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Assessing the Period between Diagnosis of Breast Cancer and Surgical Treatment among Mastectomized Female Patients in Iraq

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ABSTRACT

Introduction: *Breast cancer is the most common cancer and the major cause of cancer related deaths among Iraqi women. Due to the relatively late detection of breast cancer, the majority of the patients are still treated by modified radicle mastectomy.* ***Aim:*** *To assess the time lag between diagnosis of breast cancer and mastectomy among Iraqi patients; correlating the findings with other clinicopathological characteristics of the disease.* ***Patients and methods:*** *This retrospective study enrolled 226 Iraqi female patients who were diagnosed with breast cancer. Data were registered on the exact time period between signing the histopathological report and the surgical treatment. Other recorded variables included the age of the patients, their level of education, number of parity, age at first child birth, family history and the stage at breast cancer presentation.* ***Results:*** *In general, 51% of the patients were under the age of 50 years, 93.8% were married, 10.6% were illiterate, only 1.8% were nulliparous while positive family history of cancer was noted in 25.6%. Overall 67.7%, 87.6%, and 92% underwent mastectomy during the first month, two months and three months after diagnosis respectively. Only 3.1% were operated upon after one year. With the exception of the age at first childbirth, there was no significant correlation between the waiting times to surgery and the patients' age, education, number of parity, family history and the stage at breast cancer detection.* ***Conclusions:*** *The percentage of the patients who had surgical treatment during the first month following diagnosis seems rather satisfactory when compared to the corresponding findings reported in similar surveys from developing and some developed countries. Strengthening public education and adopting multimodality evidenced-based management protocols are crucial steps to control the waiting times among those who have delayed mastectomies.*

Keywords: Diagnosis, Treatment, Breast, Cancer, Mastectomized, Iraq

INTRODUCTION

Breast Cancer is the most common cancer in Iraq and the major cause of cancer related deaths among women [1,2]. Local studies from Iraq have demonstrated that the low survival of the affected patients is mainly attributable to the advanced stages at the time of presentation resulting from late diagnosis and management [3,4]. Although a national program for early detection of breast cancer was introduced in Iraq since 2001 nevertheless the lack of knowledge, attitudes and practice towards breast cancer has been illustrated even among the educated sample of the Iraqi population [5-7]; urging prompt action to raise the level of awareness about the significance of early detection of breast cancer among the community and to extend the coverage to include rural and remote areas.

Delays in diagnosis and treatment could be related to different aspects influencing the patients, healthcare provider or health system [8]. It has been indicated that patient delay refers to the period between the discovery of symptoms and the first medical consultation and corresponds to a delay in seeking medical advice. On the other hand, provider delay is that which takes place between the first medical diagnosis and the beginning of definitive treatment, often related to medical team and the health system; and the accepted threshold is only one month [9]. Both delays are referred to as global delay [10]. Previous studies from developed and developing countries showed that delays longer than 3-months

between the discovery of symptoms and the initiation of treatment are associated with advanced clinical stage and questioned whether the length of the interval from the biopsy to the surgery might influence survival [9-11].

Due to the relatively late detection of breast cancer in Iraq, the majority of the patients are still treated by modified radicle mastectomy [3,4]. Research on the reasons behind delays in seeking medical consultation has been published earlier [3-7,12-14], yet as far as we are aware, this is the first article that focuses on the time lag between diagnosis and starting treatment among a sample of Iraqi patients registered with breast cancer.

The aim of this study was to assess the period between the date of the histopathological reports confirming breast cancer and the time of mastectomy; correlating the findings with the age of the patients at diagnosis, their level of education, number of parity, family history, age at first child birth and the stage of the disease at presentation.

PATIENTS AND METHODS

This is a retrospective study on 226 female patients who were diagnosed as having breast cancer, at the Main Center for Early Detection of Breast Tumors in the Oncology Teaching Hospital, who were subjected to mastectomy in the period between January 2015 and November 2017. The data was extracted from the information registered in the health clinical records and the histopathology reports of confirmed cases of infiltrative breast carcinoma.

The criteria for inclusion in this study comprised the cases that showed valid information with recorded follow up belonging to female patients who were diagnosed with invasive breast cancer according to histopathology examination of mastectomy specimens, during the defined period of time. Non-invasive cases were diagnosed as carcinoma *in situ*, recurrent breast cancer and those with missing data were excluded from the study. Clinical case sheet records belonging to the examined patients were thoroughly reviewed by the authors.

