

Epidemiology of Breast Cancer in Young Lebanese Women Under the age of 40 Years: Retrospective Study in Lebanon between the Years 2011 and 2017

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Abstract

Background: Breast cancer is the most common non-skin malignancy affecting females in the world. In Lebanon, breast cancer rates are gradually increasing and young females are being more frequently affected. Few studies are available concerning this particular population.

Objectives: This study aims to estimate the epidemiology of breast cancer in the young Lebanese females below the age of 40 with identification of variable characteristics and risk factors of the disease and ultimately, comparing our findings to other Arab countries.

Methods: Breast cancer cases diagnosed at ≤ 40 years of age between 2011 and 2017 were collected from patient's files in the Lebanese Hospital Geitaoui and Mount Lebanon Hospital, including the variable risk factors and tumors characteristics. The statistical data analysis was performed using SPSS statistics software.

Results: 862 females were diagnosed with breast cancer in the aforementioned hospitals and forty-four were ≤ 40 years. The prevalence of breast cancer in the young Lebanese females is found to be 5.1%. Majority of cases (81.8%) were initially detected by breast self-examination. 20.5% had a positive family history. Infiltrative ductal carcinoma is the predominant histological subtype and grade 2 the most common histological grade. Estrogen and progesterone receptors are positive in 26 subjects and HER2/Neu receptors positive in 17 subjects. Most of cases were in stage 2A. Only 2 patients had BRCA gene testing done.

Conclusion: The early onset breast cancer is not only related to the presence of a positive family history; other factors should be actively investigated. Breast self-examination should be considered as a screening method of breast cancer in young females at high risk.

Keywords: Breast Cancer, Young, Lebanese, Females, Epidemiology

Introduction

Breast cancer is the leading type of malignancy in females second to lung and bronchus cancer, with estimated 268,600 new cases in the United States of America (USA) in 2019 [1].

Worldwide, breast cancer is the most common neoplasm among young females below the age of 40 with an estimated prevalence of 22.3% [2]. It is a leading cause of cancer death in young females below 40-years of age, only second to leukemia, with the age

standardized mortality rate ASMR of 1.5 (per 100,000) [2].

It is usually assumed that early onset of breast cancer is closely related to a positive family history or to mutations in *BRCA* genes. However, the prevalence of deleterious mutations of *BRCA* genes detected in young Lebanese female patients is 5.6% (3), this rate is lower than expected when compared to developed countries, making *BRCA* mutation itself an unsatisfactory explanation of the development of this tumor process among this population [3].

The conviction amongst regional doctors treating breast cancer is that it is diagnosed at a younger age and tends to present with a more

aggressive behavior compared to cancers diagnosed in developed countries. Investigators noticed a major lack in data gathering in Arab countries, along with missing cancer records and unavailability of public registries to fulfill research requirements [4].

Methods

Data selection

The data was collected from the archive of data base in Geitawi University Medical Center and Mount-Lebanon Hospital in Beirut. The study included patients diagnosed with breast cancer between the years 2011 and 2017.

Inclusion and exclusion criteria

A total of 862 females were diagnosed with breast cancer of all age groups in both centers

Between the year 2011 and 2017, 44 patients met the inclusion criteria and were included in the study.

Inclusion criteria were as follows:

- Female patients
- The age of diagnosis: 40-years of age or younger
- Lebanese nationality

Exclusion criteria were as follows:

- Male patients
- Age above 40 years at the time of diagnosis
- Non-Lebanese nationalities
- Benign breast lesions

Results

Out of 862 females diagnosed with breast cancer, 44 were diagnosed at the age of 40 or younger. The prevalence rate of breast cancer in young Lebanese women was 5.1%. The mean age at diagnosis was 35.3 years with the youngest female being 19 years old and the eldest 40 years. Thirty-six patients (81.8%) acknowledged the presence of a breast mass by self-detection (self-breast exam), while seven patients (18.1%) detected the presence of metastatic lesions by imaging methods which lead to the diagnosis of the primary breast cancer; two patients (4.5%) specifically had pathological bone fractures as their initial presentation. Right sided breast tumors were slightly more common than left sided ones with 54.5% of females having their cancer localized to the right, compared to 43.2% on the left side. To note that, one patient had bilateral breast lesions at the time of diagnosis. Twelve patients (27.3%) had metastasis at the time of diagnosis with bone metastasis being the most common site (Figure 1).

