Retrospective Study

Exploring the Association between Demographic Factors and Breast Cancer Diagnosis at a Holistic Breast Imaging Clinic in Cairo, Egypt

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ABSTRACT

Background
Breast cancer is among the most common cancers affecting women worldwide, including Egypt. Age is a well-known determinant of breast cancer risk; however, more data is needed to better understand the importance of age on incidence of breast cancer in the Middle East. Being overweight or obese are also known risk factors—especially for post-menopausal women—however, these data are not available for women in developing countries.

Purpose
The purpose of this study was to qualitatively explore the association between age, breast density, and demographic factors of breast cancer patients, across a spectrum of radiological breast diagnoses at a large Breast Imaging Clinic in Cairo, Egypt.

Materials and Methods
We explored the association between age, demographic factors, and Breast cancer incidence among 6,711 women undergoing mammographic screening over a consecutive period of 6-years. Data was collected from March 2007 until March 2013 and extracted from an electronic data base system.

Results
A total of 6,711 participants were included in this study. The median age of all patients was 46.1. Mean body mass index (BMI) of 28.5, where 34% of the patients were overweight and 32.4% were obese. Older women were more likely to be obese compared to younger women (38.4% vs 18.1%, p<0.001). Older females were more likely to have less dense breasts (ACR: A) compared to younger females (18.1% vs 8.7%, p<0.001). Women older than 40 had a higher confirmed number of breast cancer diagnoses compared with the younger age group (10.7% vs 3.5%, p<0.001). Women with breast cancer were more obese (p<0.001), had denser breasts (p<0.001), were post-menopausal (p=0.002), and more likely to be Muslim (p=0.0021). In the multivariate analysis, aforementioned factors were significant predictors for confirmed diagnosis.

Conclusion
To our knowledge this is the largest study to examine the association of radiological breast assessments on breast cancer incidence, obesity and demographic factors in Egypt. Although data shows the global burden of breast cancer is shifting to the developing world and affecting younger women at alarming rates, our data demonstrated a very low occurrence of breast cancer in both age groups.

Keywords
Breast cancer; Breast radiological diagnoses; Phenotypic variations; Breast imaging-reporting and data system (BI-RADS).
INTRODUCTION

Breast cancer (BC) is a disease with great association link to age, it has been well established that survival is improved significantly if detected and treated early. Delayed diagnosis and management lead to poor survival as a consequence, that creates important public health issue in the Middle East. In the Middle East and Arab population, late diagnosis has been attributed to the, illiteracy rate, lack of knowledge about BC, and to the poor resources to screening programs. Analysis of global burden of disease (GBD) 2016 data demonstrated the rising incidence of breast cancer disease in the Arab world. The breast cancer incidence in the Arab region (28/100,000) was lower than the global mean (46/100,000) in 2016. Arab countries with higher sociodemographic index tended to have a higher burden (39/100,000) of breast cancer. The rate of rise is comparable with the global trend and it is predicted to continue to rise if no interventions are implemented.

A great body of literature reviews has estimated that breast cancer accounts for 13-35% of all female cancers in Arab countries. With a clear trend toward earlier age of onset as well as presentation at advanced stages among Arab females, a recent rise of Age-Standardized Incidence Rates (ASR) is also noted. Advanced disease remains very common in Egypt, Tunisia, Saudi Arabia, Syria, Palestinians and others. A few studies have investigated individual demographics along with other factors in Breast Radiological Diagnoses in Arab countries. In this paper we conducted a retrospective study to explore the association between demographic and other factors along with radiological breast diagnoses.

MATERIALS AND METHODS

Study Population

With approval from the institutional review board, 6,711 (Table 1) women undergoing mammographic screening over a consecutive period of 6-years were studied at the Women and Fetal Imaging (WAFI) center in Cairo, Egypt. WAFI is a specialized center for mammography, fetal imaging (3D/4D fetal scan by ultrasound), dual-energy x-ray absorptiometry (DEXA) bone density scan, and Ultrasound. WAFI also provides complementary services, inclusive of medical education and research.

