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By Shahad A Ibraheem, Rozi Mahmud, Suraini Mohamad Saini, Norafida Bahari  
& Mousa Alazzwi

*Universiti Putra Malaysia*

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**Methods:** A self-administration questionnaire that included information of patients and an analytic cross-sectional study design was used to determine the morphology of normal breast among all respondents that attending the imaging department of Golden Horses Health Sanctuary, Sri-Kembangan located in Klang Valley, Selangor, Malaysia. All women were subjected to bilateral whole breast ultrasound using ultrasound.

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**GJMR-D Classification:** NLMC Code: QT 34



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Shahad A Ibraheem <sup>α</sup>, Rozi Mahmud <sup>σ</sup>, Suraini Mohamad Saini <sup>ρ</sup>, Norafida Bahari <sup>ω</sup> & Mousa Alazzwi <sup>✱</sup>

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**Results:** About 615 women were examined from October 2013 to December 2014 within age groups from 20-70 years old and different ethnic group (Malay, Chinese and Indian). The majority of mean age were 45.92, the mean of menopausal of premenopausal age was 43.00(SD5.54), while for post-menopausal age was 49.79(SD3.53). Studies were equal among age groups, religion, education level, occupation, income and marital status and some tissue in different quadrant for right and left breast i.e subcutaneous fat of left breast in UOQ (L=0.48, p-value=0.75), LOQ (L=1.82, p-value=0.13) and UIQ (L=1.27, p-value=0.24).

**Conclusion:** Study shows that there was variation and association in tissue with age, ethnic and religion in different quadrants with p-value > 0.05, except in some quadrant of other tissue of right and left breast quadrants, while in education level, occupation, income and marital status there were no association with breast morphology.

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## 1. INTRODUCTION

The breast which is primarily influenced by the endocrine system serves as a secondary sex organ in humans and also possesses the ability to produce milk in mammals. With these vital functions of the breast, it is important for the radiologist to understand the normal anatomy and physiology of the breast in order to be able to identify abnormalities which may occur in any breast [1]. The major anatomical structures in the breast include skin, fat, facial layers, Cooper ligaments, fibro glandular tissue, lymphatic, and neurovascular structures, which are all placed over the chest wall. The volume of fibro glandular tissue in women differs with age, with many women having more fat within the breasts after menopause [2]. Breast ultrasound plays a major role in the identification, diagnosis, and staging of breast cancer [3,4]. At present, it is generally assumed that glandular tissue, which is a common site for breast cancer, is the most vulnerable among the tissues (adipose, skin, and areolar tissues) making up the breast [5]. The amount of glandular tissue is linked to breast cancer risk, so an objective quantitative analysis of glandular tissue can aid in risk estimation [6]. Based on the study, the morphology of breast using ultrasound assessment suggesting that in young non lactating breast, the tissue is primarily composed of fibro glandular tissue with little or no subcutaneous fat. With increasing age and parity, fat is deposited in both the subcutaneous and retro mammary layers [7]. The difference in incidence rates between the Malays and Chinese can be explained in terms of the risk factors e.g. Increasing age, geographic location, family history, reproductive factors, oral contraceptives, Hormone replacement therapy and more, known to be associated with breast cancer. There is also a possibility of under-reporting in Malay women because they are more likely to seek alternative therapy and hence not present to the medical practitioner [8]. The main reason for conducting this study is to reduce breast cancer percentage in Malaysia by early detection of abnormalities which may lead to cancer, and that can be done by referencing the diagnosis of

**Author α σ ω:** Department of Imaging, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia.

**Author ρ:** Department of Imaging, Universiti Putra Malaysia, Faculty of Medicine and Health Sciences, 43400 Serdang, Selangor, Malaysia.  
e-mail: surainims@upm.edu.my

**Author ✱:** Public Health Clinic, Sharjah, UAE.

normality and its measurements in different age and ethnic groups.

