Associations between tea and coffee consumption and common benign breast diseases: "Hospital Based Control Study"

Zuhoor K AL-Gaithy[1], Alaa A Roublah[2], Dareen A Khawjah[2], Bushra K AL-Hawsa[2], Zahraa I AL-Ghafli[2], Esrra A Roublah[2], Laila K Ashkar[3]
[1] Department of Surgery, King Abdulaziz University Hospital, Jeddah, Saudi Arabia.
[2]King Abdulaziz University, Jeddah, Saudi Arabia
[3]Department of Radiology, King Abdulaziz University Hospital, Jeddah Saudi Arabia
[*]**Corresponding** author: Zuhoor K AL-Gaithy
Department of Surgery, King Abdulaziz University Hospital,
P.O. Box 80215, Jeddah 21589, Saudi Arabia
Email: zkngaithy@hotmail.com, **Mobile:** +966505593978

ABSTRACT

Background: Coffee drinking is popular around the world because of its aromatic flavors and delightful taste**.** The associations between coffee and health benefits are clear.

Objective: To evaluate the relationship of caffeinated and decaffeinated coffee and tea consumption with the development of common benign breast diseases (fibroadenoma and fibrocystic change) in middle aged women (18-40 years).

Design: One hundred and fifty middle aged females (18 - 40 years old) were enrolled in this prospective case-control study from King Abdulaziz University Hospital (KAUH), Jeddah, Saudi Arabia. They were 50 healthy controls, 50 women with fibroadenoma and 50 women with fibrocystic changes of the breast. Cases were collected using the radiology database between January 1st, 2014 to December 31st, 2015 with any diagnostic codes (ICD-9-CM codes 140 to 208) diagnosed by ultrasound (US) or mammogram. Excluded from the study were women with a history of breast cancer or women with age less than 18 years old or more than 40 years old.

Results: Women who consumed coffee or tea for 3-4 years were associated with increased rate of fibroadenoma (RR= 2.664, 95%CI 1.216 - 5.836, P=0.014) and fibrocystic breast

diseases (RR= 2.310, 95%CI 1.038 - 5.142, P=0.040). Women who consumed coffee or tea <1 cup/ day were associated with an increased rate of fibrocystic breast disease (RR= 3.230, 95%CI 1.333– 7.825, P=0.009). Meanwhile, women who consumed coffee or tea for >4 years were associated with reduced rate of fibrocystic breast disease (RR= 0.327, 95%CI 0.134 – 0.797, P=0.0139). Also, women who consumed caffeinated tea of 1 cup / day showed a significantly reduced rate of fibrocystic breast disease (RR= 0.580, 95%CI 0.342– 0.984, P=0.0433).

Conclusions: Our data shows an association between caffeine or tea consumption and the risk of benign breast diseases that depends on the duration and amount of beverage consumed.

Key words: benign breast diseases**;** caffeine consumption**;** fibroadenoma; fibrocystic breast disease; relative risk; tea consumption.

{**Citation:** Zuhoor K AL-Gaithy, Alaa A Roublah, Dareen A Khawjah, Bushra K AL-Hawsa, Zahraa I AL-Ghafli, Esrra A Roublah, Laila K Ashkar. Associations between tea and coffee consumption and common benign breast diseases: "Hospital Based Control Study". American Journal of Research Communication, 2017, 5(2): 1-26} www.usa-journals.com, ISSN: 2325-4076.

INTRODUCTION

Coffee drinking is popular around the world because of its aromatic flavors and delightful taste. Coffee is the second highest consumed beverage in the world, only second to water, and coffee has been consumed by millions of people across the globe for centuries (1). Coffee

contains many chemical components such as caffeine, antioxidants (polyphenols, catechins, and flavonoids) and chlorogenic acids that have been suggested to have benefits including improving concentration, alertness and enhancing physical and mental performance (2). Coffee consumption is associated with reducing Parkinson disease, type 2 diabetes, colorectal cancer and Alzheimer's (1- 3) and raising serum cholesterol, affecting coronary health, insomnia, and heart problems (1). Caffeine also exhibits notable effects on cell cycle function and regulation, apoptosis and DNA repair (4). The primary antioxidant potential of tea is attributed to its catechins, chief among them; epigallocatechin gallate (EGCG) for which green tea has a higher concentration than black tea (5).

Benign breast diseases (BBD) constitute a heterogeneous group of lesions including developmental abnormalities, inflammatory lesions, epithelial and stromal proliferations, and neoplasms. Most BBD in Saudi Arabia in women less than 25 years of age are fibroadenoma then fibrocystic disease (46.9% and 23.25%, respectively) (6, 7).

The possibility that methylxanthine (caffeine, theophylline and theobromine) may be associated with the risk of breast disease was first suggested in a report by Minton et al. (8), who found that women who abstained from methylxanthine were more likely to have a resolution of their fibrocystic disease than those who did not. Animal studies have indicated that caffeine can both stimulate and suppress mammary tumors, depending on the rodent species and strain as well as the tumorigenic phase (initiation/promotion) at the caffeine administration (9). In various studies, rats with breast tumors that were given green tea had reductions in tumor size and tumor growth (10, 11). The association between coffee and breast cancer, however, has been inconsistent in observational studies, with reports of no association (12-18), inverse association (19 - 22) and positive association (23, 24) that vary by both age (19) and body size (24).

Therefore, in light of the limited and inconsistent body of evidence, we conducted a hospital-based, case-control study to further investigate the association between benign breast diseases (fibroadenoma and fibrocystic change) in middle aged women (18-40 years old) and consumption of caffeinated and decaffeinated coffee and tea.

