RESEARCH ARTICLE

Inconsistencies of Breast Cancer Risk Factors between the Northern and Southern Regions of Vietnam

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Abstract

Background: In recent decades the amount of new breast cancer cases in the southern region has been reported to increase more rapidly than in the northernVietnam. The aim of this study is to compare breast cancer risk factors between the two regions and establish if westernized influences have an impact on any reported differences. **Method:** Data was collected from the two largest oncology hospitals in the north and the south of Vietnam in 2015. Breast density, demographic, reproductive and lifestyle data of 127 cases and 269 controls were collected in the north and 141 cases and 250 controls were gathered from the south. Baseline differences in factors between cases and age-matched controls in each region were assessed using chi-square tests and independent t-tests. Odds ratios (OR) for independent risk factors for breast cancer were obtained from conditional logistic regression. **Results:** In northern Vietnam significantly increased risks in developing breast cancer were observed for women with age at first menstrual period less than 14 years old (OR=2.1; $P<0.05$), post-menopausal status (OR=2.6; $P<0.0001$), having less than 2 babies (OR=2.1; $P<0.05$). Southern Vietnamese women having a breast density of more than 75% (OR=2.1; $P<0.01$), experiencing post-menopause (OR=1.6; $P<0.05$), having a history of less than 3 pregnancies (OR=2.6; $P<0.0001$) and drinking more than a cup of coffee per day (OR=1.9; $P<0.05$) were more likely to be diagnosed with breast cancer. **Conclusion:** We found that women living in the south had some breast cancer associations, such as increased mammographic density and coffee consumption, which are closer to the risks in westernized populations than women in the north.

Keywords: Breast cancer- case-control- epidemiology- public health

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Introduction

Breast cancer is currently known as the most common cancer affecting Vietnamese women (Ferlay et al., 2015). Although the rate of women diagnosed with breast cancer in Vietnam is relatively low at 23 per 100,000, compared to 120 per 100,000 for Caucasian women (WHO, 2012), this rate has increased by approximately 45% in the last decade, from 16 per 100,000 in 2002 resulting in breast cancer to be the most common carcinoma for women in Vietnam (Duc NB, 2009). In addition, breast cancer incidence rates within regions in Vietnam are not identical and vary based on geographic location. Hanoi and Ho Chi Minh City (HCMC) are the largest cities in the northern and the southern Vietnam with similar populations and ethnicities; yet it was reported that Hanoi had higher incidence rate of breast cancer at 26.7 per 100,000 in the 1990s , which was double the rate in HCMC (12.2 per 100,000) (Nguyen et al., 1998; Anh and Duc, 2002). Interestingly however since that time, the rate of new breast cancer cases in the south has increased much faster to 19.4 per 100,000 in the 2000s compared with the north (29.7 per 100,000) (Duc NB, 2009). Whilst the two cities are part of the same country, they have been subjected to relatively different historical events and subsequently, the south of Vietnam, particularly Ho Chi Minh City, is considered to be much more westernized than the northern areas. This westernization is probably due to the French and American presence from the mid 19th to mid 20th centuries and the rapid development of a commercial ethos within the last two decades. There are also several differences in regard to cultural customs and lifestyle behaviors between people in the northern and the southern Vietnam which might relate to regional variations in the incidence rate of breast cancer.

The aim of this study was to compare clinically recognized breast cancer risk factors in the north and the south of Vietnam. This comparison may help to explain the difference in the breast cancer incidence rates between two regions and facilitate an effective, region-specific

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national breast screening programs.

Materials and Methods

Study population

Data were gathered prospectively at the largest cancer centres located within the north (Vietnam National Cancer Hospital) and the south of Vietnam (Ho Chi Minh City Oncology Hospital) in 2015. On average, each centre attracts more than 1000 patients per day who attend for cancer screening and treatment. Referral patterns to hospitals are issued by the Vietnam Department of Health and they are similar between National Cancer Hospital and Ho Chi Minh City Oncology Hospital. The epidemiological data used in this study were gathered from three sources: a standardized clinical assessment form completed by a radiologist, a pathologist's report if a biopsy test was undertaken and a self-administered questionnaire obtained from women undergoing screening or diagnostic testing.

