Trends in Demographics and Reproductive Factors in Breast Cancer in Egypt: A Story of 25 Years

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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 lifestyle factors. Trends in these risk factors are important to demonstrate changes over time. Patients and methods: This is a cross-sectional study that included 200 breast cancer patients diagnosed during the year 2015 (group III) for the aim to compare their epidemiologic, reproductive and hormonal characteristics with two previous studies conducted in 1990 (group I) and 2005 (group II). Results: Over the past 25 years, the mean age of the patients at diagnosis became significantly older, p=0.009; (45.7, 46.1 and 49.1 years for group I, II and III respectively). The mean age at menarche became significantly younger over time (13.5, 12.5 and 12.6 years for group I, II and III respectively; p=0.003) and the percentage of patients who had their menarche under the age of 12 years was significantly higher in groups II and III compared to group I (P=0.001) while the age at menopause became significantly older (45.7, 48.5 and 48.2 years for group I, II and III respectively, p=0.006). The percentage of oral contraceptive pills intake significantly increased; it was 46.5%, 51.6% and 48.2% for group I, II and III respectively, p=0.005. Consequently, age at first full term pregnancy was significantly increased also while breast feeding tends to increase significantly over time. The percentage of oral contraceptive pills intake significantly increased; it was 46.5%, 51.6% and 61% in group I, II and III respectively, p=0.013. The percentage of working women significantly increased over time. Conclusion: There are significant changes in reproductive and hormonal pattern in Egyptian females diagnosed with breast cancer over the past 25 years. These trends should be taken into account when planning for any future national breast cancer screening or prevention plans.
II. Patients and Methods

This is a cross-sectional study that included 200 females with breast cancer diagnosed during the year 2015. Patients were asked to respond to a predesigned questionnaire including questions on demographic features, previous primary non-malignant breast diseases, family history, hormonal and reproductive history. The collected data in the study (Group III) were compared with data from previous 2 studies. The first one was conducted in 1990 and included 150 patients (Group I) while the second was in 2005 and included 126 patients (Group II). The study was approved from the ethical committee institutional review board (IRB) at National Cancer Institute.

III. Statistical methods

Data were analysed using SPSS version 22win statistical package. Numerical data were expressed as mean and standard deviation (SD), median and range as appropriate. Qualitative data were expressed as frequency and percentage. Chi-square test or Fisher's exact test were used to examine the relation between qualitative variables. Chi-square test for trend was used to examine trend between three study groups (1990, 2005 and 2015). Z test was used for pairwise comparison with Bonforoni adjusted p value. Analysis of variance (ANOVA) calculator for summary data between the three study groups were done by online calculator (www.danielsoper.com). Another calculator for comparing means was used to detect the significant group (www.medcalc.org). A p value ≤0.05 was considered significant and all tests were 2 tailed.

IV. Results

By comparing epidemiologic features among the three study groups, we found a significant increase in the age of the patients between studies through this time period (45.7, 46.1 and 49.1 years for group I, II and III respectively; p=0.004), (Figure 1). There was significant difference between group I and III as well as between groups II and III (P=0.009 and p=0.041 respectively) but no significant difference between group I and II (table 1).
The percentage of housewife women became significantly lower in group III in comparison to groups I and II (90%, 87.3 and 64% for groups I, II and III respectively; p = 0.003). The percentage of patients with a history of 1ry non-malignant breast disease was significantly decreased (28%, 12.7% and 15% for groups I, II and III respectively; p=0.005) while the presence of family history was significantly increased through these 3 studies (6%, 17.5% and 22% for group I, II and III respectively; P=0.001), (Figure 2). There were no significant trends regarding changes in the residence distribution between urban and rural nor incidence of marital status (p=0.345 and p=0.482 respectively) (table 1).

Patients in group III had irregular menstrual cycles (15.5%), which is significantly more common than those in group I (4.7%), P value < 0.001 but not different with group II, p=0.09, (Figure 3). Age at menarche showed a significant decrease over the last 25 years, the mean age at menarche of group I was significantly older than group II and III (13.5, 12.5 and 12.6 years respectively); p< 0.001, while no significant change between group II and III, p=0.473. The percentage of patients whose age at menarche was under the age of 12 years was significantly higher in groups II and III in comparison to group I; (P= 0.001), (table 2).