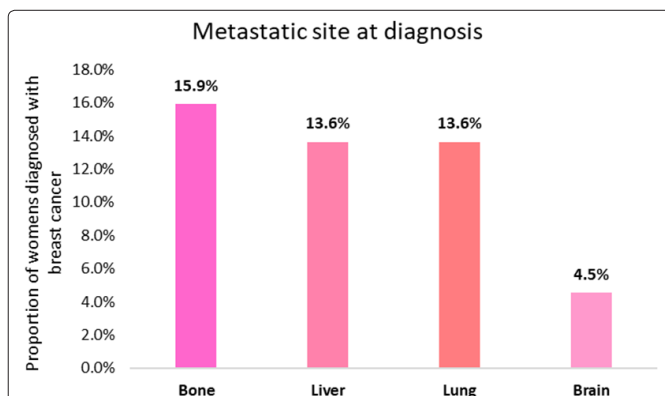


Figure 1: Percentages of metastatic sites at diagnosis

Twenty-seven patients (61.4%) were multiparous, while seventeen patients (38.6%) were nulliparous. Only fifteen patients (34.1%) breastfed their infants for more than 6 months and the majority of patients were smokers (65.9%). The presence of a positive family history for breast and ovarian cancer is a very important risk factor while assessing young females with breast cancer. In this regard, nine patients (20.5%) had a family history of breast cancer in a first degree relative, among which 80% had a mother with breast cancer and 20% had a sister with breast cancer. In addition, four patients (9.1%) had a family history of ovarian cancer, among which three patients had a mother with ovarian cancer and one patient had a sister with ovarian cancer. It is noticeable that only 2 patients had *BRCA* mutation test performed, both of which were negative. The predominant histological subtype of breast cancer cases in our study population was the infiltrative ductal carcinoma, accounting for thirty patients (69.8%). Whereas, the distribution of the other histological subtypes included 11.6 % equally for both ductal carcinoma in situ and infiltrative lobular carcinoma and 7% were lobular carcinoma in situ (Table 1). With regards to the histological grade, eleven patients (25%) had grade I cancer, while twenty-one patients (47.7%) had grade II making it the most common histological grade, and the remaining twelve patients (27.3%) had grade III cancer (Table 2).

Table 1: Histology subtypes

		Total (N=44)
Histological Subtype	DCIS	5 (11.6%)
	IDC	30 (69.8%)
	ILC	5 (11.6%)
	LCIS	3 (7.0%)
	Missing	1

N: total number of patients.

DCIS: Ductal Carcinoma In Situ

IDC: Infiltrative Ductal Carcinoma

ILC: Infiltrative Lobular Carcinoma

LCIS: Lobular Carcinoma In Situ

Table2: Histology grades

		Total (N=44)
Histology grade	G1	11 (25.0%)
	G2	21 (47.7%)
	G3	12 (27.3%)

N: total number of patients.

G: Grade

Concerning the hormone status of the breast tumors, a statistically significant finding was noticed between ER and PR receptors positivity and lower mortality ($p < 0.001$). Our study shows that twenty-six patients (60.5%) have both progesterone and estrogen receptors positive, while sixteen patients (37,2%) have double negative status (Table 3).

Table 3: ER and PR receptor status

		PR test result		Total
		Negative	Positive	
ER test result	Negative	16 (37.2%)	0 (0.0%)	16 (37.2%)
	Positive	1 (2.3%)	26 (60.5%)	27(62.8%)
	Total	17 (39.5%)	26 (60.5%)	43 (100.0)

ER: Estrogen Receptor
PR: Progesterone Receptor

Furthermore, *HER2/Neu* receptors are predominately negative (60.5%) and 39.5% are positive, in addition to one missing documentation (Figure 2).

