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The Incidence of Breast Cancer in Egyptian Females in Correlation to Different Mammographic ACR Densities

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ABSTRACT
Introduction: Breast cancer is the leading cause of illness and cancer-related death in women worldwide. Breast cancer is a complex illness, and one of the risk factors for non-familial breast cancereis breast density. Aim: To assess and detect the relationship between different breasts mammographic densities and the risk for breast cancer among asymptomatic females. Methods: An analytic cross-sectional study was conducted and included 814 women outreached for screening by digital mammography by the Presidential Program for Women Health in the period from January 2020 to December 2021. Results: 52.1% of the females had type B density, while 24.1% were type C, 21.6% were type A, and 2.2% were type D. 10.3% of the recruited females were found to suffer from breast cancer. There was a statistically significant difference between the type of breast density among the females diagnosed with breast cancer Conclusion: Breast cancer density is significantly associated with breast cancer. Female patients with type D breast density had 3 times more risk of developing breast cancer and this risk decreases as the breast density decrease.

KEYWORDS: Breast Cancer, Mammographic, ACR Densities.

INTRODUCTION

With an estimated 2.4 million new cases and 523 000 deaths recorded in 2015, breast cancer is the most frequent kind of cancer globally and the main cause of cancer-related deaths among women [1].

This illness burden presents unexpected management and outcome issues in low-income and resource-constrained nations. Cancer diagnosis and management measures have resulted in high survival rates in developed nations, but lower rates have been recorded in poorer countries [2].

The term "breast density" refers to fibroglandular mammary tissue composed of fibroblasts, epithelial cells, and connective tissue [3].

Mammograms are commonly used to examine breast density. The fatty component looks radiolucent on mammography, while the fibroglandular tissue appears radiopaque [4].

The American College of Radiology's (ACR) breast imaging reporting and data systems (BI-RADS) are the most regularly used tools for measuring mammographic density (3).

The current updated fifth edition of the BI-RADS atlas defines the four mammographic density/composition as follows: The breasts are practically fatty in ACR-a; there are scattered patches of fibroglandular density in ACR-b; and the breasts are heterogeneously dense in ACR-c, which may disguise tiny masses. ACR-d, the breasts are highly dense, lowering mammography sensitivity (4).

Mammographic density and the risk of invasive tumours have a positive correlation across all ages, with the greatest level of dense tissue showing a two-fold increase in risk compared to the average level of dense tissue (3).

Early identification of cancer is critical for a better prognosis and survival. Furthermore, mammography is the gold standard for screening, diagnosis, and early detection of breast cancer. A routine screening mammography includes images of each breast in the mediolateral oblique (MLO) and craniocaudal (CC) planes (5).

METHODS

This analytic cross-sectional study included 814 women outreached for screening by digital mammography by the Presidental Program for Women Health in the period from January 2020 to December 2021. Their data was collected from the medical records of the program.

Participants who had contraindications to mammography, such as pregnant women were excluded. Also, patients under 40 years, where US is the modality of choice were excluded from participating in the study.

Data collection tools

All patients were submitted to the following:

- **History taking** (Including patient's name, age, marital status and number of offspring's, residence and phone number, diagnosis, duration of illness, past history and family history).
- **Imaging procedure** (All patients underwent Digital Mammography, complementary US & US guided biopsy in patient with positive findings).
- **Equipments**:

At presidential program for woman health , Mammographic &ultrasound unit).

Mammographic examination was performed using a device developed by GE Healthcare allowing dual-energy CEDM acquisitions (Senographe 2000 D full field digital mammography Essential GE Healthcare).

It used a current full-field digital mammography system using a flat panel detector with CsI absorber, field size 19×23, del pitch of 100 mm, image matrix size 1,914×2,294 (Senographe DS), with some specific software and hardware adaptations for acquisition and image processing.

The digital mammography system was modified accordingly by adding a copper filter specifically used for CEDM, in addition to the usual molybdenum and rhodium filters used for standard mammography.

Moreover, a high voltage range of 45–49 kVp was used (instead of 26–32 kVp for conventional digital mammography) Typically, for a 5 cm-thick, 50% glandular breasts, exposure times were around 1 s and 3 s for the low and high energy images, respectively.

