Published in final edited form as:

Psychooncology. 2011 May ; 20(5): 532–537. doi:10.1002/pon.1767.

Patient-mediated factors predicting early- and late-stage presentation of breast cancer in Egypt

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Abstract

Objective—Breast cancer fatality rates are high in low- and middle-income countries because of the late stage at diagnosis. We investigated patient-mediated determinants for late-stage presentation of breast cancer in Egypt.

Methods—A case–case comparison was performed for 343 women with breast cancer, comparing those who had been initially diagnosed at Stage I or II with those diagnosed at Stage III or IV. Patients were recruited from the National Cancer Institute of Cairo University and Tanta Cancer Center in the Nile delta. Patients were either newly diagnosed or diagnosed within the year preceding the study. Interviews elicited information on disease history and diagnosis, beliefs and attitudes toward screening practices, distance to treatment facility, education, income, and reproductive history.

Results—Forty-six per cent of the patients had presented at late stage. Women seen in Cairo were more likely to present at late stages than patients in Tanta (OR = 5.05; 95% CI = 1.30, 19.70). Women without any pain were more likely to present at later stage (OR = 2.68; 95% CI = 1.18, 6.08). Knowledge of breast self-examination increased the likelihood of women to present in early stages significantly (OR = 0.24; 95% CI = 0.06, 0.94).

Conclusions—Despite increasing numbers of cancer centers in Egypt during the past 20 years, additional regional facilities are needed for cancer management. In addition, increasing awareness about breast cancer will have significant long-term impact on breast cancer prevention.

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The authors declare that they have no commercial or other associations that might pose a conflict of interest in connection with this article.

Keywords

patient factors; late stage; breast cancer; oncology; Egypt; global health

Introduction

As of 2002, the World Cancer Report cites breast cancer as the cause of 410 000 deaths per year worldwide with more than 70% of all cancer deaths occurring in low- and middle-income countries (LMCs) [1]. According to the American Joint Committee on Cancer classification [2], when a woman is diagnosed with breast cancer, tumors range from Stage I to Stage IV, with the latter being the most advanced cancer with the worse prognosis [3]. In LMCs, substantially more women are found at Stage III and Stage IV tumors on initial diagnosis, which is referred to as late-stage presentation. Stage of breast cancer on initial diagnosis has been found to be one of the most important determinants of successful treatment; therefore, late-stage presentation contributes to high mortality rates in these regions [4]. Five-year survival rates of 90% and 65% have been reported for Stage I and Stage II, respectively, compared with just 33% for Stage III and 6% for Stage IV in developing countries [5]. In addition, late-stage tumors are more difficult and more costly to treat compared with Stage I and Stage II tumors; hence, reducing the number of late-stage presentations in limited-resource settings should decrease government expenditures of treatment as well [6].

Late-stage presentations can be attributed to several factors that lead to delay in being treated. These factors include lack of proper health infrastructure and screening programs, lack of community awareness, limited access to health-care facilities, and social barriers impeding early detection and treatment programs [6–8]. To better understand these factors, categorizing them into two groups, those associated with providers and those mediated by patients, offers heuristic value [3]. Caplan *et al.* [9] defined delay by patients as the time it took for the patient to seek help once a symptom had been detected, while delay by providers was the time from seeking help to being treated. Although it is important to study delay factors associated with providers, the factors contributing to delay that patients mediate are less well studied, especially in under-developed settings.

Many initial breast cancer tumors are asymptomatic, so a lack of screening programs such as self-breast examination (BSE), clinical breast examinations (CBE), ultrasounds, or mammograms constitute a significant contributor to late presentation [10]. Although screening programs exist, their effect is limited if women lack knowledge of the disease and the necessity to seek regular breast screenings. In fact, a recent study of urban and rural Nigerian women showed that only 22.9% of women scored above 50% on a general breast cancer awareness test [11]. Although symptoms are manifested, which indicates that the disease has progressed to Stage III or Stage IV, treatment may not be accessible due to distance from the nearest hospital or clinic, financial constraints, or cultural acceptability to seek treatment. Even if health-care facilities are accessible, women may still not seek treatment, as they are afraid that the diagnosis of breast cancer will be a death sentence [12–14].

During the past 25 years, there has been a significant improvement in the stage of diagnosis of breast cancer in Egypt [unpublished data]. However, more than 50% of breast cancer patients in Egypt are still diagnosed at later stages and little is known about the factors that result in late presentations. Therefore, the objective of this study was to identify patient-mediated factors associated with initial diagnosis of late-stage breast cancer in Egypt.

