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Original Research Article

Incidence and characteristics of breast cancer in patients 40 years of age or younger: a study of a tertiary center in Saudi Arabia

Sahar M. Alnefaie[1]*, Nisreen R. Kanbar[2], Reem A. Alshoura[3], Amal Y. Alhefdhi[3], Saif S. Alsobhi[3]

[1]Department of Surgery, College of Medicine, Taif University, Al-Taif, Saudi Arabia
[2]Saudi German Hospital, Riyadh, Saudi Arabia
[3]Department of Surgery, King Faisal Specialist Hospital-RC, Alfaisal University, Riyadh, Saudi Arabia

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***Correspondence:**
Dr. Sahar M. Alnefaie,
E-mail: Sahar.m@tu.edu.sa

ABSTRACT

Background: Breast cancer in young women has a higher mortality rate, can show adverse outcomes, and is more likely to recur after treatment. This study evaluated the incidence and characteristics of breast cancer in female patients 40 years of age or younger.
Methods: This is a descriptive study of 234 patients, 40 years of age or younger, diagnosed with breast cancer in the period January 2010–December 2015.
Results: We included 234 out of 1026 patients (22%) that met our inclusion criteria. At the time of the diagnosis, the mean age of the patients was 34±5 years; 32 (14%) of them had a positive family history of breast cancer, and more than a fifth were found to have advanced stages of the disease. One-third of our patients were hormone receptor (HR)-positive with HER2 negative, 61 (26%) were triple negative, and a total of 98 (42%) of our patients had HER2 overexpression. Lumpectomy was performed for 89 (38%) of them. Recurrence was documented for 40 (17.4%), and approximately half of the patients, 105 (45%), had recurrence in their first two years of diagnosis.
Conclusions: Breast cancer in young patients is a very challenging entity, as they tend to be more aggressive than the older age group. The incidence of breast cancer in female patients younger than 40 is higher than that in Western countries. However, our findings align with regards to their pathology type and hormonal status.

Keywords: Breast cancer, Young women, Characteristics, Type of surgery, Recurrence

INTRODUCTION

Breast cancer is at the top of all malignancies seen in Saudi females. It accounts for 28.8, compared to 47.8 per 100,000 population worldwide. Age-standardized (worldwide) incidence rate of breast cancer at all ages in Saudi Arabia is 28.8 compared to 90.3 years in the United States.[1] According to the Saudi Health Council, cancer incidence report 2020, the highest incidence of cases diagnosed with breast cancer among Saudi females by age group is (45-49 years).[2] It was found that young age is an independent risk factor for recurrence in Saudi women who were diagnosed with breast cancer.[3] Whether there are underlying genetic or environmental factors that would render women in Saudi Arabia more prone to developing the disease at a younger age is the subject of ongoing research.[4] Breast cancer in women under the age of 40 can present differently than in older women and may be more difficult to diagnose. It tends to be larger, more advanced at diagnosis, and more aggressive. It also has a higher mortality rate, can show adverse outcomes, and is more likely to recur after treatment. There are more complex issues that arise due to a cancer diagnosis at a young age, such as considerations of pregnancy, fertility

and contraception, sexuality, and body image, as well as familial and genetic issues.[5] Thus, chemotherapy, endocrine, and local therapies have the potential to significantly impact both the physiologic health and the psychological health of young women.[6] And to this end, it is important for clinicians to clarify the existing controversy as to whether aggressive treatment for young women with breast cancer is justified.[3] This study aims to investigate the exact incidence and characteristic features of breast cancer in Saudi patients 40 years of age or younger, which have not been studied thoroughly in Saudi Arabia due to limited documented data. Based on our observation, we hypothesize that the proportion of breast cancer in young women in Saudi Arabia compared to an older age-onset population is much higher than in Western countries.

METHODS

The study was approved by the office of research affairs (ORA) at King Faisal specialist hospital and research Centre (KFSH-RC) in Riyadh, Saudi Arabia. In this descriptive, retrospective study, we collected the data of all breast cancer patients from King Faisal Specialist Hospital and Research Centre in Riyadh electronic charts. A total of 234 patients who had undergone surgery between January 2010 and December 2015 were included in this study. The characteristics of these patients and the disease biology were reviewed, including the patient's demographics, family history, pathological features, type of surgery, presence of metastatic disease, and recurrence rate. Statistics were analysed in numbers and percentage.

