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Nutrient Intake and Breast Cancer Risk in Korean Women : A case - control study

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To investigate the association between breast cancer risk and nutrient intake in Korean women, a case-control study was carried out. Incident cases (n=224) were identified through cancer biopsy between February 1999 and December 2000 at two university hospitals in Seoul. Hospital-based controls (n=250) were selected from patients in the same hospitals, during the same periods. Food intake was investigated with semi-quantitative food frequency questionnaire (98 items) by a trained dietitian. Subjects were asked to indicate the average intake, for a 12-month period of three years prior to the baseline phase. In this study, no apparent association was found between fat intake level and breast cancer risk. High fiber intake showed a significant inverse association only among premenopausal women. In terms of antioxidant vitamins, β-carotene and vitamin C among premenopausal women and vitamin C intake among postmenopausal women was significantly associated with a decreasing risk of breast cancer. A protective effect of high calcium consumption was observed among postmenopausal women. In conclusion, our findings support epidemiological evidence that antioxidant vitamin intake could lower the breast cancer risk in Korea.

Key words : breast cancer, case-control study, nutrient intake, menopausal status

INTRODUCTION

Breast cancer has increased over the last 10 years in nations with a low incidence rates, such as Asian countries, especially Korea. Breast cancer is among the second most prevalent types of cancer in Korean women. And interestingly, the age group of women with the highest breast cancer incidence rate in Korea was 40 to 49 years of age.[1)]

Studies on geographic differences in breast cancer incidence and mortality have emphasized the role of environmental factors, particularly dietary factors. Animal experiments suggest that high fat consumption promotes mammary tumorigenesis.[2)] However, the evidence from epidemiological studies is conflicting. Large scale epidemiological studies have reported the association between fat intake and breast cancer risk. [3-5)] In a pooled analysis of 12 case-control studies,[6)] a weak significant positive association was found with fat intake in postmenopausal women, whereas in other prospective cohort studies, little or no association was reported between fat intake and breast cancer risk.[6)] Interestingly, there is evidence that dietary fat may be a stronger risk factor for breast cancer for postmenopausal women than for premenopausal women.[3)] The possible protective effect of various dietary factors against breast cancer risk has received more attention, in particular antioxidant vitamin intake, such as vitamin A, C and E, and fiber intake. Some studies suggest a decreased breast cancer risk with increased intake of antioxidant vitamins,[7,8)] and fiber.[8,9)] Whereas other studies showed a no association between vitamin intake and breast cancer risk, [10,11)] and between fiber intake and breast cancer risk.[10,12)] However, evaluation of other nutrients have been more restricted. Therefore, we have examined the association of various nutrients and breast cancer risk in Korean women according to menopause status using a case-control study.

MATERIALS AND METHODS

Case and control subjects were collected from Hanyang University Hospital and Soonchunhyung University Hospital in Seoul, Korea. Breast cancer cases included in this study were histologically confirmed new patients, and the cancer stage were restricted to stage 3.

From February 1999 to December 2000, a total of 272 patients were identified and of those, 15 (5.5 %) rejected