Data was collected from March 2007 until March 2013, having been extracted from an electronic database system. Ages of the participants ranged between 30 to 70-years of age, with a median of 46.1-years. Body mass index (BMI) was calculated for the participants. Clinical breast examinations were conducted, along with which sonographic and mammographic evaluation, including family history were determined. Breast imaging and reporting data system (BI-RADS) and pathologic biopsy results were taken when obtained, with clinical follow-up and clinical outcomes.

**Table 1. Patient Characteristics of All Patients**

| Characteristics | n (%) | Age (Years) |
|-----------------|-------|-------------|
|                  |       | <40 | ≥ 40 | Total |
| **BMI** |       |     |     |     |
| Normal       | 699   | (50.87) | 885 | (27.05) | 1584 | <0.0001 |
| Overweight   | 427   | (31.08) | 1132 | (34.60) |
| Obese        | 248   | (18.05) | 1255 | (38.36) |
| **Religion** |       |     |     |     |
| Muslim       | 1840  | (89.32) | 3851 | (81.74) | <0.0001 |
| Christian    | 220   | (10.68) | 860 | (18.26) |
| **BIRAD** |       |     |     |     |
| Negative/Normal | 846 | (41.07) | 1489 | (31.61) |
| Benign       | 839   | (40.73) | 1941 | (41.20) |
| Probably Benign | 309 | (15.00) | 771 | (16.37) |
| Probably Malignant | 29 | (1.41) | 177 | (3.76) |
| **Malignant** |       |     |     |     |
| 37 | (1.80) | 333 | (7.07) |
| **ACR** |       |     |     |     |
| ACR1 | 99 | (8.86) | 786 | (18.04) | <0.0001 |
| ACR2 | 567 | (50.72) | 2341 | (53.74) |
| ACR3 | 349 | (31.22) | 1016 | (23.32) |
| ACR4 | 103 | (9.21) | 213 | (4.89) |

**Family History**

| Breast CA | 593 | (28.79) | 1433 | (30.42) | 0.0434 |
| Other CA | 25 | (1.21) | 89 | (1.89) |
| NA | 1442 | (70.00) | 3189 | (67.69) |

**Menopausal**

| Pre | 1495 | (97.27) | 1369 | (42.42) | <0.0001 |
| Peri | 19 | (1.24) | 182 | (5.64) |
| Post | 23 | (1.5) | 1676 | (51.94) |

**Breast Feeding**

| Yes | 690 | (86.25) | 2007 | (83.80) | 0.0981 |
| No | 110 | (13.75) | 388 | (16.20) |

BMI: Body mass index; ACR: American college of radiology. Total may not add up to 6,711 due to missing values.

Imaging Technique and Interpretation

For the screening and diagnostic mammography and the ultrasound examination, practice guidelines of the American College of Radiology was followed. Women under 40-years of age were first screened with ultrasound. Mammography examinations were determined through presentation of clinical symptoms or through sonographic findings. While the clinical outcome may have indicated the type of screening, the physician had discretion to modify procedure for the patient as the radiologists (both of whom had 10 to 15-years of experience in breast imaging) were the ones to provide decision as to the need to further mammographic examination.
Irrelevant of age, mammographic and sonographic findings of all the patients were described using BI-RADS lexicon whereby the final BI-RADS category was reported at the end of each examination. The BI-RADS categories for the patient outcomes were as follows.8,9

BI-RADS category 1: Negative (essentially 0% likelihood of cancer)
BI-RADS category 2: Benign (essentially 0% likelihood of cancer)
BI-RADS category 3: Probably Benign (>0% but ≤2% likelihood of cancer), short term follow-up is recommended.
BI-RADS category 4: Suspicious for malignancy (>2% but <95% likelihood of cancer), tissue diagnosis is recommended.
BI-RADS category 5: Highly suggestive of malignancy (≥95% likelihood of cancer), tissue diagnosis is recommended.

In this study, BI-RADS categories 1-3 were considered negative, while categories 4-5 were considered positive for malignancy. In addition to assigning BI-RADS to the examinations, breast parenchymal density was determined using protocols of the American college of radiology (ACR),1 whereby (ACR: A) was categorized as almost entirely fatty (less than 25% fibroglandular tissue); (ACR: B) was categorized as scattered areas of fibroglandular densities (approximately 25% to 50% fibroglandular); (ACR C) was categorized as heterogeneously dense (approximately 51% to 75% fibroglandular); and ACR 4 was categorized as extremely dense (more than 75% fibroglandular).

