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Stage at Diagnosis and Patient Delay among Breast Cancer Women in Kabul, Afghanistan

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Abstract

BACKGROUND: Breast cancer is the mostcommon cause of mortality among women. According to the WHO, about 10,300 women died because of cancers in Afghanistan in 2018. Data on breast cancer, especially stage at diagnosis and delay in seeking medical care, are very limited and scattered in Afghanistan.

AIM: The aim of the study was to obtain information about clinical stages of breast cancer of women at the time of diagnosis in Kabul, Afghanistan.

PATIENTS AND METHODS: This was a cross-sectional study conducted on 240 women diagnosed with breast cancer from March 2016 to March 2019. The diagnosis of breast cancer was made by the surgeon on the basis of physical examination and biopsy/pathological reports. Clinical staging of the tumor was recorded according to the tumor, nodal, and metastasis classification. The gap between knowing the problem and consulting a physician (Patient delay) was categorized: <3 months, 3–6 months, and >6 months.

RESULTS: The mean age of patients was 49.31 years (standard deviation ± 11.80) ranging from 18 to 76 years. The patient delay was more than 6 months (65%). Infiltrating ductal carcinoma was the most common morphological type (76.7%). Breast cancer in the left breast of patients was 52.1%. Stage II was higher in the left and Stage III in the right breast. The majority of patients were in Stages II and III at the time of diagnosis. All stages were frequent in the fourth decades of age group. The association between the clinical stages of breast cancer at the time of diagnosis, the age, and breast R/L involvement of the patients was significant ($p < 0.001$). The association between clinical stage and marital status was not significant ($p < 0.953$).

CONCLUSION: Late referrals, diagnosis delay, and advanced stages of breast cancer are still serious problems in Afghanistan. Cancer in the right breast should be given more attention because the higher stages of the disease are expected. Increasing awareness and social education are highly needed.

Introduction

Globally, cancers are one of the main causes of death and among the cancers, breast cancer is the most common cause of mortality among women: One in five people develop cancer during their lifetime, and one in eight men and one in 11 women die from the disease. Breast cancer represents one in four cancers diagnosed and the leading cancer type among women. In 2020, the number of new cases of females' breast cancer (in all ages) worldwide was 2,261,419 (24.5%). According to the WHO in 2018, about 10,300 new cases of cancers among women detected and 3062 (29.7%) were female breast cancer in Afghanistan [1], [2]. This cancer has unfavorable impacts on economic development of countries [3].

There are several methods for the diagnosis of breast cancer, such as mammography, contrast-enhanced mammography, ultrasound, magnetic resonance imaging, positron emission tomography, microwave imaging, and molecular methods [4], [5]. The differentiation of malignant tumors from the benign masses is the most important problem in clinical diagnosis and the above-mentioned methods somehow solved this issue [6].

Many studies have indicated the importance of stage at diagnosis as a prognostic factor for breast cancer [7]. Delayed presentation of breast cancer could lead to the advanced stage of the disease and subsequently, an increase in mortality [8]. In contrast, an excellent prognosis could be achieved at the early stage of the disease [5], [9]. Only 20%–50% of patients in most low- and middle-income countries, like Afghanistan, are diagnosed at early stages [10]. There are several psychosocial and cultural factors to make women avoid referring at early stages when the treatment has a great chance [11].

Many studies have been done on breast cancer and diagnosis time. In a study done by Dianatinasab *et al.* in Iran, the impact of social and clinical factors was investigated on the diagnostic delay of breast cancer [12]. In a study in India, Pakseresht *et al.* investigated the stage at diagnosis and delay in seeking medical care among women with breast cancer [13]. Malik investigated

the clinicopathological features of breast cancer in Pakistan [14]. In New Zealand, the stage of breast cancer and its screening and biology was also investigated [9].

So far, such studies have not been done in Afghanistan. The aim of this study was to determine the clinical stage of breast cancer during the first visit among Afghan women.

