Original Article

Mammographic density in relationships with relevant contributing factors: a multicentric study from Riyadh, Saudi Arabia

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Background: Mammographic breast density (MBD), a well-established factor linked to breast cancer, is the focus of this preliminary report among women across multiple centers in Riyadh. The study aims to identify risk factors associated with high breast density.

Methods: MBD was assessed at three hospitals in Riyadh, Saudi Arabia, using the American College of Radiology (ACR) categories: A (almost entirely fatty), B (scattered areas of fibroglandular density), C (heterogeneously dense), and D (extremely dense). Breast density distributions were analyzed in relation to age, body mass index (BMI), family history, parity, and hormonal therapy usage.

Results: The study included 1,530 women, revealing an inverse association between dense breast proportion and age/BMI. Notably, 43.3% [95% confidence interval (CI): 43.2% to 43.5%] of women aged 40–79 years exhibited heterogeneously or highly dense breasts, with this proportion inversely correlated with age and BMI.

Conclusions: Healthcare providers should consider breast density for appropriate screening and, if necessary, recommend supplemental methods. Policymakers and healthcare providers, when discussing breast density notification legislation, should be mindful of its high prevalence, ensuring women notified have opportunities to evaluate breast cancer risk and pursue supplemental screening options if deemed appropriate.

Keywords: Mammography; breast; cancer; surveillance; density

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Introduction

Breast cancer is a highly prevalent health issue worldwide. In Saudi Arabia, breast cancer is considered one of the most common cancers affecting women. In 2020, the age-standardized rate for incidence was 28.4 per 100,000 Saudi women (1-3). Mammographic breast density (MBD) could be assessed through subjective decision-making, visual perception, visual analog scale, and Breast Imaging-Reporting and Data System (BI-RADS). MBD is a highly heritable trait but is also influenced by well-established breast cancer risk factors (2). Body mass index (BMI), family history, and hormone therapy are major risk factors for high MBD (4). Breast density is associated with age and BMI

(2,5). Additionally, higher MBD has been documented in postmenopausal women receiving exogenous estrogen as a replacement therapy. It is known that high MBD makes the detection by mammography more challenging, suggesting that mammographic density should be considered in risk prediction models (3,4). The American College of Radiology (ACR) C and D scores are considered dense (6). Breast cancer ranks among the most prevalent cancers in females and contributes to 18.1% of all cancers (7). In 2010, breast cancer was identified as the ninth leading cause of death among females in Saudi Arabia (8). The incidence is further expected to rise over the coming years due to population growth and increasing lifespan (9). Furthermore, it affects mammographic image accuracy in detecting suspicious lesions, which may lead to delayed diagnosis (5-9). However, in Saudi Arabia, studies related to breast density prevalence are scarce (10). We conducted a study to detect risk factors related to breast density in three major hospitals in Riyadh, Saudi Arabia. We present this article in accordance with the STROBE reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-23-374/rc).

Methods

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional review board (IRB) of Dr. Sulaiman Al Habib Hospital Research Center with study number RC21.09.24. All participating institutions were also informed and agreed the study. Informed consent was waived by the IRB. All centers use the ACR BI-RADS Atlas 5th edition, using the ACR category defined as A (almost entirely fatty), B (scattered areas of fibroglandular density), C (heterogeneously dense), and D (extremely dense). This approach to categorizing density is currently the most commonly used approach in the United States and, subsequently, the most clinically applicable. We used a convenient sampling technique where patients' screening mammogram data were collected by entering the medical records and extracting the ACR score from the radiology reports and the BMI and age from patients' records. Menopausal status considers if a woman had no menstrual cycle for 6 months. Diagnostic mammograms and those done following surgery were excluded, and no personal data of the enrolled participants were recorded.

In the pursuit of methodological transparency, we acknowledge the inclusion of power calculations in our study, which, despite its exploratory nature, was guided by insights gained from preliminary data and a pilot study. These preliminary investigations offered valuable glimpses into the anticipated variability and effect size within our target population. The decision to incorporate power calculations was driven by a commitment to optimize the study's design, ensuring that the chosen sample size would be adequately powered to detect meaningful trends or patterns in the data. While the study is fundamentally exploratory, the utilization of preliminary insights reflects our dedication to balancing the inherent flexibility of exploration with the methodological rigor necessary to yield meaningful and reliable results.

