BREAST CANCER RISK MAY INCREASE AFTER CHILDBIRTH. A CLINICO-EPIDEMIOLOGICAL STUDY

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Abstract

Background: Several factors have been associated with the international variation in breast cancer incidence rates, these include epidemiologic, reproductive, hormonal and life style factors. Trends in these risk factors are important to demonstrate changes over time.

Patients and Methods: This study was done to observe affected cases of early breast cancer according to age, parity, clinical signs and symptoms, site, side of breast lesion, pathology of malignant breast lump and type of surgery performed. The study includes Seven hundred and ninety (790) patients diagnosed with early breast cancer. Patient information already present in the data-based archives at Damietta Cancer Institute, Damietta, and Mansoura University, Egypt, the period between January 2016 and December 2017.

Results: Maximum number of early breast cancer was encountered in the 5th decade of age group of patients, followed by 4th decade. All cases studied were females except 9 cases which were males. The commonest sign and symptoms of presentation was painless lump in the breast followed by referred cases after surgery along with associated features of mastalgia, nipple discharge and axillary mass. Histopathologically, infiltrating duct carcinoma represented most cases followed by medullary carcinoma & mucinous carcinoma.

Conclusion: There are significant changes in reproductive and hormonal pattern in Egyptian females diagnosed with breast cancer over the period of our study.

Key Words: Childbirth, Early breast cancer, Epidemiological study

Introduction

Breast cancer is the most common cause of cancer death among women worldwide. Incidence rates are high in more developed countries, whereas rates in less developed countries and in Japan are low but increasing. In the world, each year more than 1 million women are diagnosed with breast cancer and more than 400000 die from it. Breast cancer represents 30% of cancer new cases in developed countries and 14% in developing countries 1. In Egypt, data reported by Gharbiah population-based cancer registry indicated that breast cancer ranked first among females (37.6%). A (2001) study of migrants from the Middle East to Australia did indicate that the Egyptian women had the highest breast cancer rates of Middle Eastern Immigrants 1. In any patient who presents with a breast lump or other symptoms suspicious; assessment, radiological imaging and a tissue sample taken for exclusion of carcinoma, the diagnosis should be made by a combination of clinical, cytological or histological analysis; that so-called triple combination 2. There is a new trend for earlier diagnosis of breast cancer as stages

I & II by convention grouped together as early breast cancer. The treatment of operable primary breast cancer has also undergone a remarkable evolution in the past several decades. The standard operative procedure has changed from the radical mastectomy to the modified radical mastectomy and the use of breast conserving treatment is increasing. Radical mastectomy is no longer the only available option for potentially curative treatment of early stage breast cancer 2. The overall survival (OS) at 5 and 10 years in patients with breast cancer is 88% and 77%, respectively. Both these rates are significantly higher than the 5-year OS of all cancer together, which is 64% 3.

Patients and Methods

A permission of data collection was taken and approved by the ethical committee of the Faculty of medicine, Mansoura University, Egypt. As, most of cases from Delta area visit Damietta, Dakhlia and Gharbia Governorates oncology centers,so A retrospective observational study conducted to identify patients with early breast cancer presented at the surgical oncology unit and clinical oncology department in collaboration with pathology department at Damietta Cancer Institute over a period of two years. Out of which, 790 cases of early breast cancer were found and included in this study whose diagnosis was confirmed histologically. Other benign and locally advanced or metastatic cases were excluded from the study.

Methods of collection of data:

1. Detailed history taking.
2. Clinical Examination.
3. Routine Laboratory investigations.
4. Relevant special investigation.
5. Histological examination of the tissue was undertaken & tissue was taken from the breast by biopsy, local excision of the lump or specimen from the mastectomies.

Study Evaluation Points:

1. We stressed on: Age, gender, risk factors, parity.
2. Site of breast lesion: UOQ, UIQ, LOQ, LIQ
3. Side of breast lesion (laterality): Right, Left or bilateral
4. Presentation: Breast lump, mastalgia, nipple discharge, axillary mass, etc
5. Clinical staging.
6. Pathology of the lesion.
7. Type of surgery performed: Breast-conserving surgery (BCS) or mastectomy.

Results

Demographics characteristics: This study involved 790 patients over a period of 24 months, they were 378 cases in 2016 and 412 cases in 2017,with 781 (98.9%) females, they were 374 in 2016 and 407 in 2017and 9 males (1.1%); 4 in 2016 and 5 in 2017, the age of the studied population ranged from 20 to 86 years, with the mean was 53.1 ± 11.8.major no. of cases were encountered in the age group of 50-60 yrs. (5th decade) i.e. 30.3%, and then in 4th& 6th decades with percentage being 25.1% and 22.0% respectively Table 1.