- **Technique of Full Field Digital Mammography: (**Standard views medio-lateral-oblique and cranio-caudal views were taken for all patient). As illustrated in figure (1)

- **Ultrasound machine:**

The machine used was GE LOGIQ 57 XDclear (GE health , Chigaco,USA), using high frequency linear probe(9-12MHZ).

It is used as complementary tool for patient with BI-RADS 3,4&5 categories.

- **Image analysis and interpretation of Mammography**:

Mammograms were classified into four categories of density (MD), ACR-A, ACR-B, ACR-C & ACR-D according to ACR BI-RADS atlas fifth edition 2013.

All radiological classifications were made using both standard CC & MLO views of both breasts.

All image findings were categorized according BI-RADS (Breast imaging & reporting data system lexicon 2013).

RESULTS

Table (1) shows that the mean age of the study participants was 53.41 (± 9.44) years, and that the majority of the females lived in urban areas (62%). Moreover, 77.2 % of the females where married.

Table (2) shows that 9.5% of the females suffered from cardiac diseases, while 12.8% suffered from DM and 14.7% had hypertension. On the other hand, a minority suffered from autoimmune diseases and were smokers (0.9% and 0.4% respectively).

Furthermore, 6% only of the participants reported previous family history of breast cancer, and 1.5% stated that they had cancer previously. Additionally, the majority of the females were previously pregnant (96.3%) and 86.7% of them lactated.

Table (3) illustrates that after assessment of the breast density of the recruited females, the majority had type B density (52.1%), while 24.1% were type C, 21.6% were type A, and 2.2% were type D (Figure 1). Furthermore, 10.3% of the recruited females were found to suffer from breast cancer.

Table (4) shows that the there exists a statistically significant difference regarding the age of the females and the type of there breast density (p value= <0.001), where the oldest females where found to have breast density type A (64.34 ±5.83) years and the youngest had breast density type D (43.33 ±4.51) years. On the opposite side, no statistically significant difference was observed regarding the residence nor the marital status.

Table (5) illustrates that statistically significant difference exists regarding the presence of cardiac diseases, DM, and Hypertension among the females (p value= <0.001). Most of the females suffering from these diseases had type A breast density (22.2%, 21.6%, and 34.1% respectively). The rest of the investigated risk factors showed no statistical significance.

Table (6) demonstrates that there is a statistically significant difference between the type of breast density and the prevalence of breast cancer, where 42.8% of the females having breast cancer had a type B density, while 6% of the females had type D.

Table (7) shows that among the investigated risk factors for breast cancer, three types of breast densities increased the risk of breast cancer, where patients with type B breast density had a 1.39 times more risk of breast cancer, while type C patients had a 2.92 times more risk, and finally, type D patients had a 3.12 times more risk for breast cancer (p value= 0.010, 0.003, and 0.036 respectively).

DISCUSSION

Breast cancer is the most frequent cancer and the main cause of cancer-related mortality among women worldwide, as well as in Egypt, where breast cancer accounts for 33% of female cancer cases and over 22,000 new cases are diagnosed each year. Furthermore, 5-year survival rates in Egypt range from 28% to 68% (6,7).

As a result, screening for breast cancer is extremely valuable in finding asymptomatic disease, which results in less intrusive therapies and better outcomes because it is detected at an early stage before tumour growth (8).

Mammography is still the finest imaging technique for screening breast cancer in all women, and it is presently recognised as the only technology suitable for mass screening (6).

There has been debate over the role of mammography in predicting the risk of breast cancer occurrence among women with varying breast densities, with some studies denying the decreased sensitivity of mammography in cases of females with high breast density, while other studies finding a close relationship between breast cancer and increasing mammographic breast density (6,8).

Therefore, the aim of this study was to assess detect the relationship between different breasts mammographic densities and the risk for breast cancer among asymptomatic females through conducting an analytic cross-sectional study and performing a mammographic imaging for female patients that were recruited from Ain Shams university hospital and the national project for women health and private center.

Our study included 814 females whose age ranged from 40 to 74 years old and most of them lived in urban areas (62%) and 77.2% of them where married. Moreover, the prevalence of breast cancer among our recruited participants was 10.3%.

This current study investigated multiple risk factors for breast cancer among its participants. Among these risk factors was the presence of autoimmune diseases, where only 0.9% of our study participants suffered from autoimmune diseases.