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the interview, 11 (4.0 %) were those left out by age-matching, 10 (3.7%) were ruled out in analysis because of a surrogate interview, 12 (4.4 %) were in their 70s and were ruled out in the final analysis. Eventually, 224 (82.4%) were included in this analysis. To minimize information bias, all patients were interviewed immediately after admission and prior to surgery so that they would have no information about their exact condition. Hospital-based controls were collected using the frequency-matching method from the patients at the department of plastic surgery, general surgery, and opthalmology at the same hospital during the same period. Frequency matching variables were age (2 years), sex and menopausal status. Among the 299 control subjects, 20 (6.7%) had diabetes mellitus, 15 (5.0%) had hypertension, and the remaining 14 (4.7%) had other conditions (cataracts, tuberculosis, and thyroid disorder). Therefore, only 250 (83.6%) controls were included in this study. All cases and controls were interviewed in the hospital by a trained dietitian. The questionnaire included general information (age, sex, marital status, and socioeconomic status variables, such as education level, occupation and income), family history of breast cancer, age at menarche, menstrual periods, pregnancy and breastfeeding history, and menopausal status. We also investigated alcohol consumption, cigarette smoking, physical exercise, and nutrient supplements such as vitamin supplements and calcium supplements. Menopause was defined as not experiencing a menstrual period for the previous six months and in analysis, menopause status was restricted to natural menopause. Subjects were asked about the total duration of breastfeeding for each full term live birth and also were questioned regarding the use of oral contraceptives and hormone replacement therapy after menopause. Information about diet was collected using semi-quantitative frequency questionnaire with 98 food items. Trained dietitians interviewed the subjects as to the average frequency of consumption and portion size of each food for a 12-month period of three years prior to the baseline phase. A section on vitamin supplements included questions about the use of vitamin supplements (multivitamins, vitamin A, vitamin C, and vitamin E), average frequency of use, duration, dose and the brand name of the vitamin supplements used in a 12-month period of three years prior to the baseline phase. Irregular vitamin users (ex: reported "very occasionally use" or use < 5 times per month) were excluded from the final analysis. The semi-quantitative food frequency questionnaire of 98 items used in our study was developed by revising from the semi-quantitative food frequency questionnaire of 84 items used in a large prospective study (the Korean Cancer Research Survey).[13] Several food items that seemed to be highly associated with breast cancer were added to investigate the association of breast cancer with nutrient intake in Korea. A study of the validity and reproducibility of this semi-quantitative food frequency questionnaire has not been carried out yet, however, Kim et al[14] conducted a study of the validity and reliability of basal questionnaire with 84 food items by administering it twice at intervals of three months. The Pearson's correlation coefficients after energy adjustment between the 1st questionnaire versus 24 hr recalls and 2nd questionnaire versus 24 hr recalls were as follows: total fat r = 0.19, 0.14,(1^{st} vs 24 hr recall, 2^{nd} vs 24 hr recall) vitamin A r = 0.44, 0.35, (1^{st} vs 24 hr recall, 2^{nd} vs 24 hr recall) and vitamin C r = 0.17, 0.28. (1^{st} vs 24 hr recall, 2^{nd} vs 24 hr recall).

Information on portion size was collected through open-ended questions with the defined unit (200ml cup, bowl, etc). To help recall of food intake, the interviewers complied using significant personal events (ex: holidays, vacation, individual special event etc..). Our main goal was to investigate the effect of nutrient intake on breast cancer and thus we analyzed the following 19 nutrients: total energy, fat, carbohydrates, fiber, protein, cholesterol, vitamin A, retinol, β-carotene, vitamin C, vitamin E, thiamin, niacin, riboflavin, calcium, iron, phosphorus, sodium and potassium. In the vitamin analyses, we evaluated the risk associated with vitamin consumption from the diet and supplementation. We adjusted nutrient values for total energy intake, since most nutrient intake is positively correlated with total energy intake.

The total amount of each nutrient intake was divided into three groups (<25, 25-75, >75 percentiles) according to the criterion of the control group, and in each category the nutrient intake was compared with that in the lowest intake category. All data were analyzed through unconditional logistic regression using the SPSS (version 10.0) statistical package, and tests for trend were also performed by unconditional logistic regression analysis. Statistical analyses were done after adjustments for age and other confounding factors. The confounding factors for breast cancer in this study were as follows: In premenopausal women, age at menarche, family history of breast cancer, and total period of breastfeeding, and in postmenopausal women, current BMI, and alcohol consumption. For all, age-adjusted odds ratios (OR) and 95% confidence intervals (CIs) were calculated. All analyses were conducted according to the menopausal status to investigate a difference due to the menopause.