Participants were recruited at the radiology departments because a major aim of the study, considered partly in this paper, was to assess mammographic density. Women who came for mammography either on screening or diagnostic request were invited to fill in a questionnaire which was designed following similar studies in westernized countries (Boyd et al., 2007; Wilson et al., 2013). A subject was considered as a resident of the north or the south if they have been living in a province or a city in the north or the south region during the last 10 years. For each cancer case which was biopsy proven via pathology report, we selected data of up to one or two controls who were not diagnosed with breast cancer (confirmed by negative radiology report) but matched for age, ethnicity and region. Females with a history of breast cancer treatment or with a pending breast biopsy result were excluded from the data analysis. In total, there were 127 cancer cases and 268 controls in the north and 141 cancer cases and 250 controls in the south that fulfilled the criteria. Ages of participants were between 27 and 74 years.

Study variables

Breast densities in the form of BI-RADS (the American College of Radiology Breast Imaging Reporting and Data System) were assessed by a single reading of radiologist which is routine practice at the radiology departments in Vietnam. There were 7 radiologists in two hospitals who assessed the images with 1 representing fibroglandular tissues accounting for less than 25% of the breast; 2 representing breast density 25-50%; 3 - breast density 51-75%; and 4 for a very dense breast with breast density >75% (American-College-of-Radiology, 2004).

Other study variables consisted of demographic data (residency, ethnicity, age, body mass index (BMI - calculated as weight (kg)/height (m) squared) and reproductive information (age at first menstrual period, number of pregnancies, number of babies born, age at having first and last birth, menopause status, age at menopause). The information of current and past use of hormone replacement therapy and daily oral contraceptive was also sought. In addition, information about family history of breast cancer was requested. First degree family history of breast cancer was recorded if the participant had a mother, sister or daughter diagnosed with breast cancer whilst second degree was for the case with grandmother or relative.

Participants were also asked about their lifestyle in regard to alcohol intake, smoking, and physical activities. Alcohol consumption and smoking were identified when participants reported having ever drunk weekly at least a cup of beer, wine or spirits in half of a year months or smoked at least a cigarette per day in twelve weeks. Information about physical activity was also sought from women in form of how long they spent on physical activities weekly which was classified as: inactive, insufficient (1 to 150 minutes) and sufficient (more than 150 minutes) (AIHW, 2003). Short questions about frequency of soy drinking, coffee drinking and vegetable intake were also sought from the subjects. Informed consents were obtained from participants. Ethics approval for this study was obtained from the Research Ethics Board of University of Sydney and the Ho Chi Minh city University of Medicine and Pharmacy. Approvals for data collection were also granted by the Vietnam National Cancer Hospital and Ho Chi Minh City Oncology Hospital.

Statistical methods

The statistical methods in this study followed the approaches employed in previous studies of breast cancer risk factors (Boyd et al., 2002; Wong et al., 2011). Firstly, differences in each of features between cases and controls were assessed separately for women in the northern and southern areas using chi-square tests for categorical variables and independent t-tests for continuous variables. Secondly, optimal cut-off points obtained from a ROC curves of continuous variables were used to assign these variables into two groups: above or below the cut-off point (Barton, 2014). Thirdly, conditional logistic regression was then applied to generate odds ratios (OR) for significant factors related to breast cancer in each region and 95% confidence intervals (CI) around ORs were computed. Finally, to maintain power and avoid overfitting models, significant factors associated with breast cancer found in univariate analysis were then tested using a forwards sequential method for the conditional multiple logistic regressions. Only the significant predictors were retained in the models. This analytic process was applied for all women in each region and then reapplied for premenopausal and postmenopausal women. Due to only 22 participants from non-Kinh ethnicity, these participants were excluded from the data analysis.

The study had the power to show that an odds ratio greater than 2.0 was statistically significant when the percentage of controls exposed to the risk factor or interest was above 20%. Statistical significance required a probability value of $P<0.05$ (two-tailed test) for univariate analysis and $P<0.1$ was used as a criteria to test variables in the multivariate regression model. Levene's test was used to assess the homogeneity of controls between two regions. All analyses were conducted using SPSS statistical software package version 22 (IBM, USA).