Methods

Study design

This study was designed as a case–case comparison. Women diagnosed with Stage I and Stage II breast cancer (early stage) were included in Group 1, and women diagnosed with Stage III and Stage IV breast cancer (late stage) were included in Group 2. This study was approved by the University of Michigan Institutional Review Board and the Ethics Committees at National Cancer Institute (NCI-Cairo) of the Cairo University and Tanta Cancer Center (TCC), Tanta, Gharbiah.

The study population from which eligible participants were recruited consisted of women receiving breast cancer diagnosis and treatment at the two largest cancer centers in Egypt, the NCI-Cairo and the TCC in the Nile delta region. Almost half the patients seen at NCI-Cairo come from the Cairo metropolitan area, whereas the rest of the patients are from other regions in North and South Egypt. Patients from the non-Cairo regions seek management at NCI-Cairo because of the insufficient capabilities of the new regional cancer centers that were created in the early 1990s. In Tanta, the fourth largest city in Egypt, patients seen at TCC come from the villages and towns of the Gharbiah province and surrounding provinces.

For this study, the inclusion criterion was that patients must be women who have been clinically diagnosed with breast cancer between July 2007 and August 2008. Exclusion criteria consisted of present lactation, pregnancy, previous diagnosis of cancer, and breast cancer patients under the age of 18 years.

Recruitment

Study participants were all women breast cancer patients that were either newly diagnosed or treated at the recruitment hospitals between July 2007 and August 2008. Participants were recruited from the chemotherapy outpatient clinics of each study site. Both newly diagnosed patients and those new patients under treatment were recruited. The proportion of women from rural and urban areas, patients' ages, and percent of treated versus untreated breast cancer patients were compared with the general pool of breast cancer patients at the study hospitals. This comparison was performed to ensure that the study participants were similar to the overall patient population of the study hospitals without any bias in recruitment.

Study population

The study population consisted of 345 subjects with 200 subjects recruited from the NCI-Cairo, and 145 subjects recruited from the TCC in Tanta. Patient recruitment and interviewing began at the end of June 2008 and continued until the end of September 2008.

Data collection

The study interviewers administered a one-time 20-min questionnaire in Arabic. The questionnaire elicited information *via* both closed- and open-ended questions that pertained to reproductive history, medical history, screening practices, knowledge of disease, level of education, and travel time to the cancer center. The interviewers then collected information from the patient's medical records to confirm patient's age, cancer stage at diagnosis, tumor location, and treatment information.

Statistical analyses

All statistical analyses were conducted using SAS 9.2 (SAS Inc, Cary, NC). The outcome of interest was the stage of breast cancer at which patients were initially diagnosed. Exposures of interest included history of physician misdiagnosis, the place at which patients first sought treatment, frequency of various screening practices, patient knowledge about breast cancer, travel time to cancer center, family history of cancer, effect of disease on patient's quality of life, and self-reported factors that contributed to patient's delay in seeking treatment such as social, financial, and time constraints, lack of access to care, fear of hospitals, absence of pain associated with the condition, and knowledge about contagiousness of disease.

Several variables with multiple categories were transformed into dichotomous variables for final analyses. This was done based on the perceived patient understanding of the question and in consultation with the coauthoring treating physicians (AH, RG, and IAS). The mean for continuous variables was identified and dichotomous groups were created above and below the mean. Two participants did not have accurate breast cancer stage information and were excluded from the study making the total number of participants 343 patients.

Boxplots and histograms were created for the continuous variables to identify potential outliers. Bivariate analyses identified associations of importance, which were further evaluated through multivariate analysis using unconditional logistic regression after selecting variables with significant values from the bivariate analysis.

Results

Descriptive characteristics of the participants ($n = 343$) are shown in Table 1. The majority of participants at both early- (55.68%) and late-stage (62.42%) patients lacked formal education and a paying job (87.03%, 92.99%), for the two groups, respectively. The average age also did not differ significantly between early- (49.24 ± 10.93 years) and late-stage (49.89 ± 10.97 years) presentation. There was a significant difference in the number of early- (44.9%, 55.1%) and late-stage (34.1%, 26.0%) diagnoses in Cairo and Tanta, respectively (Table 1).