Statistical analysis

Statistical analysis was done by SPSS version 28 (IBM Co., Armonk, NY, USA). Categorical variables were presented as frequency and percentage (%) and analyzed using the chi-square test. Kendall's tau was used to study the correlation between age groups and ACR grades. Descriptive statistics for the categorical data variables are presented in the form of frequencies and relative frequencies (percentages). Ordinal logistic regression analysis was performed to assess factors associated with different ACR grades. A two-tailed P value <0.05 was considered statistically significant.

Results

This study included 1,520 females with breast cancer recorded out of which, 28.6% had ages ranging from 40 to 44 years, 27.3% had ages ranging from 45 to 49 years, 19.9% had ages ranging from 50 to 54 years, 14.2% had

Highlight box

Key findings
- Women in Saudi Arabia may have higher breast density especially from age 40 to 50 years.

What is known and what is new?
- Breast density affects mammogram sensitivity and ability for early detection.
- This report delineates mammographic density in multicentric study from Riyadh, and potential related factors.

What is the implication, and what should change now?
- Healthcare providers and patients should be aware of breast density to ensure appropriate screening options.

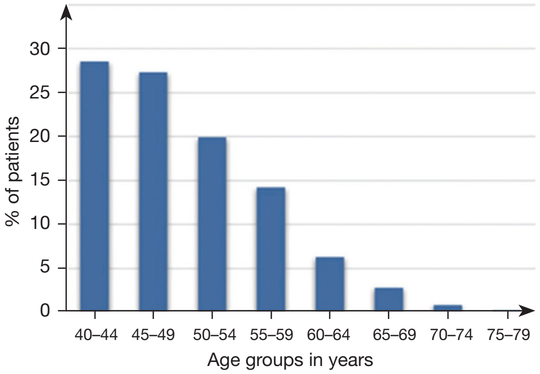

Figure 1 Age distribution of the studies patients.

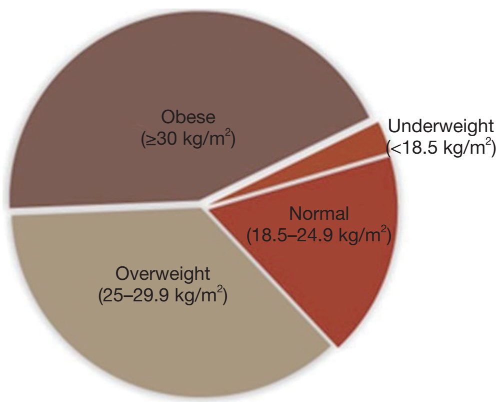

Figure 2 BMI distribution of the studied patients. BMI, body mass index.

ages ranging from 55 to 59 years as shown in *Figure 1*. The highest percentage of patients were obese with BMI ≥30.0 kg/m^2, 36.4% were overweight with BMI ranging between 25.0 and 29.9 kg/m^2, and only 2.7% were underweight with BMI <18.5 kg/m^2 as shown in *Figure 2*. More than half patients (68.7%) had ≥ one parity and 3.8% had no parity. In terms of menopausal status, 43.9% of patients were premenopausal and 25.1% were postmenopausal. Out of 1,520 patients, only 1.4% were on postmenopausal hormones at the time of the study, 11.1% had family history of breast cancer as shown in *Table 1*.

According to ACR breast density categories, 8.9% of patients were diagnosed as grade A indicating almost entirely fatty breasts with 95% confidence interval (CI) from 7.45 to 10.51, 23.3% were diagnosed as grade B indicating scattered areas of fibroglandular density with 95% CI from 20.93 to 25.85, 47.9% were given grade C indicating heterogeneously dense breasts with 95% CI from 44.48 to 51.5 and 9.9% were diagnosed as grade D indicating extremely dense breasts with 95% CI from 8.35 to 11.58 as shown in *Figure 3* and *Table 2*.

Table 1 Baseline characteristics of the studied patients (n=1,520)

Characteristics	N (%)
Age (years)	
40–44	434 (28.6)
45–49	415 (27.3)
50–54	303 (19.9)
55–59	216 (14.2)
60–64	95 (6.3)
65–69	42 (2.8)
70–74	12 (0.8)
75–79	3 (0.2)
BMI (kg/m^2)	
Underweight (<18.5)	41 (2.7)
Normal (18.5–24.9)	266 (17.5)
Overweight (25.0–29.9)	553 (36.4)
Obese (≥30.0)	660 (43.4)
Parity	
0	58 (3.8)
≥1	1,044 (68.7)
Unknown	418 (27.5)
Menopausal status	
Premenopausal	668 (43.9)
Postmenopausal	381 (25.1)
Other/unknown	471 (31.0)
Current use of postmenopausal hormones	
Yes	21 (1.4)
No	547 (36.0)
Unknown	952 (62.6)

BMI, body mass index.

