Earlier breast cancer diagnosis in Egyptian women with positive family history

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Abstract

Purpose: Epidemiological studies showed that 10% of breast cancers (BC) are associated with gene mutations. Family history (FH) is risk factor for developing BC; however, 80% of subjects with apparent familial association with BC based on analysis of pedigree have no specific gene mutation.

The aim of our study was to review the impact of presence of positive FH on age and stage at presentation with BC diagnosis.

Patients and Methods: Using data recorded from the Cairo Oncology Center database, we retrospectively identified women diagnosed with BC between Jan 1999 & Dec 2008. Variables recorded included: patients, tumor characteristics and FH for BC.

Disease free survival (DFS) is calculated and compared according to the presence of positive FH. Multivariate analysis was used to determine independent variables affecting DFS.

Results: Between 1999 and 2008, 2103 women were identified in our database with 606 cases having positive FH.

Patients with FH were more likely to be <35 years with tumors <5cm and having ER+ve/Her2 –ve phenotype.

At median follow up period of 35 months, patients with FH had median DFS of 66.4 months compared to 63.3 months for patients without FH (p=0.927).

Using multivariate analysis, FH was not an independent factor affecting DFS; however variables associated with shorter DFS were advanced T stage, node positivity, and ER negativity.

Conclusion: Due to lack of national screening program in Egypt, presence of FH raises health awareness towards earlier stage at diagnosis. Although its presence had no prognostic effect on patient's DFS, yet it results in earlier presentation which in turn improves outcome.

Background

Although family history is a strong risk factor for breast cancer [1], yet its prognostic value has not been clearly established. Population-based studies addressing this issue showed conflicting results. [2-5]

Approximately 20% of breast cancers are associated with a clear family history of the disease [6]; Yet, about 80% of patients with familial breast cancer do not have detectable mutations in any known genes. Large epidemiological studies have shown that less than 10% of all breast carcinoma may be attributed to germline mutations in well studied breast cancer susceptibility genes. [7,8]

Non-BRCA1/BRCA2- associated familial breast cancer can nevertheless confer a high estimated risk of breast cancer. Women with first degree relative affected with breast cancer are at estimated two fold increased risk of breast cancer compared with those with no family history. Thus, family history is still an established important risk factor for developing breast cancer.[9]

As family history brings together genetic and environmental factors that may cause cancer, thus our analysis aimed to study the prognostic value of the presence of positive family history in a cohort of Egyptian breast cancer patients through studying different clincopathological features of patients & through subgrouping them according to presence or absence of positive family history.

Patients and Methods

Using data recorded from the Cairo Oncology Center database, we retrospectively identified women diagnosed with breast cancer between January 1999 and December 2008. Variables recorded included patients and tumor characteristics, TNM staging, family history for breast cancer and the site of first and subsequent metastases including locoregional recurrence.

The pathological tumor characteristics were documented using the current diagnostic guidelines and TNM staging system (7th edition). ER and PgR were considered positive if >10% of tumor cells showed expression in IHC. Her2 was considered positive if scored 3+ by IHC or positive by Fluorescence in situ hybridization (FISH) or Silver in situ hybridization (SISH) test in case of IHC score 2+.

Descriptive statistical analysis was carried out to assess the patients' demographics and clinical characteristics. Categorical data were compared using Pearson chi-square test. Disease free survival (DFS) was defined as the time between histological diagnosis of the primary breast lesion and diagnosis of local or distant recurrence. Last date of follow up was July 2011. DFS for the whole cohort was calculated using Kaplan Meier method and compared according

to presence of positive family history of breast cancer using the log-rank test. Multivariate analysis using Cox proportional hazards models was then used to determine independent variables affecting DFS. SPSS program (version 17.0) was used for all analyses, and a two sided p-value less than 0.05 was considered statistically significant.