But age at marriage in females showed a trend to increase over that time period. The percentage of patients got married after the age of 25 years was significantly increased through time; it was 8.2%, 18.9% and
19.8% for group I, II and III respectively, p=0.005. Consequently, age at first full term pregnancy was significantly increased also. About two third of patients (66%) got their first full term baby after age of 20 years in 2015 compared to only half and one third in 2005 and 1990 respectively, p < 0.001. The same was observed regarding the mean age at menopause, which showed significant increase over time. It was 45.7, 48.5 and 48.2 years in the years 1990, 2005 and 2015 respectively; P= 0.006 (table 2).

Table (1): Epidemiologic features of three breast cancer groups diagnosed at 1990, 2005 and 2015.

<table>
<thead>
<tr>
<th>Epidemiologic features of breast cancer</th>
<th>Groups</th>
<th>1990 (N= 150)</th>
<th>2005 (N= 126)</th>
<th>2015 (N= 200)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td>No (%)</td>
<td>No (%)</td>
<td>No (%)</td>
<td></td>
</tr>
<tr>
<td>Mean ±SD</td>
<td></td>
<td>45.7 ± 9.9</td>
<td>46.1 ± 9.9</td>
<td>49.1 ± 11.1</td>
<td>0.004</td>
</tr>
<tr>
<td>Residence</td>
<td>Rural</td>
<td>74 (49.3)</td>
<td>33 (26.2)</td>
<td>105 (52.5)</td>
<td>0.345</td>
</tr>
<tr>
<td></td>
<td>Urban</td>
<td>76 (50.7)</td>
<td>93 (73.8)</td>
<td>95 (47.5)</td>
<td></td>
</tr>
<tr>
<td>Occupation</td>
<td>House wife</td>
<td>135 (90)</td>
<td>110 (87.3)</td>
<td>128 (64.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Un-married</td>
<td>34 (22.7)</td>
<td>14 (11.1)</td>
<td>38 (19.0)</td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td>Married</td>
<td>116 (77.3)</td>
<td>112 (88.9)</td>
<td>162 (81.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Un-married</td>
<td>34 (22.7)</td>
<td>14 (11.1)</td>
<td>38 (19.0)</td>
<td></td>
</tr>
<tr>
<td>History of 1ry non-malignant breast disease</td>
<td>Yes</td>
<td>42 (28.0)</td>
<td>16 (12.7)</td>
<td>31 (15.5)</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>9 (6.0)</td>
<td>22 (17.5)</td>
<td>44 (22.0)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

No significant change was noticed regarding parity while breast feeding tends to increase significantly over time. Women who didn’t breast fed their children became significantly lower in group II and III (5.4% and 10.1% respectively) than in group I (22%), p= 0.003. The percentage of oral contraceptive pills intake significantly increased over time. It was 46.5%, 51.6 and 61% in group I, IIandIII respectively; p=0.013 while no significant difference was noticed regarding the pattern or duration of oral contraceptive pills intake (table 2).

Table (2): Reproductive and hormonal pattern of three breast cancer groups diagnosed at 1990, 2005 and 2015

<table>
<thead>
<tr>
<th>Fertility and hormonal factors</th>
<th>Group</th>
<th>1990</th>
<th>2005</th>
<th>2015</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at Menarche</td>
<td>≤12 years</td>
<td>39</td>
<td>77</td>
<td>118</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Mean ±SD</td>
<td>13.5 ±1.3</td>
<td>12.5 ± 1.4</td>
<td>12.6 ± 1.1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Regularity of cycle</td>
<td>Irregular</td>
<td>7</td>
<td>10</td>
<td>11</td>
<td>0.001</td>
</tr>
<tr>
<td>Age at Marriage</td>
<td>≥ 25 years</td>
<td>12</td>
<td>23</td>
<td>38</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>47</td>
<td>82</td>
<td>124</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Parity</td>
<td>Nulliparity</td>
<td>31</td>
<td>6</td>
<td>19</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td>Abortion</td>
<td>79</td>
<td>47</td>
<td>100</td>
<td>0.861</td>
</tr>
<tr>
<td>Breast feeding</td>
<td>No</td>
<td>31</td>
<td>5</td>
<td>6</td>
<td>0.067</td>
</tr>
<tr>
<td></td>
<td>OCP</td>
<td>68</td>
<td>63</td>
<td>118</td>
<td>0.013</td>
</tr>
<tr>
<td>Pattern</td>
<td>Continuous</td>
<td>46</td>
<td>49</td>
<td>67</td>
<td>0.450</td>
</tr>
<tr>
<td>Duration</td>
<td>&gt; 4 years</td>
<td>34</td>
<td>15</td>
<td>14</td>
<td>0.086</td>
</tr>
<tr>
<td>Age at Menopause</td>
<td>&lt; 20 years</td>
<td>34</td>
<td>15</td>
<td>14</td>
<td>0.006</td>
</tr>
</tbody>
</table>
V. Discussion