Table 1: Frequency of cases (n=790) in each decade of age

Age	No of cases	Percentage (%)
<30 years	10 cases	1.3
30 - <40 years	102 cases	12.9
40 - <50 years	198 cases	25.1
50 - <60 years	239 cases	30.3
60 - <70 years	174 cases	22.0
70 - <80 years	58 cases	7.3
80 – 90 years	9 cases	1.1

Two-thirds 516 (66.1%) of female patients were multipara, while 110 (14.1%) nullipara and 109 (14%) grand multipara (more than 5 children) and lastly primipara 46 (5.9%) as shown in Figure1.
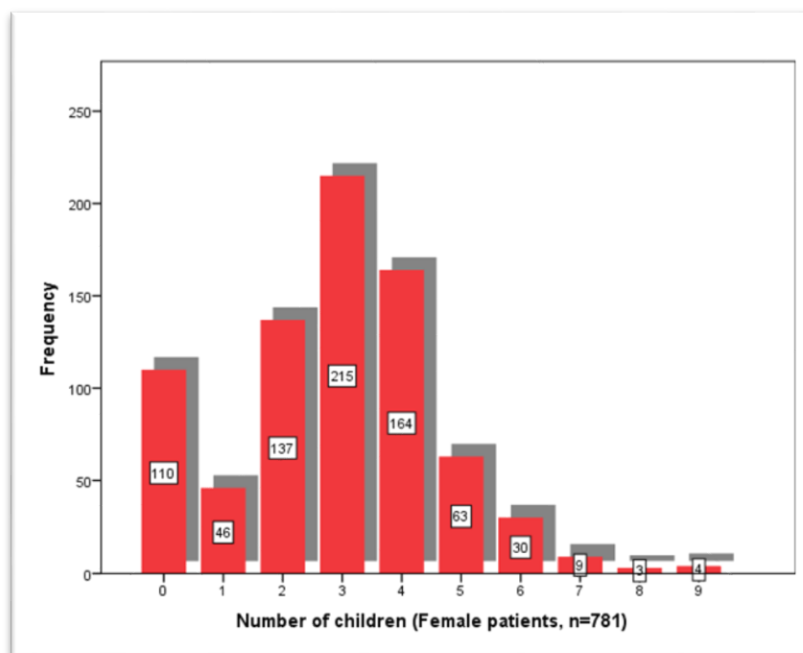
Figure (1): Frequency of parity

Most patients presented by a painless breast lump 631 (79.9%), only 19 (2.4%) presented by mastalgia, 12(1.5%) by nipple discharge and only a case with axillary mass. good number 126 (15.9%) were referred from other hospitals after surgery as shown in Table 2.

Table 2: Frequency of patient presentation

Presentation	Frequency	Percentage
Breast lump	631	79.9%
Referral after surgery	126	15.9%
Mastalgia	19	2.4%
Nipple discharge	12	1.5%
Axillary mass	2	0.3%

The right side was affected in 397 (50.8%) of women and in 4 of 9 (44.4%) men, while the left side was affected in 372 (47.6%) of women and 5 of 9 (55.6%) of men. Bilateral disease was present in 12 (1.5%) of women and was not present in men as shown in Table 3& Figure 2.

Table 3: Frequency of laterality to sex decades

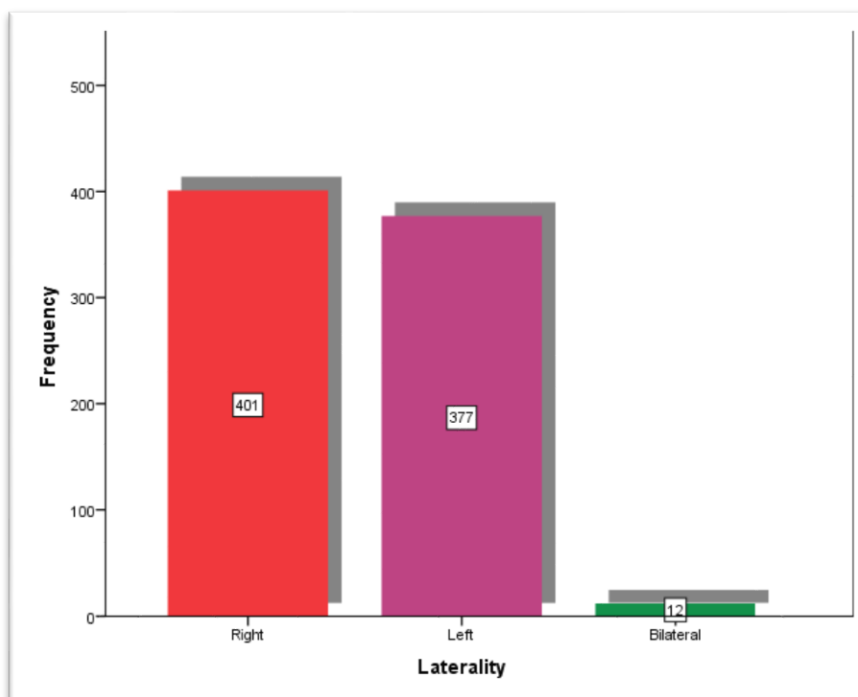| Side	Gender		χ^2	P value
	Male (n=9)	Female (n=781)		
Right	4 (44.4%)	397 (50.8%)	0.327	0.849
Left	5 (55.6%)	372 (47.6%)		
Bilateral	0 (0%)	12 (1.5%)		