Data were collected on the exact time period between the pathological diagnosis and the surgical treatment and was analyzed at the National Cancer Research Center of Baghdad University. Other recorded variables comprised the age of the patients at diagnosis, their level of education, number of parity, age at first childbirth, family history of breast cancer and the stage of the disease at presentation. The assessed period was calculated from the date of signing the histopathological report to the date of performing the mastectomy operation by the surgeon. The time intervals were categorized into <2 weeks, 2-4 weeks, 4-8 weeks, 8-12 weeks, 3-6 months, and >6 months.

The research study, which was in accordance with the ethical standards laid down by the Declaration of Helsinki, was approved by the Ethical Research Committee of the National Cancer Research Center. In general, the study protocol is part of a Regional Comparative Breast Cancer Research Project approved by IARC Ethics Committee, WHO in 2016.

Statistical Analysis

Descriptive statistical analysis was carried out on the recorded data of the study group; which were categorized by using frequencies and percentages. The information on the age of the patients was classified as those under 50 years versus patient's ≥ 50 years. Correlation of the time lag findings between diagnosis of breast cancer and mastectomy with the studied variables was performed using Chi-square test; p-values less or equivalent to 0.05 was considered significant.

RESULTS

In general, 50.9% of the patients were in their premenopausal age, 93.8% were married, 10.6% were illiterate, 20.4% had their first delivery at the age of 30 years and over while only 1.8% were nulliparous. About 55% of those who had children confirmed the history of lactation while positive family history of cancer was noted in 38%, and of breast cancer specifically in 25.6%. Palpable lumps were the main presenting sign in 96.9% while 7% complained of nipple discharge (Table 1).

Table 1 Demographic and clinical characteristics of the study group

Variable	Classification	Total=226
		N (%)
Age (years)	(<50)	115 (50.9%)
	(≥ 50)	111 (49.1%)

Marital Status	Unmarried	14 (13.0%)
	Married	212 (93.8%)
Education	Illiterate	24 (10.6%)
	Primary School and Lower	50 (22.1%)
	Secondary School	75 (33.1%)
	University	77 (34.1%)
Age at first child birth (years)	Nulliparous	4 (1.8%)
	(10-19)	35 (15.5%)
	(20-29)	108 (47.8%)
	(30-39)	42 (18.6%)
	(40-49)	4 (1.8%)
	NA*	33 (14.6%)
Lactation	Yes	125 (55.3%)
	No	59 (26.1%)
	NA*	25 (11.1%)
	Unknown	17 (7.5%)
Family History of Cancer (Any)	Positive	86 (38.0%)
	Negative	140 (61.9%)
Family History of Breast Cancer	Positive	58 (25.6%)
	Negative	168 (74.3%)
Lump	Positive	219 (96.9%)
	Negative	7 (3.0%)
Bloody Discharge	Positive	16 (7.0%)
	Negative	210 (92.9%)
Parity (No. of Children)	NA*	38 (16.8%)
	(1-5)	58 (69.9%)
	(≥ 5)	30 (13.2%)
Breast Cancer Stage	I	25 (11.0%)
	II	113 (50.0%)
	III	65 (28.7%)
	IV	23 (10.1%)
*NA=Not applicable		

Table 2 shows that about 47% of the Iraqi patients diagnosed with breast cancer in our study underwent mastectomy within the first two weeks, while 20.8% performed a surgical operation during the third and the fourth week after diagnosis. Overall 67.7%, 87.6%, and 92% received therapeutic work-up during the first month, 2 months and 3 months respectively. Only 3.1% (7 patients) were operated upon after one year.

Table 2 Distribution of patients according to the time between diagnosis of breast cancer and mastectomy

Time between Diagnosis and Treatment*	No of Patients	%	Commutative %
<2 weeks	106	46.9%	46.9%
2-4 weeks	47	20.8%	67.7%
4-8 weeks	45	19.9%	87.6%
8-12 weeks	10	4.4%	92.0%
3-6 months	7	3.1%	95.1%
6-12 months	4	1.8%	96.9%
>1 year	7	3.1%	100.0%
Total	226	100.0%	
*The overall median waiting time from the date of diagnosis to mastectomy was 17 days with a mean of 44 days; Chi-square statistic: 2.8535; p-value: 0.58263; Not significant at p<0.05			

When correlating the age of the patients with the time between diagnosing breast cancer and surgical intervention; the cases being dichotomized as those under the age of 50 years versus those aged 50 years and older, it was observed that although younger patients sought surgical therapy within relatively shorter durations than their older counterparts nevertheless these differences were not statistically significant at p<0.05 (Table 3).