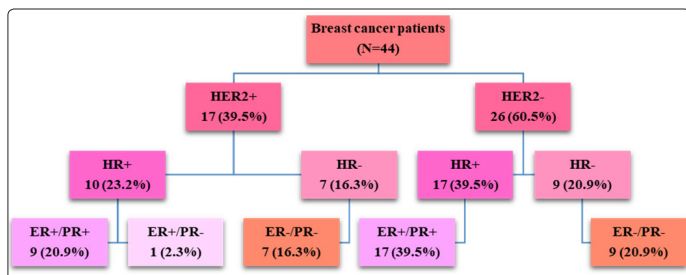


Figure 2: Distribution of breast cancer cases according to HER2/HR status

N: Total number of patients

ER: Estrogen Receptor

PR: Progesterone Receptor

HR: Hormone Receptor

HER2: Human Epidermal Growth Factor Receptor 2

The staging system is based on the size of the primary tumor, degree of spread to lymph nodes and the presence of systemic metastasis. The breast cancer staging in our study was based on TNM classification. The majority of young Lebanese females in this study had stage IIA (31.8%) with T1N1M0 being more common than T2N0M0. Of note, the second most relevant category was stage IV with 27.3%. Unfortunately, 11 patients died by the time of our data collection, with a resultant 25% mortality rate.

Discussion

Our study reveals that the prevalence of breast cancer in Lebanese females younger than the age of 40 is 5.1%. A study conducted at the American University of Beirut Medical Center (AUBMC), including 1320 patients of all ages diagnosed with breast cancer showed that: 107 subjects (8.1%) were less than 35 years of age, 526 subjects (39.9%) were between 35 and 49 and 687 subjects (52%) were aged 50 years and above [5]. The prevalence of the disease according to the latter study in young female patients was 8.1% and this is slightly higher than the rate detected by our study, knowing that the AUBMC study did not exclude non Lebanese females. Our study shows that the prevalence of breast cancer in our targeted population is 5.1% and this number is not as high as that reported for breast cancer in Lebanon, this is explained by the fact that the incidence and prevalence of breast cancer remains highest among females in the age group ranging between 45 and 55 years [6]. This coincides with a study done by Nagi El-Saghir et al. and other studies which show that fifty percent of Lebanese females diagnosed with breast malignancy are below the age of 50 with a

median age 49 years, while the median age in the developed countries is 63 years [6-9]. The prevalence rate found in our study seems to be lower than other Arabic nations. A study conducted by the Statistics and Research Center under the Ministry of Health in the UAE during the year 2014 showed that among the overall studied population: 165 patients (21.5%) were female patients and their age ranged between thirty and forty years [10]. In a retrospective study conducted in Egypt between the years 2005 and 2015 in the Oncology Center – Mansoura University, O. Farouk et al. demonstrated that three hundred and seventy-nine patients (8.19%) were aged ≤ 35 years at the time of presentation, the age ranged between 21 and 35 years and the mean age was 31 years [11]. Another significant difference is seen in Morocco, where the prevalence of breast cancer in women younger than 40 years is markedly disparate (24.8%) as shown in a retro-prospective study conducted between the years 2010 and 2015 including 331 infiltrating breast cancer cases [12]. However, Saudi Arabia is found to have concordant results with 4.1% of females younger than the age of 30 years being diagnosed with breast cancer in a 5-year retrospective study [13]. The lower prevalence rate seen in our country can be possibly explained by a higher death rate seen in Lebanon when compared to other Arabic countries such as Egypt and UAE. For instance, a study conducted by MJ. Hashim et al. in 2016 shows that Lebanon has the highest breast cancer death rate between all Arabic countries reaching a death rate of 21 per 100,000, whereas the death rate in Egypt is 7 per 100,000 and in the UAE, it reaches 10 per 100,000 [14]. Younger age can be possibly considered a poor prognostic factor, since the mortality rate tends to be higher in females younger than 40 years than in the general population and the stage at which females present is usually a bit more advanced. However, this subject remains debatable and not all studies report age being a negative prognostic factor [10,15]. Nulliparity is a known risk factor for breast cancer development [16]. However, in our study: Twenty-seven patients (61.4%) were multiparous, while seventeen patients (38.6%) were nulliparous; findings comparable to those disclosed by O. Farouk et al. declaring that 14.3% of women having breast malignancy below the age of 35 were single [11]. In fact, the social norms in our society still encourage marriage and multiparity and this might explain the higher proportion of breast cancer among multiparous females in our study. Concerning breastfeeding, a study suggests that the risk of breast cancer decreases by 4.9% with every 12-month of breast feeding [17]. Our study showed that a significant number of females did not breastfeed more than 6 months and only fifteen patients (34.1%) breastfed their infants for more than 6 months. This supports the possibility of increased breast cancer frequency in relation with uncommon breastfeeding practices. In the last few decades, Lebanese females are being more enrolled in the work environment, which limits their time and capability of breastfeeding. Regarding smoking habits, we found that the majority of our patients were smokers (65.9%). This high number can be explained by the