Materials and Methods

This was a cross-sectional study, based on a census (case series) approach to reach all women (240) diagnosed with primary breast cancer "detected in surgery outpatient department from march 2016 to march 2019" who had not started cancer treatment and admitted to surgery ward located in Aliabad Teaching Hospital, Kabul, Afghanistan. The diagnosis of breast cancer was made by the surgeon on the basis of physical examination and biopsy/pathological reports.

Women with recurrence of breast cancer, having metastasis at the time of diagnosis, reconstructive surgeries, or any other cancer were excluded from the study. The patient delay (the gap between first symptom observation by a woman and the first medical consultation) was extracted from the documents.

In symptomatic women, the patient delay was defined as the time elapsed between symptoms onset and the first medical consultation. Each medical record was reviewed to extract information about tumor characteristics. Clinical staging of the tumor according to the tumor, nodal, and metastasis classification of malignant tumors was recorded.

Of all women who registered to the surgery department in the 3 years (n = 3683), 255 (6.92%) patients had breast cancer. A total of 240 patients with breast cancer were recruited and 15 patients due to lack of documents were excluded from the study.

The analyses were done using the SPSS/PC software (version 24.0 for Windows, SPSS, Inc., Chicago, IL, USA). All statistical tests were performed at a significance level of 5% ($p < 0.05$). The authors used analytic methods (mean, standard deviation, Chi-squared, coefficient correlation, and logistic regression) for variables.

Results

In general, 255 participants were included in the study, but appropriate data to derive the stage at diagnosis were available for only 240 (94.11%) women.

The mean age of patients was 49.31 years (standard deviation [SD] ± 11.80) ranging from 18 to 76 years. Age distribution showed that 15.8% of the women were <40 years, 37.1% were aged 40–49 years, 24.6% were aged 50–59 years, and 22.5% were aged >60 years (Table 1).

Table 1: Description of study population (*n* = 240)

Variable	Categorical	Frequency (%)
Marital state	Married	202 (84.2)
	Single	38 (15.8)
Age (years)	<40	38 (15.8)
	≥40–≤49	89 (37.1)
	≥50–≤59	59 (24.6)
	≥60	54 (22.5)
Patient delay (month)	<3	35 (14.6)
	≥3–≤6	49 (20.4)
	>6	156 (65)
Breast involvement	L	125 (52.1)
	R	111 (46.3)
	L+R	4 (1.7)
Clinical stage of breast cancer at the time of diagnosis	I	44 (18.3)
	II	89 (37.1)
	III	92 (38.3)
	IV	15 (6.3)
Histopathological type	Apocrine carcinoma	2 (0.8)
	Cystosarcoma phyllodes	2 (0.8)
	Infiltrating ductal carcinoma	184 (76.7)
	Invasive lobular carcinoma	17 (7.1)
	Malignant fibrous histocytoma	1 (0.4)
	Medullary carcinoma	17 (7.1)
	Mucinous carcinoma	10 (4.2)
	Paget's disease	7 (2.9)

R: Right, L: Left.

The majority of the patients were married at the time of diagnosis (84.2%) and only 15.8% were single (Table 1).

Patient delay (the gap between first symptom observation by a woman and the first medical consultation) was categorized as follows: <3 months: 35 patients (14.6%), 3–6 months: 49 (20.4%) and >6 months: 156 (65%) (Table 1). Infiltrating ductal carcinoma was the most common morphological type (76.7%) (Table 1).

Table 2: Clinical stages of breast cancer at the time of diagnosis and position of the involved breast

Clinical stage of breast cancer at the time of diagnosis	Breast involvement (%)			Total	p
	L	R	R + L		
I	21 (16.8)	23 (20.7)	0 (0.0)	44	<0.001
II	52 (41.6)	36 (32.4)	1 (25.0)	89	
III	45 (36.0)	47 (42.3)	0 (0.0)	92	
IV	7 (5.6)	5 (4.5)	3 (75.0)	15	
Total	125	111	4	240	

R: Right, L: Left.