METHODS

A total of 150 women (50 control, 50 fibroadenoma, and 50 fibrocystic cases) were enrolled in this prospective case control study from King Abdulaziz University Hospital (KAUH), Jeddah, Saudi Arabia. The study was approved by the unit of biomedical ethics at KAUH, which is a tertiary hospital in Jeddah, Saudi Arabia.

The fibrocystic changes and fibroadenoma cases were assembled using the radiology databases between January 1st, 2014 and December 31st, 2015 with diagnostic codes (ICD-9-CM codes 140 to 208). Diagnosis was confirmed on the basis of ultrasonography or mammogram findings. Controls were enrolled simultaneously with cases when they fulfilled the following criteria: (1) age between 18 to 40 years old, (2) no personal history of any malignancy. The health status of controls was documented by collecting information from a designated data sheet. Breast history and examination were included as part of the admission examination of controls as well as cases. Participants aged less than 18 years old or older than 40 years old, patients who had a history of breast cancer and those with incomplete data were excluded from the study.

At admission, these women completed a detailed questionnaire regarding their coffee and tea consumption. The information was obtained using a 27 item questionnaire which included data on patients' demographics, anthropometric, smoking status, presence of chronic medical conditions, factors relevant to hormonal status including menstrual history, reproductive and

lactation history, oral contraceptive use, benign proliferation breast disease and family history of breast cancer. The questionnaire assessed frequency and amount of caffeinated or decaffeinated coffee and tea consumption categorized into 5 groups as following: none, <1 cup/ day, 1 cup/ day, 2-3 cups/ day and > 4 cups/ day, and the duration of consumption; >4 years, 3-4 years, 2-3 years, 1-2 years and < 1year

Statistical analysis

Descriptive statistics were analyzed using SPSS software to characterize the study population and to examine case–control differences. Demographic characteristics and potential risk factors between cases and controls were compared by OneWay ANOVA for continuous variables, and by the Chi-squared test for categorical variables. Univariate modeling was applied to identify potential confounding variables. Relative risk and 95% confidence interval was made using MedCalc program. A *P*-value < 0.05 was considered to be statistically significant.

RESULTS

Coffee and tea drinkers were more than non-drinkers in fibroadenoma (84% versus 16%), fibrocystic changes (92% versus 8%) and control (86% versus 14%) with insignificant difference between groups (P =0.457). Duration of drinking coffee or tea in fibroadenoma was mostly 3-4 years (62%) followed by >4 years (12%), 2-3 years (4%), 1-2 years (4%) and < 1year (2%); in fibrocystic changes was mostly 3-4 years (42%) followed by >4 years (26%), 1-2 years (12%), <1 year (8%) and 2-3year (4%); in control was mostly >4 years (36%) followed by 1-2 years (16%), <1 year (14%), 2-3 years (12%) and 3-4 years (8%) with significant difference between groups. The type of tea in fibroadenoma, fibrocystic changes

and controls was mostly red tea (50%, 56% and 42%) followed by green tea (26%, 22% and 40%) with insignificant differences between the groups (P =0.345). The type of coffee in fibroadenoma was mostly Arabic coffee (58%) followed by Turkish coffee (12%), Cappuccino (10%) and lastly Espresso coffee (2%); while in fibrocystic changes was mostly Arabic coffee (46%) followed by Turkish coffee (18%), Cappuccino (10%), Black coffee (8%) and lastly Espresso coffee (4%). Meanwhile in controls it was mostly Arabic coffee (36%) followed by Cappuccino (26%), Turkish coffee (8%), Black coffee (6%) and lastly Espresso coffee (4%) with insignificant differences between groups (P =0.139). Regarding the number of cups per day, in fibroadenoma it mostly was 2-3 cups/ day (28%), < 1 cup/ day (20%), 1 cup/ day (20%), > 4 cups/ day (16%) and non (16%); in fibrocystic changes it mostly was < 1 cup/ day (38%), 2-3 cups/ day (20%), 1 cup/ day (20%), none (12%) and > 4 cups/ day (10%); in controls most drank > 4 cups/ day (38%), none (26%), 2-3 cups/ day (20%), 1 cup/ day (18%), and < 1 cup/ day (8%) with significant difference between groups (P =0.015). Category of caffeinated was mostly high than low in fibroadenoma (62% versus 38%) and control (64% versus 36%); while in fibrocystic changes was more high than low (64% versus 36%) with insignificant difference between groups (P =0.085). Regarding the number of caffeinated cups drinker per day, in fibroadenoma mostly was 2-3 cups/ day (24%), 1 cup/ day (24%), none (20%), < 1 cup/ day (18%) and > 4 cups/ day (14%); in fibrocystic changes mostly was < 1 cup/ day (38%), 2-3 cups/ day (24%), none (18%), 1 cup/ day (16%), and > 4 cups/ day (4%); in control mostly was 1 cup/ day (60%), < 1 cup/ day (22%), none (14%), and > 4 cups/ day (4%) with significant difference between groups (P =0.0001). Category of decaffeinated was mostly low than high in fibroadenoma (96% versus 4%) and fibrocystic changes (98% versus 2%); while in control all was more low (100% with insignificant difference between groups (P =0.360). Regarding the number of cups drinker per day in decaffeinated, in fibroadenoma mostly was none (84%) then < 1cup/ day (12%)

and 2-3 cups / day (4%); in fibrocystic changes mostly was none (94%) then < 1cup/ day (4%) and 2-3 cups / day (2%); in control all was none (100%) with significant difference between groups (P =0.046) (Table 3).

