The Ten-Year Survival Rate for Breast Cancer Females in Kurdistan/Iraq: Special Facts and Features

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ABSTRACT

Background and objective: Worldwide, breast cancer varies widely in survival rate and age at first diagnosis. Owing to the limited follow up database in developing areas, this study aimed to estimate the 10-years survival rate for breast cancer in Kurdistan/Iraq and correlate it with clinicopathological variables.

Methodology: This follow-up study included 160 breast cancer patients diagnosed before 2010. Their data were obtained from Duhok/central lab. Survivors and families of deceased cases were contacted to approve the survivor. Cases were reviewed for variables including estrogen and HER-2 status.

Results: The mean age of patients was 44.9 years. Only 66 of them (41.2%) survived for 10-years. None of the survivors was below 30 or above 70 years. Death rate was significantly high between 30-39 years. The survival rate was highest (75.8%) between 40-49 years. The lymph nodes involvement was seen in 61.87% with statistically higher mortality rate. Estrogen was positive in > ¾ of patients (76.9%) which was statistically high among survivors. However, in deceased group estrogen positivity was also high (41.88%), while HER-2 were only significant between 40-49 years.

Conclusion: The relatively low survival rate, the young age at first diagnosis, despite the high estrogen receptors positivity are facts can't be explained by delay treatment and need thorough search for a possible genetic or other underling rezone.

Keywords: Ten-Year; Survival rate; Breast Cancer; Kurdistan.

INTRODUCTION

There are great variations in both breast cancer (BC) incidences and outcomes from region to region,[1,2] but still this tariffing cancer is the leading cancer, and cancer related death in females worldwide.[2,3] The incidence is relatively low in developing countries and seems to rise with the development, reaching its highest numbers in Europe and the United States of America (USA).[4] However, this increase is inversely proportional to the

prognosis and outcome,[5] since the survival rate towering in advanced countries, reaching to 80% in the United Kingdom,[6] and 90% in the USA.[7]

The prognostic factors are complexly diversified. With the exception of the distant metastasis, (which turn the cancer to stage IV) the lymph nodes (LNs) involvement represents an important independent prognostic factor more than the size of the tumor.[8] Nevertheless, other prognostic factors like: the age, the ethnic origin,[2,9,10] the grade, the histological type and the hormonal status, all play important and somehow intermingling roles in the prognosis.[10,11]

The overlap effects among the prognostic factor are noticeable in the action of estrogen receptors (ER) and the HER-2 (or HER-2 Neu). The HER-2 is the target of the antibody Trastuzumab (known in the market as Herceptin). When the HER-2 is over expressed the Trastuzumab will be effective in the treatment,[12] as the later will bind to the HER-2 and this will increase the p27, which will in-turn pause the cell proliferation.[13] It has been reported that ER signaling regulate the HER-2 expression and ER+/HER-2+ patients may signify more than ER-/HER-2+ patients from drugs inhibiting the PI3K/AKT pathway.[14,15] There is a revolution in studying the prognosis of BC patients all over the developed world, on the contrary, there is a remarkable finite information, if ever, on the survivors of this cancer in developing regions and their clinical and pathological features.

The aim of this study is to estimate a primary 10 years survival rate among BC female patients in Kurdistan region and highlight the relation between the 10 years survival rates and the age, LNs involvement, ER and HER-2 status.

PATIENTS AND METHODS

The study ethical approval was obtained from the official ethical committee for research in Duhok and the scientific approval was taken from the scientific committee for research in College of Medicine/ University of Duhok.

The study collected retrospectively 160 cases of BC female patient diagnosed in the three governorates in Kurdistan: Duhok, Erbil and Sulaymany before 2010. Most BC cases diagnosed at that period have been sent to Duhok central lab for the ER and HER-2, since it was the only lab doing these investigations at that time. All the data have been collected from the pathological reports, including the histological type of the cancer, the LNs involvement, ER and HER-2 status. Cases were grouped according to the age at time of diagnoses. Results of the LNs involvement, hormonal receptors and the HER-2 status were analyzed. All the patients and the families of the deceased patients have been contacted to confirm the survival or the death of the

patient and the cause of death. Then the patients were divided into three groups; those how are below 40 years, those between 40-49 and those how are equal or above 50 years. The clinicopathological features of the three groups were analyzed and the survival rate was statistically assessed. Chi-square (x2) test was used to compare proportions. P values ≤ 0.05 were considered statistically significant.

Criteria for inclusion:

1. Females diagnosed before 2010 as BC cases
2. Cases with confirmation about the survival status, whether by talking to the patient herself or the relatives of the deceased person.
3. Cases with slides and reports contain information about the LNs, ER, and HER-2 status

Criteria for exclusion:

1. Cases diagnosed by tru-cut biopsy only, since they contain no information about the LNs involvement.
2. Patient died during that period from any cause other than the BC.
3. Any case that has not been confirmed to be survived or died due to breast cancer, whether by talking to the patient herself or the relatives of the deceased person.