Figure 2: Frequency of laterality in the study group

Breast cancer was located in the upper outer quadrant in 601(76.1%) in the study group, upper inner quadrant in 71 (9%) of them and located centrally in 54 (6.8%) as shown in Figure 3.
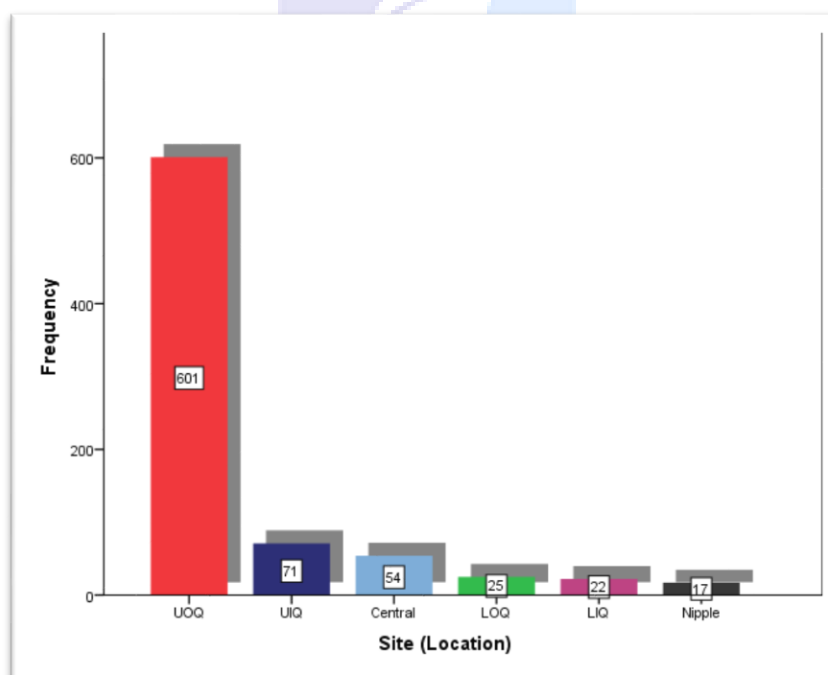

Figure 3: Site (location) of breast cancer in the study group

Most of patients 398 (50.4%) had tumor stage T1, and 351 (44.4%) of them had T2, only 41 (5.2%) had TX. Also, Ipsilateral axillary lymph node affection was present in 541 (68.5%) of patients and was negative in 249 (31.5%) of them as shown in Table 4. This table also showed a statistically significant higher proportion of N1 versus N0 and a statistically significant higher proportions of T1 and T2 versus TX.

Table 4: Clinical staging by Lymph node and Tumor size

Parameter	Frequency (%)	χ^2	P value
LN: **N0** **N1**	 249 (31.5%) 541 (68.5%)	107.929	**<0.0005**
Tumor: **Tx** **T1** **T2**	 41 (5.2%) 398 (50.4%) 351 (44.4%)	285.770	**<0.0005**

Histopathologically, most of patients had Infiltrating duct carcinoma 748 (94.7%) as shown in Table 5, as pathological types as medullary carcinoma 10 (1.3%) and mucinous carcinoma 11 (1.4%).

Table 5: Histopathological diagnosis

Histopathology	Frequency	Percentage	χ^2	P value
Infiltrating duct carcinoma	748	94.7%	7.004.9	**<0.0005**
Medullary carcinoma	10	1.3%		
Mucinous carcinoma	11	1.4%		
Colloid carcinoma	2	0.3%		
Intra-ductal carcinoma	7	0.9%		
Intra-cystic papillary carcinoma	5	0.6%		
Tubular carcinoma	1	0.13%		
Paget disease	2	0.3%		
Undifferentiated carcinoma	2	0.3%		
Malignant lymphoma	1	0.13%		
Cystosarcoma phylloides	1	0.13%		

Modified radical mastectomy was done for all males 9 (100%) and for 524 (67.1%) females, but conservative breast surgery was done for 252 (32.9) females as shown in Table 6 which show a significant difference in type of surgery used.