Table (1): Sociodemographic, menstrual, reproductive and anthropometric characteristics, of patients with benign breast diseases and control

Characteristics	**Women with fibroadenoma** (n= 50)	**Women with fibrocystic** (n= 50)	**Control women** (n= 50)
Nationality			
Saudi	33 (66.00%)	26 (52.00%)	47 (94.00%)
Non- Saudi	17 (34.00%)	24 (48.00%)	3 (6.00%)
Age group at diagnosis			
18-25 years	15 (30.00%)	7 (14.00%)	41 (82.00%)
26-30 years	11 (22.00%)	7 (14.00%)	5 (10.00%)
31-35 years	12 (24.00%)	14 (28.00%)	2 (4.00%)
36-40 years	12 (24.00%)	22 (44.00%)	2 (4.00%)
Weight (kgs)	59.10±13.88	60.68±13.81	62.48±18.10
Height (cm)	159.16±5.20	158.76±7.24	158.36±7.92
BMI group			
underweight	7 (14.00%)	5 (10.00%)	3 (6.00%)
normal	30 (60.00%)	29 (58.00%)	24 (48.00%)
overweight	9 (18.00%)	11 (22.00%)	18 (36.00%)
obese	4 (8.00%)	6 (12.00%)	5 (10.00%)

Social status			
single	18 (36.00%)	16 (32.00%)	42 (84.00%)
married	27 (54.00%)	30 (60.00%)	8 (16.00%)
widow	1 (2.00%)	2 (4.00%)	-
divorced	4 (8.00%)	2 (4.00%)	-
Occupation			
students	10 (20.00%)	10 (20.00%)	40 (80.00%)
house wife	19 (38.00%)	23 (46.00%)	8 (16.00%)
teacher	4 (8.00%)	4 (8.00%)	2 (4.00%)
doctor	2 (4.00%)	1 (2.00%)	-
others	15 (30.00%)	12 (24.00%)	-
Multiparous			
no	26 (52.00%)	20 (40.00%)	43 (86.00%)
yes	24 (48.00%)	30 (60.00%)	7 (14.00%)
Number of live births			
none	26 (52.00%)	20 (40.00%)	43 (86.00%)
1	12 (24.00%)	6 (12.00%)	2 (4.00%)
2-3	8 (16.00%)	14 (28.00%)	1 (2.10%)
≥4	4 (8.00%)	10 (20.00%)	4 (8.30%)
Number of breastfed children			
none	31 (62.00%)	21 (42.00%)	43 (86.00%)
1	10 (20.00%)	7 (14.00%)	3 (6.00%)
2-3	7 (14.00%)	14 (26.00%)	1 (2.00%)
≥4	2 (4.00%)	8 (16.00%)	3 (6.00%)

Table (2): History of the patients with benign breast diseases and control

Data	Fibroadenoma (n= 50)	Fibrocystic (n= 50)	Control (n= 50)	Significance
Tobacco smoking status				**0.001**
never smoker	45 (90.00%)	44 (88.00%)	31 (62.00%)	
current smoking	4 (8.00%)	6 (12.00%)	19 (38.00%)	
former smoking	1 (2.00%)	-	-	
Exposure - passive smoking				**0.0001**
no	34 (68.00%)	31 (62.00%)	49 (98.00%)	
yes	16 (32.00%)	19 (38.00%)	1 (2.00%)	
Chronic illness				0.353
no	41 (82.00%)	40 (80.00%)	45 (90.00%)	
yes	9 (18.00%)	10 (20.00%)	5 (10.00%)	
Exercise				0.673
no	32 (64.00%)	30 (60.00%)	25 (50.00%)	
1-4 hrs/week	15 (30.00%)	17 (34.00%)	22 (44.00%)	
≥ 5 hrs/ week	3 (6.00%)	3 (6.00%)	3 (6.00%)	
Age of menarche				**0.004**
< 11 years	4 (8.00%)	6 (12.00%)	8 (16.00%)	
12-15 years	36 (72.00%)	43 (86.00%)	41 (82.00%)	
>15 years	10 (20.00%)	1 (2.00%)	1 (2.00%)	
Contraceptive used				**0.001**
no	42 (84.00%)	35 (70.00%)	49 (98.00%)	
< 5 years	7 (14.00%)	8 (16.00%)	-	
≥5 years	1 (2.00%)	7 (14.00%)	1 (2.00%)	

Positive family history				**0.007**
no	28 (56.00%)	28 (56.00%)	41 (82.00%)	
yes	22 (44.00%)	22 (44.00%)	9 (18.00%)	
Number of relatives	0.40±1.18	0.88±1.80	0.28±0.73	0.065
Degree of relationship				**0.003**
1st degree	14 (28.60%)	5 (10.00%)	3 (6.00%)	
2nd degree	7 (14.00%)	13 (26.00%)	4 (8.00%)	
3rd degree	1 (2.00%)	4 (8.00%)	2 (4.00%)	
Age of diseased relative	23.00±32.500	18.36±24.35	19.98±35.92	0.754
Disease duration (months)	50.58±54.00	4.20±00.08	-	**0.0001**
Side of breast				**0.0001**
right side	18 (36.00%)	13 (26.00%)	-	
left side	8 (16.00%)	19 (38.00%)	-	
both sides	24 (48.00%)	18 (36.00%)	-	
Self-examination of breast				**0.0001**
no	16 (32.00%)	19 (38.00%)	42 (84.00%)	
yes	34 (68.00%)	31 (62.00%)	8 (16.00%)	
Last time of breast examination				
During 6 months	25 (50.00%)	17 (34.00%)	4 (8.00%)	**0.0001**
During a year	3 (6.00%)	12 (24.00%)	3 (6.00%)	
During 2 years	6 (12.00%)	2 (4.00%)	1 (2.00%)	