RESULTS

The mean age of the 160 BC patients included in the study at time of diagnosis was 44.9 years, 120 of them (75%) were below 50 years. The 10-years survival rate was 41.2%. Death rate was significantly high at age group 30-39 years (23.1%), while the survival rate of this group was only 1.9% among all patients. On the other hand, the survival rate in patient diagnosed between 40-49 years was the highest among others (31.2%); however, the last result was not significant statistically. None of the patients that have been diagnosed bellow 30 or above 70 years survived for 10 years. (Table 1).

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Table 1: The relation of breast cancer survival and mortality rates with the age.

Age	Survivors No. (%)	Dead No. (%)	Total No. (%)	P-value
20-29	0 (0)	3 (1.9)	3 (1.9)	
30-39	3 (1.9)	37 (23.1)	40 (25)	<0.01
40-49	50 (31.2)	27 (16.9)	77 (48.1)	>0.05
50-59	10 (6.2)	20 (12.5)	30 (18.7)	>0.05
60-69	3 (1.9)	4 (2.5)	7 (4.4)	>0.05
70-79	0 (0)	3 (1.9)	3 (1.9)	
Total	66 (41.2)	94 (58.8)	160 (100)	

The survival rate after the age of 50 years returns back to decrease but this decrease was also not significant statistically. Therefore, the subsequent age grouping was studied as the following: those below 40 years, those from 40-49 years and those equal or above 50 years (Table 2). Among the 43 patients diagnosed bellow 40 years only 3 patients survived. This result was statistically highly significant.

Table 2: The relation of breast cancer survival and mortality rates with special age grouping.

Age	Survivors No. (%)	Dead No. (%)	Total No. (%)	P-value
<40	3 (1.9)	40 (25)	43 (26.9)	<0.01
40-49	50 (31.2)	27 (16.9)	77 (48.1)	>0.05
≥50	13 (8.1)	27 (16.9)	40 (25)	>0.05
Total	66 (41.2)	94 (58.8)	160 (100)	

A relatively large percentage of patients (No.99) presented at time of diagnosis with positive LNs (61.87%). Death within 10 years was statistically high in these patients (53.12%) when compared with those without LNs involvement (5.63%) as seen in Table 3.

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Table 3: The relation of breast cancer survival and mortality rates with the LNs status.

Lymph nodes	Survivors No. %	Dead No. %	Total No. (%)
LNs-	**52 (32.5)**	**9 (5.63)**	**61 (38.13)**
LNs+	**14 (8.75)**	**85 (53.12)**	**99 (61.87)**
Total	**66 (41.2)**	**94 (58.8)**	**160 (100)**
P-value		**<0.01**	

The total number of ER+ patients was 123 (76.9%). Among the 66 survivors 56 were ER + (35%) and only 10 were ER- (6.25%), the difference was statistically high. However, in the deceased group the percentage of ER + cases was also high (41.88%) and higher than that of ER- cases (16.87%), as seen in Table 4. Although the last difference was not significant statistically, these results needed further analyzed and therefore they were analyzed later according the age groups.

Table 4: The relation of breast cancer survival and mortality rates with the ER status.

ER status	Survivors No. (%)	Dead No. (%)	Total No. (%)	P-value
+ve	**56 (35)**	**67 (41.88)**	**123 (**76.9**)**	**P-value >0.05**
-ve	**10 (6.25)**	**27 (16.87)**	**37 (23.1)**	**P-value <0.05**
	P-value <0.05 **66 (41.25)**	**P-value >0.05** **94 (58.75)**	**160 (100)**	

In an opposite way, among the 66 survivors, only 10 were HER-2 + (6.25%) and 56 were HER-2 - (35%) and again the difference was statistically high. On the other hand, a significant difference was seen between

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the survivors and deceased group and the positive HER-2 results were significantly higher in the deceased group.

However, the deference between HER-2 positive and negative cases in the deceased group was statistically not significant as seen in Table 5. Therefore, both ER and HER-2 results were correlated later according to the age groups.

Table 5: The relation of breast cancer survival and mortality rates with the HER-2 status.

HER-2 Status	Survivors No. (%)	Dead No. (%)	Total No. (%)	P-value
+ve	10 (6.25)	44 (27.5)	54 (33.75)	<0.05
-ve	56 (35)	50 (31.25)	106 (66.25)	>0.05
P-value	<0.05	>0.05	160 (100)	
	66 (41.25)	94 (58.75)		

Out of the 66 survived patients 50 were between 40-49 years (75.8%). Among them 43 patients (65.2%) were ER+ and only 7 (10.6%) were ER-, this result was statistically significant. Similar significant results were among patients equal and above 50 years (Table 6). On the other hand, results in 94 deceased patients were significant only in the group bellow 40 years.

