RESEARCH ARTICLE

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Mammographic Density Distribution in Ras Al Khaimah (RAK): Relationships with Demographic and Reproductive Factors

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Abstract

Objective: Mammographic density is an important risk factor for breast cancer and determines to a large extent mammographic screening efficacy. This study aims to provide baseline data for mammographic density profiling of women living in Ras Al Khaimah (RAK) and to identify risk factors associated with high mammographic density. **Methods:** A cross-sectional design was used to examine a series of 366 mammography cases. The Breast Imaging Reporting and Data System (BI-RADS, 5th edition) was used to evaluate mammographic density. Pearson's chi-squared, Mann-Whitney U test and multivariate logistic regression were used for statistical analysis. **Results:** Most participants (67%) fell into BI-RADS b and c mammographic density categories. Of the total sample, women who were aged ≤ 45 years (p=0.004, OR=1.9), weighed ≤ 71kg (p=<0.0001, OR=4.8), had a body mass index of ≤ 27 kg/m^2 (p=<0.0001, OR=5.1) and were of non-Arab descent (p=0.007, OR=1.8) were significantly more likely to have denser breast tissue. Adjusted ethnicity regression analysis showed that Emirati women were significantly less likely to have dense breast tissue compared with Western women (p=0.04, OR=0.4). Among the sample of survey participants, increased odds of having mammographic density were among women who were full-time workers (p=0.02, OR=2.8), of Christian faith (p=0.007, OR=4.4), nulliparous (p=0.003, OR=10.8), had three or fewer children (p=0.03, OR=3.8), and had used oral contraceptives for three years or more (p=0.01, OR=6.1). **Conclusion:** This study indicated that because Emirati women have a low mammographic density profile, screening mammography can be considered as an effective early detection imaging modality.

Keywords: Breast cancer- breast density- Mammography- risk factors

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Introduction

Breast cancer is the leading cancer-related cause of death among women worldwide, accounting for more than 500,000 deaths in 2012 (International Agency for Research on Cancer, 2012). Although United Arab Emirates (UAE) women have a lower breast cancer incidence rate than Western women, the rate has recently doubled over a ten year period to 40 per 100,000 women, which is amongst the highest in the Gulf Cooperation Council (GCC) region (International Agency for Research on Cancer, 2012). In addition, Emirati women are more likely to have an elevated risk of mortality from breast cancer due to initial clinical diagnoses occurring at advanced stages (Health Authority Abu Dhabi, 2008). Whilst it is known for instance, that prevalence and age of manifestation of breast cancer in the UAE are different from those in Western countries, little attention has been paid to mammographic density as a key risk factor of breast cancer (Boyd et al., 2011).

Mammographic density is defined as a measure of the amount of fibroglandular (radiopaque or white) tissue relative to the amount of fat tissue (radiolucent or black) in the breast (Boyd et al., 2011). In 1976, John Wolfe and his colleagues were the first to qualitatively assess variations in breast density and propose an association with the risk of breast cancer (Wolfe, 1976). Following Wolfe's work, several qualitative and quantitative (automated, semi-automated, and volumetric) methods have been developed to measure mammographic density and its association with breast cancer risk (Boyd et al., 2011). It has been reported that the risk of developing breast cancer is 4-6 times higher in women with extremely dense tissue (>75% density) than in

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women with almost entirely fatty tissue (<25% density) (McCormack and dos Santos Silva, 2006).

Although knowledge related to mammographic density has mainly been derived from Western population, some research has been conducted in other regions including Asia and South America (Jeon et al., 2011; Casado et al., 2015; Kawahara, 2015). There is, however, a paucity of information around this feature for Emirati women. Therefore, it is unclear if mammography is the most appropriate screening modality in the UAE. Researchers studying mammographic density among Japanese women aged 40-49 years, concluded that due to increased mammographic density, mammography may not be the optimum screening tool, and proposed the use of alternative imaging modalities such as ultrasonography (Kawahara, 2015). Such country-specific variations on this important morphological agent highlight the importance of not relying on one imaging paradigm across different world regions.

Currently no mammographic density data exist for Emirati women. Without these data breast cancer risk factors cannot be fully explored nor can imaging strategies be optimized since optimum imaging modalities depend on knowledge of typical levels of mammographic density. The present study is the first to evaluate the mammographic density profile of women living in RAK, a northern emirate within the UAE, and the first to identify factors associated with mammographic density. The findings are expected to feed decision-making around breast cancer prevention and screening strategies in this part of the world where breast cancer is becoming an increasingly important health policy issue.