Patients with known ACR grades (1,367 patients) were analyzed according to age, BMI and state of menopausal status: the comparison between different age groups in terms of ACR breast density grades revealed a statistically significant difference (P<0.001) as younger patients of age groups 40–44 and 45–49 years had significantly denser ACR grades when compared to older age groups 50–54, 55–59,

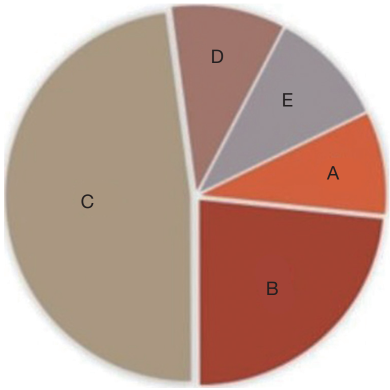

Figure 3 ACR breast density classification of the studied patients. A: almost entirely fatty breasts; B: scattered areas of fibroglandular density; C: heterogeneously dense breasts; D: extremely dense breasts; E: unknown. ACR, American College of Radiology.

Table 2 ACR breast density classification of the studied patients (n=1,520)

ACR grade	N (%)	95% CI
A	135 (8.9)	7.45 to 10.51
B	354 (23.3)	20.93 to 25.85
C	728 (47.9)	44.48 to 51.5
D	150 (9.9)	8.35 to 11.58
Unknown	153 (10.1)	8.53 to 11.79

A: almost entirely fatty breasts; B: scattered areas of fibroglandular density; C: heterogeneously dense breasts; D: extremely dense breasts. ACR, American College of Radiology; CI, confidence interval.

60–64, 65–69, and 70–74 years old patients. Likewise, patients of age group 50–54 years old had significantly denser ACR grades when compared to those with 55–59 and 65–69 years old (*Table 3*, *Figure 4*). Kendall's tau correlation showed a statistically significant negative weak correlation 155 between ACR grade and age group (correlation coefficient =–0.165, P value <0.001). Younger age groups had more dense breasts.

The comparison between BMI groups in terms of their ACR breast density grades revealed a statistically significant difference (P<0.001) as normal and overweight patients had relatively denser ACR grade than the underweight and obese ones (*Table 4*, *Figure 5*). Ordinal logistic regression was used to study the factors associated with denser ACR. An OR of higher than 1 indicates that the associated group tends to have a higher (denser) ACR category as compared to the reference group, and an OR <1 indicates a lower tendency to have dense ACR as shown in *Table 5*. For the age groups, as compared to the reference group (40–44 years), those in the age groups 50–54, 55–59, 60–64, and 65–69 years, tend to have less dense ACR, OR: 0.72, 0.47, 0.52, and 0.44, respectively. For the BMI groups, as compared to the reference group (normal weight), those in the other groups underweight, overweight and obese, tend to have less dense ACR, OR: 0.34, 0.59, and 0.62, respectively. For the menopausal status group, as compared to the reference group (normal weight), those in the other groups Premenopausal women tend to have more risk than other groups, OR: 1.22, 1.00, and 0.64, respectively.

Table 3 Relation between ACR grades and age of patients

Age groups (years)	Number of patients	Grade A	Grade B	Grade C	Grade D	P value
40–44	389	30 (7.7)	78 (20.1)	226 (58.1)	55 (14.1)	<0.001
45–49	372	30 (8.1)	75 (20.2)	214 (57.5)	53 (14.2)	
50–54	273	20 (7.3)	84 (30.8)	150 (54.9)	19 (7.0)	
55–59	195	39 (20.0)	56 (28.7)	85 (43.6)	15 (7.7)	
60–64	87	10 (11.5)	36 (41.4)	36 (41.4)	5 (5.7)	
65–69	37	5 (13.5)	18 (48.6)	11 (29.7)	3 (8.1)	
70–74	11	0 (0.0)	6 (54.5)	5 (45.5)	0 (0.0)	
75–79	3	1 (33.3)	1 (33.3)	1 (33.3)	0 (0.0)	

Data are presented as n (%). A: almost entirely fatty breasts; B: scattered areas of fibroglandular density; C: heterogeneously dense breasts; D: extremely dense breasts. Statistical significance at P value <0.05. ACR, American College of Radiology.