RESULTS

Table 1 shows the distribution of cases and controls by age and marital status. Total number of cases was 224, of those, premenopausal women accounted for 122 (54.5%). The age group showing a high breast cancer

Table 1. The distribution of the subjects by age and marital status

Variables	Premenopausal women		Postmenopausal women	
	Case	Control	Case	Control
Number of subjects	122(100)[2]	131(100)	102(100)	119(100)
Age(yr)				
20-29	14(11.5)	18(13.7)	-	-
30-39	38(31.1)	35(26.7)	-	-
40-49	65(53.3)	69(52.7)	6(5.9)	13(10.9)
50-59	5(4.1)	9(6.9)	68(66.7)	72(60.5)
60-69			28(27.4)	34(28.6)
Marital status				
Married	98(80.3)	104(79.4)	80(78.4)	95(79.8)
Unmarried	21(17.2)	17(16.0)	5(4.9)	6(5.0)
Widowed	3(2.5)	6(4.6)	17(16.7)	18(15.2)

[1] This category included only naturally menopaused women.
[2] Number(%)

Table 2. Odds ratios (OR) of breast cancer in relation to reproductive factors, and breastfeeding in Korean women

Variables	Premenopausal women		Postmenopausal women	
	OR[1]	95% CI	OR[2]	95% CI
Age at menarche(year)				
<13	1.00		1.00	
14-16	0.64	0.34-1.37	0.69	0.84-2.31
>17	0.45	0.31-0.94*	1.02	0.62-2.87
p-value for trend=0.0323*			*p*-value for trend=0.0653	
Total menstrual period(years)				
<25	-	-	1.00	
25-35	-	-	1.03	0.74-2.53
>35	-	-	1.23	0.87-3.21
			p-value for trend=0.1723	
Pregnancy				
Never	1.00		1.00	
Ever	0.74	0.57-1.49	0.69	0.48-1.57
p-value for trend=0.0529			*p*-value for trend=0.0523	
Total number of full term delivery[3]				
None	1.00		1.00	
1-3	0.79	0.53-1.92	0.83	0.47-1.89
>3	0.68	0.39-1.04	0.91	0.45-1.67
p-value for trend=0.0528			*p*-value for trend=0.0423*	
Total periods of breastfeeding (total months)[3]				
None	1.00		1.00	
<13	1.08	0.79-4.32	0.97	0.49-1.98
13-35	0.56	0.38-1.95	0.86	0.58-1.72
>35	0.47	0.31-0.99*	0.74	0.42-1.44
p-value for trend=0.0618			*p*-value for trend=0.0693	

[1] Odds ratio in premenopausal women adjusted for age
[2] Odds ratio in postmenopausal women adjusted for age
[3] This category included only women ever pregnant
*$p<0.05$; ** $p<0.01$

Table 3. Odds ratios (OR) of breast cancer in relation to family history of breast cancer and current BMI in Korean women

Variables	Premenopausal women		Postmenopausal women	
	OR[1]	95% CI	OR[2]	95% CI
Family history of breast cancer[3]				
No	1.00		1.00	
Yes	2.13	1.04-4.37*	2.09	0.87-3.09
p-value for trend=0.0203*			*p*-value for trend=0.0653	
Current BMI(body mass index)				
<20	1.00		1.00	
20.00-24.99	0.91	0.67-2.10	0.83	0.45-1.92
25.00-29.99	1.31	0.46-3.23	1.21	0.86-3.27
>30	1.83	0.86-3.21	2.19	1.02-3.83*
p-value for trend=0.0643			*p*-value for trend=0.0231	

[1] Odds ratio in premenopausal women adjusted for age
[2] Odds ratio in postmenopausal women adjusted for age
[3] This category included only the first degree relatives
*$p<0.05$; ** $p<0.01$

Table 4. Odds ratios (OR) of breast cancer according to the intake of macronutrients in Korean women