Table 6: Frequency of surgery done

Surgery	Sex		χ^2	P value
	Male (n=9)	Female (n=781)		
CBS	0 (0%)	257 (32.9%)	4.390	**0.035**
MRM	9 (100%)	524 (67.1%)		

Image 1: Showing female patient with Lt breast cancer (peri auricular mass) underwent Lt BCS

Image 2: Showing female patient with Rt breast cancer (UIQ mass) underwent Rt BCS

Discussion

Breast cancer is the most frequent malignant tumor in females. Its morbidity and mortality continue to increase, despite remarkable progresses in the field of early diagnosis and adjuvant therapy. In the United States (US), breast cancer is the most common among females representing 30% of all cancers, the second most common cause of cancer deaths in women, and the main cause of deaths in women aged 40 to 59 years4. In Egypt, according to population-based registry in three governorates, breast cancer was the most common cancer among females (32.9%) and the second common of both sexes. At NCI, Cairo University, breast cancer ranked the first in females (38.8%) and in both genders (19.6%) according to NCI-Hospital based registry 5. Several factors have been reported to be associated with the international variation in breast cancer incidence rates including differences in reproductive, hormonal and lifestyle factors. Contributing factors also include differences in population size, age structure and availability of early detection and screening services 6. Postponement of child bearing or having no children, which were part of family planning policies in many countries as Brazil, India and China added also to the increase in breast cancer incidence. With declining parity, the lifetime duration of breastfeeding will also decrease representing increased risk for breast cancer 7. Worldwide, Breast cancer is mainly a disease of females. More than 99% of cancer occur in females and less than 1 % in males 8. The present study documented that female patients were 781 (98.9%) with only 9 (1.1%) male patients which close to global one. In our study we found that most patients who had been diagnosed with early breast cancer ranged in age between 50 years old and 60 years (mean age 53.1 ± 11.8 years) with 30.3% of all patients, and these values appear to be highly compatible with the results of Chen et al., (2016) in which the 50-59 year age group was the largest group of patients enrolled in his study (26.4%), and El Saghir et al., (2007), in which the median age was between 49-52 years. Our results were in contrast with the study done by Sant et al., (2004) in which approximately 50% of all women with newly diagnosed breast cancer were older than 63 years, and the study done by Holmes and Muss, (2003), in which 50% of patients with breast cancer were those older than 65 years of age and 35% were older than 70 years, this difference may be due to environmental and racial factors9,10,11,12. We

found that Two-thirds 516 (66.1%) of female patients were multipara, while 110 (14.1%) nullipara and 109 (14%) grand multipara (more than 5 children) and lastly primipara 46 (5.9%), these results coincide with Singh et al., (2016), who submitted that 47.37% of patients had more than 3 up to 6 children followed by up to 3 children (36.84%) and 5.26% had no children while 10.53% had more than 6 children13. In contrary, nulliparity was associated with a high risk of breast cancer as compared to uniparous women, in the study done by Butt et al., (2009), and the study carried by Lambertini et al., (2016) showed that having a first child before age 35 and having a greater number of children was associated with decreased risk of HR+ breast cancer. Also, Palmer et al., (2003), suggested that multiparity modestly decreases the risk of breast cancer in older women, this difference may be due to racial factors, different life style, and inter-population differences14,15,16. 631 (79.9%) patients presented by a breast lump only 19 (2.4%) presented by mastalgia, 12 (1.5%) by nipple discharge in our study, these results were similar to the study done by Soylar and Genc, (2016), in which 69.5% stated that the first symptom they noticed was a mass in the breast/axilla; 13% had pain in the breast and 10.5% reported breast deformity and discharge. The study done by Özgün, Soyder and Tunçyürek, (2009), reported 77.8% of the patients in their study had a breast mass, 14.2% had mass and pain in the breast, 3.1% had pain, and 3.8% had breast deformity and discharge as their first symptom the difference in pain and discharge percentage may be due to difference in sample size or inter-population differences17,18. The right side was affected in 397 (50.8%) of women and in 4 of 9 (44.4%) men, while the left side was affected in 372 (47.6%) of women and 5 of 9 (55.6%) of men. Bilateral disease was present in 12 (1.5%) in this study, these results similar to study carried by Orang, Marzony and Afsharfard, (2013), in which 51.5% of cases, tumor was detected in right side and in 47.4% of cases the location of tumor in breast was in left side. In 1.1% of cases tumors were bilateral. while in the study carried by Zeeneldin et al (2013) reported that out of 5459 cases of invasive breast cancers (BCs), 2928 cases (53.64%) were left-sided and 2531 cases were right-sided (46.36%), this discrepancy possibly related to difference in sample size19,20. Out of 790 patients with early breast cancer 601 (76.1%) patients had mass located in the upper outer quadrant in in the study group, upper inner quadrant in 71 (9%) of them, and located centrally in 54 (6.8%), this compatible with Eisemann, Waldmann and Katalinic, (2013), in which the most frequent