Table 3 Relationship of patients' age at breast cancer detection with the time between diagnosis and mastectomy

Time between Diagnosis and Mastectomy	Age (>50 Years)	Age (≥ 50 Years)	Total
	No (%)	No (%)	
<2 weeks	54 (50.9%)	52 (49.1%)	106
2-4 weeks	26 (55.3%)	21 (44.7%)	47
4-8 weeks	23 (51.1%)	22 (48.9%)	45
2-6 months	9 (52.9%)	8 (47.1%)	17
>6 months	3 (27.3%)	8 (72.7%)	11
Total	115 (50.9%)	111 (49.1%)	226
Mean age: 49.36; SD: 8.816; Chi-square statistic: 2.8535; p: 0.58263; Not significant at p<0.05			

No statistical relationship was elicited between the level of education and the time between breast cancer detection and receiving treatment among Iraqi patients in this study (Table 4).

Table 4 Relationship of the level of education with the time between diagnosis and mastectomy among breast cancer patients

Time between diagnosis and mastectomy	Primary School	Secondary School	University	Total
	No (%)	No (%)	No (%)	
1st month	45 (29.4%)	52 (34.0%)	56 (36.6%)	153
2nd month	18 (40.0%)	14 (31.1%)	13 (28.9%)	45
3rd month	7 (70.0%)	2 (20.0%)	1 (10.0%)	10
3-6 months	1 (14.3%)	2 (28.6%)	4 (57.1%)	7
>6 months	3 (27.3%)	5 (45.5%)	3 (27.3%)	11
Total	74 (32.7%)	75 (33.2%)	77 (34.1%)	226
*Chi-square statistic: 11.0518; p-value: 0.19878; Not significant at p<0.05				

Likewise, no differences were noted regarding the relationship of the studied time intervals between diagnosis and treatment with the number of children the patients delivered (Table 5).

Table 5 Relationship of the number of parity with the time between diagnosis and mastectomy among breast cancer patients

Time between Diagnosis and Mastectomy	Nulliparous	1-5 Children	≥ 6	Total
	No (%)	No (%)	No (%)	
1st month	23 (15.0%)	111 (72.5%)	19 (12.4%)	153
2nd month	8 (17.8%)	32 (71.1%)	5 (11.1%)	45
3rd month	2 (20.0%)	5 (50.0%)	3 (30.0%)	10
3-6 months	1 (14.3%)	5 (71.4%)	1 (14.3%)	7
>6 months	4 (36.4%)	5 (45.5%)	2 (18.1%)	11
Total (%)	38 (16.8%)	158 (69.9%)	30 (13.3%)	226
*Chi-square statistic: 7.1284; p-value: 0.522842; Not significant at p<0.05				

In general, 62.8% of the study sample gave birth for the first child before the age of 30 years, 17.7% were between 30-39 years of age while only 2.7% were aged 40 years and over. More than two third of the patients (68.6%) who were treated within the first month of diagnosis had their first delivery when they were younger than 30 years versus (1.3%) who were older than 39 years. Such a difference was statistically significant at p<0.05 (Table 6).

Table 6 Relationship of the age at first childbirth with the time between diagnosis and mastectomy among breast cancer patients

Time between diagnosis and mastectomy	≤ 30 years	(30-39) years	≥ 40 years	NA	Total
	No (%)	No (%)	No (%)	No (%)	
1st month	105 (68.6%)	23 (15.0%)	2 (1.3%)	23 (15.0%)	153
2nd month	23 (51.1%)	13 (28.9%)	1 (2.2%)	8 (17.8%)	45
3rd month	6 (60.0%)	1 (10.0%)	1 (10.0%)	2 (20.0%)	10
3-6 months	3 (42.9%)	2 (28.6%)	1 (14.3%)	1 (14.3%)	7
>6 months	5 (45.5%)	1 (9.1%)	1 (9.1%)	4 (36.4%)	11

Total	142 (62.8%)	40 (17.7%)	6 (2.7%)	38 (16.8%)	226
*Chi-square statistic: 16.2927; p-value: 0.038377; Not significant at p<0.05					

Overall 25.7% of the patients in this study registered were having relative(s) with breast cancer. Table 7 illustrates that no significant correlation was noted regarding family history of breast cancer with the time between diagnosis and treatment among the studied group.