Results

Between 1999 and 2008, 2387 women were identified in our database, with 606 cases (25.4%) having positive family history (+veFH). More than half of cases (326 cases) have the disease in their 1st degree relatives while the rest (260 cases) have history of breast cancer in their 2nd or 3rd degree relatives.

The median age of the whole cohort was 49 years (19 – 88 years) and it was similar in both groups +veFH and –veFH. Although patients younger than 35 years at presentation represented 6.6% among the former group compared to 10.1% among the latter; yet this difference was reversed in age group 36-40 years (14.6% versus 11.2%) resulting in similar percentage if we used age 40 as the cutoff (21.2% versus 21.3%). [Table 1]

Regarding TNM stage at presentation, 10.8% of +veFH patients presented advanced stage (T_3 or T_4), 55.3% with lymph node involvement and 5% with metastatic disease compared to 14.8%, 60.4% and 9.4% among the –veFH group respectively and this difference was statistically significant for T and M (p=0.034, 0.001) while N showed borderline significance (p=0.053).

The percentage of patients presenting with bilateral disease, high grade tumors or lobular histological subtype was similar among both groups. Regarding immunohistochemistry, there was also no difference between the groups regarding both Hormone receptors positivity and Her2 overexpression. Detailed patients' clinicopathological characteristics at diagnosis of breast cancer are summarized in Table 1.

At a median follow up period of 35 months, median disease free survival (DFS) for the whole cohort was 63.5 months. Patients with +veFH had median DFS of 66.4 months compared to 63.3 months for –veFH patients which was not statistically significant (p=0.927). [Figure 1]

Using univariate analysis for the data of the whole cohort, +veFH was not a factor affecting DFS; however the following variables were associated with shorter DFS: age less than 35 years, advanced T stage, lymph node involvement, ER negativity and Her2 overexpression. [Table 2]

Multivariate analysis confirmed independent effect of Tumor, nodal stage and ER status on DFS while age and Her2 expression did not show statistical significance. [Table 3]

Discussion

This study showed that tumours detected in Egyptian women with a family history of breast cancer were smaller, less likely to be node positive and less likely to be metastatic than those with no family history.

Although it was reported that women with +veFH of breast cancer not only have higher risk of developing this cancer, but their risk increases at a younger age.[10,11] This was not shown in our study where the median age was similar between both groups.

Comparing our study to the large Sweden population-based study which included more than 17000 cases with a median follow up period of 36 months, 13% of patients had 1st degree relative with breast and/or ovarian cancers [12] which is similar to our study (326/2387).

In our study, women with +veFH presented with relatively smaller tumours. This observation was also reported by Nomizu et al [2] and Cao et al.[11] A possible explanation may be that individuals with +veFH prefer to undergo regular screening of breasts and present with a small tumour size at initial diagnosis.

In the Sweden study, no information about the stage of breast cancer at diagnosis was indicated, yet the authors supposed that breast cancer arising in women with a genetic predisposition might have a different, presumably more aggressive, biologic behaviour than sporadic cancer with a nongenetic aetiology.[12] As we had the baseline clinicopathological characteristics of patients with family history in our database; those with +veFH did not show difference in hormonal or Her2 overexpression status denoting aggressive biological behavior, and these findings were also demonstrated in other studies.[11]

Our study confirms the results of other population based studies both European and American that the presence of +veFH is not a poor prognostic factor per se with no negative impact on Disease Free survival; [5,13-14] Yet it raises the awareness of the individual for rapidly seeking medical advice in case of accidental finding of a breast lump as well as self motivation for screening mammography in spite of the absence of a national screening program in countries like Egypt.

In conclusion, due to the lack of genetic counseling in Egypt, family history still represents an important risk factor because it raises public health awareness towards earlier diagnosis. As disease free and overall survival in patients with hereditary cancer does not differ significantly from survival in sporadic patients, this makes every effort done to detect breast cancer at an earlier stage worthwhile.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST The authors indicated no potential conflicts of interest.

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