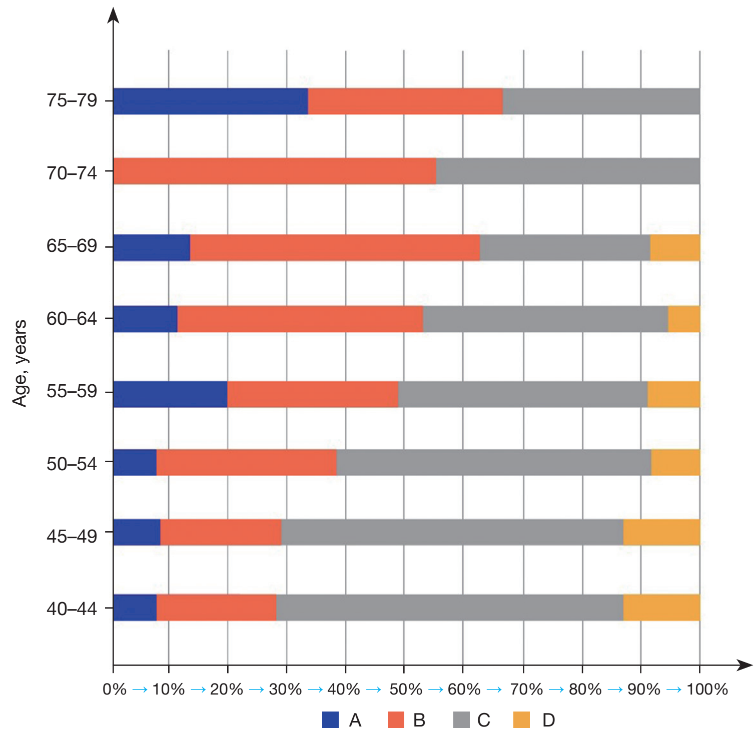

Figure 4 Relation between ACR grades and age of patients. A: almost entirely fatty breasts; B: scattered areas of fibroglandular density; C: heterogeneously dense breasts; D: extremely dense breasts. ACR, American College of Radiology.

Table 4 Relation between ACR grades and BMI of patients

BMI groups (kg/m^2)	Number of patients	Grade A	Grade B	Grade C	Grade D	P value
Underweight (<18.5)	34	6 (17.6)$_a$	9 (26.5)$_{a,b}$	17 (50.0)$_{a,b}$	2 (5.9)$_{a,b}$	<0.001
Normal (18.5–24.9)	239	10 (4.2)$_b$	40 (16.7)$_b$	133 (55.6)$_b$	56 (23.4)$_c$	
Overweight (25.0–29.9)	495	28 (5.7)$_b$	107 (21.6)$_b$	305 (61.6)$_b$	55 (11.1)$_b$	
Obese (≥30.0)	599	91 (15.2)$_a$	198 (33.1)$_a$	273 (45.6)$_a$	37 (6.2)$_a$	

Data are presented as n (%). Statistical significance as P value <0.05. Each subscript letter denotes a subset of BMI categories who proportions do not differ significantly from each other at the 0.05 level. A: almost entirely fatty breasts; B: scattered areas of fibroglandular density; C: heterogeneously dense breasts; D: extremely dense breasts. ACR, American College of Radiology; BMI, body mass index.

Discussion

To the best of our knowledge, this is the first study reporting MBD and factors related to this among Saudi women (11,12). More than half of our sample size at the age of 40–50 years has dense breast. This signifies that the majority of women who attend screening in Saudi may have high-density breasts. This is important information for stakeholders when allocating resources, as high density entails that there will be a necessity for additional imaging.

MBD is a dynamic trait that typically declines with increasing age (6,13). The study demonstrated an inverse relationship between age and MBD, where women at 40–50 years reported high (MBD) ACR BI-RADS C. This is akin to other data that has shown this inverse relation (14). This is predicted as estrogen levels decline with age. Estrogen has a proliferative effect on breast epithelial cells (6,13,15,16), thus it is anticipated that any condition increasing estrogen will increase MBD. It is noteworthy that our result is comparable to the United Arab Emirates, which shares the same demographic and lifestyle (17).