location of the cancer is the upper outer quadrant of the afflicted breast, which represent 36.1% this is followed by the upper inner quadrant (9.4%) then the central portion (4.5%). Also, the study done by Rummel et al (2015), stated that Tumor location in the UOQ (51.5%) was significantly higher than in the UIQ (15.6%) followed by central (10.6%)21,22. This study revealed that most of patients 398 (50.4%) had tumor stage T1, and 351 (44.4%) of them had T2, only 41 (5.2%) had TX, Also Ipsilateral axillary lymph node affection was present in 541 (68.5%) of patients, and was negative in 249 (31.5%) of them, these results compatible with the study done by Eisemann, Waldmann and Katalinic, (2013), in which 40% were in stage T1 and 30% T2 and 70.4% of the patients had lymph node metastasis at the time of diagnosis and 29.6% were negative. However, Maffuz-Aziz et al (2017), showed that, 16.3% T1, 38.2% T2 and 3.8% TX, lymph node stage at the time of diagnosis was 46.2% at N0, N1 in 33%21,23. The majority of tumors in our study was invasive duct carcinoma (IDC) 748 (94.7%), other pathological types as medullary carcinoma 10 (1.3%) and mucinous carcinoma 11 (1.4%), these results matched with Maffuz-Aziz et al (2017), who showed that 78% of all the cases were invasive ductal carcinoma, medullary carcinoma (0.4%) and mucinous carcinoma (3.3%), and Denewer et al (2013) in his study over 35 patients reported 29 cases of IDC, 4 cases of medullary carcinoma and 2 cases of mucinous carcinoma23,24. In contrary Rambau et al., (2011), reported that all patients, 91.5% (300) had invasive ductal carcinoma, 3% (10) had Invasive lobular carcinoma and 5.2% (17) had mucinous carcinoma. Also, Singh, (2012) demonstrated that invasive ductal carcinoma that accounts for about 80% of breast carcinomas. Invasive lobular carcinoma accounts for about 10% of breast carcinoma while the other types as the medullary, mucinous and tubular types account for the remaining 10% these variations possibly related to difference in sample size25,26. Modified radical mastectomy was done for all males 9 (100%) and for 524 (67.1%) females, but conservative breast surgery was done for 252 (32.9) females as shown in our study, and these values appear to be highly compatible with the results of the following studies: Yu et al., (2007), which the modified radical mastectomy (MRM) was 55.7% and breast-conserving surgery (BCS) was 6.3% of patients, and Raina et al., (2005) in which 11.3% patients opted for breast-conserving surgery (BCS) while the remaining 88.7% underwent modified radical mastectomy (MRM)27,28. Our results were in contrast with the study done by Veronesi et al.,

(2002), in which 349 underwent a radical mastectomy and 352 underwent breast-conserving surgery, and Onitilo et al., (2014), in which 62.6% underwent BCS and 37.4% underwent mastectomy[29,30].

Conclusion

The epidemiology of breast cancer has changed markedly in the past years; the number of afflicted women has increased further. Breast cancer is the most common cancer diagnosis made for women. There are significant changes in reproductive and hormonal pattern in Egyptian females diagnosed with breast cancer over the period of our study. It was noticed that parity is not absolute protector of breast cancer; neither marriage nor more children protect females from having breast cancer or decrease its risk. These trends should be taken into account when planning for any future national breast cancer screening or prevention plans. Awareness campaigns and screening should be applied according to resources. Awareness campaigns should also be directed at husbands to encourage women to enroll in early detection programs. Medical research, including cancer research, deserves to be given priority in the Arab world. Research into etiology, local characteristics and new therapies should be further developed. The medical community in the Arab World is urged to publish its findings in peer-reviewed scientific journals.

Declaration of interest: None.

Ethical approval: The study was approved by Institutional Research Board (IRB), Mansoura University.

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