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Table 6: The relation of breast cancer survival and mortality rates with the ER and HER-2 status according to the age groups

		Survival			Death		
		Age at diagnosis			Age at diagnosis		
		<40	40-49	≥50	<40	40-49	≥50
		No.	No.	No.	No.	No.	No.
		%	%	%	%	%	%
ER	-ve	1 (1.5)	7 (10.6)	2 (3.0)	7 (7.5)	11 (11.7)	9 (9.6)
	+ve	2 (3.0)	43 (65.2)	11 (16.7)	33 (35.1)	16 (17.0)	18 (19.1)
	Total	3 (4.5)	50 (75.8)	13 (19.7)	40 (42.6)	27 (28.7)	27 (28.7)
	P-value	>0.05	<0.05	<0.05	<0.05	>0.05	>0.05
HER2	-ve	3 (1.9)	39 (24.3)	7 (4.4)	30 (18.7)	11 (6.9)	16 (10)
	+ve	0 (0.0)	11 (6.9)	6 (3.7)	10 (6.3)	16 (10)	11 (6.9)
	Total	3 (1.9)	50 (31.2)	13 (8.1)	40 (25)	27 (16.9)	27 (16.9)
	P-value		<0.05	>0.05	>0.05	>0.05	>0.05

The results for HER-2 were only significant in one age group, between 40- 49 years, where among the 66 survivors, 39 patients (24.3%) were HER-2 negative when compared with 11 (6.9%) HER-2 positive patients.

DISCUSSION

Despite the great concern about the prognosis of BC patients, the efforts to estimate the survival rate and to do follow up studies in developing areas, including this region, are limited and humble. This attempt to estimate the 10-years survival rate for the BC females in Kurdistan, a revealed relatively low survival rate when compared with that reported all over the world. In Turkey, the nearest country to Kurdistan, the overall

10-year survival rate was estimated in a large study, included 20.000 BC patients, to be 76%.[16] A higher survival rate has been reported in USA and the mortality rate has decreased even more in recent years particularly in the White population, and to a lesser extent in some ethnic populations, like the African American and Hispanic population.[17]

The mean age of BC patients was below 45 years. In a previous study of 324 BC cases in Duhok (directorate of Kurdistan) the mean age was 46.8 years,[18] and in Sulaimaniyah, (another directorate) a study of 539 BC women, reported a mean age of 47.4.[19]

However, asymptotic result to this study has been reported in Saudi Arabia (45 years),[20] and close results in Egypt and Baghdad (46 and 46.5 years respectively).[21,22] However, in Turkey, in a large study included 13,240 BC patients, the mean age was 51.6 years,[23] which is relatively low when compared it with other parts of the world

In USA, a large statistical study reviewed cancer cases between 1975 and 2016 found that the median age of first diagnosis breast cancer is 62 years and that black American women tend to be diagnosed at a younger age than white American women.[24] According to some authors breast cancer is strongly related to age with only 5% of all breast cancers occurring in women under 40 years old.[25] However, in this study patients bellow 40 years represented more than ¼ of the patients and those below 50 more than ¾ of the patients.

The relatively large percentage of patients presented at time of diagnosis with positive LNs cannot be completely explain by; the late presentation or inappropriate treatment, with the presence of such low mean age. And if the mammography performed for patients above 50, as in England and some other countries,[26] we will lose more than ¾ of the patient who had the cancer before that age. Furthermore, some authors revealed that women younger than 40 years or older than 80 years, more likely to have a poorer prognosis than others, probably due to changes in the breast with the menstrual cycles in younger women. Also, there may be biologic factors contributing to the higher stage (represented mainly by the increase in LNs involvement) and also to the risk of recurrence in younger females.[27]

The other finding of high ER+ cases despite the low age also needs explanation. This ER positivity was high in young patients who survived for 10 years, however, in the deceased group the percentage of ER + cases was also high. Oppositely, among the survivors the percentage of HER-2 positivity was low (6.25%). In Turkey, the results of ER+ cases were in agreement to our results (76.9% in this study and 72.5% in their study), while a higher percentage was reported for HER-2 + receptor (21.8%) and during their 51.6 months of follow-up, the recurrence rates was 5.2%, and the five and 10-year overall survival rates were 86% and

76%, respectively for their cases.[16] However, the HER-2 results in the current study were only significant in one age group, between 40- 49 years.

The low mean age 44.9 years, the relatively high % below 40 and the very high % below 50 (75%) in addition to the very low number of patients survived bellow 40 years, despite the high % of ER+ patients, all these facts need thorough study for a possible ethnic related genes or other underlying causes, that make this discrepancy. Several studies suggested poor prognosis in young patients and additionally expressed the suspicion that breast cancer incidence and prognosis differ according to ethnicity.[10,28,29]

CONCLUSION

The 10-years survival rate in this region is low, when compared with other parts of the world, yet there are several specific criteria related to BC in Kurdistan region: low mean age, high number of patients presented at time of diagnosis with positive LNs, significantly high death rate at age group 30-39 years, despite the high percentage of ER + in cases, including the younger age group, indicating that ER+ receptor status is not protective at young age nor the HER-2 negativity.

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