Table 7 Relationship of family history of breast cancer with the time between diagnosis and mastectomy among breast cancer patients

Time between Diagnosis and Mastectomy	(-ve) Family History	(+ve) Family History	Total
	No (%)	No (%)	
1st month	115 (75.20%)	38 (24.80%)	153
2nd month	34 (75.60%)	11 (24.40%)	45
3rd month	8 (80.00%)	2 (20.00%)	10
(3-6) months	5 (71.40%)	2 (28.60%)	7
>6 months	6 (54.50%)	5 (45.50%)	11
Total (%)	168 (74.34%)	58 (25.70%)	226
*Chi-square statistic: 2.5475; p-value: 0.636151; Not significant at p<0.05			

Overall, 11.1%, 50%, 28.8% and 10.2% of patients in the study were diagnosed with breast cancers at Stages I, II, III and IV respectively. Table 8 displays that there was no significant difference with respect to the correlation between the stage of breast cancer at detection and the time between diagnosis and starting treatment of the disease.

Table 8 Relationship of the stage at detection with the time between diagnosis and mastectomy among breast cancer patients

Time between Diagnosis and Mastectomy	Stage I	Stage II	Stage III	Stage IV	Total
	No (%)	No (%)	No (%)	No (%)	
1st month	20 (13.1%)	79 (51.6%)	40 (26.1%)	14 (9.2%)	153
2nd month	3 (6.7%)	21 (46.7%)	14 (31.1%)	7 (15.6%)	45
3rd month	1 (10.0%)	5 (50.0%)	4 (40.0%)	0 (0.0%)	10
3-6 months	1 (14.3%)	2 (28.6%)	3 (42.9%)	1 (14.3%)	7
>6 months	0 (0.0%)	6 (54.5%)	4 (36.3%)	1 (9.1%)	11
Total	25 (11.1%)	113 (50.0%)	65 (28.8%)	23 (10.2%)	226
*Chi-square statistic: 5.105; p-value: 0.954381; Not significant at p<0.05					

DISCUSSION

Although breast cancer is currently diagnosed and treated at early stages in most developed regions of the world, yet in many developing countries there are still great disparities in the clinico-pathological profiles, stage at presentation and treatment outcomes among patients affected by this type of cancer [14]. Advanced stages as a consequence of diagnostic delays in low and middle income countries, including Iraq, are mainly attributable to the lack of affordable access to appropriate medical care, deficient knowledge regarding breast cancer, stigma, and myths pertaining to the disease [5-10,12-14]. On the other hand, the impact of delays in initiating treatment, after diagnosis, on the prognosis and survival is still ill defined [10,11,15-17]. It has been well documented that delays of 3-6 months are often associated with poor outcomes when the stages at detection of the disease are not taken into consideration [18].

The results of the present work revealed that almost two-third of the Iraqi patients diagnosed with breast cancer at the Main Center for Early Detection of Breast Cancer in Baghdad (67.7%) underwent mastectomy during the first month after diagnosis, with an overall median waiting time of 17 days from receiving the histopathology report to surgery; only 3.1% started therapeutic work-up after one year. That period is significantly shorter that what has been reported in a previous study carried out 10 years ago, on patients who referred to the same center, which showed that 32% sought medical advice within the first month, while 16% consulted medical doctors one year later [19]. The difference in the attitude most probably illustrates the early outputs of the Iraqi National Program for Early Detection of Breast Cancer which was established in 2001 [3-6,19].

In general, waiting times are key indicators of the performance of the health care system and reflect the capacity to deal with the work load in terms of availability of resources and professional efficiencies. In a critical review assessing breast cancer treatment delay impact on prognosis and survival, "treatment delay interval" was defined as the time period from the date of biopsy and/or diagnosis to the start of first treatment which could be surgery, chemotherapy, radiation, or hormonal therapy. More than 50% of the studies in that survey expressed the interval time in weeks, 27% classified the delays in days while few reports categorized such period in months [15]. Research studies on the impact of delays in the treatment of breast cancer, after definitive diagnosis, display great differences in the examined time lag among developed versus developing countries that suffer from lack of quality infrastructure and multimodality protocol based therapy due to deficient financial resources [10].