Table (3): Comparison of drinking coffee or tea between different groups

Risk factors	Fibroadenoma (n= 50)	Fibrocystic (n= 50)	Control (n= 50)	Significance
Drink coffee or tea				0.457
no	8 (16.00%)	4 (8.00%)	7 (14.00%)	
yes	42 (84.00%)	46 (92.00%)	43 (86.00%)	
Duration of drinking coffee or tea				**0.0001**
< 1 year	1 (2.00%)	4 (8.00%)	7 (14.00%)	
1-2 years	2 (4.00%)	6 (12.00%)	8 (16.00%)	
2-3 years	2 (4.00%)	2 (4.00%)	6 (12.00%)	
3-4 years	31 (62.00%)	21 (42.00%)	4 (8.00%)	
> 4 years	6 (12.00%)	13 (26.00%)	18 (36.00%)	
Type of drinker tea				0.345
None	12 (24.50%)	11 (22.00%)	9 (18.00%)	
Red tea	25 (50.00%)	28 (56.00%)	21 (42.00%)	
Green tea	13 (26.00%)	11 (22.00%)	20 (40.00%)	
Type of drinker coffee				0.139
none	9 (18.00%)	7 (14.00%)	10 (20.00%)	
Arabic coffee	29 (58.00%)	23 (46.00%)	18 (36.00%)	
Turkish coffee	6 (12.00%)	9 (18.00%)	4 (8.00%)	
Black coffee	-	4 (8.00%)	3 (6.00%)	
Espresso coffee	1 (2.00%)	2 (4.00%)	2 (4.00%)	
Cappuccino	5 (10.00%)	5 (10.00%)	13 (26.00%)	

Category of drinker				0.157
low (≤1 cup/ day)	28 (56.00%)	35 (70.00%)	26 (52.00%)	
high (>1cup/ day)	22 (44.00%)	15 (30.00%)	24 (48.00%)	
Cups drinker per day				**0.015**
none	8 (16.00%)	6 (12.00%)	13 (26.00%)	
<1 cup/ day	10 (20.00%)	19 (38.00%)	4 (8.00%)	
1 cup/ day	10 (20.00%)	10 (20.00%)	9 (18.00%)	
2-3 cups/ day	14 (28.00%)	10 (20.00%)	10 (20.00%)	
> 4 cups/ day	8 (16.00%)	5 (10.00%)	14 (28.00%)	
Category of caffeinated				0.085
low (≤1cup/ day)	19 (38.00%)	28 (56.00%)	18 (36.00%)	
high (> 1cup/ day)	31 (62.00%)	22 (44.00%)	32 (64.00%)	
Caffeinated				**0.0001**
none	10 (20.00%)	9 (18.00%)	7 (14.00%)	
<1 cup/ day	9 (18.00%)	19 (38.00%)	11 (22.00%)	
1 cup/ day	12 (24.00%)	8 (16.00%)	30 (60.00%)	
2-3 cups/ day	12 (24.00%)	12 (24.00%)	-	
> 4 cups/ day	7 (14.00%)	2 (4.00%)	2 (4.00%)	
Category of decaffeinated				0.360
low (≤1cup/ day)	48 (96.00%)	49 (98.00%)	50 (100.00%)	
high (> 1cup/ day)	2 (4.00%)	1 (2.00%)	-	
Decaffeinated				**0.046**
none	42 (84.00%)	47 (94.00%)	50 (100.00%)	
< 1cup/ day	6 (12.00%)	2 (4.00%)	-	
2-3 cups/ day	2 (4.00%)	1 (2.00%)	-	

Table (4): Associations between coffee consumption and benign breast diseases risk

Risk factors	Fibroadenoma		Fibrocystic	
	RR (95% CI)	***P*- value**	**RR (95% CI)**	***P*- value**
Drink coffee or tea				
no	1		1	
yes	0.977 (0.83 - 1.15)	0.780	1.070 (0.931 - 1.229)	0.340
Duration of drinking coffee or tea				
< 1 year	1		1	
1-2 years	1.250 (0.493 - 3.167)	0.470	1.125 (0.563 - 2.250)	0.333
2-3 years	1.444 (0.535 - 3.897)	0.726	0.722 (0.202 - 2.584)	0.500
3-4 years	2.664 (1.216 - 5.836)	**0.014**	2.310 (1.038 - 5.142)	**0.0403**
> 4 years	1.191 (0.807 - 1.756)	0.379	0.327 (0.134 – 0.797)	**0.0139**
Type of drinker tea				
None	1		1	
Red tea	0.965 (0.698 - 1.334)	0.830	1.026 (0.755 - 1.393)	0.8711
Green tea	0.754 (0.481- 1.181)	0.218	0.725 (0.447 – 1.176)	0.1928
Type of drinker coffee				
none	1		1	
Arabic coffee	1.187 (0.855 - 1.648)	0.305	1.193 (0.849 - 1.675)	0.3091
Turkish coffee	1.400 (0.4976 - 3.939)	0.524	1.969 (0.774 - 5.011)	0.1553
Black coffee	0.200 (0.0116 - 3.457)	0.268	1.576 (0.446 - 5.574)	0.4805
Espresso coffee	0.600 (0.063 - 5.687)	0.656	1.333 (0.230 - 7.743)	0.7486
Cappuccino	0.632 (0.287 - 1.391)	0.254	0.737 (0.345 - 1.575)	0.4313