In 52.1% of patients left breast, 46.3% right breast, and 1.7% both breast were involved (Table 1). Stage II was higher in the left breast (41.6%) and Stage III in the right breast (42.3%) (Table 2). There were four cases (100%) with both breast involvement at Stage IV in the married group and no cases of both breast involvement in the single group (Table 3).

Table 3: Clinical stages of breast cancer at the time of diagnosis and marital status

Clinical stage of breast cancer at the time of diagnosis	Marital status		Total	p
	Married	Single		
I	37	7	44	0.953
II	76	13	89	
III	76	16	92	
IV	13	2	15	
Total	202	38	240	

Out of 240 selected participants, 44 cases (18.3%) were diagnosed with Stage I, 89 (37.1%)

with stage II, 92 (38.3%) with Stage III, and 15 (6.3%) with Stage IV. The majority of patients (75.4%) were presented with Stages II and III at the time of diagnosis (Tables 1 and 4). The mean age of patients with Stage I was 43.86 (SD ± 9.96), at Stage II, 46.44 (SD ± 11.59), with Stage III, 54.75 (SD ± 10.53), and with Stage IV, 48.93 (SD ± 12.88) (Table 1). The mean gap between knowing the problem and consulting a physician (patient delay) was 15.70 months (SD ± 19.01) ranging from 0.2 to 96 months. The association between clinical stage and marital status was not significant (p < 0.953) (Table 3).

Table 4: Gap between the first symptom observation by a woman to the first medical consultation (patient delay) and clinical stages of breast cancer

Clinical stage of breast cancer at the time of diagnosis	Patient delay (months)			Total	p
	<3	≥3–≤6	>6		
I	12	13	19	44	<0.001
II	18	30	41	89	
III	4	4	84	92	
IV	1	2	12	15	
Total	35	49	156	240	

The analysis revealed a statistically significant association between the patient's stage of cancer and consultation gap and more than 50% of the patients had Stage II and III and were referred after 6 months delay (p < 0.001) (Table 4). The association between the clinical stages of breast cancer at the time of diagnosis and the age of the patients was significant and the stages were frequent in the 40 ≤ age <50 age group (p < 0.001) (Table 5).

Table 5: Clinical stages of breast cancer at the time of diagnosis and age of the patients

Clinical stage of breast cancer at the time of diagnosis	Age				Total	p
	<40	≥40–≤49	≥50–≤59	≥60		
I	11	21	9	3	44	<0.001
II	22	34	19	14	89	
III	3	28	27	34	92	
IV	2	6	4	3	15	
Total	38	89	59	54	240	

The relationship between the clinical stages of breast cancer at the time of presentation and the R/L breast involvement was significant (p > 0.001) (Table 2).

As illustrated in Table 6, the multivariable models evaluated the association of staging in breast cancer, by age and the gap which came out to have significant association at the multivariate level (p < 0.05). In the case of Stage I compared to Stage IV, the gap variable is clinically effective. The odds ratio in the gap category Gap < 3 is 3.69E + 09, which indicates that a change from a gap category of Gap < 3 to a gap category of Gap ≥ 6 increases the likelihood of early breast cancer (p < 0.001). Furthermore, the odds ratio in the gap category of 3 ≤ Gap < 6 is equal to 1.71E + 09, which indicates that changing from this category to category of Gap ≥6 increases the risk of breast cancer (p < 0.001).

In the case of Stage II compared to Stage IV, the gap variable is clinically effective. The odds ratio in the gap category Gap < 3 is equal to 109,596, which indicates that by changing from the gap category < 3 to the category Gap ≥ 6, the probability of starting breast cancer increases (p < 0.001). The gap between 3 and 6 is equal to 58.891, which indicates that changing the gap between this category to Gap ≥ 6 increases the risk of breast cancer (p = 0.002). Furthermore, the odds ratio in the category 3 ≤ Gap < 6 is equal to 21.864, which shows that by changing the 3 ≤ Gap < 6 category to a category Gap ≥ 6, the probability of breast cancer increases (p = 0.027).