### Standard Definitions

**Data collection:** The study received approval from the Mulago Hospital Research and Ethics Committee (Protocol No: MHREC 1545). Informed consent was obtained from all the participants prior to conducting the focus groups and interviews. The participants were also assured of the anonymity and confidentiality of their responses and no names were to be tagged to any response. Participants were also informed that they were free to withdraw from the study at any one time.

**Mammography:** Routine craniocaudal and oblique mediolateral views of both breasts were part of our examination protocol. Mammography exams were consistently performed using the in-clinic unit (Selenium, Hologic ™ 2D Digital Mammography, USA). Images were reviewed using Belgian American Radio Corporation (BARCO) SecurView® DX digital 5 megapixels workstation.

Mammograms in our breast imaging unit were viewed by the radiologist for immediate workup. No further recalls were required for any presented images. The BI-RADS assessments given after imaging review were used for both sonographic and mammographic examinations.8,9 No retrospective second interpretation was made. Final results of the mammograms were categorized as true positive, true negative, false positive, or false negative according to standard definitions in the fifth edition of the BI-RADS atlas.10

### Ultrasonography:

Women deemed qualified for breast ultrasound examinations were examined on both breasts, including regional lymphatic areas. This was performed by the same radiologist interpreting final diagnostics results, and the real-time dynamic equipment (GE: Voluson 730 pro, GE Healthcare, USA) was used for it has a high resolution phased-array transducer with a frequency that ranges from 7.0 to 12.0 MHz. Colour and Power Doppler were also available on the equipment.

### Statistical Analysis

The collected data was analyzed using SPSS® for Windows®, version 15.0 (SPSS, Inc., USA). Quantitative (numerical) variables were represented for mean, range and standard deviation; qualitative (categorical) data was represented by number of cases and percentage. Analysis of categorical data was performed via a chi-square test. Multivariable analyses were done using logistic regression. p-value less than 0.05 was considered statistically significant.

### RESULTS

A total of 4,791 participants were included in this study. The patient median age was 46.1. Approximately 31% (n=1,462) of the participants were less than 40-years-old. The participants had a mean (Standard Deviation) BMI of 28.2 (10.51). Thirty four % of the patients were overweight and 30.2% were obese. Majority of women (83.3%) had Muslim religion followed by 16.7% Christian. Patient characteristics are summarized according to their age categories in Table 1.

Older women had a higher obesity status compared to younger women (36.1% vs 16.6%, p<0.0001). Younger women had a higher Muslim religion compared to older women (89.5% vs 80.6%, p<0.0001). Older women had a higher malignant status (BI-RADS results in ‘malignant’, or ‘probably malignant’) compared to younger women (6.8%; 3.8% vs 1.7%; 1.0%, p<0.0001)

The ACR density differed by age group. Older female presented more ACR1 density than younger female (15.3% vs 8.6%, p<0.001). The family history of breast cancer was similar in both younger and older women (28.7% vs 29.3%). The breast feeding history was similar in both younger and older women (88.5% vs 88.4%). Additional patient characteristics are summarized according to their malignancy status in Table 2.

The older age group (older than 40-years) had a higher confirmed diagnosis of breast cancer status than the younger age group (10.0% vs 2.9%, p<0.001). Obese women had a higher confirmation status than the normal or overweight group (14.4%; 8.6%; 5.8%, p<0.001. Post-menopausal women had the highest malignant status, followed by pre-menopausal, and then peri-menopausal women (17.8%; 7.5%; 5.6%, p<0.001). Women with a family history for breast cancer had similar proportions of confirmation compared to the other cancer group (6.2% vs 4.8%). Muslim women had a higher malignant status than Christian women (8.6% vs 5.5%, p=0.0268). Women who breast fed had similar proportions of confirmation compared to the non-breast feeding
women (11.2% vs 9.4%, \( p=0.2027 \)).