Our finding was consistent with previous studies that found increased risk of breast cancer among cases of diffuse scleroderma and psoriasis (9,10). The underlying mechanism illustrated by these studies was that the increased levels of autoantibodies found in these autoimmune diseases was responsible for the increased risk of breast cancer, for instance, patients with diffuse scleroderma has increased the anti-pol III autoantibodies that was found to increase the risk of developing breast cancer within the first three years of being diagnosed with diffuse scleroderma when compared to the general population.

The current study found that 6% of the participants had a positive family history of cancer, and this is consistent with the decreased incidence of breast cancer among our participants; compared to the national incidence rate of breast cancer, because family history especially among first degree relatives is an established risk factor of breast cancer (11).

In our study, 15.2% of the females used hormonal contraceptives, with a mean duration of 32.94 (±15.38) months. This decreased prevalence along with the decreased prevalence of breast cancer among our participants is consistent with previous studies that showed that the use of hormonal contraceptives whether combined of progesterone only contraceptives, are associated with 20 to 30% more risk of breast cancer.

The effect by which hormonal contraceptives are thought to influence breast cancer risk could be due to direct stimulatory action on breast tissue, for instance, via cross regulatory signaling networks between the estrogen receptor (ER) alpha and BRCA or indirectly via delayed childbirth and lower parity (12).

In our study, the breast densities of the participants were distributed as follows, 21.6% of the females had a type A breast density, 52.1% had a type B breast density, 24.1% had type C density, and 2.2% had type D density.

This is similar to a study by Ali et al. who reported that the distribution of the type of breast densities of a cohort of Egyptian females was 23% type A, 49% type B, 25% type C, and 3% type D (8).

Our study investigated the relation between multiple breast cancer risk factors and the type of breast density, where we found that age, presence of cardiac diseases, DM, and hypertension differed significantly according to the type of breast density (p value = <0.001). We found that 22.2% of the females whose breast density was type A had cardiac disease, while 21.6% of them had DM, and 34.1% of them had hypertension. On the other hand, a minority of the females in the remaining breast density categories reported these comorbidities.

Grassmann et al. reported similar results to ours, where they found that higher breast density was associated with lower incidence of DM and hypertension. Nevertheless, they did not find any significant association between breast density and cardiac diseases (13).

Nevertheless, Miller et al. [14] found contradicting results, where they stated that diabetic women are more likely to have denser breasts. This was in agreement to a previous study by Borgquist et al. who explained their findings through the role of exogenous insulin on promoting breast tissue grouth either directly by signaling mitogenic effects through the insulin receptor isoform A and the insulin-like growth factor 1 (IGF-1) receptor or indirectly by altering the levels of circulating estrogens [15].

The difference between our results and theirs could be attributed to the missing data regarding the type of DM our participants suffer from, because there is a probability that a minority only receives insulin treatment.

In regard to the females that suffered from breast cancer, 42.8% of them had type B breast density, while 38.1% of them had type C, 13.1% had type A and 6% had type D breast density. Moreover, this difference was statistically significant (p value= <0.001).

On the opposite hand, on examining the prevalence of breast cancer in each breast density category, 27.7% of the females categorized as Type D had breast cancer, compared to 16.3% in type C, 8.4% in type B, and only 6.2% in type A.

Nevertheless, our study found that females patients with type D breast density had 3 times more risk of developing breast cancer, while this risk decreased as the breast density category decreased, where type C density was associated with a 2.92 more risk of breast cancer, and type B increased the risk 1.39 times more. As for type A breast density, we did not find a statististically significant assoc了itation between it and breast cancer.

Our results are strengthened and are consistent with all of the previous studies that stated the increased risk of breast cancer among females with increased breast density, where Ali et al. found that the positive breast cancer cases was the highest among type C and type D breast densities (3.3% and 13.7% respectively), while lower prevalence of breast cancer was observed among type A and B (2.2% and 2.7% respectively) [8].

Additionally, Bodewes et al. stated that type D breast density is associated with a 2 fold increase of breast cancer compared to type B breast density [7].

Likewise, Sajjad et al. stated that breast densities of type B and C are significantly associated with breast cancer, especially if the female's age is above 40 years old [16].