## II. PATIENTS AND METHOD

### a) Study design and population

Analytic cross-sectional research design was conducted from October 2013 to December 2014 on females admitted to the imaging department of Golden Horses Health Sanctuary (GHHS) for breast checking in Seri Kembangan district located within Klang Valley, Selangor, Malaysia. Respondents were identified and selected using modest random sampling method. Subjects were randomly selected from the list of respondents that went to the Imaging Department in the GHHS using SPSS. This list was used as sample frame. A total of 615 females were selected.

### b) Data collection

Data was collected using self – administered questionnaires which was developed and validated especially for this study. All women subjected to bilateral whole breast ultrasound examination using Philips ultrasound iu22. Both breasts were scanned utilizing clockwise, overlapping radial approach. The breast divided into four quadrants. Each quadrant was scanned in a radial fashion to accommodate the arrangement of ducts in the breast with a linear array probe L17-5 (5-17MHz), depth 3.5-4.0 cm and gain 86%-87%. Data are acquired at the region of interest (ROI).

### c) Inclusion Criteria

The inclusion criteria for normal breast respondents were females aged 20 to 70 years.

### d) Exclusion Criteria

- A. Male
- B. Females < 20 years old because permission was needed from parents
- C. Females > 70 years old because no obvious changes occurred on breast
- D. Women that used contraceptive pills or device.
- E. Women that used hormone replacement therapy.
- F. Women with history of breast diseases such as:
  - i. *Benign breast tumors*: fibrosis or cysts and fibroadenoma or intraductal papilloma are abnormal growths which caused a change in the breast tissues.
  - ii. *Malignant breast tumors*: carcinoma, adenocarcinoma, carcinoma in situ, invasive carcinoma and sarcoma are types of breast cancer that grow in glandular tissue and breast duct.
  - iii. Breast infections such as mastitis occurred frequently during breast feeding.
  - iv. Nipple infections, mammary duct ectasia and intraductal papilloma caused nipple discharge.

### e) Ethical consideration

Ethical approval to conduct the study was obtained from medical research ethnics committee of the Universiti Putra Malaysia. Then approval was obtained from The Medical Research and Ethics Committee, Ministry of Health - Malaysia. A written consent was taken from each respondent before conducting the survey.

### f) Statistical analyses

All analyses were performed using SPSS<sup>®</sup> software, version 21.0 (SPSS Inc., Chicago, IL, USA). Normality test were done and all of the quantitative data were found to be normally distributed. Descriptive statistical analysis, which included frequency, mean and standard deviation (SD), was used to characterize the data. Parametric test (one-way ANOVA and t-test) and non-parametric test (Kruskal Wallis and Mann-Whitney) employed to determine the association between normal breast morphology and socio-demographic factors, family information and gynecology history. The level of statistical significance was set at  $\alpha < 0.05$ .

### g) Breast image analysis

For measuring and analyzing the breast tissues, Philips DICOM Viewer software (R 3.0- SP03) was used. The measuring unit for each tissue is (mm), and the dimensions were obtained. Furthermore, all the measured data were collected by uni-dimensional (length) for subcutaneous fat while two-dimensional (length × width) for glandular tissue and fat lobules, sizing from three different areas for each tissue three readings were taken and average obtained to minimize errors.

## III. RESULT

Total of 700 respondents were selected as sample for this study. However 85 respondents (12.14%) returned questionnaires were omitted due to either incomplete answers or were inaccurately completed. Hence, 615 females participated in this study were counted. The giving response rate in this study was 87.9%.