Variables	Premenopausal women		Postmenopausal women	
	OR[1]	95% CI[4]	OR[2]	95% CI
Energy				
Low[3]	1.00		1.00	
Medium	0.64	0.34-1.37	0.69	0.84-2.31
High	0.95	0.31-0.94*	1.02	0.62-2.87
p-value for trend=0.1523*			*p*-value for trend=0.0821	
Carbohydrate				
Low	1.00		1.00	
Medium	1.02	0.75-1.24	1.03	0.74-2.53
High	0.81	0.48-2.39	1.23	0.87-3.21
p-value for trend=0.0923			*p*-value for trend=0.0523	
Fiber				
Low	1.00		1.00	
Medium	0.72	0.58-1.29	0.49	0.73-1.93
High	0.44	0.35-0.93*	0.69	0.57-2.14
p-value for trend=0.0351*			*p*-value for trend=0.1680	
Protein				
Low	1.00		1.00	
Medium	0.79	0.53-1.92	0.83	0.47-1.89
High	0.68	0.39-1.04	0.91	0.45-1.67
p-value for trend=0.0828			*p*-value for trend=0.1729	
Total fat				
Low	1.00		1.00	
Medium	1.03	0.45-2.11	0.95	0.77-1.57
High	1.24	0.56-1.56	1.05	0.86-2.19
p-value for trend=0.0618			*p*-value for trend=0.0693	
Cholesterol				
Low	1.00		1.00	
Medium	1.58	0.38-3.21	1.53	0.58-2.31
High	2.01	0.83-2.39	1.93	0.93-3.42
p-value for trend=0.0618			*p*-value for trend=0.0693	

[1] energy adjusted odds ratios for age, age at menarche, family history of breast cancer and total periods of breastfeeding
[2] energy adjusted odds ratios for age, current body mass index (BMI), alcohol consumption
[3] classified with quartile according to nutrients intake level of control group, and low means 1st quartile and high means 4th quartile
[4] 95% confidence interval
*$p<0.05$; **$p<0.01$

Table 5. Odds ratios (OR) of breast cancer according to the intake of vitamins from dietary sources in Korean women

Variables	Premenopausal women		Postmenopausal women	
	OR[1]	95% CI[4]	OR[2]	95% CI
Vitamin A				
Low[3]	1.00		1.00	
Medium	0.48	0.74-1.97	0.67	0.80-1.39
High	0.72	0.88-2.92	0.88	0.68-1.87
p-value for trend=0.0598			*p*-value for trend=0.071	
Retinol				
Low	1.00		1.00	
Medium	0.82	0.75-1.24	1.64	0.74-2.53
High	0.63	0.48-2.39	0.78	0.87-3.21
p-value for trend=0.0581			*p*-value for trend=0.1231	
β-carotene				
Low	1.00		1.00	
Medium	0.71	0.58-1.29	0.64	0.73-1.93
High	0.41	0.33-0.91*	0.58	0.57-1.02
p-value for trend=0.0325*			*p*-value for trend=0.1081	
Thiamin				
Low	1.00		1.00	
Medium	0.85	0.53-1.92	0.89	0.47-1.89
High	0.79	0.39-1.04	0.92	0.45-1.67
p-value for trend=0.0728			*p*-value for trend=0.0692	
Niacin				
Low	1.00		1.00	
Medium	0.72	0.39-1.99	0.83	0.59-2.36
High	0.63	0.74-2.10	0.89	0.31-2.95
p-value for trend=0.0598			*p*-value for trend=0.0601	
Riboflavin				
Low	1.00		1.00	
Medium	0.82	0.56-2.39	0.49	0.55-1.91
High	0.51	0.47-1.83	0.78	0.83-3.01
p-value for trend=0.0618			*p*-value for trend=0.0693	
Vitamin C				
Low	1.00		1.00	
Medium	0.53	0.45-1.95	0.65	0.47-1.47
High	0.35	0.25-0.89*	0.45	0.52-0.98*
p-value for trend=0.0392*			*p*-value for trend=0.0632	
Vitamin E				
Low	1.00		1.00	
Medium	0.86	0.38-1.92	0.62	0.83-2.31
High	0.64	0.73-2.19	0.87	0.76-1.92
p-value for trend=0.0993			*p*-value for trend=0.0501	