Table 2 shows several variables that were significantly associated with the stage at diagnosis. A referral to a cancer center by the first physician visited was significantly associated with late stage (53.6%) rather than early stage (38.0%) at diagnosis ($P = 0.004$). Women diagnosed at an early stage (37.3%) rather than late stage (26.6%) were more likely to have sought a second diagnosis ($P = 0.035$; Table 2). Women diagnosed at an early stage

(38.7%) rather than late stages (59.4%) were also less likely to be unsure about the contagiousness of breast cancer ($P < 0.0001$). Women who were diagnosed at early stages were also more likely to report delays in seeking treatment due to social, financial, and time restraints (23.9%) compared with those diagnosed at late stages (11.2%) and less likely to report delay in seeking treatment due to lack of pain (2.7%, 5.2%). Women diagnosed at late stages were more likely to report delays due to the previous factors together (31.6%) compared with those in the early-stage diagnosis group (21.2%) ($P = 0.043$; Table 2).

Associations between screening practices and stage at diagnosis were captured by several variables. Women diagnosed at late stages (3.2%) rather than early stage (10.9%) were less likely to have knowledge of BSEs ($P = 0.007$; Table 2). Late-stage rather than early-stage diagnosis was also significantly associated with no previous CBE (12.9% vs 23.9%, respectively; $P = 0.01$) and no previous mammogram (11.4% vs 22.2%, respectively; $P = 0.008$).

Patients reported several reasons for delay in seeking medical care after initially noticing symptoms. More women who were diagnosed at early stages reported no delay (52.2%) compared with women diagnosed at late stages (38.7%; Table 2). Longer time between onset of symptoms and seeking medical care was associated with late-stage diagnosis ($P = 0.001$). The average travel time in minutes also significantly ($P = 0.05$) differed between the two groups with the late-stage diagnosis group having longer average travel time (120 min) compared with early-stage diagnosis group (60 min; Table 2).

Table 3 shows our results of the unconditional logistic regression model. Women were more likely to be diagnosed at later stages if they were diagnosed in Cairo at the NCI compared with TCC (OR = 5.05; 95% CI = 1.29, 19.07). Women with no pain had a higher propensity to be diagnosed at later stages (OR = 2.68; 95% CI = 1.18, 6.08). However, if women knew about BSE they were less likely to present at later stages (OR = 0.24; 95% CI = 0.06, 0.94). Although it did not reach significance, if women had to travel for more than 1 h to reach a health facility, it increased their odds of presenting at late stage (OR = 1.64; 95% CI = 0.96, 2.79).

Discussion

This is the first study to investigate patient-mediated factors influencing late-stage presentation of breast cancer in Egypt. This study analyzed patient-mediated predictors of late-stage presentation of breast cancer in Egypt. As a part of our initial analyses, we found that women who were referred to a cancer facility by the first physician they saw were more likely to present with late-stage presentation. Women who sought a second opinion at the study cancer centers were more likely to present at early stages. Women presenting at an early stage were more likely to be sure about breast cancer not being contagious. Lack of knowledge about BSE and not having a previous CBE or a mammogram were also associated with late stage at presentation. In addition, if patients reporting having social, financial, or time constraints, it increased the probability of late stages at presentation. Not seeking care soon and longer travel times were also associated with late stages at presentation. Finally, patients at NCI-Cairo were more likely to have late-stage presentation

on diagnosis. Our multivariate analysis confirmed some of those findings further including higher propensity of latestage presentation at NCI-Cairo, pain as an important factor in seeking care early, knowledge of BSE being an important factor for early stage at presentation, and the importance of shorter travel time to health-care facilities.

NCI-Cairo is a much larger cancer center than the TCC. It is quite likely that more severe cases of breast cancer visit NCI-Cairo from farther distances and which are also more likely to be in later stages. This may explain why women at NCI-Cairo were at greater odds of having a late-stage diagnosis. We also found lack of pain to be an important factor leading to late stage of diagnosis. Pain is a very common symptom of any disease that draws attention to the site of the disease. In case of breast cancer, pain is most likely to occur in case of large tumors or ulceration, both of which are indicative of late-stage disease. In settings with low screening or early detection, lack of pain will delay a patient's attention toward a growing tumor and delay the process of seeking treatment. Previous research showed that breast cancer symptoms other than lumps are more likely to be ignored [3,15–18]. It is imperative that breast cancer awareness campaigns emphasize on the fact that breast cancer is mostly asymptomatic and pain is a rare symptom, which happens quite late in the disease process.