Materials and Methods

The study was approved by the Human Research Ethics Committee of the University of Sydney. All women who agreed to participate, signed a consent form prior to the interview and mammography screenings.

Study design and data source

This cross-sectional study was conducted at Ras Al Khaimah private hospital from June 2015 to January 2016. There were two forms of data collection. The first data set comprised of 263 mammogram cases from women attending RAK hospital for diagnostic purpose. These data were collected retrospectively from Picture Archiving and Communication System (PACS) and demographic information (age, marital status, nationality, height, and weight) was collected from the Hospital Information System (HIS).

The second data set was collected prospectively. Interviews and mammography screenings were conducted with 111 women who responded to a RAK private hospital advertising campaign for free mammography screening. Four women aged < 30 years and four women with breast diseases were excluded. In total, data from 366 cases were included in the analysis. A structured questionnaire was used to collect basic demographic and reproductive data at the time of mammography screening. Demographic data included age, nationality, marital status, religion, educational level, occupational status, and monthly family income. Participants were also asked about age at first menarche, menopausal status, age at first delivery, number of children, breastfeeding, hormone replacement therapy (HRT) and oral contraceptives (OC). For each participant, height and weight were measured and body mass index (BMI) was calculated (weight in kilograms/square of height in meters) at the time of the survey.

The interviews were conducted by a female staff member from RAK private hospital who was fluent in both Arabic and English. Forward and backward translations of the questionnaire and related documents between English and Arabic were carried out to ensure lexical equivalence. These translations were later attested by a Justice of the Peace (JP), who was authorized by the Australian Government, NSW, Australia.

Mammographic density classification

Mammographic density scores were measured by a qualified radiologist affiliated to the University of Sydney. Mammographic density was classified according to the American College of Radiology Breast Imaging Reporting and Data System (ACR, BI-RADS, 5th edition) into four categories (Sickles et al., 2013): a (the breasts are entirely fatty), b (there are scattered areas of fibroglandular density), c (heterogeneously dense breast tissue, which may obscure small masses) and d (extremely dense breast tissue, which lowers the sensitivity of mammography).

Data analysis

Mammographic density was categorized as either low (BI-RADS categories a and b) or high (BI-RADS categories c and d). For univariate analysis, Mann–Whitney U test was used to assess relationships between continuous variables while Pearson's chi-squared (χ^2) was used to assess relationships between categorical variables for the two mammographic density groups. To categorize the continuous variables into two groups, a receiver operating characteristic (ROC) curve analysis was conducted to find the optimal cut off point with the area under the curve (AUC).

Multivariate logistic regression using the Enter method was performed to derive adjusted odds ratio (OR) for variables that showed statistical significance at the univariate level. P values were obtained from two tailed tests, and an alpha level of ≤ 0.05 was considered significant. All analyses were conducted using statistical software package SPSS (version 22.0).

Results

Total sample

The distribution of study participants into the four BI-RADS density categories according to basic demographic characteristics is shown in Table 1. The average age was 45.8 years (ranging from 30 to 69 years) and the average BMI was 29 kg/ m^2 (ranging from 18 to 60 kg/ m^2). Three quarters of women were overweight or obese (BMI $\geq$ 25 kg/ m^2). Emirati and Arab women had the highest body weight compared with other ethnicities in the study (Figure 10). Among all women, scattered

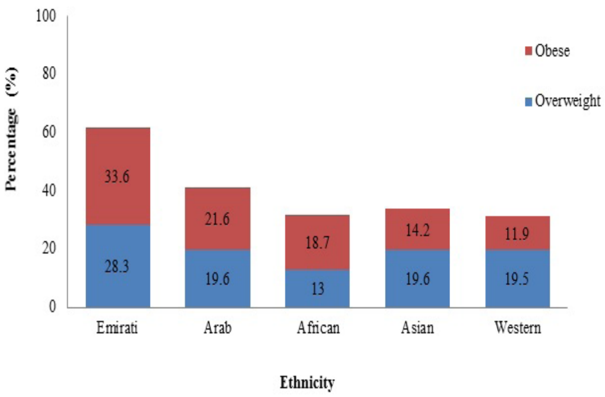

Figure 1. Distribution of Overweight and Obesity by Women's Ethnicity

fibroglandular breast tissue (BI-RADS b category) was the most commonly recorded form (n=156, 43.1%) whilst only 11% (n=40) of participants had extremely dense breast tissue.