A previous similar study performed in Antalya University Medical Hospital, Turkey, demonstrated that the median time to surgery for breast cancer was 7.5 days and only 25% of their patients registered delays over 2 weeks (versus approximately 50% in the present study). The authors concluded that delay in surgery up to several weeks had no detrimental effect on the outcome of the disease and that patients should be given time to accept the situation calmly since mastectomy is not considered as an emergency [11]. On the other hand, in Germany, a population-based study on 380 patients diagnosed with breast cancer documented that 11% had provider delays greater than 3 months [20], as compared to 8% in our report. More recently, it has been noted in France that the overall median waiting time between the pathological diagnosis and the first treatment was 31 days. Excluding social support, other socio-economic and behavioral factors had a limited impact [21]. An earlier population based study among French patients showed that the median waiting time from the first imaging detection of breast cancer to the treatment initiation was 34 days [22]. The same figure was reported in a descriptive, observational retrospective study among 493 Spanish patients which displayed that the median of days from biopsy to surgery was 34; concluding that there was no influence of delays on survival [23]. A retrospective analysis focusing on disparities in time to definitive surgical treatment conducted on 37 American black women matched with 37 while women, treated for ductal carcinoma *in situ* of the breast, illustrated that black patients were 64% more likely to undergo a delay in surgery of more than 50 days [24,25].

Prolonged waiting times to treatment were significantly registered among breast cancer patients in developing countries. That was obviously reported among older patients in Ghana specifically when they were unmarried, from lower educational and socioeconomic standards who did not receive adequate information from the health workers [26]. In Mexico, where 48% of the breast cancer cases were diagnosed at stages III and IV, the median time between problem identification and the beginning of treatment was 7 months. Multivariate analyses showed independent correlations of patient and health system delay with the probability of beginning treatment in an advanced stage [27]. The waiting time intervals were longer among those who were single, younger, from lower socioeconomic working classes and in those who visited several health care services before the hospital [28]. However, a recently published study involving another Mexican cohort demonstrated that the delay intervals were not associated with age or educational status [29]. Similar findings were observed in this study regarding the relationship of delays with the age and the level of education where 54% of the Iraqi patients were premenopausal and 10.6% were illiterate. On the other hand, a systematic review on the influence of waiting times to treatment on survival from breast cancer indicated that low standards of education were significantly related to longer delays [18].

In the current study, with the exception of the age at first childbirth, there was no significant correlation between the waiting times to surgery and the family history of breast cancer, number of parity and stage at breast cancer detection including tumor size. Consistent results were observed in earlier surveys from well-developed regions of the world which revealed that cancers of patients with delay were surprisingly similar to those of patients with no delay [25]. Other multivariate models illustrated that older patients, smaller size cancers and multidisciplinary consulting meetings were related to increased waiting times [22]. In general, it has been widely reported in the literature that delays in seeking medical care are mainly attributable to misinterpretations of the signs and symptoms of breast cancer by the patients as being not serious; specifically in low and middle income countries [28,30]. Nigerian patients delayed surgical treatment of breast cancer for causes related to fear of mastectomy (45%), triage of herbal treatment (23%) and prayers (13.5%), economic reasons (10.2%) and misbelief that the lesion was inflammatory benign (8.5%) [31].

In general, the exact impact of treatment delays on the survival of patients with invasive breast cancer remains controversial. Some studies showed no influence, others indicated that early diagnosis and initiation of treatment within 90 days could increase survival, while research on low income women documented that waiting exceeding 60 days to start treatment was associated with a significantly increased risk of breast cancer-related mortality [23,32,33].

CONCLUSION

In conclusion, the presented time lag between breast cancer diagnosis and surgical treatment in this study, focusing specifically on those who underwent mastectomy during the first month (67.7%) seems rather satisfactory when compared to the corresponding findings reported in similar surveys from developing and some developed countries. That is obviously attributable to the fact that all the patients included in this work were managed in the biggest comprehensive tertiary cancer center in Baghdad where health services are delivered "free of charge". The relationship of waiting times with financial constraints has been well documented in the literature. Nevertheless, that could also point out to the achieved positive outcomes of establishing the National Program for Early Detection of Breast Cancer in Iraq. Strengthening the public educational campaigns on breast cancer awareness and adopting multimodality evidenced-based management protocols are crucial steps to control the prolonged waiting times among those patients who have surgical treatment after one month following diagnosis. As delays often reflect inability to pay, poor access to services and limited professional and/or infrastructure resources, it is recommended to include "delays to treatment" within the national health policy guidelines as an index to address standard waiting times between the diagnosis of cancer and the initiation of therapy. Research on health services and the associated socio-economic related factors for delay should be invested in establishing breast cancer control strategies amenable for implementation in developing countries.

DECLARATIONS

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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