| Characteristics          | n (%) | \( p \)-value |
|--------------------------|-------|---------------|
| Age                      |       |               |
| <40                      | 38    | 3.51          | < 0.0001 |
| \( \geq 40 \)            | 300   | 10.70         |          |
| BMI                      |       |               |
| Normal                   | 45    | 5.06          | < 0.0001 |
| Overweight               | 87    | 9.73          |          |
| Obese                    | 109   | 12.73         |          |
| Religion                 |       |               |
| Muslim                   | 300   | 9.33          | 0.0021   |
| Christian                | 38    | 5.65          |          |
| BIRAD                    |       |               |
| Negative/Normal/Probable/| 0     | 0             | <0.0001  |
| Possibly Malignant       | 81    | 59.56         |          |
| Malignant                | 250   | 90.58         |          |
| ACR                      |       |               |
| ACR1                     | 60    | 12.63         | 0.0227   |
| ACR2                     | 147   | 8.84          |          |
| ACR3                     | 79    | 9.61          |          |
| ACR4                     | 12    | 5.83          |          |
| Family History           |       |               |
| Breast CA                | 84    | 7.11          | 0.0543   |
| Other CA                 | 5     | 7.14          |          |
| NA                       | 249   | 9.45          |          |
| Menopausal               |       |               |
| Pre                      | 103   | 6.25          | <0.0001  |
| Peri                     | 11    | 8.03          |          |
| Post                     | 171   | 16.18         |          |
| Breast Feeding           |       |               |
| Yes                      | 159   | 11.55         | 0.0019   |
| No                       | 48    | 18.53         |          |

**DISCUSSION**

We found that older females were more likely to have less dense breasts (ACR A) compared to younger females, while women older than 40 had a higher confirmed number of breast cancer diagnoses compared with the younger age group. In addition, our results suggested that women with breast cancer were more obese and not having breast feeding history. Studies have suggested that Arab women present with breast cancer at younger ages.11 In contrast to these reports, in our study older women had higher confirmed cases of BC. Our study is limited by the quality of information reported from a large imaging center and a retrospective review although the study is based on the best available data. Statistical analysis is based on association not causation.

Our study is limited by the quality of information reported from a large imaging center and a retrospective review although the study is based on the best available data. Statistical analysis is based on association not causation.

Age-standardized cancer incidence varied substantially between EMR countries with infection-related cancers playing a more important role in low and low-middle income countries (e.g., stomach
cancer having the highest ASIR in Afghanistan, Iran, Yemen, and Sudan, and cancers related to low physical activity and cancers with strong lifestyle-related risk factors such as colorectal cancer being more common in middle- and high-income EMR countries such as Lebanon, the UAE, and Libya). Breast cancer is markedly affected by association between age, breast density, and other demographic factors of breast cancer patients, and with different radiological breast diagnoses categories.

Environmental factors might contribute to breast cancer incidence rate and prevalence. Studies show high BMI is linked with increased risk for breast cancer for women in post-menopausal stage.5

Taken together, our study conducted in this large cohort demonstrated that trends of BC in Egypt, including risk factors resemble that of women of European descent. This is akin to a study published by Salhia et al demonstrating that Egyptians appear to have a molecular subtype distribution like that of Western women, where Luminal A BC represents the largest fraction of cases.11 Still women of Egyptian and Arab descent have advanced disease at diagnosis and high mortality. Awareness, early detection, lifestyle and access to care are the key to combating BC in Egypt. Intervention at the public health level, including education on the benefits of early detection is necessary and would likely have tremendous impact on breast cancer outcome in Egypt. Obesity is a risk factor for BC, prevention strategies including engaging women in healthy eating and physical activity would also have an impact on BC epidemiology in the area.

**CONCLUSION**

BC epidemiology in the Arab region remains understudied compared with Western countries. Women in the Eastern Mediterranean Area (EMR) have higher cancer incidence rate but less cancer deaths in comparison to males, which might be attributed to less aggressive cancers (breast, cervical) being among the top cancers in females compared to lung and stomach cancer in males.12

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**DISCLOSURES**

Gewefel HS disclosed no relevant relationships. Michelen S disclosed no relevant relationships.

**CONFLICTS OF INTEREST**

The authors declare that they have no conflicts of interest.

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