Mammographic density was further categorized as fatty breast tissue or dense breast tissue to facilitate the univariate analysis, as shown in Table 2. Based on cut-off points, there were age, weight, and BMI differences between women in the fatty and dense mammographic density categories. Women in the high mammographic density category had a lower median age (43 vs 46years), body weight (65.3 vs 77.5 kg) and BMI (25.2 vs 29.9 kg/m^2) than women in the low mammographic density group (p=<0.0001). Although there was a tendency for women with dense breast tissue to be taller (median 162 cm), there was no statistically significant relationship between mammographic density and height (p=0.2).

In relation to the unadjusted OR, increased mammographic density was significantly higher in women in the younger age group (OR=1.9; p=0.04), who had a lower body weight (OR=4.8; p=<0.0001) and a lower BMI (OR=5.1; p=<0.0001). Higher mammographic density was significantly more likely among non-Arab women compared with Arab women (OR=1.8; p=0.007), as shown in (Table 2). There were no significant associations between mammographic density and marital status (p=0.06).

The multivariate logistic regression analysis Table 2 showed similar results to the univariate analyses in that women who were younger (OR=1.7), lower BMI (OR=4.4) and were of non-Arab descent (OR=1.6) were more likely to have denser breast tissue. Because of collinearity issue between weight and BMI, only BMI was used in the model.

Further analysis of the data stratified by ethnicity was performed to determine if the ethnic differences in mammographic density were independent of other confounding risk factors. The unadjusted analysis showed that Emirati and African women were significantly less likely to have denser breast tissue than Western women (Table 3).

After controlling for relevant confounders such as age and BMI, African women were not at increased risk of having denser breast tissue, but the association remained

Table 1. Distribution of Mammographic Density patterns by Demographic Characteristics of the Total Sample

	BI-RADS categories[a]			
Factors (Mean ± SD)	a. Entirely fatty N (%)	b. Scattered fibroglandular N (%)	c. Heterogeneously dense N (%)	d. Extremely dense N (%)
Age (45.8 ± 8.1)				
> 45	50 (29.2)	74 (43.3)	34 (19.9)	13 (7.6)
≤ 45	29 (15.2)	82 (42.9)	53 (27.7)	27 (14.1)
Height (161.2 ± 8.1)[a]				
> 161	29 (16.9)	75 (43.6)	45 (26.2)	23 (13.4)
≤ 161	50 (26.7)	80 (42.8)	41 (21.9)	16 (8.6)
Weight (75 ±14)[b]				
> 71	65 (32)	98 (48.3)	32 (15.8)	8 (3.9)
≤ 71	14 (9)	57 (36.5)	54 (34.6)	31 (19.9)
BMI (29 ± 5.9)[b]				
Normal (18.5- 24.9)	6 (6.6)	28 (30.8)	34 (37.4)	23 (25.3)
Overweight (25-29.9)	20 (14.8)	65 (48.1)	37 (27.4)	13 (9.6)
Obese (≥ 30)	53 (39.8)	62 (46.6)	15 (11.3)	3 (2.3)
Marital status				
Married[c]	72 (23)	137 (43.8)	71 (22.7)	33 (10.5)
Single	7 (14.3)	19 (38.8)	16 (32.7)	7 (14.3)
Ethnicity[d]				
Emirati	27 (27.6)	48 (49)	14 (14.3)	9 (9.2)
Arab	18 (26.1)	28 (40.6)	16 (23.2)	7 (10.1)
African	16 (31.4)	22 (43.1)	11 (21.6)	2 (3.9)
Asian	11 (17.2)	22 (34.4)	22 (34.4)	9 (14.1)
Western	7 (9.1)	35 (45.5)	23 (29.9)	12 (15.6)

a 4 missing values; b 3 missing values; c 7 separated and 7 widowed women were considered as "Married"; d 3 missing values. Abbreviation: N, Number, BMI, Body Mass Index; SD, Standard Deviation.

Table 2. Results of Univariate Analysis of Total Women's Demographic Characteristics by Mammographic Density Patterns