### a) Factors associated with performing US on breast morphology

Table 1 shows the distribution of respondents according socio-demographic factors (age, race, religion, education level, occupation, and income), family information (marital status), and gynecology history (menarche age, menopause age and family history of breast cancer). Overall, the majority of mean age were 45.92 (SD= 12.94), Chinese 326(51.4%), Buddhism 282(45.9%), having degree 114 (18.5%), most of them working 209(60%), having income rang 1001-3000RM, married 538(87.5%), the mean of first menstrual cycle was 12.1(SD0.64), the mean of menopausal of premenopausal age was 43.00(SD5.54),

while for post-menopausal age was 49.79(SD3.53) and 46(7.5%) of respondents reported having a family history of breast cancer.

*Table 1:* Socio-demographic data of respondents (n=615)

Characteristics	Frequency	Percent (%)	Mean±SD
<b>Age groups</b>			45.92 ± 12.94
20-29	78	12.7	
30-39	137	22.3	
40-49	112	18.2	
50-59	184	29.9	
60-70	104	16.9	
<b>Ethnicity</b>			
Malay	203	33	
Chinese	326	51.4	
Indian	96	15.6	
<b>Religion</b>			
Muslim	208	33.8	
Christian	40	6.5	
Buddhism	282	45.9	
Hinduism	85	13.8	
<b>Educational level (n=237)</b>			
Primary/ secondary	28	4.6	
Diploma	82	13.3	
Degree	114	18.5	
Postgraduate	13	2.1	
<b>Employment status (n=349)</b>			
Student	25	7.2	
Working	209	60	
Housewife/retiree	115	32.4	
<b>Income (n=221)</b>			
<1000	7	3.2	
1001-3000	105	47.5	
3001-5000	94	42.5	
>5000	15	6.8	
<b>Marital status</b>			
Single	75	12.2	
Married	538	87.5	
Widower	2	0.3	
<b>Age of first menstrual</b>			12.1 ± 0.64
<b>Menopausal age</b>			
Premenopausal age			43.00 ± 5.54
Postmenopausal age			49.79 ± 3.53
<b>Family history of breast cancer</b>			
Yes	46	7.5	
No	569	92.5	

Data presented as mean ± SD for age groups

The percentage of participants who performed Ultrasound was 615 (100%). Among those who did ultrasound wide range of breast tissue size founded.

As shown on Table 2 and Table 3 the relationship between breast morphology and socio demographic parameter, family information and gynecology history. In each quadrant of the breast, the distribution varied between normal and non-normal. For analyzing normal data one-way ANOVA and t-test was used to find the association between breast morphology and socio demographic factors, marital status and breast cancer history after using homogeneity test of

variance, and according to that test plus Levene statistics, variances were equal among age groups, religion, education level, occupation, income and marital status and some tissue in different quadrant for right and left breast i.e subcutaneous fat of left breast in UOQ (L=0.48, p-value=0.75), LOQ (L=1.82, p-value=0.13) and UIQ (L=1.27, p-value=0.24) respectively. For non-normal data, nonparametric test of Kruskal Wallis and Mann-Whitney was used. At the current study, there was

variation and association in tissue with age, ethnic and religion in different quadrants with p-value > 0.05, except in some quadrant of other tissue of right and left

breast quadrants, while in education level, occupation, income and marital status there were no association with breast morphology.

**Table 2:** Association between right breast morphology and socio demographic in different quadrants for normal and non-normal distribution