Regarding the mechanism underlying the relation between breast cancer and breast density, multiple mechanisms have been postulated. A potential mechanism is hypercellularity and increased breast epithelium in dense breasts that may lead to increased rates of somatic mutations. In addition, dense breasts contain a large amount of stroma with aromatase activity, which has been associated with an increased release of estrogen that may lead to carcinogenesis [17].

Another explanation is that mammographic sensitivity was 80% in women with predominantly fatty breasts and 30% in women with mammographically dense breasts. Also, it was previously demonstrated that dense tissue could obscure subtle signs of malignancy and thereby decrease the sensitivity of mammography. Accordingly, several asymptomatic cases may be missed because of the density of the breast tissue when they undergo mammograophy, a phenomenon called “radiologic masking of tumors” [16].

CONCLUSION

Breast cancer density is significantly associated with breast cancer. Female patients with type D breast density had 3 times more risk of developing breast cancer and this risk decreases as the breast density decrease.

Conflict of interest statement

The authors affirm that they do not have any competing interests.

Ethical approval

• The Research Ethics Committee's administrative permission was granted on October 2020(approval number 236).

• The Ethics Committee of the Ain Shams University, Faculty of Medicine, accepted the study protocol.

• No vested interests.

• Before collecting any data or conducting any investigations, we obtained fully informed consent from each participant.

• No other use will be made of the participant information gathered.

The consent contained:

• A short and understandable explanation of the study's objectives for laypeople.

• No hazardous actions or methods were employed.

• All information was regarded as private and will not be shared outside of this study without the consent of the participants.

• The patients' or their families' contact information, including the researcher's phone number, was provided so they could get in touch with them if they wanted an explanation.

• The study's findings were shared with all participants.

• Without giving a reason or impacting the standard of medical treatment they get; every participant had the freedom to leave the research at any time.

Authors contribution

All authors are equally contributed.

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TABLES

Table (1): Demographic characteristics of the study participants.

Characteristics	No.	%
Age (years)		
Min. – Max.	40	74
Mean ± SD.	53.41	±9.44
Median	52	-
Residence		
Urban	505	62%
Rural	309	38%
Marital status, (yes)	629	77.2%

Table (2). Distribution of the risk factors among the study participants.

Characteristics	No.	%
Cardiac disease, (yes)	77	9.5%
Diabetes Mellitus, (yes)	104	12.8%
Hypertension, (yes)	120	14.7%
Family history, (+ve)	49	6%
Autoimmune Disease, (yes)	7	0.9%

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Smoking	3	0.4%
Hormonal contraception, (yes)	124	15.2%
Duration of use (months)		
Mean ± SD.	32.94	± 15.38
Min. – Max.	10	72
Previous pregnancy, (yes)	784	96.3%
Lactation, (yes)	706	86.7%
Previous cancer, (yes)	12	1.5%

Table (3). Clinical findings of the current breast cancer.

Characteristics	No.	%
Presence of breast cancer, (yes)	84	10.3
Type of breast density		
Type A	176	21.6%
Type B	424	52.1%
Type C	196	24.1%
Type D	18	2.2%

Table (4). Comparison of the demographic data of the study participants according to their type of breast density.

Characteristics	Type A No. (%)	Type B No. (%)	Type C No. (%)	Type D No. (%)	P value
Age (Mean ± SD)	64.34 (±5.83)	53.18 (±7.95)	45.02 (±3.72)	43.33 (±4.51)	**<0.001*** [a]
Residence					0.383 [b]
Urban	117 (66.5)	253 (59.7)	125 (63.8)	10 (55.6)	
Rural	59 (33.5)	171 (40.3)	71 (36.2)	8 (44.4)	
Marital status, (yes)	130 (73.9)	333 (78.5)	155 (79.1)	11 (61.1)	0.204 [b]

Table (5). Comparison of the risk factors of the study participants according to their type of breast density.