	Mammographic density patterns[a]					
Factors	Fatty breast tissue N (%)	Dense breast tissue N (%)	P-value[b]	Unadjusted OR (95% CI)[c]	P-value[b]	Adjusted OR (95% CI)[d]
Age						
Median ± SD	46 ± 8.4	43 ± 6.7	**<0.0001**			
> 45*	124 (72.5)	47 (27.5)				
≤ 45	111 (58.1)	80 (41.9)	**0.004**	**1.90 (1.22, 2.96)**	**0.02**	**1.80 (1.09, 2.95)**
Height						
Median ± SD	160 ± 8.6	162 ± 7.1	0.21			
> 161*	104 (60.5)	68 (39.5)				
≤ 161	130 (69.5)	57 (30.5)	0.07	0.67 (0.43, 1.04)		
Weight						
Median ± SD	77.5 ± 13.8	65.3 ± 10.9	**<0.0001**			
> 71*	163 (80.3)	40 (19.7)				
≤ 71	71 (45.5)	85 (54.5)	**<0.0001**	**4.88 (3.06, 7.79)**		
BMI						
Median ± SD	29.9 ± 6	25.2 ± 4.2	**<0.0001**			
> 27*	169 (80.1)	42 (19.9)				
≤ 27	65 (43.9)	83 (56.1)	**<0.0001**	**5.14 (3.22, 8.21)**	**<0.0001**	**4.41 (2.73, 7.13)**
Marital status						
Married*	209 (66.8)	104 (33.2)				
Single	26 (53.1)	23 (46.9)	0.06	1.78 (0.97, 3.27)		
Ethnicity						
Arab*	121 (72.5)	46 (27.5)				
Non-Arab	113 (58.9)	79 (41.1)	**0.007**	**1.84 (1.18, 2.87)**	**0.03**	**1.69 (1.03, 2.79)**

Note. **Boldface items** indicate statistically significant associations ($P < 0.05$); [a] Fatty breast tissue includes " entirely fatty breast and scattered fibroglandular dense tissues" whereas dense breast tissue includes " heterogeneously breast and extremely dense breast tissues"; [b]Obtained from Pearson's chi-squared test for categorical variables and Mann-Whitney U test for continuous variables; [c]Obtained from binary logistic regression. [d]Obtained from multivariate logistic regression (R^2= 20.7%); *Reference group for odds ratio; Abbreviation: N= Number, SD= Standard Deviation, BMI= Body Mass Index, OR=Odds Ratio, CI= Confidence Interval.

significant for Emirati women.

Interviewed sample

The majority of interviewed participants were Arabs (80.7%), married (92.7%), and postmenopausal (70.8%). Homemakers and women with school or college level qualifications comprised more than half of interviewed participants. Slightly more than one quarter (26.5%) of participants reported a positive family history of breast cancer. Full details on the profile of interviewed candidates are shown in Table 4.

With regard to reproductive factors, 65.7% of women reported being 13 years or less at their first menarche. Almost 12% of women were nulliparous and 72.7% had their first child at the age of 25 years or younger. Half of the participants reported using OC in the past, and 85.7% had never used HRT. Slightly more than three quarters of participants (n=86, 79%) had breastfeeding experience and approximately 50% had breastfed their children for a year or more (Table 4).

When evaluating statistical associations, increased mammographic density was significantly associated with women who reported a lower height, body weight, and BMI (p=>0.05, Table 5). Increased mammographic density was also more likely in women who were non-Arab, full-time workers, and Christian (p=<0.05) compared with those who were Arab, homemakers, and Muslim women, respectively. Similarly, high mammographic density was more likely in nulliparous women, women who had three or fewer children, and women who had used OC for three years or more (p<0.05). It should be acknowledged that these unadjusted associations should be interpreted with caution due to the small number of observations in each cell, as reflected by the large CI for some ORs Table 5.

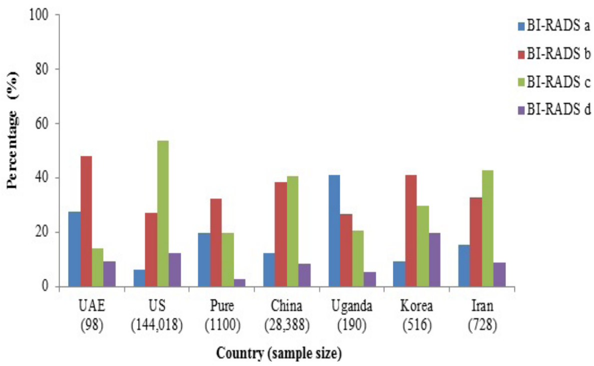

Figure 2. BI-RADS Density Distribution of Emirati Women Compared with other Populations.UAE=United Arab Emirates, US= United States; References: (Titus-Ernstoff et al., 2006; Jeon et al., 2011; Galukande and Kiguli-Malwadde, 2012; Rahmani et al., 2013; Dai et al., 2014; Casado et al., 2015). Generated from (Casado et al., 2015).