[1]energy adjusted odds ratios for age, age at menarche, family history of breast cancer and total periods of breastfeeding
[2]energy adjusted odds ratios for age, current body mass index(BMI), alcohol consumption
[3]classified with quartile according to nutrients intake level of control group, and low means 1st quartile and high means 4th quartile
[4]95% confidence interval
*$p<0.05$; ** $p<0.01$

incidence rate was that for women from 40 to 59 years of age. Table 2 presents odds ratios (OR) of breast cancer in relation to reproductive factors and breastfeeding. In premenopausal women, age at menarche for ≥17 year was significantly related to the decreased risk of breast

Table 6. Odds ratio (OR) of breast cancer according to the intake of vitamins from dietary sources and vitamin supplement

Variables	Premenopausal women		Postmenopausal women	
	OR[1]	95% CI[4]	OR[2]	95% CI
Vitamin A				
Low[3]	1.00		1.00	
Medium	0.68	0.84-2.34	0.79	0.72-1.92
High	0.92	0.68-3.02	0.62	0.89-2.27
p-value for trend=0.1508			*p*-value for trend=0.0911	
Thiamin				
Low	1.00		1.00	
Medium	0.95	0.79-1.90	0.60	0.66-2.21
High	0.76	0.65-2.01	0.88	0.73-3.02
p-value for trend=0.0820			*p*-value for trend=0.1093	
Niacin				
Low	1.00		1.00	
Medium	0.91	0.46-1.96	0.69	0.94-1.83
High	0.84	0.54-1.98	0.79	0.71-1.82
p-value for trend=0.0902			*p*-value for trend=0.0811	
Riboflavin				
Low	1.00		1.00	
Medium	0.89	0.74-2.12	0.89	0.47-1.89
High	0.56	0.59-1.81	0.92	0.45-1.67
p-value for trend=0.0543			*p*-value for trend=0.1502	
Vitamin C				
Low	1.00		1.00	
Medium	0.63	0.79-2.69	0.73	0.69-2.66
High	0.49	0.65-1.21	0.70	0.51-2.88
p-value for trend=0.0502*			*p*-value for trend=0.0932	
Vitamin E				
Low	1.00		1.00	
Medium	0.72	0.56-2.39	0.52	0.75-1.90
High	0.65	0.42-2.29	0.69	0.72-2.91
p-value for trend=0.0798			*p*-value for trend=0.0802	

[1]energy adjusted odds ratios for age, age at menarche, family history of breast cancer and total periods of breastfeeding
[2]energy adjusted odds ratios for age, current body mass index(BMI), alcohol consumption
[3]classified with quartile according to nutrients intake level of control group, and low means 1st quartile and high means 4th quartile
[4]95% confidence interval
*$p<0.05$; ** $p<0.01$

cancer (OR=0.45, CI=0.31-0.94). In analyses for an association between breast cancer risk and total period of breastfeeding, premenopausal women who had lactated for a total of ≥36 months showed the lowest risk of breast cancer (OR=0.47, 95% CI=0.31-0.99) compared with women who had never breast-fed. In our data, protective effects from breastfeeding were observed only among premenopausal women.

Table 3 presents the odds ratios (OR) of breast cancer in relation to family history of breast cancer and current body mass index (BMI). Family history of breast cancer was related to the risk of breast cancer only among premenopausal women (OR=2.13, 95% CI=1.04-4.37). High body mass index (≥30) significantly increased the

Table 7. Odds ratios (OR) of breast cancer according to the intake of minerals in Korean women

Variables	Premenopausal women		Postmenopausal women	
	OR[1]	95% CI[4]	OR[2]	95% CI
Calcium				
Low[3]	1.00		1.00	
Medium	0.76	0.84-3.97	0.71	0.40-1.89
High	0.98	0.58-4.12	0.43	0.28-0.87*
p-value for trend=0.0891			*p*-value for trend=0.0493*	
Phosphorus				
Low	1.00		1.00	
Medium	0.87	0.85-2.29	0.54	0.89-2.72
High	0.93	0.58-4.31	0.78	0.74-3.11
p-value for trend=0.0711			*p*-value for trend=0.3204	
Iron				
Low	1.00		1.00	
Medium	0.91	0.57-2.93	0.44	0.77-1.83
High	1.21	0.83-3.98	0.58	0.49-2.39
p-value for trend=0.0581			*p*-value for trend=0.0811	
Sodium				
Low	1.00		1.00	
Medium	0.95	0.63-2.42	0.89	0.67-2.82
High	1.29	0.89-4.04	0.92	0.76-2.77
p-value for trend=0.1028			*p*-value for trend=0.1092	
Potassium				
Low	1.00		1.00	
Medium	0.83	0.75-3.12	0.65	0.87-3.77
High	0.95	0.55-2.87	0.45	0.62-2.88
p-value for trend=0.0622			*p*-value for trend=0.0631	