fact that social habits have been rapidly changing over time and that hubble bubble smoking is becoming a trend and socially accepted attitude among young Arab females who were limited by the concealed habit of cigarette. Many of the aforementioned factors can be explained by the likelihood of adapting a more industrialized lifestyle similar to that in the western world. Mutations in the *BRCA1* and *BRCA2* genes are of a great concern in the early onset breast cancer. Unfortunately, we had a major lack in this field in our study. In fact, only two patients had the *BRCA* mutation test performed and came out with negative results. The lack of *BRCA* mutation testing in our studied population might be explained by the absence of adequate awareness of the general population concerning the importance of this test. In addition to the high-cost of the test and the insufficient financial coverage by the ministry of public health, social security and healthcare insurance companies. Our study taught us that, nine patients (20.5%) had a family history of breast cancer in a first degree relative and four patients (9.1%) had a family history of ovarian cancer. One study done among Lebanese subjects showed that: 238 patients (18.3%) with breast cancer, among all age groups, had a family history of breast cancer [5]. None, ever mentioned a precise number of patients with a family history of ovarian cancer. When it comes to other Arabic countries, a hospital-based study conducted in Egypt including 150 patients with breast cancer found that 19% had a familial breast cancer and among those three quarters had a first degree relative with breast cancer [18]. J. Bekkach et al. revealed in a 5-year retrospective study in Morocco including 331 subjects with infiltrating breast cancer that 26% of all patients (young and old) had a family history of either breast cancer in a first or second degree relative or ovarian cancer [12]. The presence of breast cancer in the young age group was not always accompanied by the presence of a family history of breast cancer. This raises the question of the possibility of having other unknown factors that play a role in the occurrence of breast cancer in this age group. An important consideration in Lebanon is the frequent war experiences (the Lebanese civil war in 1975-1990, 1993, 1996 and the 2006 war) and subsequent exposure to unknown chemicals and stressful events. Several other Arabic countries also experienced wars over years (Iraq, Syria, Yemen...) but no studies regarding the risk breast cancer development in relation to war has been done. Moreover, in Lebanon, the uprising reports concerning pollution may also be an additional causative etiology. In fact, the newest pollution reports show that the pollution index in Lebanon is 87.39, making it the fifth most polluted country in the world [19]. These rates have been progressively increasing in the last few years going from rank 13 in 2013 to rank 5 in 2019 (19). To note that both air pollution and water pollution indices are high (76.91 and 78.08, respectively) [19]. Although, the impact of pollution on the development of breast cancer remains debatable; certain studies affirm a completely negative association linking air pollution to breast cancer [20]. Notably, the psychological and emotional impact of breast cancer diagnosis seen among young patients is stronger and more detrimental when compared to the impact seen in older patients [21]. Upon the young population, the emotional and psychological distress stems from concerns about future pregnancies, childcare, personal career, body image, and sexuality.

Conclusion

In conclusion, the prevalence of breast cancer in our studied population among females younger than forty years of age was 5.1%. Further studies should be conducted in the genetic fields for the detection of other gene mutations that could be associated

with breast cancer. Additionally, profound research evaluating the environmental factors can also help in establishing a positive correlation of increasing risk of breast cancer especially among young females. The development of nation-wide social support groups is also mandatory and is very helpful in providing social and psychological support for patients. Lastly, breast cancer remains the most common cancer in females and a significant cause of mortality which has the capacity to greatly impact the lives of patients. Our study is a step forward to better understand this disease.

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