Table 1. Homogeneity of Ages (Years) of Controls in Two Regions in Vietnam

Controls	N	Mean ± SD	Levene Statistics	P value
Northern region	268	47.9± 9.7	1.92	0.16
Southern region	250	49.5 ± 8.6		

Results

Results show that the mean ages of women with breast cancer in the north and the south were 49.2 and 49.3 years and the mean ages of controls were 47.9 and 49.5 years. Levene test showed that there was no significant difference in age between controls in the two regions

Table 2. Distribution of Cancer Cases and Controls by Potential Risk Factors among Women in the North

Factors	Category	All women					Pre-menopause women	Post-menopause women
		Cases N(%)[a]	Controls N(%)[a]	P value[b]	Unadjusted OR (95% CI)[c]	Adjusted OR (95% CI)[d]	Unadjusted OR (95% CI)[c]	Unadjusted OR (95% CI)[c]
Age (years)		127 (32.1)	268 (67.9)					
	Mean ± SD	49.2 ± 9.8	47.9 ± 9.7	0.22				
Breast density percentage								
	≤ 75	86 (67.7)	183 (68.3)	0.91	1.0 (0.6-1.6)		1	1
	>75	41 (32.3)	85 (31.7)		1		1.1 (0.6-2.1)	1.8 (0.8-4.1)
Height (cm)								
	Mean ± SD	154.3 ± 4.8	154.1 ± 5.6	0.77				
	< 155	63 (49.6)	130 (48.5)	0.84	1		1	1
	≥ 155	64 (50.4)	138 (51.5)		1.0 (0.6-1.5)		1.1 (0.6-2.0)	1.0 (0.6-1.9)
Weight (kg)								
	Mean ± SD	51.8 ± 6.8	51.9 ± 7.2	0.85				
	< 55	85 (66.9)	174 (64.9)	0.7	1		1	1
	≥ 55	42 (33.1)	94 (35.1)		0.9 (0.6-1.4)		0.6 (0.3-1.2)	1.2 (0.6-2.3)
BMI								
	Mean ± SD	21.8 ± 2.7	21.8 ± 2.7	0.77				
	< 23	89 (70.1)	191 (71.3)	0.81	1		1	1
	≥ 23	38 (29.9)	77 (28.7)		1.1 (0.7-1.7)		1.0 (0.5-2.1)	0.8 (0.4-1.5)
Age at first menstrual period								
	Mean ± SD	15.4 ± 1.9	15.8 ± 2.0	0.08				
	< 14	24 (19.0)	27 (10.1)	0.01	2.1 (1.1-3.8)*	2.1 (1.1-3.8)*	2.0 (0.9-4.7)	2.0 (0.8-5.1)
	≥ 14	102 (81.0)	240 (89.9)		1	1	1	1.0
Menopause status								
	Pre	55 (43.3)	177 (66.0)	<0.0001	1	1		
	Post	72 (56.7)	91 (34.0)		2.6 (1.7-3.9)*	2.5 (1.6-3.9)*		
Age at menopause								
	Mean ± SD	48.4 ± 4.7	48.8 ± 4.4	0.55				
	< 50	39 (54.2)	42 (46.2)	0.31	1			1
	≥ 50	33 (45.8)	49 (53.8)		0.7 (0.4-1.4)			0.7 (0.4-1.4)
Age at first giving birth								
	Mean ± SD	24.2 ± 4.2	23.7 ± 3.8	0.21				
	< 23	44 (36.7)	123 (46.1)	0.22	1		1	1
	23-29	65 (54.2)	124 (46.4)		1.5 (0.9-2.3)		1.4 (0.8-2.7)	1.3 (0.7-2.6)
	≥ 30	11 (9.2)	20 (7.5)		1.4 (0.6-3.2)		2.6 (0.8-8.8)	0.8 (0.2-2.3)
Age at last giving birth								
	Mean ± SD	30.0 ± 5.3	29.5 ± 4.6	0.38				
	< 30	60 (50.0)	142 (53.2)	0.56	1		1	1
	≥ 30	60 (50.0)	125 (46.8)		1.1 (0.7-1.7)		1.0 (0.5-1.8)	1.2 (0.6-2.2)

