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Case Report

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Exploring of Breast Cancer Characteristic Features and Their Influences on Survival Rates

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Abstract

Breast cancer stands as the most predominant form of neoplasm and it remains the main cause of cancer-related deaths among females. Over the last four decades; a significant reduction in breast cancer mortality has been achieved due the substantial progress in the management of the disease.This retrospective study aims to evaluate the clinical and pathological features along with breast cancer molecular sub-types in city of Kirkuk-Iraq.

In this study data were collected from 280 breast cancer patient who were under the care of Kirkuk oncology center from April 2020 and for nine months, patient's average age was 50.05 years and the most of the patient diagnosed with luminal A breast cancer (57%) of the cases, with the majority (56.9%) falling within the 41 to 50-year-old age range, results shows a significant correlation between menopausal status and the survival rate (p=0.002). A significant correlation (p=0.002) between tumor stage (AIII) and postmenopausal statutes has been noticed. On the same time a higher survival rate (≥5 years) has been recorded among those who diagnosed with tumor stage AIII, whereas in 85% of the cases who diagnosed with tumor stage IV showed survival rate for less than five years.

Results from this study highlights the importance of considering the stage and molecular subtypes along with patient's age in the management of the disease and addressing the outcome associated with luminal A (Her2 negative) breast cancer via developing more reliable diagnoses tools and therapeutic targets among different molecular subtypes and finally enhancing women's awareness of the importance of early detection as a principle objective.

Introduction

Breast cancer, the most frequently occurring cancer in women, is a major public health problem. Data from Global Cancer Incidence, Mortality and Prevalence (GLOBOCAN) which is released by the International Agency for Research on Cancer estimated 2,261,419 new cases in 2020 worldwide with nearly 684,996 related deaths in both sexes [1]. In Asia, including Iraq, breast cancer incidence frequently diagnosed among women at their forties, whereas the disease most often affects elderly women in Europe and United States [2,3]. There are a multiple factors might causes this variation in incidence, including geographic variation along with other factors such as genetic factors, life style, ethnic background and other known risk factors [4,5].

For more effective treatments of breast cancer and in order to categorizing and tailoring a successful personal treatment strategies, oncologists has identified several clinical and molecular characteristics resulting in considerable declines in breast cancer deaths and rising the prevalence of women living with the disease worldwide [6,7]. Hence, significant progress continues to be made in for a specific, rigorous and reproducible method of identifying successful treatment algorithms utilizing biological markers such as ER/PR or Her2 in the developing field of personalized medicine [8]. Variances in the molecular subtypes of the breast cancer has been noticed amongst women from different racial and ethnic backgrounds, in particular few studies showed fairly high incidence of triple negative breast cancer with poorer prognoses among African-American women compared to Caucasian females [9]. In recent decades, breast cancer incidence and survival have changed considerably, in many developed countries and despite of high the incidence rate a significant survival improvement amongst breast cancer patients has been recorded, whereas a short life span is highly expected in developing countries, due to the late women's present and insufficient management of the disease [10]. Although the correlation between the survival rate and breast cancer characteristics such as histopathological and molecular has been studied in other parts of the country, but it is not enough to draw a clear pattern of presentation for breast cancer patient or those who are at risk of developing breast cancer [11-13]. Therefore, the goal of this study is to determine the molecular subtypes according to

the age groups among Kirkuk women. Furthermore, the correlation between menopause states, tumor stage and the survival rate has been investigated in this study.

Methodology

Ethical Considerations

This is a retrospective study; patient identity and confidentiality were protected. Since consent form was not applicable to this research work, a prior approval from the college ethical board were obtained.

Data Collection and Statistical Analysis

This retrospective study was conducted at Kirkuk Oncology Center which is the main referral cancer facility in the city of Kirkuk, patients who has been diagnosed with breast cancer from period from April 2020 to January 2021 were included, patients who didn't turn up for treatment were excluded from this study. Guideline of College of American pathologist test for the breast cancer was used to score the expression of the ER, PR and HER2 amongst Patient were diagnosed with breast cancer [14], they have been categorized into four molecular subtypes; luminal A (ER+ and/or PR+ and HER2-), luminal B (ER+ and/or PR+/HER2+), HER2- (ER- and PR-/HER2+) and triple negative (ER- and PR-/HER2-) [15]. Other predictor variables (age, menopause state, stage at diagnosis and survival rate) were collected along with molecular subtypes. The patients were then grouped on the basis of menopause statute as shown in Table 1 and on the basis of the age as shown in Table 2.

Statistical Analyses

All collected data from the patient was analyzed using Statistical Package for Social Sciences (SPSS) version 25, unpaired t-test and chi- squared test were used to express and compare the data, were $p \leq 0.05$ has been considered statistically significant [16].

Results

Table1 represents the relation between the menopause state of the 280 breast cancer patients who participate in this study and the survival rate. Mean age of the included cases were 50.05 year, whereas the median was 48 years and the ages range of the patients 25 to 90 years old. The mean value of the survival rate according to time of menopause was significantly higher amongst premenopausal BC (6.2 ±3.87) years and P value by unpaired t-test was (p=0.002) with mean value of (4.82 ±3.66 years) amongst postmenopausal BC.

