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Association between dietary total antioxidant capacity and breast cancer: a case–control study in a Middle Eastern country

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Abstract

Objective: The aim of this study was to determine the relationship between dietary total antioxidant capacity (dTAC) and risk of breast cancer among Iranian women.
Design: In this hospital-based case–control study, dietary intake of participants was collected using a 168-item validated FFQ. Dietary TAC was assessed using FRAP assay considering. Logistic regression was used to obtain ORs for breast cancer across quartiles of dTAC.
Setting: Cancer Institute, Iran.
Participants: We included 412 women with pathologically confirmed breast cancer and 456 apparently healthy controls.
Results: Mean dTAC was 11·3 ± 5·8 for cases and 12·1 ± 7·9 for controls. A trend towards significant inverse association was seen between dTAC and odds of breast cancer in the whole population; such that after controlling for several potential confounders, individuals in the highest quartile of dTAC were 0·39 times less likely to have breast cancer than those in the lowest quartile (0·61; 95 % CI: 0·38, 0·99, $P < 0·05$). In the stratified analysis by menopausal status, we found that postmenopausal women with the greatest dTAC had lower odds for breast cancer, compared with those with the lowest dTAC (0·47; 95 % CI: 0·24, 0·93, $P < 0·05$). This association strengthened after additional adjustment for BMI (0·28; 95 % CI: 0·11, 0·72, $P < 0·05$). No significant association was seen between dTAC and odds of breast cancer in premenopausal women.
Conclusions: We found that dietary TAC was inversely associated with risk of breast cancer, in particular among postmenopausal women. Prospective cohort studies are needed to confirm these findings.

Keywords
Total antioxidant capacity
Breast neoplasms
Diet
Case–control

Closely following lung cancer, breast cancer is the most commonly diagnosed cancer in women worldwide[1]. The WHO reported that 28 % of women are affected by breast cancer in Europe[2]. In Iran, 13 776 cases of breast cancer were diagnosed in 2018, and age standardised incidence of breast cancer was 31·0 per 100 000 in women in 2015–2016[3].

Besides genetic factors, other factors such as age of menarche and menopause, smoking and postmenopausal hormone therapy contribute to the risk of breast cancer[4]. Diet is a modifiable risk factor that can influence the risk[5–7]. Among dietary factors, consumption of alcohol and processed meat has positive association and that of fruits and vegetables has inverse association with the risk of breast cancer[8–10]. Although the contribution of individual antioxidants to the risk of breast cancer has earlier been reported, limited data are available linking dietary total antioxidant capacity (dTAC) to the risk of breast cancer.

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Previous investigations have considered dietary intakes of individual antioxidants, their blood levels or concentrations inside breast cells[11–14]. The contribution of total antioxidants together has received limited attention in this regard. Individual antioxidants may not reflect the total antioxidant power of the whole diet. In addition, due to the interactions among nutrients or synergetic effects of antioxidants, it is better to consider TAC, which considers the overall dietary antioxidants[15]. Findings from *in vitro* studies demonstrated the protective role of antioxidants against the risk of cancer[16]. In epidemiologic studies, dTAC has been linked to the reduced risk of colorectal, gastric, pancreatic and prostate cancers[17–20]. However, little information is available with regard to dTAC and risk of breast cancer. In the Rotterdam study, Patavos *et al.* reported an inverse association between dTAC and risk of breast cancer[21]. In a case–control study, no significant association was seen between dTAC and breast cancer in Iranian women[22].

Overall, data on diet–disease associations are limited in Middle-Eastern countries and most information in this regard came from Western nations. It is worth noting that dietary habits have unique characteristics in this region, and environmental factors are different in this region compared with other parts of world. The traditional Middle-Eastern diet contains high amounts of fruits and vegetables, rich sources of antioxidants, along with a large amount of refined carbohydrates and detrimental fats. Therefore, assessment of contribution of dTAC to prevalent diseases in the region might be of great importance. The current study was, therefore, done to examine the association between dTAC and odds of breast cancer in a large case–control study of Iranian women.

Subjects and methods

Participants

This hospital-based case–control study was conducted among women between May 2014 and April 2016. A total of 1030 (503 cases, 506 controls) women aged 19–80 years were recruited in the current study. Cases were patients with pathologically confirmed breast cancer that was diagnosed within the previous year. All patients were those that referred to the surgery, chemotherapy or radiotherapy departments of Iran Cancer Institute that is located at Imam Khomeini Complex in Tehran. Patients had to have no history of any other cancers. Controls were apparently healthy subjects that had attended the hospital as relatives of patients or those that had referred to the same hospital for other diseases. Controls were selected based on convenience sampling method from those that had no dietary restrictions for long term. All controls were matched to cases in terms of age category (10-year interval) and geographic location. All cases and their matched controls were included at the study at the same time to avoid biases that might occur in this regard. In the current study, we excluded those that had no response for more than seventy items of FFQ (*n* 25) as well as those with a reported total energy intake of >18 900 or <3360 kJ/d (*n* 116). Finally, 412 cases and 456 controls remained for the current analysis. All patients signed an informed written consent.