Category of drinker				
low (≤1cup/ day)	1		1	
high (> 1cup/ day)	0.917 (0.599 - 1.403)	0.689	0.625 (0.374 - 1.043)	0.072
Cups drinker per day				
none	1		1	
<1 cup/ day	2.361 (0912- 6.114)	0.077	3.230 (1.333 – 7.825)	**0.009**
1 cup/ day	1.1358 (0.709 – 2.602)	0.411	1.528 (0.814 – 2.867)	0.187
2-3 cups/ day	1.463 (0.834 – 2.570)	0.185	1.438 (0.788 – 2.622)	0.237
> 4 cups/ day	0.964 (0.524 - 1.775)	0.907	0.877(0.417 - 1.842)	0.348
Category of caffeinated				
low (≤1cup/ day)	1		1	
high (> 1cup/ day)	0.969 (0.717- 1.308)	0.836	0.688 (0.472 – 1.001)	0.0505
Caffeinated				
none	1		1	
<1 cup/ day	0.775 (0.425 -1.413)	0.406	1.110 (0.709 - 1.738)	0.6470
1 cup/ day	0.673 (0.446 - 1.017)	0.059	0.580 (0.342 - 0.984)	**0.0433**
2-3 cups/ day	8.696 (0.579- 130.670)	0.118	9.091(0.606 -136.418)	0.1102
> 4 cups/ day	1.853 (0.481 -7.132)	0.370	0.818 (0.142 - 4.712)	0.8223
Category of decaffeinated				
low (≤1cup/ day)	1		1	
high (> 1cup/ day)	5.000 (0.246- 101.590)	0.295	3.000 (0.125 - 71.927)	0.498
Decaffeinated				
none	1		1	
< 1cup/ day	13.531 (0.7823 - 233.83)	0.073	5.100 (0.251-103.596)	0.2889
2-3 cups/ day	5.667 (0.279 - 114.944)	0.259	3.122 (0.130 - 74.827)	0.4823

RR: relative risk. The p-value for heterogeneity obtained through multivariable logistic regression.

DISCUSSION

Results of studies investigating the association between caffeine and/or methylxanthine intake and BBD are conflicting. Results from this hospital-based study provided additional evidence for an association between the consumption of coffee or tea for 3-4 years and fibroadenoma (RR= 2.664, 95% CI 1.216 - 5.836, P= 0.014) and fibrocystic breast disease (RR= 2.310, 95% CI 1.038 - 5.142, P= 0.0403) in middle age women. This relation was more associated with women who drank Turkish coffee and had either fibroadenoma (RR= 1.400, 95% CI 0.4976 - 3.939, P= 0.524) or fibrocystic breast disease (RR= 1.969, 95% CI 0.774 - 5.011, P= 0.1553).

Minton et al. (8) were the first to suggest that caffeine consumption was associated with the symptoms of fibrocystic breast diseases (FBD). When caffeine and other methylxanthines (MX) –containing beverages were eliminated from the diet of women with clinically diagnosed FBD, a majority of women (13 of 20) experienced complete disappearance of palpable breast nodules and other symptoms (e.g. pain) within 1-6 months after completely abstaining from all methylxanthines consumption. Only 1 of 27 women who continued MX consumption experienced resolution of her disease. Cyclic AMP and cyclic GMP levels were found to be higher in fibrocystic breast tissue when compared with normal breast tissue. Brooks et al. (25) found that among women who abstained from MX consumption for 6 months, 91% had improvements in palpable breast findings and 88% had improvements in self-reported breast symptoms. In addition, 85% of patients exhibited improvements in graphic thermal patterns using graphic stress telethermometer. Minton et al. (26) presented a third report supporting the hypothesis that MX consumption is associated with the symptoms of FBD. In women who completely abstained from MX consumption, 83% experienced complete resolution of their disease and 15% experienced a significant improvement. Symptoms resolved in 25% and improved in 50% of women who reduced their MX

consumption by more than half. Among women who did not alter their MX consumption, only 17% experienced a resolution of their symptoms, and 8% experienced an improvement. More studies have required histological confirmation of BBD and have evaluated the risk separately for different types of BBD. Of these, two studies reported significant positive associations that were strongest among women with high-risk types of BBD (27, 28); while a third found no association overall but an increased risk among the 40 women with severe atypia (29). Boyle et al. (27) reported that the occurrence of FBD was positively associated with average daily consumption of caffeine. The OR ranged from 1.5 (3 1-150 mg caffeine/day) to 2.3 (greater than 500 mg caffeine/ day). The OR was approximately the same when acute or chronic disease controls were considered separately. Women who had FBD along with concomitant fibroadenoma also showed a positive association with caffeine consumption. The OR were 1.9 (31-250 mg caffeine/day), 2.7 (25-500 mg caffeine/day), and 2.5 (greater than 500 mg caffeine/day). For breast pain, the OR was 3.2 when comparing controls who consumed greater than 500 mg caffeine/day with those consuming 30 mg or less/day. The corresponding OR was 1.9 for the formation of breast lumps. No relationship was found between caffeine consumption and the presence of fibroadenomas. La Vecchia et al. (28) also showed a definite caffeine dose response relationship and an association specific for FBD. The relative risk (RR) estimates of FBD for women who consumed 1-2, or 3 or more, cups of coffee/day were 4.1 and 6.4, respectively, when hospitalized controls were the comparison group, and 2.0 and 3.7, respectively, when outpatient controls were the comparison group. The RR estimates were higher, but not significantly changed, when total MX consumption (coffee plus tea) was considered. The relationship between total MX consumption and FBD was increased with increasing duration of use. No association was found between MX consumption and the presence of fibroadenomas. The highest quartile of coffee consumption was associated with an increased incidence of atypical hyperplasia for a

small subsample of women (30). Using discordant twins in a case control study, Odenheimer et al. (31) showed a significantly positive association between FBD and coffee consumption. Two groups were studied: 90 pairs of twins in which one twin had a history of biopsy-proven FBD and her twin did not (44 monozygotic pairs and 46 dizygotic pairs) and 48 pairs of twins in which one twin had clinically diagnosed FBD and her twin was free of disease at examination and reported no history of breast disease (25 monozygotic pairs and 23 dizygotic pairs). In the cases with a history of biopsy-proven FBD, the odds ratio (OR) for moderate coffee consumption (1-4 cups/day) versus none, or moderate consumption versus heavy consumption (at least 5 cups/day) was 1.6. In the cases with clinically diagnosed FBD, women with FBD were more likely to consume coffee than their twins (OR: 4.2, P <0.05). In both groups, the association was stronger for the monozygotic than the dizygotic twins.

