggests that practicing BSE might not only influence early detection; it might also be a predictor of the willingness or motivation to follow through with timely diagnosis and treatment, with the strongest association among women practicing BSE in the standard monthly schedule.

The influence of the common socio-demographic factors on delay varies remarkably within and across regions of Africa. Such factors as age, level of education, marital status, residing remotely, and employment status did not influence detection size and risk of disease

progression in the cohort studied here. Nevertheless, these factors merit further research as they often contribute to delay and treatment challenges in SSA.

The influence of symptomatology on delay is fairly consistent in the literature; the absence of breast lump, pain, and ulceration are linked to delays. Recently, the implication of laterality is becoming more apparent. A report in India [21] found right-sided tumors were diagnosed at later stages compared to left-sided tumors, suggesting the impact of handedness. It is reassuring in this study that tumor laterality did not appear to diminish the effect of BSE on detecting small tumors.

Another possibly advantageous exploratory finding pertinent to the challenges of managing BC in poor-resource centers is that receiving information from non-medics might not negatively affect its benefit. Getting comprehensible breast health messages to as many women as possible might be more important than the source. Similarly, A recent report from Uganda found that irrespective of the source, women who received breast health education previously participated more in BSE and CBE [22]. However, there was segregation depending on the place of health care service, with women receiving care in public services preferring messages from healthcare providers. In contrast, those paying out of pocket preferred messages from friends and family.

Africa needs more context-specific interventional research similar to the effort in Sudan [12] using locally trained personnel for CBE and in Ghana [17] intervening on BC patients' micro-communities using CBE and BSE. Such studies should assess the feasibility, cost-effectiveness, and benefit of the BC down-staging strategies. Simple assumptions or over-generalization of research findings should be avoided in rolling out interventional programs or policies because of unexpected and counterintuitive findings. For instance, family history of BC and history of benign lesions were associated with increased risk of endstage disease [21], negating the expected positive effect of prior knowledge in an Iranian study. Our findings showed significant use of alternatives and a higher proportion of disease progression among those living close to referral centers, thus negating the expected effect of distance.

Being a secondary analysis limits our findings. Also, we did not directly determine that the tumors were detected during BSE, and we did not assess the knowledge of BSE and the method. Furthermore, we could not evaluate the association between detection, time to treatment, and treatment outcome. Notwithstanding, the present report is one of few studies on factors associated with advanced-stage diagnosis in Africa, providing insight into some previously unreported and under-researched associations that might aid down-staging breast cancer in Africa.

Conclusion

Most of the socioeconomic and demographic risk factors commonly influencing late presentation and diagnosis of BC in Africa did not affect early detection or risk of progression among patients who detected their disease early. High knowledge of BC and practicing BSE were consistently associated with early detection and early diagnosis. Additionally, the simple habit of checking the breast might increase early BC detection while adhering to the standard routines of BSE might be associated with detecting even smaller tumors and following through with early diagnosis in the face of common barriers.

Supporting information

S1 Data. Minimum data file. (XLSX)

Author Contributions

Conceptualization: Olayide Agodirin, Samuel Olatoke, Ganiyu Rahman.

Data curation: Olayide Agodirin. **Formal analysis:** Olayide Agodirin.

Methodology: Olayide Agodirin, Samuel Olatoke, Ganiyu Rahman.

Project administration: Olayide Agodirin.

Visualization: Samuel Olatoke.

Writing – original draft: Olayide Agodirin, Samuel Olatoke, Ganiyu Rahman, Oladapo Kolawole, Saliu Oguntola, Olalekan Olasehinde, Omobolaji Ayandipo, Julius Olaogun, Aba Katung, Amarachukwu Etonyeaku, Olufemi Habeeb, Ademola Adeyeye, John Agboola, Halimat Akande, Olusola Akanbi, Oluwafemi Fatudimu, Anthony Ajiboye.

Writing – review & editing: Olayide Agodirin, Samuel Olatoke, Ganiyu Rahman, Oladapo Kolawole, Saliu Oguntola, Olalekan Olasehinde, Omobolaji Ayandipo, Julius Olaogun, Aba Katung, Amarachukwu Etonyeaku, Olufemi Habeeb, Ademola Adeyeye, John Agboola, Halimat Akande, Olusola Akanbi, Oluwafemi Fatudimu, Anthony Ajiboye.