Table 2. Continued

Factors	Category	All women					Pre-menopause women	Post-menopause women
		Cases	Controls	P value[b]	Unadjusted OR	Adjusted OR	Unadjusted OR	Unadjusted OR
		N(%)[a]	N(%)[a]		(95% CI)[c]	(95% CI)[d]	(95% CI)[c]	(95% CI)[c]
Number of pregnancy								
	Mean ± SD	3.6 ± 1.9	4.0 ± 1.9	0.03				
	< 3	40 (31.5)	207 (77.2)	0.06	1.6 (1.0-2.5)		1.4 (0.7-2.7)	1.9 (0.9-3.9)
	≥ 3	87 (68.5)	61 (22.8)		1		1	1
Number of babies born								
	Mean ± SD	2.1 ± 0.9	2.4 ± 1.0	0.006				
	< 2	26 (20.5)	29 (10.8)	0.01	2.1(1.2-3.8)*	1.9 (1.1-3.5)*	1.3 (0.5-3.0)	3.4 (1.4-8.5)*
	≥ 2	101 (79.5)	239 (89.2)		1	1	1	1
Number of months of breastfeeding								
	Mean ± SD	15.6 ± 6.1	16.1 ± 6.0	0.43				
	< 15	48 (40)	108 (40.4)	0.93	1.0 (0.6-1.5)		0.8 (0.4-1.6)	0.9 (0.5-1.7)
	≥ 15	72 (60)	159 (59.6)		1		1	1
Hormone use								
	No	96 (75.6)	210 (78.4)	0.54	1		1	1
	Yes	31 (24.4)	58 (21.6)		1.2 (0.7-1.9)		2.1 (1.1-4.2)*	0.6 (0.3-1.3)
Family history of breast cancer								
	No	121 (95.3)	252 (94)	0.2	1		1	1
	1st degree	2 (1.6)	12 (4.5)		0.3 (0.1-1.6)		0.4 (0.05-3.4)	0.3 (0.03-2.8)
	2nd degree	4 (3.1)	4 (1.5)		2.1 (0.5-8.5)		2.2 (0.4-23.4)	1.2 (0.2-9.0)
Smoking								
	No	124 (97.6)	258 (96.3)	0.48	1		1	1
	Yes	3 (2.4)	10 (3.7)		0.6 (0.2-2.3)		0.5 (0.05-3.7)	0.8 (0.1-5.1)
Alcohol drinking								
	No	127 (100)	266 (99.3)	0.33	N/A		N/A	N/A
	Yes	0 (0)	2 (0.7)		N/A		N/A	N/A
Soy drinking								
	< 1 cup per day	114 (89.8)	230 (85.8)	0.28	1		1	1
	≥ 1 cup per day	13 (10.2)	38 (14.2)		0.7 (0.3-1.3)		0.5 (0.2-1.4)	0.9 (0.3-2.1)
Coffee drinking								
	< 1 cup per day	124 (97.6)	254 (94.8)	0.19	1		1	N/A
	≥ 1 cup per day	3 (2.4)	14 (5.2)		0.4 (0.1-1.6)		1.6 (0.4-6.8)	N/A
Vegetable consumption (serves)								
	≤ 1	6 (4.7)	13 (4.9)	0.67	1		1	1
	2—3	75 (59.1)	170 (63.4)		0.9 (0.4-2.1)		1.5 (1.2-1.5)	0.3 (0.1-1.3)
	≥ 4	46 (36.2)	85 (31.7)		1.1 (0.4-2.7)		1.3 (1.1-1.5)	0.5 (0.1-2.4)
Physical activities								
	No (Inactive)	11 (8.7)	13 (4.9)	0.14	1.9 (0.8-4.3)		1.9 (0.6-5.8)	2.0 (0.5-7.3)
	Yes (Insufficient and Sufficient)	116 (91.3)	255 (95.1)		1		1	1

[a], Number of participants (Percentage); [b], Obtained from t-test for continuous variables and chi-square test for categorical variables; [c], Unadjusted odd ratios (95% confidence interval) - Obtained from binary logistic regression; [d], Multivariable adjusted odd ratios (95% confidence interval) - Obtained from multiple logistic regression; *, Statistically significant (P < 0.05); N/A, Due to low number of cases

(P=0.16) (Table 1).