Inclusion and exclusion criteria

We included all female patients with breast cancer who were operated on at King Faisal Specialist Hospital, Riyadh, in the period from January 2010 to December 2015. Also, we included patients who were diagnosed with breast cancer at the age of 40 years or younger and all patients' nationalities, religions, and racial and ethnic groups. Male patients and patients who were diagnosed with breast cancer above the age of 40 years were excluded.

RESULTS

A total of 1026 patients with breast cancer were recognized at KFSH-RC, Riyadh, in the period between January 2010 and December 2015. We included 234 patients (22% of the cases) that met our inclusion criteria.

Clinicopathological characteristics

At the time of the diagnosis, the mean age of the patients was 34±5 years, and 32 (14%) of them had a positive family history of breast cancer. Also, we found that 18 (7.7%) of our patients had stage III disease, while 35 (15%) were found to have advanced stages of the disease with evidence of distant metastasis. Pathological data has shown that the majority of the patients were diagnosed with invasive ductal carcinoma (IDC), which accounts for 198 (84.6%), while 13 (5.6%) of them were diagnosed with pure ductal carcinoma in situ (DCIS), and 7 (3%) had malignant phyllodes. As most of the patients were diagnosed with IDC, further pathological data were evaluated, and we found that more than half of these cases, 120 (51.3%), had IDC grade 3. Moreover, 216 (92.3%) had Ki67 of more than 20. Regarding the hormonal status, it has been observed that about one-third of our patients were hormone receptor (HR)-positive with HER2 negative, 61 (26%) were triple negative, 68 (29%) of them were triple positive, and 30 (13%) of them were hormonal receptor-negative with HER2 overexpression, so a total of 98 (42%) of our patients had HER2 overexpression. These findings from pathological data, as well as tumor biology, indicate the aggressiveness of breast cancer when it occurs in women younger than 40 years (Table 1).

Table 1: Clinicopathological characteristics.

Character	N	%
Age (years)		
Mean	34.5	-
Range	20-40	-
Final histology		
Total cases of IDC*	198	84.6
Total cases of DCIS*	105	44.87
Pure DCIS	13	5.65
Pure IDC	110	47.83
DCIS+IDC	88	38.26
DCIS+IPC*	1	0.43
DCIS+IDP*	2	0.87
DCIS+Paget's disease	1	0.43
Malignant Phyllodes	7	3.04
ILC*	4	1.74
IPC	1	0.43
IDP	1	0.43
Metaplastic carcinoma	2	0.87
Hormonal receptors and HER2 status		
HR+HER2+(triple +ve)	68	29
HR-HER2-(triple -ve)	61	26
HR+HER2-	75	32
HR-HER2+	30	13

*IDC: Invasive ductal carcinoma, DCIS: Ductal carcinoma in situ, IPC: Intracystic papillary carcinoma, IDP: Intraductal papilloma, ILC: Invasive lobular carcinoma.

Treatment

All of the included patients had undergone different types of operations; 89 (38%) of them had undergone lumpectomy, 52 (22%) skin-sparing mastectomy, 31 (13%) simple mastectomy, and only 24 (10%) had undergone modified radical mastectomy. This shows that the surgeons were aiming to achieve more cosmetic operations and breast preservation once feasible in such a young age group of patients, provided that these

operations do not affect the safety of the oncological resection (Table 2).

Table 2: Type of surgery and disease-free survival.

Type of surgery	N	%
Lumpectomy	89	38
SSM*	52	22
Simple Mastectomy	31	13
MRM*	24	10
Palliative Surgery	15	6
NSM*	10	4
Wire localization lumpectomy	10	4
Bilateral surgery	8	3
Disease-free survival		
Recurrence	40	17.4
Recurrence in the first two years of diagnosis	105	45

*SSM: skin-sparing mastectomy, MRM: modified radical mastectomy, NSM: nipple-sparing mastectomy.

Outcomes

Lastly, we have also evaluated the disease-free survival, and we have noticed that 40 (17.4%) had recurrence, and approximately half of these patients, 105 (45%), had recurrence in their first two years of diagnosis (Table 2).