Objectives of this study were to find trend in epidemiologic features within three-time periods that involve two and half decades. In the current study, we showed that the mean age at presentation in women with breast cancer who were diagnosed and treated at NCI became progressively older along the past 25 years. This trend may reflect both population growth and/or demographic change mainly due to aging of population. It is expected that population growth alone would increase the number of incident cases by 55.2% in 2015 and to 67.2% in 2050 (6).

A study in Lebanon showed a steeper increase in breast cancer incidence which was found between 2004 and 2010 and largely confined to women above age of 40 years. It was explained that this increase is corresponding to the target population of the national awareness campaign. They also found that Age-Standardized Incidence Rates was elevated which may be attributed to an improved awareness of breast cancer early signs, since the initiation of the annual national breast cancer awareness campaigns in 2002 (7).

The percentage of working women increased significantly over time. This increase may reflect changes in educational and socioeconomic characteristics. This is in contrast to a study conducted in US to examine trends in breast cancer by race, healthcare coverage, and socio-economic status (SES) before the Great Recession (2003–2005), during the recession (2007–2009), and post-recession period (2010–2012). It reported that percentage of employed breast cancer patients, before recession was 85.9%, during the recession was 85.4% and after the recession was 83.9% (8). Despite this increase noticed in Egyptian females, the percentage of working women still far lower than the American women mainly due to differences in the structure and beliefs of the families from both countries. Although marital status didn’t show significant trend for change over the three study periods, though percentage of unmarried in group I (including widows and divorced) was unexceptionally high which may be attributed to educational and socioeconomic factors.

History of primary non-malignant breast disease was significantly higher in group I as compared to group II and group III, this could be explained by more rapidly growing tumour in the latter groups. By comparing our figures to that in the US, comparable estimates were found specifically to the recent two study periods. Two large databases in US have found that history of benign breast biopsy was reported by 17.1% of Breast Cancer Surveillance Consortium (BCSC) and by 23.5% of Collaborative Breast Cancer Study cases (CBCS) (9).

Family history of breast cancer is widely recognized as an important risk factor for breast cancer. About 13-19% of women diagnosed with breast cancer have an affected first-degree relative compared to 8-12% of women without breast cancer (10). We found that family history of breast cancer in 2015 at National Cancer Institute was 22% which was similar to that reported by Collaborative Breast Cancer Study which was 21% (9). The current study showed a trend of increased proportion of breast cancer patients with positive family history over last 25 years. This came in agreement with a previous study describing secular changes in the proportion of women with a self-reported first-degree family history of breast cancer over the past three decades. The study reported increased prevalence of first degree family history over time from 12.3% in 1996 to 16.0% in 2010 (9). Increased prevalence of patients with positive family history in our study as well as other studies could be explained by increased mammography screening rates. Increased uptake of screening mammography has resulted in an increase in breast cancer incidence especially in early stage disease. Consequently, more women now report a family history of breast cancer (11).

Breast cancer risk factors that are more prevalent in developed countries than developing ones include having children (if any) at an older age, inappropriate breastfeeding, use of oral contraceptives and postmenopausal hormone-replacement therapy, obesity with high body mass index, poor physical activity and excessive alcohol consumption (12). In the present study, it showed significant trend in decrease age at menarche by an average of 0.9 years from 13.5 years in group I to 12.6 years in group III similar to results from a study that found mean age at menarche in the US to decline from 13.3 years to 12.4 years, with a significant decline in the age of menarche by an average of 0.9 year (13). Again the same trend was noted in Korean (14) and a Chinese (15) study that found a drop of 1.1 years in the mean age at menarche over a 30-year period and such a drop would be associated with a 5% increase in breast cancer incidence rates.