Risk factors of breast cancer in northern Vietnam

Table 2 shows the distribution of risk factors in the northern region. In the univariate analysis, significantly increased risks in developing breast cancer were observed for women with age first menstrual period earlier than 14 years old (OR=2.1; P=0.01), post-menopausal status

Table 3. Distribution of Cancer Cases and Controls by Potential Risk Factors among Women in the South

Factors	Category	All women					Pre-menopause women		Post-menopause women	
		Cases	Controls	P value[b]	Unadjusted OR	Adjusted OR	Unadjusted OR	Adjusted OR	Unadjusted OR	Adjusted OR
		N(%)[a]	N(%)[a]		(95% CI)[c]	(95% CI)[d]	(95% CI)[c]	(95% CI)[d]	(95% CI)[c]	(95% CI)[d]
Age (years)		141 (36.1)	250 (63.9)							
	Mean ± SD	49.3 ± 9.9	49.5 ± 8.6	0.91						
Breast density percentage										
	≤ 75	94 (66.7)	201 (80.4)	0.002	1	1	1	1	1	1
	>75	47 (33.3)	49 (19.6)		2.1 (1.3-3.3)*	2.1 (1.3-3.6)*	2.5 (1.4-4.7)*	2.2 (1.1-4.4)*	2.2 (1.0-5.0)*	2.1 (0.9-4.8)
Height (cm)										
	Mean ± SD	154.1 ± 5.7	154 ± 5.3	0.83						
	< 155	75 (53.2)	137 (54.8)	0.76	1		1		1	
	≥ 155	66 (46.8)	113(45.2)		1.1 (0.7-1.6)		1.0 (0.5-1.7)		1.4 (0.7-2.5)	
Weight (kg)										
	Mean ± SD	56.2 ± 8.8	55.8 ± 7.6	0.66						
	< 55	59 (41.8)	114 (45.6)	0.47	1		1		1	
	≥ 55	82 (58.2)	136 (54.4)		1.2 (0.8-1.8)		1.1 (0.6-2.0)		1.2 (0.7-2.3)	
BMI										
	Mean ± SD	23.6 ± 3.3	23.5 ± 2.9	0.74						
	< 23	57 (40.4)	112 (44.8)	0.4	1		1		1	
	≥ 23	84 (59.6)	138 (55.2)		1.2 (0.8-1.8)		1.0 (0.5-1.8)		1.4 (0.8-2.6)	
Age at first menstrual period										
	Mean ± SD	15.1 ± 2.1	15.3 ± 2.0	0.27						
	< 14	34 (25)	31 (12.8)	0.002	2.3 (1.3-3.9)*	1.9 (1.1-3.4)	3.0 (1.4-6.6)*	2.4 (1.0 -5.7)*	1.7 (0.8-3.6)	
	≥ 14	102 (75)	212 (87.2)		1	1	1	1	1	
Menopause status										
	Pre	65 (46.1)	146 (58.4)	0.02	1	1				
	Post	76 (53.9)	104 (41.6)		1.6 (1.1-2.5)*	2.6 (1.6-4.2)*				
Age at menopause										
	Mean ± SD	48.9 ± 4.7	49.3 ± 5.0	0.55						
	< 50	35 (46.1)	42 (40.4)	0.45	1				1	
	≥ 50	41 (53.9)	62 (59.6)		0.8 (0.4-1.4)				0.8 (0.4-1.4)	
Age at first giving birth										
	Mean ± SD	24.8 ± 4.6	24.1 ± 4.8	0.19						
	< 23	43 (37.1)	100 (45.2)	0.35	1		1		1	
	23-29	56 (48.3)	93 (42.1)		1.3 (0.8-2.2)		1.2 (0.6-2.5)		1.6 (0.8-3.3)	
	≥ 30	17 (14.7)	28 (12.7)		1.6 (0.8-3.1)		1.0 (0.4-3.0)		1.8 (0.7 - 4.6)	
Age at last giving birth										
	Mean ± SD	30.7 ± 5.7	30.8 ± 5.4	0.78						
	< 30	50 (43.1)	95 (43.0)	0.98	1		1		1	
	≥ 30	66 (56.9)	126 (57.0)		1.0 (0.6-1.6)		1.2 (0.6-2.2)		0.7 (0.4-1.4)	
Number of pregnancy										
	Mean ± SD	2.6 ± 2.0	3.4 ± 2.2	<0.0001						
	< 3	80 (56.7)	84 (33.6)	<0.0001	2.6 (1.7-4.0)*	2.9 (1.8-4.7)*	3.2 (1.7-6.0)*	3.1 (1.6-6.2)*	2.8 (1.5-5.4)*	2.7 (1.4-5.1)*
	≥ 3	61 (43.3)	166 (66.4)		1	1	1	1	1	1
Number of babies born										
	Mean ± SD	2.1 ± 1.6	2.4 ± 1.7	0.05						
	< 2	49 (34.8)	65 (26.0)	0.09	1.5 (0.9-2.3)		1.2 (0.7-2.3)		1.9 (0.9-3.8)*	0.8 (0.3-2.0)
	≥ 2	92 (65.2)	185 (74.0)		1		1		1	1
Number of months of breastfeeding										
	Mean ± SD	14.4 ± 6.5	13.9 ± 6.0	0.56						
	< 15	65 (56.5)	117 (53.2)	0.56	1.1 (0.7-1.8)		1.0 (0.5-1.9)		1.2 (0.6-2.4)	
	≥ 15	50 (43.5)	103 (46.8)		1		1		1	