Breast morphology	Socio demographic factors											
	Age				Ethnic				Religion			
	F	P-value	$\chi^2$	P-value	F	P-value	$\chi^2$	P-value	F	P-value	$\chi^2$	P-value
<b>Subcutaneous fat</b>												
Upper outer	23.62	0.000*										
Lower outer	25.46	0.000*			8.47	0.000*			6.48	0.000*		1.34 0.260
Lower inner			65.8	0.000*	11.99	0.000*			7.20	0.000*		4.81 0.003*
Upper inner	24.4	0.000*			12.40	0.000*			7.76	0.000*		3.53 0.016*
							13.11	0.001*			12.26	0.007* 3.23 0.023*
<b>Glandular tissue</b>												
Upper outer	3.82	0.004*			19.48	0.000*			13.62	0.000*		2.44 0.065
Lower outer			14.52	0.006*	17.12	0.000*			11.57	0.000*		1.91 0.129
Lower inner			14.12	0.007*	6.68	0.001*			5.21	0.001*		2.82 0.039*
Upper inner			14.57	0.006*	14.60	0.000*			9.38	0.000*		1.20 0.310
<b>Fat lobules</b>												
Upper outer			12.64	0.013*	27.13	0.000*			19.03	0.000*		2.41 0.067
Lower outer			11.58	0.021*	36.56	0.000*			23.56	0.000*		2.82 0.04*
Lower inner			9.83	0.043*	38.12	0.000*			26.19	0.000*		1.99 0.12*
Upper inner			13.49	0.009*	30.68	0.000*			22.35	0.000*		2.23 0.085

\*significance value at level  $p < 0.005$

Breast morphology	Socio demographic factors									
	Occupation				Income				Marital status	
	F	P-value	$\chi^2$	P-value	F	P-value	$\chi^2$	P-value	F	P-value
<b>Subcutaneous fat</b>										
Upper outer	14.51	0.000*								
Lower outer			33.52	0.000*	2.24	0.084			1.34	0.260
Lower inner			24.14	0.000*	2.87	0.037*			4.81	0.003*
Upper inner	10.21	0.000*			4.62	0.004*			3.53	0.016*
					3.95	0.009*			3.23	0.023*
<b>Glandular tissue</b>										
Upper outer	1.53	0.22			1.76	0.16			2.44	0.065
Lower outer	1.48	0.23			1.66	0.18			1.91	0.129
Lower inner			4.65	0.098			10.43	0.02*	2.82	0.039*
Upper inner	1.78	0.17			0.58	0.63			1.20	0.310
										-0.76 0.011*
<b>Fat lobules</b>										
Upper outer	2.90	0.057			2.49	0.061			2.41	0.067
Lower outer	5.10	0.007*			3.37	0.019*			2.82	0.04*
Lower inner	7.86	0.000*					2.07	0.56	1.99	0.12*
Upper inner	3.15	0.044*			1.52	0.21			2.23	0.085
										-0.73 0.064

\*significance value at level  $p < 0.005$

Table 3: Association between left breast morphology and socio demographic in different quadrants for normal and non-normal distribution

Breast morphology	Socio demographic factors											
	Age			Ethnic			Religion			Education level		
	F	P-value	χ <sup>2</sup>	P-value	F	P-value	χ <sup>2</sup>	P-value	F	P-value	χ <sup>2</sup>	P-value
<b>Subcutaneous fat</b>												
Upper outer	8.66	0.000*										
Lower outer	5.51	0.000*			7.61	0.001*					19.14	0.000*
Lower inner			7.33	0.000*			17.95	0.000*	6.69	0.000*	3.68	0.013*
Upper inner	4.19	0.002*					33.91	0.000*			30.87	0.000*
							15.22	0.000*			14.03	0.003*
											2.92	0.035*
<b>Glandular tissue</b>												
Upper outer												
Lower outer			68.41	0.000*	28.04	0.000*			19.43	0.000*	4.05	0.008*
Lower inner			31.84	0.000*	22.12	0.000*			14.08	0.000*	3.07	0.029*
Upper inner			26.61	0.000*	16.05	0.000*			11.64	0.000*		10.08
			47.37	0.000*	24.90	0.000*			17.56	0.000*	3.59	0.014*
<b>Fat lobules</b>												
Upper outer			24.85	0.000*	27.36	0.000*			17.22	0.000*	0.93	0.430
Lower outer			40.27	0.000*	31.78	0.000*			19.79	0.000*	4.01	0.008*
Lower inner			69.59	0.000*	26.68	0.000*			18.39	0.000*	1.73	0.160
Upper inner			46.77	0.000*	30.09	0.000*			18.31	0.000*	2.21	0.087