Knowledge and possible practice of BSE was found to be quite instrumental in avoiding late stage at presentation. A number of studies have found BSE to be ineffective in reducing mortality from breast cancer [19] and among other limitations it has been pointed out that even with best training it is difficult for humans to detect tumors less than 1 cm in size [20]. However, BSE can be effective in combination with other screening methods, such as CBE and mammograms [21]. Enhanced breast health awareness may motivate women to seek treatment for breast-related symptoms earlier than women who did not know about BSE resulting in downsizing of symptomatic tumors. Even in criticisms regarding the effectiveness of BSE, the importance of awareness created by BSE has been shown to be important in lowresource areas [22,23].

We also observed a weak association of patients with longer travel times more likely to present with late stage at diagnosis. On one hand, travel time represents a physical barrier to access healthcare, whereas on the other, it may represent a proxy for an increase in other delay factors. This is quite possible because the cancer centers where this study was conducted are located in urban areas and patients with longer travel times most probably were from rural areas. However, in this setting, the presence of effective and cheap transportation, and good network of roads especially near the TCC, seemed to lessen geographical distance as a strong determinant of stage of presentation in this population.

In addition, it is likely that women who had less aggressive breast tumors presented at earlier stages and thus had opportunities to seek more than one medical opinion before presenting to the cancer centers. Increased risks for late stage were also found in women who reported delay of treatment due to social, financial, or time constraints although not significant. Social and financial factors included fear of hospitals, busy clinics, and lack of access to hospitals with most women reporting more than one factor as has also been observed previously [24].

This study is unique in that it is one of the first studies to investigate patient-mediated factors that may be associated with late-stage diagnosis at initial presentation in this population. The study population captured a large number of rural and urban patients seen at the NCI-Cairo and TCC, Tanta, the largest cancer centers in Egypt. However, the study did not corroborate patients' reporting with any first-diagnosing physicians outside the participating cancer centers.

It is important to disseminate the information that breast cancer is not rapidly fatal and can be cured if detected early. This can reduce the fear of diagnosis [12–14], which prevents patients from seeking treatment long after onset of symptoms. A very important measure in this direction could be developing educational programs for patient education that include breast cancer survivors. Better dissemination of information and inclusion of cancer survivors could result in creation of a critical mass in the population before more advanced measures such as opportunistic mammography are introduced in LMCs such as Egypt.

In conclusion, increasing incidence and mortality rates of breast cancer in LMCs highlight the need for public health measures to improve early detection of breast cancer in these regions. The results of this study will allow for a better understanding of barriers to effective care confronting cancer patients, specifically those in Egypt. In addition, this study will contribute to the growing body of research identifying factors of delay related to health outcomes and health practices in limited-resource environments [25,26]. Because many of the health resources used to screen for breast cancer in high-resource countries are not available in LMCs, it is important to understand the likely cost-effectiveness of interventions that can be feasibly implemented in these areas. The results of this study can aid health-care providers and policy makers in understanding ways to provide effective education and screening tools within the general population. Ideally, these measures will reduce the number of late-stage presentations, therefore, reducing mortality rates of breast cancer in Egypt and other LMCs. In addition, this study can contribute to global health scholarship, in that the factors we examined could inform health issues that transcend national boundaries [27]. Although this study has developed initial information on multiple determinants of late-stage presentation in Egypt, much remains unanswered. Future studies should conduct a more qualitative, in-depth analysis to capture women's knowledge and attitudes regarding screening practices. In addition, research to better define delay factors associated with providers of treatment in this population is warranted.

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Table 1

Descriptive variables for Egyptian breast cancer patients (by stage at presentation)

Variable	Early-stage diagnosis N = 185 (%)	Late-stage diagnosis N = 158 (%)	P
Education (185, 157)			
No formal schooling	103 (55.68)	98 (62.42)	0.21 ^a
Completed primary school	33 (17.84)	30 (19.11)	
Completed secondary school	49 (26.49)	29 (18.47)	
Treatment status (185, 158)			
Under treatment	80 (43.24)	85 (53.80)	0.05 ^a
Not under treatment	105 (56.76)	73 (46.20)	
Occupation (185, 157)			
Doesn't have paying job	161 (87.03)	146 (92.99)	0.16 ^a
Has paying job	24 (12.97)	11 (7.01)	
Age (185, 158)			
Median (min–max)	48 (22–81)	49 (24–75)	0.58 ^b
Mean±SD	49.24±10.93	49.89±10.97	
Site of treatment (185, 158)			
Tanta	102 (55.14)	41 (25.95)	<0.0001 ^a
Cairo	83 (44.86)	117 (34.11)	

^a χ^2 test.^b*T*-test.