Characteristics	Type A No. (%)	Type B No. (%)	Type C No. (%)	Type D No. (%)	P value
Cardiac disease, (yes)	39 (22.2)	33 (7.8)	4 (2.0)	1 (5.6)	**<0.001*** [b]
Diabetes Mellitus, (yes)	38 (21.6)	48 (11.3)	15 (7.7)	3 (16.7)	**<0.001*** [b]
Hypertension, (yes)	60 (34.1)	52 (12.3)	8 (4.1)	0 (0)	**<0.001*** [b]
Family history, (+ve)	13 (7.4)	26 (6.1)	10 (5.1)	0 (0)	0.565[b]
Autoimmune Disease, (yes)	2 (1.1)	3 (0.7)	2 (1.0)	0 (0)	0.921[b]
Smoking	1 (0.6)	1 (0.2)	1 (0.5)	0 (0)	0.904[b]
Hormonal contraception, (yes)	27 (15.3)	60 (14.2)	36 (18.4)	1 (5.6)	0.364[b]
Duration of use (months)					
Mean ± SD.	36.3 (±16.85)	32.34 (±14.47)	31.67 (±15.93)	24.00 (-)	0.651[a]
Min. – Max.	12 - 72	12 - 60	10 - 60	-	
Previous pregnancy, (yes)	169 (96)	407 (96)	190 (96.9)	18 (100)	0.784[b]
Lactation, (yes)	149 (84.7)	368 (86.8)	172 (87.8)	17 (94.4)	0.622[b]
Previous cancer, (yes)	2 (1.1%)	6 (1.4%)	3 (1.5%)	1 (5.6%)	0.746[b]

Table (6). Distribution of the positive breast cancer lesions according to each type of breast density among the study participants.

Breast density	Positive breast cancer		P value*
	No.	%	
Type A	11	13.1	**<0.001***
Type B	36	42.8	
Type C	32	38.1	

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Type D	5	6.0	

Table (7). Logistic regression for the various risk factors for breast cancer among the study participants.

Characteristics	OR[a]	CI	P value
Age	0.97	0.942 – 1.007	0.124
Cardiac comorbidities	1.56	0.528 – 4.631	0.419
Diabetes Mellitus	0.92	0.461 – 2.033	0.793
Type A	0.54	1.740 – 19.125	0.068
Type B	1.39	1.399 – 12.286	**0.010***
Type C	2.92	1.323 – 3.410	**0.003***
Type D	3.12	0.169 – 1.522	**0.036***

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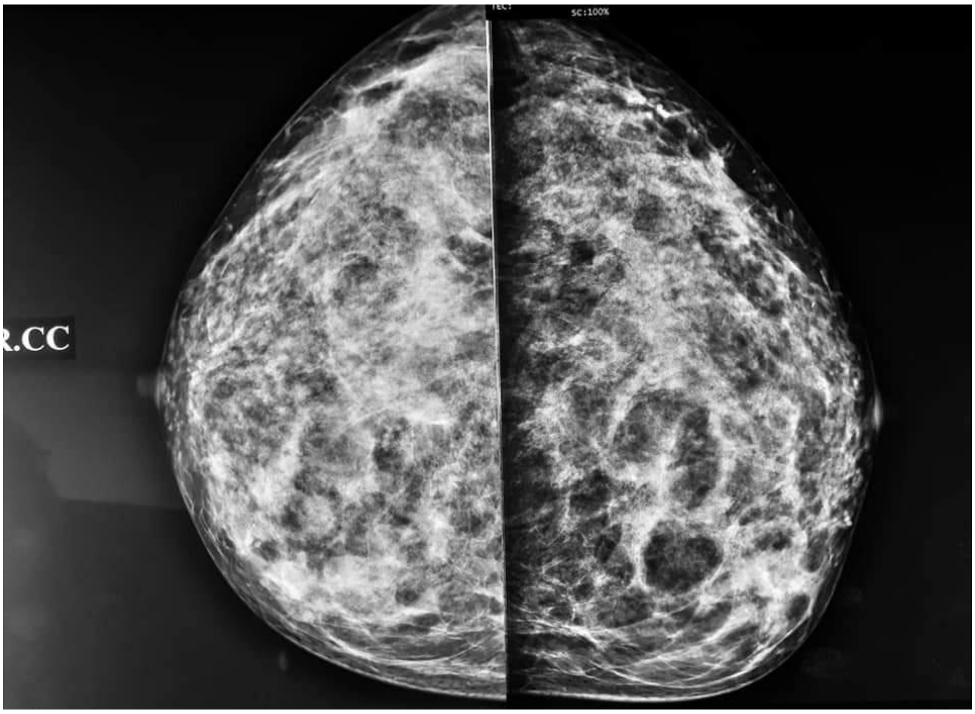
Figure (1). Mediolateral and oblique views of both breasts.



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