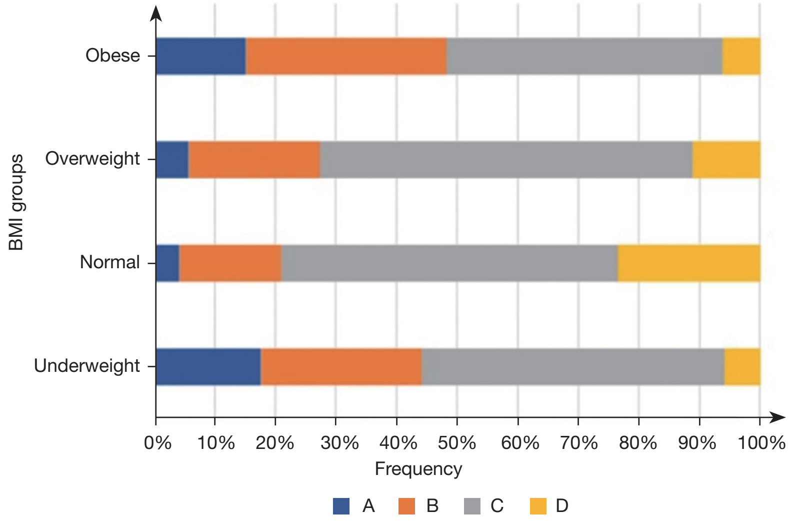

Figure 5 Relation between ACR grades and BMI of patients. A: almost entirely fatty breasts; B: scattered areas of fibroglandular density; C: heterogeneously dense breasts; D: extremely dense breasts. BMI, body mass index; ACR, American College of Radiology.

Table 5 Ordinal logistic regression for factors associated with ACR grades

Factors	OR (95% CI)	P value
Age groups (years)		
40–44	1.00	
45–49	1.10 (0.83–1.46)	0.50
50–54	0.72 (0.53–0.97)	0.033
55–59	0.47 (0.33–0.66)	<0.001
60–64	0.52 (0.34–0.81)	0.004
65–69	0.44 (0.24–0.84)	0.012
70–74	0.49 (0.17–1.38)	0.178
75–79	0.22 (0.03–1.71)	0.147
BMI groups (kg/m^2)		
Normal (18.5–24.9)	1.00	
Underweight (<18.5)	0.34 (0.17–0.69)	0.003
Overweight (25.0–29.9)	0.59 (0.43–0.81)	0.001
Obese (≥30.0)	0.26 (0.19–0.36)	<0.001
Menopausal status		
Premenopausal	1.22 (0.12–0.74)	0.002
Postmenopausal	1.00 (0.28–0.93)	0.024
Other/unknown	0.64 (0.02–1.34)	0.163

Reference categories are age group 40–44 years, normal BMI, and zero parity. Statistical significance at P<0.05. ACR, American College of Radiology; OR, odds ratio; CI, confidence interval; BMI, body mass index.

In addition, breast cancer in Saudi women may occur at a younger age compared to western countries (18,19), raising questions about the accuracy of implementing western guidelines in our local society. Moreover, increased density renders mammography a less sensitive tool for early detection (10,20-28). In the USA, many state medical boards mandate reporting patient notification of their breast density (10), which we recommend adopting this recommendation by stakeholders and educating women about their breast density.

Our results are consistent with prior studies demonstrating strong inverse associations of BMI with MBD (1,4,6,10-16). Breast fat is needed to allow the proliferation of fibroglandular tissue (18-21). Given that 79.8% were overweight or obese, it may lessen the sensitivity of mammogram as a screening tool. According to the World Health Organization (WHO), in the Kingdom of Saudi Arabia (KSA), the overall prevalence of obesity is estimated to be 33.7%, and of overweight is 68.2% (20,22,25). This cohort cannot analyze the relationship of family history of breast cancer and increased density as we have overly many missing data. Although other studies indicate that family history may play an important role in MBD (23-25).

One important clinical implication of our study is that screening mammography could be impaired as an early detection imaging modality for Saudi women, due to the high mammographic density profile. Other modalities may need to be considered. It also seems advisable to educate women about their mammogram's density.

Limitations

Limitations to our study include its retrospective nature, small sample size, were not able to collect for other factors such as a family history of breast cancer, parity, or the use of postmenopausal hormones.

Conclusions

Healthcare practitioners should be aware of breast density to provide adequate screening choices and, if necessary, consider supplementary procedures. Local healthcare providers shall be aware of such finding of relatively high breast density when screening women. And carefully choose appropriate supplemental imaging if indicated.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-23-374/rc

Data Sharing Statement: Available at https://gs.amegroups.com/article/view/10.21037/gs-23-374/dss

Peer Review File: Available at https://gs.amegroups.com/article/view/10.21037/gs-23-374/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-23-374/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional review board (IRB) of Dr. Sulaiman Al Habib Hospital Research Center with study number RC21.09.24. All participating institutions were also informed and agreed the study. Informed consent was waived by the IRB.

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