\*significance value at level p<0.005

Breast morphology	Socio demographic factors											
	Occupation				Income				Marital status			
	F	P-value	$\chi^2$	P-value	F	P-value	$\chi^2$	P-value	F	P-value	$\chi^2$	P-value
<b>Subcutaneous fat</b>												
Upper outer	9.61	0.000*		3.26	0.02*				9.98	0.000*		
Lower outer	13.14	0.000*		4.47	0.005*				10.41	0.000*		
Lower inner	19.84	0.000*		4.10	0.007*				13.47	0.000*		
Upper inner	13.37	0.000*		6.03	0.001*				9.87	0.000*		
											13053.5	0.977
<b>Glandular tissue</b>												
Upper outer			9.50	0.009*								
Lower outer	1.35	0.26					6.82	0.078			1.92	0.38
Lower inner	2.27	0.11		1.14	0.34						5.02	0.081
Upper inner	0.83	0.44					6.75	0.08			5.88	0.05*
				2.41	0.07						0.35	0.84
<b>Fat lobules</b>												
Upper outer	0.96	0.38					2.49	0.48			5.10	0.078
Lower outer			11.74	0.003*			5.66	0.13			4.06	0.13
Lower inner	3.72	0.025*		1.52	0.21						6.76	0.034*
Upper inner	2.77	0.064					9.91	0.02*			3.84	0.15

\*significance value at level  $p < 0.005$



## IV. DISCUSSION

Aging of human breast tissue is often followed by particular structural and functional changes and these changes have been linked by several research findings to the development of aging-related cancer. At the cellular level, morphological and functional changes which may include increased cell size and decreased proliferation may result in aging of human mammary epithelial cells [9]. The development of the breast begins from the stage of fetal development with mammary ridge or milk line which is usually a thickening in the chest region after which the nipples and milk duct system begin to develop when the baby is born, then at puberty stage, child-bearing phase, during menstrual cycle and finally at menopause [10].

In the present study the finding is consistent as in other studies which linked age with breast changes [11, 12]. Our work confirms that an increase in age is associated with a reduction in glandular tissue. Moreover the increment of fat in the breast and the radiographic appearance of the breast vary among women of the same age because of variations in breast tissue composition [13]. Most of the studies done in Malaysia, focused on the knowledge of breast cancer screening using mammography or breast self-examination with socio demographic factors such as [14-16]. These studies have similar findings of the association of women with ethnicity, religion, occupation, income, marital status, degree level of education. Family history of breast cancer was higher than those with secondary or primary level of education ( $p < 0.001$ ). Only a few studies have reported on the variation of breast density by race, however, one study done in Department of Imaging, Country Height Health Sanctuary, Malaysia With the total number of 610 subjects, there were significant associations between breast density and age group and there were no significant association with ethnic groups [17-20]. This is important, because different racial/ethnic groups have different breast cancer risk and these differences change with age [21]. Furthermore, some studies found higher breast cancer risk among women with professional occupations such as nursing [22] and teaching [23-26]. A study by Rubin et al., (1993) found teachers to be twice at risk of breast cancer mortality compared to other women. Although marital status have been commonly identified by various studies [27-30] as a positive factor in early cancer diagnosis and better survival, local studies [31,32] to date have not established any significant relationship between marriage and uptake of breast cancer screening. However, there was a study among female secondary school teachers from 20 selected secondary schools in Selangor, Malaysia to determine the knowledge and practices on breast cancer screening and socio demographic but there was no significant knowledge

[33]. Yet no studies have been carried out on normal breast morphology related to the socio demographic factors using ultrasound.

## V. LIMITATION

As this study was designed to be cross-sectional. It may not be possible to conclude that the factors were found to be associated with normal breast morphology predated onset. Incidentally all the respondents that were selected from GHHS which is located in urban area; hence, the result cannot be generalized to both urban and rural.

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