Table 3. Results of Regression Analysis of Mammographic Density Patterns by Ethnicity (Fatty vs Dense)*

Ethnicity	P value	Unadjusted OR (95% CI)[a]	P value	Adjusted OR (95% CI)[b]
Western (Reference)				
Emirati	0.002	0.37 (0.19, .070)	0.04	0.46 (0.22, 0.95)
Arab	0.14	0.60 (0.31, 1.18)	0.47	0.76 (0.36, 1.60)
African	0.02	0.41 (0.19, 0.89)	0.31	0.65 (0.28, 1.49)
Asian	0.72	1.13 (0.58, 2.19)	0.56	1.24 (0.60, 2.56)

*Fatty breast tissue includes "entirely fatty breast and scattered fibroglandualr dense tissues" whereas dense breast tissue includes "heterogeneously breast and extremely dense breast tissues"; [a]Logistic regression model with ethnicity alone (R^2=63%); [b]Fully-adjusted model for age and Body Mass Index (R^2=22%); Abbreviation: OR=Odds Ratio, CI= Confidence Interval.

Table 4. Distribution of Demographic and Reproductive Characteristics of the Interviewed Participants

Characteristic	N (%)	Characteristic	N (%)
Age (years) (Mean ± SD)	43.6 ± 8.1	Height (Mean ± SD)	(161.2 ± 8.2)
> 40	58 (53.2)	Weight (Mean ± SD)	(75.2 ± 13.5)
≤ 40	51 (46.8)	BMI (Mean ± SD)	(29.2 ± 6.4)
Nationality		Normal (18.5- 24.9)	34 (31.2)
Emirati	52 (47.7)	Overweight (25-29.9)	33 (30.3)
Arab	36 (33)	Obese (≥ 30)	42 (38.5)
Non-Arab	21 (19.3)	Mammographic density distribution[h]	
Marital status		a. Entirely fatty	27 (25.7)
Single	8 (7.3)	b. Scattered fibroglandular	53 (50.5)
Married	101 (92.7)	c. Heterogeneously dense	19 (18.1)
Menopause status[a]		d. Extremely dense	6 (5.7)
Pre	31 (29.6)	Family history of breast cancer[j]	
Post	75 (70.8)	Yes	26 (26.5)
Religion[b]		No	72 (73.5)
Muslim	86 (80.4)	Age at first birth (Mean ± SD)[k]	(23 ± 4.8)
Christian	21 (19.6)	> 25	24 (27.3)
Education level[c]		≤ 25	64 (72.7)
School / Collage level	56 (53.3)	Number of children (Mean ± SD)[i]	(3 ± 2.6)
University/ Higher education level	49 (46.7)	Nulliparous	12 (11.8)
Monthly family income[d]		> 3	42 (41.2)
> 30, 000 ADE	12 (12.1)	≤ 3	48 (47.1)
≤ 30, 000 ADE	46 (46.5)	Breast feeding (months) (Mean ± SD)[m]	(13.7 ±7.8)
I do not know / Refuse[d]	41 (41.4)	> 12 months	40 (46.5)
Employment status[e]		≤ 12 months	46 (53.5)
Homemaker	61 (57)	Age at first menstrual period (Mean ± SD)[n]	(12.9 ± 1.4)
Full time/ Part time	46 (43)	> 13	37 (34.3)
OC use[f]		≤ 13	71 (65.7)
Ever	50 (50)	HRT use[o]	
Never	50 (50)	Ever	14 (14.3)
OC duration (Years)[g]		Never	84 (85.7)
< 3	26 (53.1)		
≥ 3	23(46.9)		

[a] 3 missing values; [b] 2 Hindu participants were removed from the analysis; [c] 4 participants never went to school; [d] 10 missing values; [e] One full-time student and one missing value; [f] 9 missing values; [g] One participant did not specify the period of usage; [h] 4 missing values; [j] 6 participants did not know the answer and 5 missing values; [k] 21 participants were removed from the analysis (12 nulliparous and 9 missing values); [l] 7 missing values; [m] 5participants answered "No", 12 nulliparous and 6 missing values; [n] One missing value; [o] 2 participants did not know the answer and 9 missing values; Abbreviations: N, Number; SD, Standard Deviation; BMI, Body Mass Index; OR, Odds Ratio; CI, Confidence Interval; OC, Oral Contraceptives; HRT, Hormone Replacement Therapy.