Meanwhile, results of this study showed reduced rate of fibrocystic breast disease in middle aged women who consumed coffee or tea for > 4 years (RR = 0.327, 95% CI 0.134 – 0.797, P =0.0139) and women who drank 1 caffeinated cup / day (RR= 0.580, 95% CI 0.342– 0.984, P =0.0433). Other studies showed that caffeinated beverages alter sex hormone binding globulin and estradiol that potentially reducing the risk of developing breast cancer (32). Although both black tea and decaffeinated coffee have been studied considerably less than regular coffee, previous studies have been consistent in failing to find a significant association between these 2 beverages and breast cancer risk (19, 33, 34). Baker et al. (35) found a significant reduction in risk for lobular type breast cancer among consumers of black tea, suggesting the importance of further consideration of histological type in future research.

There are several plausible mechanisms by which coffee, tea, and caffeine may affect breast cancer risk. Coffee and tea contain a wide variety of phytochemicals, many of which are antioxidants (36), and coffee compounds such as caffeine, chlorogenic acid, kahweol, and cafestol have known biologic effects (37). Coffee may inhibit DNA methylation (38),

influence tumor differentiation (39); and alter sex hormone levels (40). Theaflavins and thearubigins, the oxidized derivatives of black tea catechins, may enhance apoptosis, suppress cell proliferation, and inhibit angiogenesis, although black tea polyphenols have low or no bioavailability (41). Tea polyphenols, in particular (-)-epigallocatechin-3-gallate, inhibit enzyme activities and signal transduction pathways, resulting in the suppression of cell proliferation and the enhancement of apoptosis, as well as the inhibition of cell invasion, angiogenesis, and metastasis (41). Cancer risk reduction is observed more frequently in studies on green tea than in those on black tea, which is probably because many polyphenols in black tea are poorly bioavailable, or not bioavailable due to fermentation. As a chemical, EGCG can exert its actions in the form of an antioxidant or a pro-oxidant. It can also bind to target molecules and trigger cascades of signaling or metabolic pathways that lead to the inhibition of carcinogenesis. The antioxidative activity of tea polyphenols could decrease oxidative DNA damage, which has been shown in both human and animal models (41).

Many studies reported no association between BBD and caffeine. Heyden (42) in an editorial review of the original work of Minton et al. (8) concluded that there was no reason to associate caffeine and FBD. Lawson et al. (12) reported a modest positive association between caffeine and FBD. The RR was: 1.4 (1-3 cups of coffee/day), 1.5 (4-6 cups of coffee/ day), and 1.3 (7 or more cups of coffee/day). However, the authors concluded that the data gave little support for a role of MX in the development of FBD. Ernster et al. (43) found a statistically significant ($P < 0.001$) reduction in clinically palpable breast findings in women abstaining from MX consumption when compared with controls. However, the absolute reduction was slight (a mean of one-half point per quadrant), and before-after mammograms for a small subset of women abstaining from MX consumption were unchanged. Marshall et al. (44) noted no difference in coffee and tea consumption patterns between controls and women with BBD. Higher levels of coffee consumption were not associated with an elevated

risk of BBD. When high coffee consumption was adjusted for high tea consumption, no increase in risk was observed. Higher levels of tea consumption were associated with a decreased risk of BBD even when adjusted for coffee consumption. The clinical course of FBD over a 6-month period was followed by Heyden and Muhlbaier (45), while recording the usual MX consumption of the study subjects. All nodules disappeared from 21 (15% of all) breasts, and 125 (87% of all) breasts showed some change in position or number of nodules during the 6-month study period. The MX consumption remained constant throughout the study (4.2 mg/day decrease from the start to the finish of the study).

Lubin et al. (19) reported that the histological type of BBD and degree of ductal atypia showed no association with coffee or MX consumption. No dose response effect was observed. Schairer et al. (46) found no evidence for an association between MX consumption and BBD (trend test P = 0.47). When cases with FBD were examined separately according to pathological subtypes (atypia, hyperplasia, sclerosing adenosis, and cysts) no association was also found. No relationship was observed between menstrual breast tenderness and MX consumption among women with FBD. A 5-year retrospective study and a 6-month prospective study of women with FBD were done by Heyden and Foder (47). No association between MX consumption and FBD was reported. A critical review of the literature on the association between caffeine and FBD was written by Levinson and Dunn (48) which concluded that there was little evidence to support the association. Allen and Frobery (49) reported that decreased caffeine consumption did not result in any significant reduction in palpable breast nodules or in a lessening of breast pain and tenderness. However, the authors found discrepancies between the actual study results and the follow-up survey results. The follow-up survey revealed that 42% of the study subjects who had reduced their caffeine consumption during the study reported a decrease in nodularity and breast pain and tenderness during the study. The actual study results did not support the follow-up survey

results. A review of clinical trials in which women with BBD excluded caffeine from their diet found inconsistent results regarding the association between caffeine and BBD progression (50). Additionally, the authors pointed out that “benign breast disease” is really an umbrella term used to broadly classify a set of closely related non-neoplastic breast syndromes, further complicating the interpretation of studies that do not discern among subtypes (50). In prospective study of dietary influences on BBD, caffeine was not significantly associated with the incidence of non-proliferative BBD or proliferative BBD without atypia (30).