[1]energy adjusted odds ratios for age, age at menarche, family history of breast cancer and total periods of breastfeeding
[2]energy adjusted odds ratios for age, current body mass index(BMI), alcohol consumption
[3]classified with quartile according to nutrients intake level of control group, and low means 1st quartile and high means 4th quartile
[4]95% confidence interval
*$p<0.05$; ** $p<0.01$

breast cancer risk among postmenopausal women (OR=2.19, 95% CI= 1.02-3.83). Adjusted odds ratios (OR) of breast cancer in relation to macronutrient intake are shown in Table 4. We observed no association for the risk of breast cancer and intake of carbohydrates, protein and total fat among premenopausal and postmenopausal women. Although overall major nutrient intake showed no clear association with breast cancer risk, high cholesterol intake, especially among premenopausal women, tended to increase risk, and the test for trend was significant (*p*-value for trend = 0.0423). The breast cancer risk was decreased significantly with high fiber intake among premenopausal women (OR= 0.44, CI=0.35-0.93) and the test for trend was also significant (*p*-value for trend = 0.0351). But, for postmenopausal women, the protective effect of fiber intake was not significant. We evaluated the risk associated with breast cancer and vitamin intake from the diet (Table 5). For premenopausal women, the protective effect of high intake of β-carotene (OR=0.41, CI= 0.33-0.91) and vitamin C (OR=0.35, CI=0.25-0.89) were significant, and the tests for trend were also significant. For postmenopausal women, high consumption of vitamin C had a protective effect on breast cancer (OR=0.45, CI=0.52-0.98). β-carotene also had a protective effect but was not significant (OR=0.58, CI=0.57-1.02). Another antioxidant vitamin, vitamin E, did not significantly decrease the breast cancer risk in either pre or postmenopausal women. Although consumption of other vitamins was not significantly associated with breast cancer risk, overall intake of vitamins showed protective effects when adjusted for age, energy and other potential confounding factors in our study. We also assessed the association between vitamin intake from diet plus vitamin supplements and the risk of breast cancer, but it did not show any association (Table 6). Results of analyses according to mineral intake are shown in Table 7. High calcium intake appeared to have a protective effect for breast cancer risk only among postmenopausal women (OR=0.43 ,CI= 0.28-0.87), and the test for trend was significant (*p*-value for trend = 0.0493). Intake of other minerals did not show any significant association with breast cancer risk in either pre or postmenopausal women.

DISCUSSION

In this case-control study, we found no association between total fat intake and breast cancer risk in Korean women. Our results are generally consistent with evidence from previous epidemiological studies. In our study, fat intake of the subjects ranged from 11.2-27.9% of total energy, and mean value was 17.9% (39.8 g per day) of total energy intake.

In a recent study carried out in the United States,[15] mean value of total fat intake was 35.0% of total energy, which is almost two times higher than that among the Korean population. In addition to a low amount of fat intake, a narrow range of fat intake, the relatively homogeneous fat intake in this study's subjects may contribute to the inability to detect a strong association of fat intake and breast cancer risk in the present study.

It is difficult to conclude that there is an association between fat intake and breast cancer due to the various classifications of fat. Therefore, it is necessary to investigate the association of fat sub-types and breast cancer.