In a study to examine trends in US women born from 1912 to 1969. They observed an increase in the average age at menopause from 49.1 years in 1915–1919 birth cohort to 50.5 years in the other birth cohort (15). Menarche and menopause mark the onset and cessation of ovarian activity associated with reproduction and affect breast cancer risk. Data from 117 epidemiological studies, including women with invasive breast cancer concluded that breast cancer risk increased for every year younger at menarche and for every year older at menopause. The younger women were at menarche, the greater was their subsequent risk of breast cancer, the relative risk (RR) increasing by a factor of 1.050 (95% CI 1.044–1.057, p<0.0001) and the older age at menopause the greater the risk, the RR increasing by a factor of 1.029 (95% CI 1.025–1.033) (16).

The higher breast cancer risk in women with a late menopause is most likely explained by both the longer duration and higher level of exposure to estrogen and progesterone experienced by these women. They
also may experience a larger number of anovulatory cycles resultin in a lack of cyclic progesterone(17). There are many speculated causes of delays in age at menopause, but no one hypothesis has gained widespread support. Potential delays in age at menopause may be associated with genetic, social, environmental, and/or hormonal exposure associations. As breast cancer is a multifactorial disease, its risk is associated with an increased tendency to postpone the first childbirth, combined with a low parity and short duration of breastfeeding (5). The present study showed that age at marriage of patients in 2015 was significantly older when compared to the previous two studies and eventually age at first full term pregnancy became significantly older, where both represent important determinants for risk of breast cancer.

In the National health survey of India, two different population studied at 1998-1999 and 2005-2006 and reported that age at first full term pregnancy showed an evidence of increase overtime (18). Other studies done in Brazil for two groups of patients in 1996 and 2006 also documented an increase in age at first full term pregnancy (4). Similarly, in Nigeria the median age at first full term pregnancy increased from 18.5 to 20.3 year over a period of twenty years (19). We can claim that family planning programs in Egypt could add to the risk of breast cancer. In a study done by Jansen, Herrán, and Villamor 2015, an increase in breast cancer incidence was found to be between 8% and 20% due to a range of reduction in parity from 1 to 2.5 births. Another finding by the same author was that breastfeeding a child for 1 year provides a 4.3% reduction in breast cancer risk for the mother, independent of the protective effect of the pregnancy itself.

The present study also found that breast feeding, in the two recent groups was significantly lower than older group. In Kazakhstan during the middle of the 20th century, it was reported that breast cancer in Slavic women is three times more frequent than Kazakh women which remained the same over timemostly due to preservation of their reproductive function. Kazakh women marry at younger age, they usually have more pregnancies and fewer abortions, often practice breastfeeding and their lactation period is longer (21). Moreover, many studies recommend prolonged breastfeeding as a protective behaviour against breast cancer, though the optimal interval is not identified (5, 22). Breastfeeding is considered as one of the most important protective factors against breast cancer, claiming that it would seem simple and trivial procedure and an important aspect in prevention of breast cancer (7).

Results of the current study showed that usage of oral contraceptive pills increased significantly over the past 25 years (45.3%, 50% and 59.0%). Although different contraceptive methods are easily accessible at low prices and without a prescription, contraceptive use rate varies in different regions. In the present study, the rate of OCP use was 59% in 2015 which was similar to that found in Lebanon (58%) (7). These numbers were relatively low when compared to another EMRO country (73.8% in Iran) and Western countries; France: 81.8% and US: 72.8%. Collaborative reanalysis of data on 53, 297 women with breast cancer and 100, 239 women without breast cancer from 54 epidemiological studies found that the relative risk of breast cancer in women using birth control pills was 10 to 30 percent (or 1.1-1.3-fold) higher than that of women who had never used these control pills. Once women stopped taking the pill, however, their risk began to diminish and returned to normal within about 10 years (Collaborative Group on Hormonal Factors in Breast Cancer, 1996). In most of the studies in this analysis, the women were taking older, higher-dose versions of the pill, and so one area under active study is how today’s slower-dose pills might affect the risk of breast cancer. The evidence to date hasn’t been able to answer this question confidently (22).

Many lifestyle changes had occurred during modernization; thus, if the younger adult generation has a 1-year delay in menarche, two less births and average age at first full term birth 2 years older than the previous generation, these changes would combine to produce a 25% increase in breast cancer incidence (4).So, these trends should be taken into account during planning of any national prevention program as they may contribute to the increased incidence in breast cancer.

VI. Conclusion

There are significant changes in reproductive and hormonal pattern in Egyptian females diagnosed with breast cancer over the past 25 years. These trends should be taken into account when planning for any future national breast cancer screening or prevention plans.

References

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