In conclusion, our data showed an association between caffeine or tea consumption and risk of benign breast diseases that depends on the duration and amount consumed.

Results from this study provided additional evidence for an association between the consumption of coffee or tea for 3-4 years and fibroadenoma، fibrocystic changes in middle aged women. Meanwhile, this study also showed a reduced rate of fibrocystic breast disease in women who consumed coffee or tea for > 4 years and women who drank 1 caffeinated cup / day. Additional research is warranted to better understand the potential roles of compounds in coffee and tea on benign breast diseases, and how these influence benign breast disease risks in response to the amount and duration of beverage consumption.

We thank the Medical Record Department at King Abdulaziz University Hospital for assisting with the collection of data.

The authors responsibilities were as follows—ZKG: conducted the research, analyzed the data, and wrote the manuscript; AAR, DAK, BKH, ZIG, EAR and LKA: designed the study; conducted the research and shared the writing and editing of the manuscript.

The authors reported no conflicts of interest related to the study.

Abbreviations used: BBD, benign breast diseases; EGCG, epigallocatechin gallate; FBD, fibrocystic breast diseases; KAUH, King Abdulaziz University Hospital; MX, methylxanthines; OR, odds ratio; RR, relative risk; US, ultrasound.

Clinical Trial Registry number and website: non applicable

REFERENCES:

1. Butt M, Sultan M. Coffee and its Consumption: Benefits and Risks. Critical Reviews In Food Science & Nutrition 2011; 51:363–73.
2. George S, Ramalakshmi K, Mohan Rao LJ. A perception on health benefits of coffee. Crit Rev Food Sci Nutr 2008; 48:464–486.
3. Yu X, Bao Z, Zou J, Dong J. Coffee consumption and risk of cancers: a meta-analysis of cohort studies. BMC Cancer 2011; 11:96.
4. Bode AM, Dong Z. The enigmatic effects of caffeine in cell cycle and cancer. Cancer Lett 2007; 247:26–39.
5. Kavanagh KT, Hafer LJ, Kim DW, Mann KK, Sherr DH, Rogers AE, Sonenshein GE. Green tea extracts decrease carcinogen-induced mammary tumor burden in rats and rate of breast cancer cell proliferation in culture. J Cell Biochem. 2001; 82:387–98.
6. Amr SS, Sa'di ARM, Ilahi F, Sheikh SS. The spectrum of breast diseases in Saudi Arab females: a 26-year pathological survey at Dhahran Health Center. Ann Saudi Med 1995; 15:125–32.
7. Mansoor I. Profile of female breast lesions in Saudi Arabia. Journal Pakistan Medical Association 2001; 51:243–6.

8. Minton J, Foecking M, Webster D, Matthews R. Caffeine, cyclic nucleotides, and breast disease. Surgery 1979; 86:105–9.
9. Welsch CW. Caffeine and the development of the normal and neoplastic mammary gland. Proc Soc Exp Biol Med 1994; 207:1–12.
10. Hirose M, Hoshiya T, Akagi K, Futakuchi M, Ito N. Inhibition of mammary gland carcinogenesis by green tea catechins and other naturally occurring antioxidants in female Sprague-Dawley rats pretreated with 7, 12-dimethylbenz [alpha] anthracene. Cancer Lett 1994; 83:149–56.
11. Tanaka H, Hirose M, Kawabe M, Sano M, Takesada Y, Hagiwara A, Shirai T. Post-initiation inhibitory effects of green tea catechins on 7,12-dimethylbenz[a]anthracene-induced mammary gland carcinogenesis in female Sprague-Dawley rats. Cancer Lett 1997; 116:47–52.
12. Lawson DH, Jick H, Rothman KJ. Coffee and tea consumption and breast disease. Surgery 1981; 90:801–3.
13. Rohan TE, McMichael AJ. Methylxanthines and breast cancer. Int J Cancer 1988; 41:390–3.
14. Ewertz M, Gill C. Dietary factors and breast-cancer risk in Denmark. Int J Cancer. 1990; 46:779–84.
15. Ewertz M. Breast cancer in Denmark. Incidence, risk factors, and characteristics of survival. Acta Oncol 1993; 32:595–615.
16. Folsom AR, McKenzie DR, Bisgard KM, Kushi LH, Sellers TA. No association between caffeine intake and postmenopausal breast cancer incidence in the Iowa Women's Health Study. Am J Epidemiol 1993; 138:380–3.
17. Tavani A, Pregnolato A, La Vecchia C, Favero A, Franceschi S. Coffee consumption and the risk of breast cancer. Eur J Cancer Prev 1998; 7:77–82.