Table 3. Continued

Factors	Category	All women					Pre-menopause women		Post-menopause women	
		Cases	Controls	P value[b]	Unadjusted OR	Adjusted OR	Unadjusted OR	Adjusted OR	Unadjusted OR	Adjusted OR
		N(%)[a]	N(%)[a]		(95% CI)[c]	(95% CI)[d]	(95% CI)[c]	(95% CI)[d]	(95% CI)[c]	(95% CI)[d]
Hormone use										
	No	94 (66.7)	174 (69.6)	0.55	1		1		1	
	Yes	47 (33.3)	76 (30.4)		1.1 (0.7-1.8)		1.5 (0.8-2.7)		0.9 (0.5-1.7)	
Family history of breast cancer										
	No	130 (92.1)	232 (92.8)	0.58	1		1		1	
	1st degree	4 (2.9)	10 (4)		0.7 (0.2-2.3)		0.9 (0.2-4.9)		0.5 (0.1-2.9)	
	2nd degree	7 (5)	8 (3.2)		1.6 (0.6-4.4)		1.8 (0.5-7.1)		1.4 (0.3-6.9)	
Smoking										
	No	140 (99.3)	249 (100)	0.18	N/A		N/A		N/A	
	Yes	1 (0.7)	0 (0)		N/A		N/A		N/A	
Alcohol drinking										
	No	140 (99.3)	248 (99.2)	0.92	1		N/A		1	
	Yes	1 (0.7)	2 (0.8)		0.9 (0.1-9.8)		N/A		0.7 (0.1-7.6)	
Soy drinking										
	< 1 cup per day	113 (80.2)	218 (87.2)	0.06	1		1		1	
	≥ 1 cup per day	28 (19.8)	32 (12.8)		1.7 (1.0-2.9)		1.5 (0.6-3.5)		1.7 (0.8-3.6)	
Coffee drinking										
	< 1 cup per day	99 (70.2)	202 (80.8)	0.02	1	1	1		1	1.0
	≥ 1 cup per day	42 (29.8)	48 (19.2)		1.9 (1.1-2.9)*	1.5 (1.0-2.6)	1.5 (0.8-2.9)		2.4 (1.1-5.1)*	2.1 (1.0-4.6)*
Vegetable consumption (serves)										
	≤ 1	28 (20)	31 (12.5)	0.07	1		1		1	
	2—3	66 (46.7)	142 (57.1)		0.5 (0.3-0.9)		0.4 (0.2-0.8)		0.8 (0.3-2.0)	
	≥ 4	47 (33.3)	76 (30.4)		0.7 (0.4-1.3)		0.4 (0.2-1.0)		1.4 (0.5-3.5)	
Physical activities										
	No (Inactive)	17 (12.2)	36 (14.4)	0.51	0.8 (0.4-1.5)		2.2 (0.9-5.6)		0.4 (0.2-1.2)	
	Yes (Insufficient and Sufficient)	124 (87.8)	213 (85.6)		1		1		1	

[a], Number of participants (Percentage); [b], Obtained from t-test for continuous variables and chi-square test for categorical variables; [c], Unadjusted odd ratios (95% confidence interval); - Obtained from binary logistic regression; [d], Multivariable adjusted odd ratios (95% confidence interval) - Obtained from multiple logistic regression;*, Statistically significant (P < 0.05); N/A, Due to low number of cases

(OR=2.6; P<0.0001), having less than 2 babies born (OR=2.1; P=0.01). All these factors, age at first menstrual period (OR=2.1; P=0.02), menopausal status (OR=2.5; P <0.0001) and number of babies born (OR=1.9; P=0.03), maintained their associations with breast cancer in the multivariable adjusted OR analysis. When the data were stratified by menopausal status, a significant association with breast cancer among premenopausal women was only shown for hormone use (OR=2.1; P=0.02) while having less than 2 children (OR=3.4; P=0.005) was found to be the only significant risk factor for postmenopausal women.