References

- Black E, Richmond R. Improving early detection of breast cancer in sub-Saharan Africa: why mammography may not be the way forward. Global Health. 2019; 15(1):3. https://doi.org/10.1186/s12992-018-0446-6 PMID: 30621753
- dos Santos Silva I, McCormack V, Jedy-Agba E, Adebamowo C. Downstaging Breast Cancer in sub-Saharan Africa: A realistic target? Cancer Control. 2017:46–52.
- Pace LE, Mpunga T, Hategekimana V, Dusengimana JM, Habineza H, Bigirimana JB, et al. Delays in Breast Cancer Presentation and Diagnosis at Two Rural Cancer Referral Centers in Rwanda. Oncologist. 2015; 20(7):780–8. https://doi.org/10.1634/theoncologist.2014-0493 PMID: 26032138
- Moodley J, Cairncross L, Naiker T, Constant D. From symptom discovery to treatment—women's pathways to breast cancer care: a cross-sectional study. BMC Cancer. 2018; 18(1):312. https://doi.org/10.1186/s12885-018-4219-7 PMID: 29562894
- Moodley J, Cairncross L, Naiker T, Momberg M. Understanding pathways to breast cancer diagnosis among women in the Western Cape Province, South Africa: a qualitative study. BMJ open. 2016; 6(1). https://doi.org/10.1136/bmjopen-2015-009905 PMID: 26729392
- Otieno ES, Micheni JN, Kimende SK, Mutai KK. Delayed presentation of breast cancer patients. East African medical journal. 2010; 87(4):147–50. https://doi.org/10.4314/eamj.v87i4.62410 PMID: 23057289
- Agodirin O, Olatoke S, Rahman G, Olaogun J, Olasehinde O, Katung A, et al. Presentation intervals and the impact of delay on breast cancer progression in a black African population. BMC public health. 2020; 20(1):962. https://doi.org/10.1186/s12889-020-09074-w PMID: 32560711
- Szukis HA, Qin B, Xing CY, Doose M, Xu B, Tsui J, et al. Factors Associated with Initial Mode of Breast Cancer Detection among Black Women in the Women's Circle of Health Study. Journal of Oncology. 2019; 2019;3529651. https://doi.org/10.1155/2019/3529651 PMID: 31354818
- 9. Austoker J. Screening and self examination for breast cancer. Bmj. 1994; 309(6948):168-74.
- Kearney AJ, Murray M. Commentary: Evidence against Breast Self Examination Is Not Conclusive: What Policymakers and Health Professionals Need to Know. Journal of Public Health Policy. 2006; 27 (3):282–92. https://doi.org/10.1057/palgrave.jphp.3200086 PMID: 17042125
- Semiglazov VF, Moiseyenko VM, Bavli JL, Migmanova NS, Seleznyov NK, Popova RT, et al. The Role
 of Breast Self-Examination in Early Breast Cancer Detection (Results of the 5-Years USSR/WHO Randomized Study in Leningrad). European Journal of Epidemiology. 1992; 8(4):498–502. https://doi.org/10.1007/BF00146366 PMID: 1397215
- Abuidris DO, Elsheikh A, Ali M, Musa H, Elgaili E, Ahmed AO, et al. Breast-cancer screening with trained volunteers in a rural area of Sudan: a pilot study. Lancet Oncol. 2013; 14(4):363–70. https://doi. org/10.1016/S1470-2045(12)70583-1 PMID: 23375833

- 13. Devi BC, Tang TS, Corbex M. Reducing by half the percentage of late-stage presentation for breast and cervix cancer over 4 years: a pilot study of clinical downstaging in Sarawak, Malaysia. Ann Oncol. 2007; 18(7):1172–6. https://doi.org/10.1093/annonc/mdm105 PMID: 17434897
- Mittra I, Mishra GA, Dikshit RP, Gupta S, Kulkarni VY, Shaikh HKA, et al. Effect of screening by clinical breast examination on breast cancer incidence and mortality after 20 years: prospective, cluster randomised controlled trial in Mumbai. BMJ. 2021; 372:n256. https://doi.org/10.1136/bmj.n256 PMID: 33627312
- Romanoff A, Constant TH, Johnson KM, Guadiamos MC, Vega AMB, Zunt J, et al. Association of Previous Clinical Breast Examination With Reduced Delays and Earlier-Stage Breast Cancer Diagnosis Among Women in Peru. JAMA oncology. 2017; 3(11):1563–7. https://doi.org/10.1001/jamaoncol.2017. 1023 PMID: 28542677
- Ginsburg O, Yip CH, Brooks A, Cabanes A, Caleffi M, Dunstan Yataco JA, et al. Breast cancer early detection: A phased approach to implementation. Cancer. 2020; 126 Suppl 10(Suppl 10):2379–93.
- Bonsu AB, Ncama BP. Integration of breast cancer prevention and early detection into cancer palliative care model. PLoS ONE. 2019; 14(3):e0212806. https://doi.org/10.1371/journal.pone.0212806 PMID: 30893313
- Johnson OE. Awareness and Practice of Breast Self Examination among Women in Different African Countries: A 10-Year Review of Literature. Niger Med J. 2019; 60(5):219–25. https://doi.org/10.4103/nmj.NMJ_84_19 PMID: 31844349
- Lera T, Beyene A, Bekele B, Abreha S. Breast self-examination and associated factors among women in Wolaita Sodo, Ethiopia: a community-based cross-sectional study. BMC Women's Health. 2020; 20 (1):167. https://doi.org/10.1186/s12905-020-01042-1 PMID: 32770978
- Birhane K, Alemayehu M, Anawte B, Gebremariyam G, Daniel R, Addis S, et al. Practices of Breast Self-Examination and Associated Factors among Female Debre Berhan University Students. International Journal of Breast Cancer. 2017; 2017:8026297. https://doi.org/10.1155/2017/8026297 PMID: 28596921
- Foroozani E, Ghiasvand R, Mohammadianpanah M, Afrashteh S, Bastam D, Kashefi F, et al. Determinants of delay in diagnosis and end stage at presentation among breast cancer patients in Iran: a multicenter study. Sci Rep. 2020; 10(1):21477. https://doi.org/10.1038/s41598-020-78517-6 PMID: 33293634
- Scheel JR, Molina Y, Patrick DL, Anderson BO, Nakigudde G, Lehman CD, et al. Breast Cancer Downstaging Practices and Breast Health Messaging Preferences Among a Community Sample of Urban and Rural Ugandan Women. J Glob Oncol. 2017; 3(2):105–13. https://doi.org/10.1200/JGO.2015.
 001198 PMID: 28503660