Table 5. Results of Univariate Analysis of Interviewed Women's Demographic Characteristics by Mammographic Density Patterns

	Mammographic density patterns			
Factors	Fatty breast tissue N (%)	Dense breast tissue N (%)	P-value[b]	Unadjusted OR (95% CI)[c]
Age				
Median ± SD	42 ± 8.2	39 ± 6.8	0.29	
> 40*	44 (80)	11 (20)		
≤ 40	36 (72)	14 (28)	0.34	1.56 (0.63, 3.84)
Height				
Median ± SD	160 ± 8.9	164 ± 5.2	**0.015**	
> 161*	51 (86.4)	8 (13.6)		
≤ 161	29 (63)	17 (37)	**0.005**	**3.74 (1.44, 9.72)**
Weight				
Median ± SD	75 ± 13.2	62 ± 11.3	**<0.0001**	
> 70*	55 (90.2)	6 (9.8)		
≤ 70	25 (56.8)	19 (43.2)	**<0.0001**	**6.97 (2.48, 19.56)**
BMI				
Median ± SD	29.5 ± 6.5	23.7 ± 4.2	**<0.0001**	
> 25*	64 (90.1)	7 (9.9)		
≤ 25	16 (47.1)	18 (52.9)	**<0.0001**	**10.27 (3.67, 28.83)**
Marital status				
Married*	6 (75)	2 (25)		
Single	74 (76.3)	23 (23.7)	0.94	1.06 (0.37, 2.77)
Nationality				
Arab*	70 (83.3)	14 (16.7)		
Non-Arab	10 (47.6)	11 (52.4)	**0.001**	**5.50 (1.96, 15.42)**
Menopause status				
Pre*	23 (76.7)	7 (23.3)		
Post	55 (76.4)	17 (23.6)	0.98	1.02 (0.37, 2.78)
Religion				
Muslim*	68 (82.9)	14 (17.1)		
Christian	11 (52.4)	10 (47.6)	**0.007**[d]	**4.42 (1.57, 12.39)**
Education level				
School/Collage*	43 (81.1)	10 (18.9)		
University/Higher education	34 (70.8)	14 (29.2)	0.23	1.77 (0.70, 4.48)
Monthly income				
> 30, 000 ADE*	30 (68.2)	14 (31.8)		
≤ 30, 000 ADE	10 (83.3)	2 (16.7)	0.30	0.43 (0.83, 2.22)
Employment status				
Homemaker*	50 (84.7)	9 (15.3)		
Full time/ Part time	29 (65.9)	15 (34.1)	**0.02**	**2.87 (1.12, 7.39)**
Oral contraceptive pills use				
Never*	37 (77.1)	11 (22.9)		
Ever	35 (72.9)	13 (27.1)	0.64	1.25 (0.50, 3.16)
Oral contraceptive pills duration				
< 3 years*	22 (88.0)	3 (12.0)		
≥ 3 years	12 (54.5)	10 (45.5)	**0.01**	**6.11 (1.41, 26.57)**
HRT use				
Never*	58 (72.5)	22 (27.5)		
Ever	13 (92.9)	1 (7.1)	0.10	0.20 (0.03, 1.64)
Family history of breast cancer				
No*	49 (71)	20 (29)		
Yes	21 (84)	4 (16)	0.20	0.47 (0.14, 1.53)

Table 5. Continued

Factors	Mammographic density patterns		P-value[b]	Unadjusted OR (95% CI)[c]
	Fatty breast tissue N (%)	Dense breast tissue N (%)		
Age at first menarche				
Median ± SD	22 ± 4.5	24.5 ± 5.3	0.89	
> 13*	25 (69.4)	11 (30.6)		
≤ 13	54 (79.4)	14 (20.6)	0.26	0.59 (0.24, 1.48)
Age at first delivery				
Median ± SD	13 ± 1.3	13 ± 1.7	0.09	
> 25*	18 (75)	6 (25)		
≤ 25	49 (80.3)	12 (19.7)	0.58	0.74 (0.24, 2.25)
Number of children				
Median ± SD	3 ± 2.63	2 ± 1.91	**0.002**	
> 3*	33 (70.2)	14 (29.8)		
Nulliparous	5 (45.5)	6 (54.5)	**0.003**	**10.8 (2.23, 52.08)**
≤ 3	36 (90)	4 (10)	**0.03**	**3.81 (1.14, 12.77)**
Breast feeding				
Median ± SD	12 ± 7.7	12 ± 7.8	0.40	
> 12 months*	32 (84.2)	6 (15.8)		
≤ 12 months	35 (77.8)	10 (22.2)	0.46	0.66 (0.21, 2.01)

Note. **Boldface items** indicate statistically significant associations (P < 0.05); [a] Fatty breast density includes "entirely fatty breast and scattered fibroglandular dense tissues" whereas dense breast density includes "heterogeneously breast and extremely dense breast tissues"; [b]Obtained from Pearson's chi-squared test for categorical variables and Mann-Whitney U test for continuous variables; [c]Obtained from binary logistic regression; [d] Obtained from Fisher's Exact Test. One cell has an expected frequency less than 5.; *Reference group for odds ratio; Abbreviation: N= Number, SD, Standard Deviation; BMI, Body Mass Index; OR, Odds Ratio; CI, Confidence Interval; OC, Oral Contraceptive; HRT, Hormone Replacement Therapy.