Risk factors of breast cancer in the southern Vietnam

Southern Vietnamese women who had a breast density more than 75% (OR=2.1; P=0.002), were post-menopausal status (OR=1.6; P=0.02), had the first menstrual period before 14 years old (OR=2.3; P=0.002), had less than 3 pregnancies (OR=2.6; P<0.0001) or who drank more than a cup of coffee per day (OR=1.9; P=0.02) had a higher risk of with breast cancer in the univariate analysis. Among these factors, breast density (OR=2.1; P=0.004), menopausal status (OR=2.6; P<0.0001), number of pregnancies (OR=2.9; P<0.0001) and coffee drinking (OR=1.5; P=0.13) remained significant predictors of breast cancer in the multivariable adjusted risk model.

Breast cancer in premenopausal women in the south was found to have a significant relationship with high breast density (OR=2.5; P=0.003), the first menstrual period earlier than 14 years old (OR=3.0; P=0.004) or less than 3 pregnancies (OR=3.2; P<0.0001). High breast density (OR=2.2; P=0.04), low number of pregnancy (OR=2.8; P=0.001), low number of live birth (OR=1.9; P=0.04) or drinking more than a cup of coffee daily (OR=2.4; P=0.02) were also related to breast cancer among postmenopausal women. Whilst breast density (OR=2.2; P=0.02), age at first menstrual period (OR=2.4; P=0.04) and number of pregnancies (OR=3.1; P=0.001) retained their significant relationships with breast cancer in a multivariable adjusted model for premenopausal women, number of pregnancies (OR=2.7; P=0.003) and coffee drinking (OR=2.1; P=0.04) were the factors significantly associated with breast cancer in the adjusted model for postmenopausal women (Table 3).

Discussion

The aim of this study was to compare female breast cancer risk factors in the north and the south of Vietnam. Our findings showed that there were variances in the distribution of breast cancer risk between the two populations. According to the multivariable analysis, early age at first menstrual period and post-menopause status were factors that maintained a significant association with breast cancer for both women in the north and in the south, a finding which is in line with other studies in Asian and westernized populations (Kelsey et al., 1993; Key et al., 2001). We also found that the risk of post-menopausal women in northern Vietnam developing breast cancer was higher than that of women in the south (OR=2.6 vs OR=1.6) in univariate analysis. The reasons for this and indeed higher (current) incidence rates in the north compared with the south of Vietnam (29.7 per 100,000 vs 19.4 per 100,000) (Duc NB, 2009), which was reported previously, may be multi-factorial. It is tempting to look for origins arising from the war with America, however toxic chemicals such as dioxin were actually used in greater amounts in southern Vietnam compared with the north (Schecter et al., 1995). One more acceptable possibility is around the use of monosodium glutamate (MSG), a chemical linked with carcinogenesis: MSG was probably introduced to Vietnam by the Japanese when the army invaded northern Vietnam in the period of 1940-1945 whilst concomitantly the French colonized the south of the country. To ameliorate the effects of the 1944-1945 famine in the north which dramatically affected millions of civilians, MSG was provided by the Japanese as an additive for cooking, and often as a supplement to rice dishes. In modern day Vietnam (in the northern region) MSG is still a very important part of the diet, where in contrast the southern Vietnamese preferentially use sugar in cooking due to sugar cane availability in the Mekong Delta area. Although the evidence about the association between MSG and breast cancer does not exist, a study in Turkey showed that MSG had caused DNA damage in isolated human lymphocytes (Ataseven et al., 2016). There are of course other potential causal agents. Smoking and alcohol consumption were shown in previous studies to be more common in women in the north than in the south with rates being almost a factor of three and two greater (Oanh et al., 2009; Nguyen et al., 2012). Moreover, a lower number of doctors is evident in the north, with only 72% of commune health stations in the north having a doctor compared with 85% in the southern areas (Nguyen, 2013) potentially impacting on preventative and monitoring activities.