Table 2

Characteristics of study population (by stage at presentation)

Variable by category	Early-stage diagnosis <i>N</i> = 185 (%)	Late-stage diagnosis <i>N</i> = 158 (%)	<i>P</i>
<i>Referral by first physician</i> (184, 155)			
No referral	114 (61.96)	72 (46.45)	0.0043 ^a
Referral	70 (38.04)	83 (53.55)	
<i>Second place of diagnosis</i> (185, 158)			
Yes	69 (37.30)	42 (26.58)	0.0345 ^a
No	116 (62.70)	116 (73.42)	
<i>Breast cancer is contagious</i> (185, 155)			
Yes	2 (1.08)	0 (0.00)	<0.0001 ^b
No	117 (63.24)	63 (40.65)	
Unsure	66 (35.68)	92 (59.35)	
<i>Patient reasons for delay in seeking medical care</i> (184, 155)			
No delay	96 (52.17)	60 (38.71)	0.0429 ^a
Social, financial, and time constraints	44 (23.91)	38 (11.21)	
No pain	5 (2.72)	8 (5.16)	
Both	39 (21.20)	49 (31.61)	
<i>Knowledge of BSE</i> (184, 158)			
Yes	20 (10.87)	5 (3.16)	0.0065 ^b
No	164 (89.13)	153 (96.84)	
<i>Knowledge of BSE from physician</i> (185, 158)			
Yes	11 (5.95)	3 (1.90)	0.0974 ^b
No	174 (94.05)	155 (98.10)	
<i>Previous CBE</i> (180, 155)			
Yes	43 (23.89)	20 (12.90)	0.0103 ^a
No	137 (76.11)	135 (87.10)	
<i>Previous mammogram</i> (185, 158)			
Yes	41 (22.16)	18 (11.39)	0.0084 ^a
No	144 (77.84)	140 (88.61)	
<i>Time between onset of symptoms and seeking medical care</i>			
<1 month	156 (85.25)	103 (66.45)	0.0012 ^b
2 months	14 (7.65)	25 (16.13)	
3 months	0 (0.0)	1 (0.65)	
4 months	10 (5.46)	13 (8.39)	
5 months	0 (0.0)	4 (2.58)	
6 months	0	0	
>6 months	3 (1.64)	9 (5.81)	
<i>Travel time in minutes</i> (185,157)			

Variable by category	Early-stage diagnosis <i>N</i> = 185 (%)	Late-stage diagnosis <i>N</i> = 158 (%)	<i>P</i>
Median (min–max)	60 (10–1440)	120 (15–1200)	0.0486 ^c
Mean±SD	105.49±124.52	133.47±136.84	

^a χ^2 test.

^b *T*-test.

^c Fisher's exact test.

Table 3

Logistic regression model to predict late versus early stage on initial diagnosis in Egyptian patients

Variable	Multivariate OR ^a (95% CI)	P
<i>Site of treatment</i> (185, 158)		
Tanta	1	
Cairo	5.05 (1.30, 19.70)	0.0146
<i>Visited a second facility</i>		
No	1	
Yes	0.72 (0.30, 1.74)	0.462
<i>First diagnosed as breast cancer</i>		
No	1	
Yes	0.99 (0.52, 1.89)	0.985
<i>Suggested treatment</i> (184, 155)		
No referral	1	
Referral	1.10 (0.57, 2.12)	0.782
<i>Treated in a hospital or present facility</i>		
No	1	
Yes	0.80 (0.43, 1.48)	0.479
<i>Delay factors</i> (184, 155)		
No delay	1	
Social, financial, and time constraints	1.72 (0.86, 3.46)	0.127
No pain	2.68 (1.18, 6.08)	0.018
Both	1.19 (0.32, 4.41)	0.794
<i>Knowledge of BSE</i> (184, 158)		
No	1	
Yes	0.24 (0.06, 0.94)	0.041
<i>Previous CBE</i> (180, 155)		
No	1	
Yes	1.00 (0.28, 3.62)	0.999
<i>Previous mammogram</i> (185, 158)		
No	1	
Yes	2.17 (0.48, 9.72)	0.312
<i>Delay in seeking treatment</i>		
33 weeks	1	
>33 weeks	1.57 (0.76, 3.23)	0.22
<i>Travel time to a facility</i> (185, 157)		
1 h	1	
>1 h	1.64 (0.96, 2.79)	0.071

^a Unconditional logistic regression adjusted for all variables in this model.