18. Michels KB, Holmberg L, Bergkvist L, Wolk A. Coffee, tea, and caffeine consumption and breast cancer incidence in a cohort of Swedish women. Ann Epidemiol. 2002; 12:21–6.
19. Lubin F, Ron E, Wax Y, Black M, Funaro M, Shitrit A. A case-control study of caffeine and methylxanthines in benign breast disease. J Am Med Assoc 1985; 253:2388-92.
20. Le MG. Coffee consumption, benign breast disease, and breast cancer. Am J Epidemiol. 1985; 122:721.
21. Hunter DJ, Manson JE, Stampfer MJ, Colditz GA, Rosner B, Hennekens CH, Speizer FE, Willett WC. A prospective study of caffeine, coffee, tea, and breast cancer. (Abstract) Am J Epidemiol 1992; 136:1000–1.
22. Mannisto S, Virtanen M, Mikkonen T, Pietinen P. Reproducibility and validity of a food frequency questionnaire in a case-control study on breast cancer. J Clin Epidemiol. 1996; 49:401–9.
23. Mansel RE, Webster DJT, Burr M, St Leger S. Is there a relationship between coffee consumption and breast disease? (Abstract) Br J Surg. 1982; 69:295–6.
24. Vatten LJ, Solvoll K, Løken EB. Coffee consumption and risk of breast cancer. A prospective study of 14,593 Norwegian women. Br J Cancer. 1990; 62:267–70.
25. Brooks PG, Gart S, Heldfond AJ, Margolin ML, Allen AS. Measuring the effect of caffeine restriction on fibrocystic breast disease: The role of graphic stress telethermometry as an objective monitor of disease. J Reprod Med 1981; 26:279–82.
26. Minton J, Abou-Issa H, Reiches N, Roseman J. Clinical and biochemical studies on methylxanthine-related fibrocystic breast disease. Surgery.1981; 90:299–304.

27. Boyle CA, Berkowitz GS, LiVolsi VA, Ort S, Merino MJ, White C, Kelsey JL. Caffeine consumption and fibrocystic breast disease: a case-control epidemiologic study. J Natl Cancer Inst 1984; 72:1015–9.
28. La Vecchia C, Talamini R, Decarli A, Franceschi S, Parazzini F, Tognoni G. Coffee consumption and the risk of breast cancer. Surgery1986; 100:477–81.
29. Rohan TE, Cook MG, McMichael AJ. Methylxanthines and benign proliferative epithelial disorders of the breast in women. Int J Epidemiol 1989; 18:626–33.
30. Webb P, Byrne C, Schnitt S, Connolly J, Jacobs T, Baer H, Willett W. A prospective study of diet and benign breast disease. Cancer Epidemiol Biomarkers Prev 2004; 13:1106–13.
31. Odenheimer DJ, Zunzunegui MV, King MC. Risk factors for benign breast disease: a case control study of discordant twins. Am J Epidemiol. 1984; 120:565–71.
32. Nagata C, Kabuto M, Shimizu H. Association of coffee, green tea, and caffeine intakes with serum concentrations of estradiol and sex hormone–binding globulin in premenopausal Japanese women. Nutr Cancer 1998; 30:21–4.
33. Goldbohm RA, Hertog MG, Brants HA, van Poppel G, van den Brandt PA. Consumption of black tea and cancer risk: a prospective cohort study. J Natl Cancer Inst, 1996, 88:93–100.
34. Wu AH, Yu MC, Tseng CC, Hankin J, Pike MC. Green tea and risk of breast cancer in Asian Americans. Int J Cancer 2003; 106:574–9.
35. Baker JA, Beehler GP, Sawant AC, Jayaprakash V, McCann SE, Moysich KB. Consumption of coffee, but not black tea, is associated with decreased risk of premenopausal breast cancer. J Nutr 2006; 136:166-71.

36. Halvorsen BL, Carlsen MH, Phillips KM, Bøhn SK, Holte K, Jacobs DR Jr, Blomhoff R. Content of redox-active compounds (i.e., antioxidants) in foods consumed in the United States. Am J Clin Nutr 2006; 84:95–135.
37. Bohn SK, Blomhoff R, Paur I. Coffee and cancer risk, epidemiological evidence, and molecular mechanisms. Mol Nutr Food Res 2014; 58:915–30.
38. Lee WJ, Zhu BT. Inhibition of DNA methylation by caffeic acid and chlorogenic acid, two common catechol-containing coffee polyphenols. Carcinogenesis 2006; 27:269–77.
39. Pozner J, Papatestas AE, Fagerstorm R, Schwartz I, Saevitz J, Feinberg M, Aufses AH. Association of tumor differentiation with caffeine and coffee intake in women with breast cancer. Surgery 1986; 100:482–8.
40. Kotsopoulos J, Eliassen AH, Missmer SA, Hankinson SE, Tworoger SS. Relationship between caffeine intake and plasma sex hormone concentrations in premenopausal and postmenopausal women. Cancer 2009; 115:2765–74.
41. Yang CS, Wang H. Mechanistic issues concerning cancer prevention by tea catechins. Mol Nutr Food Res 2011; 55:819–31.
42. Heyden S. Coffee and fibrocystic breast disease. Surgery 88:741–2.
43. Ernster VL, Mason L, Goodson WH 111, Sickles EA, Sacks ST, Selvin S, Dupuy ME, Hawkinson J, Hunt TK. Effects of caffeine free diet on benign breast disease: A randomized trial. Surgery 1982; 91:263–7.
44. Marshall J, Graham S, Swanson M. Caffeine consumption and benign breast disease: a case-control comparison. Am J Public Health 1982; 72:610–2.
45. Heyden S, Muhlbaier LH. Prospective study of fibrocystic breast disease and caffeine consumption. Surgery 1984; 96:479–83.

46. Schairer C, Brinton LA, Hoover RN. Methylxanthines and benign breast disease. Am J Epidemiol 1986; 124:603–11.

47. Heyden S, Foder JG. Coffee consumption and fibrocystic breasts: An unlikely association. Can J Surgery 1986; 29:208–11.

48. Levinson W, Dunn PM. Nonassociation of caffeine and fibrocystic breast disease. Arch Intern Med 1986; 146:1773–5.

49. Allen SS, Froberg DG. The effect of decreased caffeine consumption on benign proliferative breast disease. Surgery 1987; 101:720–30.

50. Horner NK, Lampe JW. Potential mechanisms of diet therapy for fibrocystic breast conditions show inadequate evidence of effectiveness. J Am Diet Assoc 2000; 100:1368–80.