Discussion

Breast cancer is the most common cause of cancer mortality for women worldwide, especially in low-income countries, which experience sharp slopes

Table 6: Multivariate logistic regression of staging in breast cancer, by age, and the patient delay

Parameter estimates							
Clinical stage of breast cancer at the time of diagnosis[a]	Variable	*B*	SE	P	OR	95% CI for OR	
						Lower bound	Upper bound
I	Intercept	−21.190	1.205	0.000			
	Patient delay<3	22.028	1.049	0.000	3.69E + 09	4.71E + 08	2.88E + 10
	≥3–<6	21.258	1.017	0.000	1.71E + 09	2.33E + 08	1.25E + 10
	Patient delay≥6	19.969	0.000		4.70E + 08	4.70E + 08	4.70E + 08
	Age<40	2.380	1.291	0.065	10.800	0.860	135.600
	≥40–≤49	1.361	0.978	0.164	3.901	0.574	26.532
	≥50–≤59	1.205	1.072	0.261	3.338	0.408	27.280
	≥60	-	-	-	-	-	-
II	Intercept	−2.388	1.331	0.073			
	Patient delay<3	4.697	1.316	0.000	109.596	8.315	1444.528
	≥3–<6	4.076	1.293	0.002	58.891	4.673	742.098
	Patient delay≥6	3.085	1.392	0.027	21.864	1.428	334.649
	Age<40	1.521	1.156	0.188	4.576	0.474	44.149
	≥ 40–≤ 49	0.263	0.816	0.748	1.300	0.263	6.440
	≥ 50–≤ 59	0.354	0.903	0.695	1.425	0.243	8.356
	≥ 60	-	-	-	-	-	-
III	Intercept	2.189	0.754	0.004			
	Patient delay<3	−0.530	0.878	0.546	0.588	0.105	3.290
	≥3–<6	0.385	0.781	0.622	1.470	0.318	6.793
	Patient delay≥6	1.337	0.840	0.111	3.807	0.734	19.747
	Age<40	−1.801	1.122	0.108	0.165	0.018	1.488
	≥40–≤49	−1.203	0.776	0.121	0.300	0.066	1.374
	≥50–≤59	−0.944	0.842	0.263	0.389	0.075	2.029
	≥60	-	-	-	-	-	-

AQ3 [a]The reference category is: IV, [b]This parameter is set to zero because it is redundant. SE: Standard error, OR: Odds ratio, CI: Confidence interval.

of breast cancer mortality rate [15]. This work indicated that the diagnosis delay of breast cancer is a serious problem in Afghanistan. Here, we have focused on factors associated with late-stage breast cancer in Afghanistan. Understanding the causes of delay may help health authorities to apply policies to reduce the consequences of breast cancer due to diagnosis delay.

The mean age in our study was 49.31 years. In one study, the average age of women with breast cancer was reported to be 46.99 years, and in our study, the highest number of patients was in the age group of 40–49 years [13]. In a study conducted in Asian countries, the highest number of patients was observed in the same age group [16]. In this study, as in a study conducted in Iran, 38% of patients were under 40 years of age [13]. According to the research in Iraq, the highest incidence of breast cancer was in the age group of 40–49 years, and 15.4% of patients were over 60 years old [17]. In another study, 88.35% of patients presented with Stages III and IV, of whom more than 77% were under 50 years of age. In this study, a significant relationship was found between patients' age and breast cancer stage at the time of diagnosis. In another study, it was reported that there was no association between patients' age and stage of breast cancer at the time of diagnosis [17].

