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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.[1] 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.[2,3] Analysis of global burden of disease (GBD) 2016 data demonstrated the rising incidence of breast cancer disease in the Arab world.[4] The breast cancer incidence in the Arab region (28/100,000) was lower than the global mean (46/100,000) in 2016.[5] 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,[6] 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.[7] 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 age 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**
	2060	(30.42)	4711	(69.58)	6711
BMI					***p*-value**
Normal	699	(50.87)	885	(27.05)	<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					<0.0001
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 6,771 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.

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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 tirm 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 (Selenia, 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.[1,2] 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 (BIRAD 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 ACR[1] 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).

Table 2. *Confirmed Diagnosis and Patient Characteristics*

Characteristics n (%)	n	(%)	p-value
Age			
<40	38	3.51	< 0.0001
≥ 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			<0.0001
Negative/Normal/Benign/ Probably Benign	0	0	
Probably 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	

BMI: Body mass index; ACR: American college of radiology; CA: Cancer; NA: Not available

To test whether age was an independent risk factor of malignancy status, a multivariate analysis was performed using a logistic regression. In the multivariate analysis, being older (>=40-years), being obese, and being post-menopausal were significant predictors for confirmed diagnosis. A woman's religion was marginally significant (p=0.0899), Table 3.

The unadjusted odds ratio (OR) of confirmed status associated with older age women was 3.3. After the adjustment for clinical and other demographic factors, OR (95% confidence interval) of older women having confirmed diagnosis was 2.32 (1.19, 4.50) times more likely than younger women. BMI, menopausal status, breast feeding history did contribute to the improvement of the model. The obese group was 1.83 (1.10, 3.03) times more likely to present the confirmed status than the normal group. The post-menopausal group was 1.64 (1.07, 2.50) times more likely to present the confirmed status.

Table 3. *Multivariate Logistic Regression Analysis: Predictors of Malignant Diagnosis*

Variables	OR	95% CI	p-value
Age			
<40	1		0.0481
≥ 40	1.75	(1.01, 3.05)	
BMI			
Normal	1		0.0017
Overweight	1.72	(1.09, 2.70)	
Obese	2.23	(1.44, 3.45)	
Religion			0.0086
Muslim	1		
Christian	0.48	(0.28, 0.83)	
Menopausal			0.0023
Pre	1		
Peri	1.74	(0.83, 3.67)	
Post	1.93	(1.33, 2.81)	
Breast Feeding			0.0002
Yes	1		
No	2.12	(1.43, 3.14)	

BMI: Body mass index

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.[13] 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.

REFERENCES

1. O'Mahony M, Hegarty J. Factors influencing women in seeking help from a health care professional on self discovery of a breast symptom, in an Irish context. *J Clin Nurs*. 2009; 18(14): 2020-2029. doi: 10.1111/j.1365-2702.2008.02564.x

2. Altwalbeh D, Dahshan MEAE, Yaseen R Factors influencing delayed presentation of breast cancer among saudi women. *International Journal of Science and Research*. 2013; 4(1): 967-974.

3. Lodhi FB, Ahmad B, Shah SIH, et al. Determinants of delayed presentation in breast cancer. *APMC*. 2010; 4: 9-16.

4. Global Burden of Disease Collaborative Network. Global burden of disease study 2016 (GBD 2016) cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life years 1990-2016. Web site. http://ghdx.healthdata.org/record/ihme-data/gbd-2016-cancer-incidence-mortality-years-life-lost-years. Accessed July 6th, 2019. 2018.

5. Hashim MJ, Al-Shamsi FA, Al-Marzooqi NA, Al-Qasemi SS, Mokdad AH, Khan G. Burden of breast cancer in the arab world: Findings from global burden of disease, 2016. *J Epidemiol Glob Health*. 2018; 8(1-2): 54-58. doi: 10.2991/j.jegh.2018.09.003

6. Anderson BO, Ilbawi AM, El Saghir NS. Breast cancer in low and middle income countries (LMICs): A shifting tide in global health. *Breast J*. 2015; 21(1): 111-118. doi: 10.1111/tbj.12357

7. Sickles EA, D'Orsi CJ, Bassett LW. Breast imaging reporting and data system (BI-RADS): Mammography. 4 . Reston, VA, USA: American College of Radiology; 2003. Web site. https://radiopaedia.org/articles/breast-density?lang=gb. Accessed July 6th, 2019.

8. Mendelson EB, Baum JK, Berg WA, Merritt CRB, Rubin E. Breast imaging reporting and data system (BI-RADS): Ultrasound. 1. Reston, VA, USA: American College of Radiology; 2003. Web site. https://radiopaedia.org/articles/breast-echotexture-bi-rads-categories-1?lang=gb. Accessed July 6th, 2019.

9. Sickles EA, D'Orsi CJ, Bassett LW, et al. ACR BI-RADS mammography. In: *ACR BI-RADS Atlas, Breast Imaging Reporting and Data System*. Reston, VA, USA: American College of Radiology; 2013: 134-136.

10. GBD 2015 Eastern Mediterranean Region Cancer Collaborators. Burden of cancer in the Eastern Mediterranean Region, 2005-2015: Findings from the Global Burden of Disease 2015 Study. *Int J Public Health*. 2018; 63(Suppl 1): 151-164. doi: 10.1007/s00038-017-0999-9

11. El Saghir NS, Shamseddine AI, Geara F, et al. Age distribution of breast cancer in Lebanon: Increased percentages and age adjusted incidence rates of younger-aged groups at presentation. *J Med Liban*. 2002; 50: 3-9.

12. Najjar H, Easson A. Age at diagnosis of breast cancer in Arab nations. *Int J Surg*. 2010; 8: 448-452. doi: 10.1016/j.ijsu.2010.05.012

13. Salhia B, Tapia C, Ishak EA, et al. Molecular subtype analysis determines the association of advanced breast cancer in Egypt with favorable biology. *BMC Womens Health*. 2011; 11: 44. doi: 10.1186/1472-6874-11-44