Discussion

The study found that the majority of participants fell into BI-RADS b and c mammographic density categories, which is similar to findings in the United States (US) and Asian states (Titus-Ernstoff et al., 2006; Jeon et al., 2011; Dai et al., 2014). This distribution of BI-RADS density in our sample might, however, have been influenced by the high degree of ethnic diversity in the RAK emirate. As the first investigation of its kind in the GCC region, the ethnicity analysis showed that of all ethnic groups included in the study, Emirati women had the lowest mammographic density categories (BI-RADS a and b). When we compared these Emirati specific findings with those from other populations, we did not observe a similar BI-RADS distribution as shown in Figure 2. It has been suggested that genetic predisposition is by far the most attributable reason for racial differences in mammographic density as it accounts to up to 60% of reported variance in density (Boyd et al., 2002). This rational might support the assumption that breast composition is not consistent across global regions, and may also indicate a possible epidemiological difference in breast cancer etiology for Emirati women (Casado et al., 2015).

Our findings from the interview sample were commensurate with those from previous studies in that high BMI and parity were associated with lower mammographic density (Titus-Ernstoff et al., 2006; Jeon et al., 2011). However, as most of the previous studies have reported only BMI (without its constituent factors of body height and weight), it was difficult to validate our finding that lower body height was significantly associated with increased mammographic density.

The positive association between high BMI and lower mammographic density is well-established (Boyd et al., 2005). Therefore, our finding that Emirati women were in the lowest mammographic density categories (BI-RADS a and b, Table 1) was expected because of the substantial number of overweight and obese women recorded in this study (Figure 1). Our results are supported by a recently published study among Croatian women which found that approximately 87% of women fell into the lowest mammographic density categories (BI-RADS a and b) and that 71% of participants were overweight or obese (BMI ≥ 25 kg/m^2) (Tesic et al., 2013). We acknowledge, however, that lower mammographic density distribution among Emirati women remained significant after controlling for BMI in our ethnicity stratified regression analysis presented in Table 3. This suggests that other possible attributable agents for the reported low mammographic density among Emirati women that need to be considered.

Low mammographic density patterns among Emirati women could be partly explained by the use of reproductive medication explored in this study. It has been reported that the combined use of estrogen and progesterone therapy significantly increases mammographic density as a result of increased epithelial cell proliferation (Couto et al., 2012). The proportion of current HRT users in our study was low (14.3%, 6 women were Emirati) which is comparable to the proportion reported in studies of Croatian (5.8%)

(Tesic et al., 2013) and Jamaican (14%) (Soares et al., 2002) women. In comparison, the proportion of postmenopausal US women who have used HRT ranged from 48% to 55.5% (El-Bastawissi et al., 2001; Barlow et al., 2006).

The observed association between mammographic density and occupation seen here is consistent with a report from Iran (Rahmani et al., 2013), which reported that employed women were more likely to have denser breasts. The author argued that high mammographic density observed among employed women might be due to the relatively increased prevalence of physical activity compared to unemployed women. Although evidence around the association between mammographic density and physical activity is unclear (Ekpo et al., 2016), reduction in the amount of adipose tissue corresponding to the increase in muscle mass seen in physically active individuals (Ekpo et al., 2016) might serve as a potential explanation.

In the current investigation, the results of unadjusted ORs showed that that Christian women were significantly more likely to have denser breasts compared with Muslim women. As the majority of Christian participants were women from Western countries, it could be inferred that the Western lifestyle involving the use of HRT (Couto et al., 2012) and alcohol consumption (Cabanes et al., 2011) might explain this association. However, when adjusted for ethnicity, the significant association disappeared indicating the confounding effect of ethnicity on mammographic density.