	Pre. N=150 Mean ±SD	**Post. N=130 Mean ±SD**	**P-value**
Survival rate (yr)	6.2 ±3.87	4.82 ±3.66	0.002

Table 1: Survival rate according to time of menopause-P value by unpaired t-test.

Results shown in table 2 revealed that the most frequent molecular subtype who have positive ER and PR tend to have negative Her2- (p=0.016), amongst them 66 BC (56.9%) were at 41-50 years old.

Mol. Subtypes	**Age (year)**						**P- Value**
	≤30 N=3 N(%)	**31-40 N=44 N(%)**	**41-50 N=116 N(%)**	**51-60 N=66 N(%)**	**61-70 N=41 N(%)**	**>70 N=10 N(%)**	
$ER^-/PR^-/HER2^-$	1(33.3)	2(20.0)	3(7.3)	7(10.6)	14(12.1)	3(6.8)	0.016
$ER^-/PR^-/HER2^+$	0(0.0)	1(10.0)	3(7.3)	5(7.6)	11(9.5)	5(11.4)	
$ER^-/PR^+/HER2^-$	1(33.3)	0(0.0)	2(4.9)	0(0.0)	4(3.4)	4(9.1)	
$ER^-/PR^+/HER2^+$	0(0.0)	0(0.0)	0(0.0)	3(4.5)	1(0.9)	0(0.0)	
$ER^+/PR^-/HER2^-$	0(0.0)	0(0.0)	1(2.4)	3(4.5)	8(6.9)	4(9.1)	
$ER^+/PR^-/HER2^+$	1(33.3)	0(0.0)	0(0.0)	1(1.5)	5(4.3)	0(0.0)	
$ER^+/PR^+/HER^+$	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(0.9)	0(0.0)	
$ER^+/PR^+/HER2^-$	0(0.0)	6(60.0)	29(70.7)	42(63.6)	66(56.9)	19(43.2)	
$ER^+/PR^+/HER2^+$	0(0.0)	1(10.0)	3(7.3)	5(7.6)	6(5.2)	9(20.5)	

Table 2: All receptors together according to age groups- P value by Yates chi square test.

Almost 78% of BC patients with Her2 positive belongs to 41-50 years old age group and less than 1% were 30 years old or younger. This invers association between the age of the patients at diagnoses time and the expression of Her2 was statistically significant (p=0.015) as shown in Table 3.

Her2 statute	Age (year)						P- Value
	≤30 N=3 N(%)	31-40 N=44 N(%)	41-50 N=116 N(%)	51-60 N=66 N(%)	61-70 N=41 N(%)	>70 N=10 N(%)	
Her2^{+}	1(33.3)	14(31.8)	24(20.6)	14(21.2)	6(14.6)	2(20)	0.015
Her2^{-}	2(66.7)	30(68.2)	92(79.4)	52(78.8)	35(85.4)	8(80)	

Table 3: Age group according to Her2 expression.

Among postmenopausal breast cancer patients; stage IIIA tumour were more frequently observed (p=0.022) as shown in Figure 1.

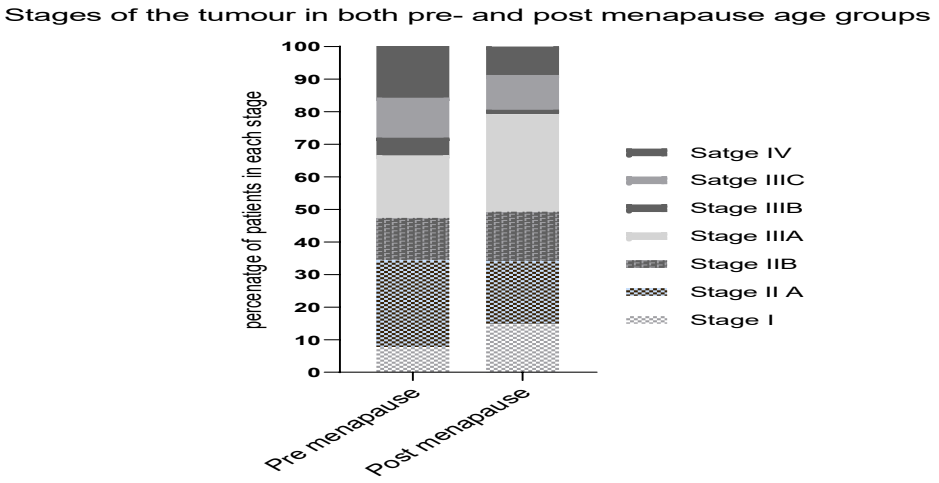

Figure 1: Stages of the tumour in both pre and post menopause age group.

With regards to the relation between tumour stage and the survival rate, almost (75%) of those who diagnosed with stage I tumour presented with best survived rate for more than 5 years and (85%) those who diagnosed with stage IV tumour a survived for less than 5 years as shows in Figure 2.