DISCUSSION

It has been observed that breast cancer is uncommonly seen in young females, with only 5% to 7% below the age of 40 in developed countries, and it is believed that this early onset of breast cancer has special characteristics with more aggressive behavior and a poor prognosis in comparison to the older age group.[4] As described in a previous study by Najjar et al it has been found that Arab women are more likely to get breast cancer in an earlier decade than in Western countries.[7] Focusing more on our region, studies have shown that one of the main characteristics of Saudi females with breast cancer is their presentation at a young age.[8] In our study, we evaluated the clinic-pathological features of young breast cancer patients, the recurrence rate of the disease, and the surgical treatment that was done for this group of patients to get a better overview of their disease behavior and course. The number of patients who were diagnosed with breast cancer below the age of 40 was 234 (22%), with a mean age of 34.5. In comparison with Western countries like the United States, age-standardized (worldwide) incidence rates of breast cancer at all ages are 90.3 years.[1] These data may point toward clear socioeconomic factors that caused these differences between Arab and Western countries in the course of the disease.[8] Going through the background of these patients, our study showed that 32 (14%) of them had a positive family history of breast cancer in one or more members of the family. On the other hand, other studies showed that most young women with breast cancer had a familial history of breast cancer.[4] Therefore, it was recommended that this group of young patients with breast cancer go for genetic counselling and testing for BRCA1/2 genes.[9]

Many of the previous studies demonstrated that young females with breast cancer usually present with an advanced stage of the disease; 66.1% of them were diagnosed with stage III.[10] In our data, we found that 18 (7.7%) of our patients had stage III disease, and 35 (15%) of them presented with metastatic disease, so a total of more than a fifth (22.7%) of our patients were diagnosed with advanced stage (III or IV), which indicates the aggressiveness of breast cancer in female patients younger than 40 years. This necessitates early detection and prompt treatment of these young patients, as the delay in management may have a huge impact on their survival.[11] Also, this can be of interest in upcoming studies. To gain a better understanding of the behavior of breast cancer in young women, we analyzed the pathological and biological features of the disease. We found that one-third of them were hormone receptor-positive with HER2 negative, 61 (26%) were triple negative, 68 (29%) of them were triple positive, and 30 (13%) of our patients were estrogen receptor (ER) and progesterone receptor (PR) negative with HER2 overexpression, so a total of 98 (42%) of our patients had HER2 overexpression, which confirms the aggressiveness of this disease when it occurs in young female patients. Previous research has revealed that unfavorable prognostic factors are associated with young women. It has been seen that most of these tumors are estrogen (ER) and progesterone (PR) negative, with HER2 overexpression and vascular invasion.[12] Further analysis of the pathological features of breast cancer in young females revealed that most of the patients were found to have invasive ductal carcinoma, which accounts for 198 (84.6%) of the cases, and 120 (51.3%) of them were grade 3 tumors. Also, similar results have been noticed in previous studies.[12]

Operative options for this group of patients are somewhat challenging. It depends on several factors, such as the loco-regional recurrence, the ratio of cosmetic/ oncological results, and the patient's preference. Although young females with breast cancer are a predisposing factor for local recurrence, patients who underwent radical mastectomies had no survival advantages in comparison with patients with breast conserving treatment (BCT).[9] Our study reported that 89 (38%) of our patients underwent lumpectomy. We have also found that 31 (13%) underwent simple mastectomy, 52 (22%) underwent skin-sparing mastectomy, and only 24 (10%) of the patients had modified radical mastectomy (MRM). Hence, these data can explain the aim of the surgeons in dealing with these young patients with breast cancer in more conservative management once feasible with better cosmetic results, given the evidence that BCT was found to be as safe as modified radical mastectomy in previous research in terms of overall survival.[13] It is important to shed light on the disease-free survival (DFS) of this unique group of

patients. So, we analyzed the patient data during the 5-year follow-up period to evaluate for recurrence, and it was observed that 40 (17.4%) of our patients had recurrence, and 105 (45%) had recurrence in the first or second year. However, we endorse a long-term follow-up of 10 years for better evaluation of outcomes. In a prospective study that was done in the UK, they found that 24% of their patients had distant recurrence.[14] Another study showed that 5.6% of their patients had loco-regional recurrence, 15.2% developed metastatic recurrence, and 8% died.[11]

CONCLUSION

In conclusion, breast cancer in young patients is a very challenging entity, as they tend to be more aggressive than the older age group. In comparison to other studies, we found that the incidence of breast cancer in female patients younger than 40 is higher than that in Western countries (22% compared with 5–7%). However, we have found similar results in describing this group of patients in relation to their pathology type, hormonal status, and management modality. Regardless of the aggressive behavior, surgeons could achieve more conservative management with these patients. Long-term follow-up of these patients may be addressed in future research for better management.

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