Consistent with some (Jeon et al., 2011; Rahmani et al., 2013) but not all previous work (Tesic et al., 2013), there was no significant association between the use of OC and increased mammographic density. On the other hand, the duration of OC use was significantly associated with increased mammographic density in our study (≥ 3 years, Table 5). Since previous works did not report the duration of oral OC use, comparisons between current and past studies are difficult. From a clinical perspective given the proportion of women seen in this study who used OC (36% of users were Emirati women), consideration should be given to informing Emirati women that there is a slightly increased risk of developing breast cancer for recent OC users (1.1-2 Relative Risk). The risk diminishes after cessation of OC for 10 years or more (American Cancer Society, 2013).

Our finding in regard to the lack of association between mammographic density and age at first menarche and age at first delivery differs from a number of published reports (Jeon et al., 2011; Tesic et al., 2013; Kawahara, 2015). However, in a New Hampshire study of more than 140,000 US women aged 40-89 years the impact of reproductive factors on mammographic density was less evident in women with high BMI (≥ 30 kg/m^2) (Titus-Ernstoff et al., 2006). Taking into account the high proportion of Emirati women were obese (Figure 1), this could possibly explain the lack of associations between mammographic density and age at first menarche and age at first delivery in the current work.

It is well-established that increased mammographic density plays an important role in reducing mammographic sensitivity (Ekpo et al., 2015). It is also responsible for nearly 50% of interval breast cancer rates (cancer diagnosed within a year after a negative mammography) as a result of the masking effect (Ekpo et al., 2015). In addition, higher mammographic sensitivity has been reported in women with low breast density grading. A large cohort study of more than 2,000 US women aged 40-89 years, showed that the adjusted sensitivity of mammography in women with BI-RADS a and b density categories were 87% and 82%, respectively, compared with 69% and 63% in women with BI-RADS c and b density categories (Carney et al., 2003). Considering that the majority of Emirati women were in the lowest mammographic density categories (BI-RADS a and b), one important potential implication of our study is that mammography would be an effective screening tool for Emirati women (del Carmen et al., 2007), since arguably subtle lesions would be less obscured by dense breast tissue (Galukande and Kiguli-Malwadde, 2012; Kerlikowske et al., 2013). It should be acknowledged, however, this is an argument is based on film screen technology, and therefore according to (Mousa et al., 2014), does need further digitally-based studies to support the contention.

Another important implication could be derived from the current work is regarding the appropriate age to start screening by mammography (Soares et al., 2002; Galukande and Kiguli-Malwadde, 2012). The current mammography screening guideline for Emirati women is to start screening at 40 years and return every 2 years thereafter. According to the World Health Organization (WHO), the highest breast cancer incidence in the UAE is found among women in the 40-49 years age group with age-standardized rate of 162.4/100,000 women (International Agency for Research on Cancer, 2012). In our study the prevalence of high breast density (BI-RADS c and d) in Emirati women aged 40-49 years was only 9.2% (n=98) compared with 38.3% among Korean women (Jeon et al., 2011). Therefore, based on current results which are supported by other recent suggestions (Soares et al., 2002; Galukande and Kiguli-Malwadde, 2012), it seems advisable to at least maintain the current starting age for screening and also to explore if it may be potentially advantageous to invite younger women to be screened, particularly if higher mammographic density may not be a major impediment to screening and a high incidence of breast cancer persists at earlier ages.

The current paper has some limitations. First, it can be argued that the BI-RADS method of mammographic density assessment is a subjective approach. It should be acknowledged, however, that good inter-observer agreement has been reported for BI-RADS b, c, and d density categories and excellent for the BI-RADS a density category (Roubidoux et al., 2003). Second, the study involved a relatively small sample size of women even though we obtained all available mammography cases from 2014 and 2015. It should be noted that we do not know if our findings apply to a wider population of Emirati women since RAK population represents only 4.8% of the UAE population (Government of Ras Al Khaimah, 2013). Therefore, additional studies using volumetric mammographic density measurement at population level are needed to validate our findings and to enhance our understanding of mammographic density in Emirati women.

This cross-sectional study is the first of its kind to evaluate the mammographic density profile of women living in RAK. It showed that Emirati women had the most fatty breast parenchyma compared with other ethnic groups in the study. It also highlighted significant associations of mammographic density with age, weight, height, BMI, ethnicity, employment, parity, religion, and the duration of OC use. One important clinical implication of our study is that due to the low mammographic density profile, screening mammography can be considered as an appropriate early detection imaging modality for Emirati women. It also seems advisable to at least maintain the current starting age for mammography screening and to explore if potential advantages could result from inviting younger women.

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Conflict of Interests

The authors have no conflict of interest to declare.

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