During the past twenty years, Vietnam has had rapid social and economic growth. Studies in westernized populations reported that socioeconomic disparity might link with various distributions of breast cancer risk factors, especially reproductive control (Lea et al., 2009). Some of our findings indicate a shift towards Western patterns with regard to reproductive factors for women in the south where women had fewer pregnancies in both control and cancer groups than women in the north of Vietnam. These reproductive findings are in line with Teerawichitchainan et al., (2010) who showed that the fertility ratios of south and north of Vietnam were 1.7 and 2.6 respectively (Teerawichitchainan and Amin, 2010), and this may explain at least in part the more rapid upsurge in the number of new breast cancer cases in the south in the last two decades (Trieu et al., 2015). The reasons for this reproductive difference between the two regions may be twofold: developing urbanization and modernization in the south has led local women to adopt more westernized lifestyles, including those involving reproductive control; the two-child policy in Vietnam might be more strictly enforced for families in the south compared with the north.

In addition, we found that though the consumption of more than 1 cup of coffee per day was not a predictor of breast cancer for women in the north, it is the risk factor for southern women, especially postmenopausal women. In the southern Vietnam, there is a large coffee consumption, a habit which has been developing since 1945 and the increased involvement with western nations, while people in the north prefer drinking soy milk as a result of 1,000 years of Chinese influence. The growing cancer risk with coffee drinking is in line with a study in Singapore showing that drinking two or more cups of coffee per day elevated the estrogen-related risk of advanced breast cancer (OR=2.3) (Lei, 2013). No engagement in soy consumption, vegetable intake or physical activities was reported to be related to breast cancer for women in either region.

There are several estimates of association (although not statistically significant) such as increased vegetable intake associated with breast cancer risk; protective effect of smoking; first degree family history being protective but second degree family history increasing the risk that are relatively unusual compared with the general knowledge about breast cancer. Our results, rather than indicating the inverse relationship, may be more linked to the limited number of women in this study who had a smoking habit (1.8%), consumed less vegetables (9.9%) or had mother or sister ever diagnosed with breast cancer (3.6%) though these numbers are in line with low incidence rate of breast cancer and common lifestyles among Vietnamese women (Ginsburg et al., 2011; Trieu et al., 2015). It might be necessary in the future to elucidate the relationship of these factors with breast cancer in a larger sample study.

Based on the differences in reproductive, diet and lifestyle factors discussed above, it is interesting to note that women in the south seem to have breast cancer risk factors that are closer to westernized populations whilst this is not necessarily the case for women in the northern Vietnam. Findings in westernized populations show that reproductive and lifestyle factors are associated with breast density and women with breast density >75% have an increased risk (OR=3-5) to develop breast cancer than women with less dense breast tissue (Boyd et al., 2007; Wong et al., 2011). Women in the south of Vietnam (both pre-menopausal and post-menopausal) have an increased OR in developing breast cancer with breast density >75% (OR=2.1) compared with lower density. In contrast, in the northern region even though our data suggest a higher proportion of women with high dense breasts compared with the south, there was no significant difference in breast density between normal and cancer women and fewer of the westernized-based associations with breast cancer that have impacted on breast density such as low number of pregnancies or coffee drinking were found apart from hormone use which was significantly associated with breast cancer among premenopausal northern women. This could potentially be the most important output of this work since it suggests that even within a single country, if westernized lifestyles are not adopted, established knowledge about breast density and breast cancer risks may not apply. Vietnam has served as an excellent model to examine this due to its geographical arrangement and its short and long term political histories.

Strengths of this study are that it was the first study investigating a wide range of breast cancer risk factors in two different regions in Vietnam and it has revealed key demographic, reproductive and lifestyle factors relating to breast cancer for women each region. However, the study has several limitations. Firstly, data were collected through hospital-based systems with the inability to consider individually screened or diagnostic cases separately due to lack of population-based disease surveillance systems in the hospitals. Secondly, breast density was assessed by single reading of radiologists which is in line with the clinical procedure in Vietnam, but it could cause subjective bias compared with routine practice of double reading in Westernzied countries.

In conclusion, this study shows that several risk factors of breast cancer in the south of Vietnam similar to findings in Westernized populations were not found in the northern region. This distinction highlights the need to undertake region-dependent studies in Vietnam if causal agents for breast cancer are comprehensively understood.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest of this article.

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