The mean gap (the time between awareness of the problem and consultation with the physician [patients' delay]) in our study was 15.70 months and only 84 patients (35%) sought treatment in 6 months. Furthermore, 35 patients (14.60%) had <3 months of delay and 156 patients (65%) were treated after 6 months. In another study, 38.4% of patients sought medical consultation within 3 months [13]. Furthermore, 19% of women presented with a delay of 12 weeks or more, and in the study performed by Brzozowska *et al.*, the mean delay of the patient was 32.2 weeks [18], [19]. A systematic review showed that a delay of 3–6 months is clearly associated with increased tumor size, disease progression, and poor prognosis. Another study also found that a delay of >12 weeks endangered survival [20], [21]. In another study, the mean gap was 10.9 months [13].

In the present study, 18.3% of patients were referred with Stage I and 37.1% with Stage II, 38.3% with Stage III, and 6.3% with Stage IV of breast cancer. The mean age at Stage III, which has the highest number of patients, was 54.75 (SD ± 10.53) years. In a study conducted in India, 27.1% and 61% of the patients at the time of diagnosis presented with Stage III and Stage IV, respectively [13]. In another study performed in Nepal, 76.79%, 10.7%, and 2.50% were at Grade II, III, and I, respectively [22]. In another study, 65.5%–70.5% of cases were in the early stages of diagnosis (I and II) and <30% in the advanced Stages (III and IV) [23].

In our study, the most common type of tumor was infiltrating ductal carcinoma (184 (76.7%) cases), the second most common was invasive lobular carcinoma, medullary carcinoma (17 [7.1%] cases for both of them), and malignant fibrous histiocytoma had the lowest number of cases (1 (0.4%). In a study conducted in Iran, the highest number of cases had invasive ductal carcinoma (75%), while medullary carcinoma was 5.4% and lobular carcinoma had the lowest number of cases, which is consistent with our research [22]. In another study, infiltrating ductal carcinoma was the most common type of breast cancer (81.4%), and invasive lobular carcinoma was responsible for only 6.3% of the cases [21].

In our study, 202 (84.2%) of the patients were married and 38 cases (15.8%) were single. Furthermore, 17 (44.7%) of the single patients presented in the advanced Stage (III and IV) with a gap of more than 6 months. The married women, on the other hand, presented with the advanced stage with a gap of more than 6 months (79 [31.1%] patients). In another study, single patients were 1.8 times more likely to be diagnosed with the final stages than married women, and it was also found that breast cancer was more likely to be diagnosed in the final stages among single patients than in pregnant women [24]. Furthermore, it was found that marital status has a significant relationship with the clinical stage at the time of diagnosis, which may be diagnosed at an early stage. In a meta-analysis study, single patients were more prone to late-stage breast cancer [25]. Another study showed that single patients may be diagnosed with Stages II, III, and IV [26].

In the present study, 125 (52.1%) and 111 (46.3%) of the patients had breast cancers in the left and right breast, respectively, and 4 (1.7%) of them showed cancer in either right or left breasts. Many studies have shown that unilateral breast cancer is more common on the left side than on the right. Primary cancer of both breasts was diagnosed in 3.7% of patients [27]. Another study showed that breast cancer is more common in the left breast, which is consistent with our study. Another study found that breast cancer was 5% more common on the left side [28]. In the surveillance, epidemiology, and end results database, it was reported that 50.8% and 49.2% of the patients in the United States had the left and right sides involved, respectively [29].

Limited access of women to doctors (especially lack of female health workers in distant area), social media due to special culture in Afghan society, economic problems, and lack of awareness of the dire consequences of breast cancer are possible causes of late referral with breast cancers in Afghanistan. Inadequate campaigns of health awareness of the risks of breast cancer in women (especially the breast self-exam) due to social, economic, and security factors are the other reason.

Conclusion

Despite awareness of women for early presentation to detect early-stages of breast cancer over the past two decades, late referrals and advanced stages of breast cancer are still a major problem that requires more nationwide awareness programs. It seems that women who are experiencing cancer in their right breast should be given more attention because higher stages of the disease are expected in them and more studies are needed in this regard. Breast cancer awareness programs should also be implemented.

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