Among antioxidant vitamins, the most consistent findings in our study were the inverse associations of vitamin C intake and cancer risk both in premenopausal and postmenopausal women. Lee et al[7] reported inverse

associations between dietary vitamin C and breast cancer risk in a case-control study in Singapore. Some studies about the survival rate of breast cancer patients reported that women with a greater intake of vitamin C were at a lower risk of dying from cancer.[11,16] Consistent with our results, high intake of antioxidant vitamin, especially β-carotene, was associated with a decreased risk of breast cancer among premenopausal women in another epidemiological study.[17] For retinol, in a similar finding to our study, no significant inverse association with breast cancer risk was observed in most epidimiologic studies.[10,11] However, in most animal studies, retinoids inhibited the progression phase of mammary carcinogenesis.[18,19] The most promising retinoids are retinyl acetate (RA) and N-4-hydroxyphenyl retinamide (4-HPR). Som et al[20] reported that beta-carotene inhibited DMBA-induced transformation of the mammary glands in vitro, acting both at the initiation and the promotion stages. Vitamin C, β-carotene and vitamin E have antioxidant activity and thus are thought to provide a cellular defense mechanism against reactive oxygen species that damage DNA.[21]

High consumption of fiber showed an inverse association with breast cancer risk among premenopausal women in our study. There were some results for an inverse association between consumption of fiber and breast cancer risk.[22,23] However, a recent case-control study reported no association between fiber intake and breast cancer risk.[24] Rose[25] reported that dietary fiber can influence oestrogen metabolism, which is probably involved in the aetiology of breast cancer. Dietary fiber could interfere with the enterohepatic cycling of oestrogen, and the oestrogenic stimulus to the breast could be thus modified and oestrogen levels in circulation reduced. [26]

In the present study, we analyzed the effect of crude fiber not dietary fiber, because there was a shortage of exact dietary fiber contents data in the Korean food composition table.

Although we could not observe the association of other minerals with the risk of breast cancer, there were possible weak inverse associations of dietary calcium intake with the risk of breast cancer among postmenopausal women. Some studies[27,28] reported a protective effect of calcium for colon cancer and stomach cancer. Nevertheless, few studies have focused on the association of breast cancer and calcium but they support our findings. Further epidemiological investigations of the protective effects of calcium against breast cancer are needed. Also needed are approaches that may provide a chemical mechanism and additional discussion of the issue of calcium intake and breast cancer must be conducted.

In hospital-based case-control studies, the bias cannot be totally excluded, and there are also several limitations to our study. However, the hospital was considered as a proper matching factor (or place) based on the fact that most of the cases and controls in this study seem to reside in areas near the hospital. The potential problem comes from the disease condition for which the controls were hospitalized. Therefore in the future study, a community based case-control study also needed. Owing to the retrospective design of the present study, recall bias is also a limitation. Therefore, interviewers complied by using significant personal events to help past food intake. (individual event, and domestic event etc..) And misclassification of exposure may have influenced the results. We used the semi-quantitative food frequency questionnaire method to measure the usual nutrient intake of the subjects. From a validation study, it was concluded that the questionnaire could satisfactorily rank subjects according to intake of nutrients and food groups.[29]

In this study, nutrient intake estimated from the food-frequency questionnaire was calculated as amount per day. Nutrient intake often strongly correlates with total energy intake, therefore, we analyzed the association of nutrient intake with breast cancer risk using the method of energy adjustment: The "residual" method suggested by Willett and Stampfer.[30]

In this study, we calculated caloric adjusted value using 2,000 kcal for a constant value. Finally, the issue of bias in this study arises owing to a limited number of cases and controls. In this study, the modest sample size may be due to the fact the analyses was done according to the menopausal status to examine the effect of menopause and, therefore, further study with a greater number of subjects should be conducted.

In conclusion, we found no overall association between intake of total fat and breast cancer risk among Korean women. However, we found a significant reduction in breast cancer risk associated with the intake of antioxidant vitamins such as β-carotene, vitamin C, and fiber intake. Interestingly, the overall protective effects of diet shown in this study appeared to be stronger among premenopausal than postmenopausal women. In a future study, it would be interesting to analyze the association between many fat subtypes and breast cancer risk. Above all, a comprehensive and well-constructed cohort study is needed to assess the relation of dietary factors and breast cancer in Korean women.

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