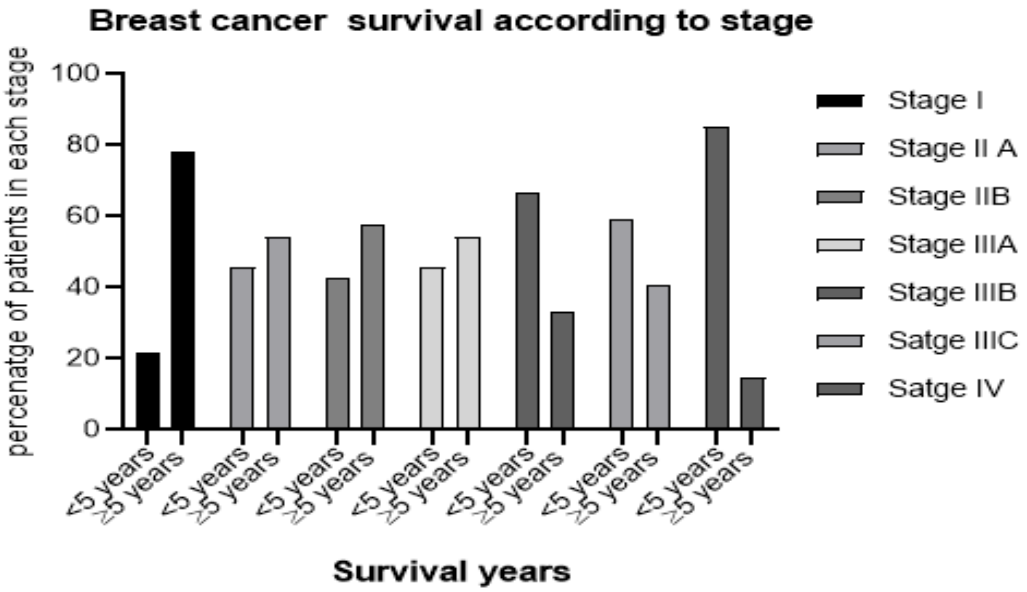

Figure 2: Bresat cancer survival rate acording to the tumour stages.

Discussion

In Iraq, according to the cancer registry office; almost one- third of the registered cancer amongst female is a breast cancer and a significant increase in the incidence has been noticed among 50-59 year age group 2. These results were in agreement to those in US, as 65.1% of the breast cancer reported case was found to be older than 55 years of age [17]. These dramatic increases of breast cancer incidence in parallel with treatment improvement have resulted in escalating the prevalence of breast cancer patient worldwide [18]. Our data showed a significant association between menopausal state and the average survival rate (p=0.002), this result is in accordance with the results found in previous published studies [19,20]. Saying that, our findings were supported the hypotheses that the slower growth of the breast tumour amongst elderly breast cancer patient [21-23]. The status of ER and PR and Her2 are very important indicators in the treatment of the breast cancer; A positive expression of these favourable molecular markers oestrogen receptor (ER) and progesterone receptor (PR) has been noticed amongst women 40 years and older (Table -2), which is inversely associated with a low expression of Her2 (p=0.016). Nevertheless, significant increase of the survival rate amongst elderly patient might partly be explained by the fact that there is a positive expression of the favourable molecular markers in advancing age breast cancer patients [24]. The positive expression of the Her2 is significantly seen in younger women; for example, for those who are (41-50) years old, the proportion of those who showed Her2 negative was 79.4% versus 20.6 in the same age group, as in (Table-3).this result is in consistent with previous studies [25,26].

In this study; tumour characteristics has been assessed in relation to the menopausal statute and the relative survival rate. The results shown a significant association between tumour stage (IIIA) and postmenopausal statue, unfortunately the diagnoses of the tumour at the advanced stage can't be fully explained because of the limitation of the study, however a possible role of the combined hormone therapy amongst postmenopausal women, socioeconomic factors and the strong culture of local people might be one of the reasons behind the late diagnoses [27,28]. Furthermore, results from this study showed that tumour staging at the diagnoses time might have an influence on average survival rate of the patients, however there many other factors such as early diagnoses and the molecular subtypes, histological grade, and other related risk factors might play a great role in increasing survival rate and our results are in consistent with above previous study [29]. Saying that some other studies are in disagreement with our finding and they suggest that the above diagnostic factors are independently associated with the survival rate [30]. Since the results from this study showed a negative association between the average survival rate and tumour advanced stage, it is become clear that diagnosis of an earlier stage breast cancer will leads to longer survival rates [31].

Conclusion

These types of the studies have shown a possible association between clinicopathological characteristics and the survival rate amongst breast cancer patients. Our study found that breast cancer age group in the city of Kirkuk are mainly (40-50) years old and a significant correlation between the age group, menopause status, molecular subtypes and the survival rate were indicted, further studies are needed to establish which maters is the most. The variation between our findings with the other studies in other region(s) highlights the needs of increasing breast cancer awareness amongst the local communities and encouraging the screening and early diagnoses programmes.

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