Assessment of dietary intake

Trained interviewers administered a valid and reliable FFQ containing 168 food items to all participants. The FFQ was a block-format questionnaire that contained standard portion sizes of all food items. Controls were requested to report the frequency of food consumption during the past year based on daily, weekly or monthly consumptions. Cases were asked to report their consumption in the year preceding diagnosis. Individuals who could not report their frequency of consumption based on the mentioned serving sizes were requested to report the frequency considering their own portion sizes and then the dietitians converted these portions sized to those that were mentioned in the original FFQ. To cover seasonal variations in dietary intakes, all participants were requested to report their consumption frequency of several foods during the time in the last year when these foods were available without considering the current time. We calculated daily intakes of all consumed foods and then converted them to grams by a program made by authors in access. Total energy intake was computed by summing up energy content of all foods. Nutrient composition of consumed foods was determined based on USDA food composition database that were modified for Iranian foods[23]. A previous study revealed good validity and reliability of the FFQ by comparing two similar FFQ completed 1 year apart and twelve dietary recalls[24,25].

Assessment of total antioxidant capacity

Dietary antioxidant capacity was assessed based on the impacts of food intakes on ferric reducing antioxidant potential (FRAP). The FRAP measures the power of dietary antioxidants to reduction of Fe^{3+} (ferric ion) to Fe^{2+} (ferrous ion), it can be a good index to obtain total effect of antioxidants of dietary components[26]. We considered a FRAP value for each food item based on their capacity to reduce ferric iron to Ferro using published data[27,28]. For food items that we did not find TAC values, we assumed the value of similar food as their FRAP value. TAC was computed for each person considering daily food intake multiplied by corresponding FRAP value (in mmol/100 g).

Assessment of other variables

Weight was measured to the nearest 100 g using digital scales with minimal clothes while not wearing shoes. Height was measured to the nearest 0·5 cm by tape meter mounted on the wall, whereas subject without shoes stand in a normal position. BMI was calculated by weight in kilograms divided by height in meters squared. Physical

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activity (PA) was assessed using the standardised Global Physical Activity Questionnaire (GPAQ), translated to Persian. This questionnaire has been carried out in forty-nine countries including Iran[29]. GPAQ questionnaire consists of sixteen questions in four physical activity domains: job-related activities; transportation activities; recreation and sport activities and sedentary behaviors. Data on physical activity were analysed according to the GPAQ analysis Guide[30], and MET-hours per week values was computed. Additional information on age, educational level, family history of breast cancer, alcohol and tobacco use, age at menarche, marriage history, pregnancy history, stillbirth, infertility treatment, menopause age, postmenopausal hormone therapy and contraceptive use was collected through questionnaire by a face to face interview.

Statistical methods

Data were analysed in whole study population as well as stratified by pre- and postmenopausal status. Dietary TAC was adjusted for total energy intake using the residual method. Then participants were categorised based on quartiles of dTAC. We used one-way ANOVA or *t*-test and χ^2 test to compare continuous and categorical variables, respectively, across quartiles of dTAC. To examine the association of dietary TAC and odds of breast cancer, multivariable logistic regression analysis was used in which we controlled for several covariates. The first model was adjusted for age (continuous) and energy intake. Additional adjustments were done for physical activity (continuous, Met-h/w), family history of breast cancer (yes *v.* no), educational level (Un university/university), parity (nulliparous, 1, 2–3, ≥4), oral contraceptive use (yes *v.* no), menopausal hormone use (yes *v.* no), tobacco use (yes *v.* no), alcohol use (yes *v.* no), infertility treatment (yes *v.* no), marital status (married, unmarried), folic acid (continuous, μg/d) and BMI (continuous) in the second model. The trend of ORs across quartiles of dTAC was examined by considering the median value of dTAC in each category as a continuous variable. *P* values < 0·05 were considered statistically significant. Analysis was performed by STATA version 14 (State Corp.).

Results

Table 1 indicates the sociodemographic, anthropometric and lifestyle-related characteristics of participants in cases and controls. Patients with BC were slightly older, had lower BMI and were more likely to have family history of breast cancer compared with controls. They were less likely to be physically active, married, use oral contraceptives, use postmenopausal hormones and alcohol users than controls. Patients had lower intakes of red meat and protein than controls.

Premenopausal women in the highest quartile of dTAC were older, had greater BMI and were less likely to be smoker than those in the lowest quartile (Table 2). We also found a significant difference across quartiles of dTAC in premenopausal group in terms of parity. Compared with subjects in the lower quartile, postmenopausal women in the top quartile of dTAC were more likely to be current smoker.

Pre- and postmenopausal women in the highest quartile of dTAC had higher intake of fruits, vegetables, carbohydrate, proteins, fibre, folic acid and vitamin B6 and lower intake of refined grains, energy, fat and saturated fat than those in the lowest quartile (Table 3). Compared with subjects in the lower quartile, premenopausal women in the top quartile of dTAC had higher intakes of iron. No other significant differences were seen in other dietary variables across categories of dTAC in pre- and postmenopausal women.

Multivariable-adjusted ORs and 95 % CIs for breast cancer, separately for whole population, pre- and postmenopausal women, across quartile categories of dTAC are presented in Table 4. A trend towards significant inverse association was seen between dTAC and odds of breast cancer in the whole population; such that after controlling for several potential confounders, individuals in the highest quartile of dTAC were 0·39 times less likely to have breast cancer than those in the lowest quartile (OR: 0·61; 95 % CI: 0·38, 0·99). When stratified by menopausal status, we found that postmenopausal women in the top category of dTAC had lower odds of breast cancer, compared with those in the bottom category, after adjustment for age and energy intake (OR: 0·47; 95 % CI: 0·24, 0·93). This association remained significant when we further controlled for other potential confounders, such that those in the top category had lower odds of breast cancer than those in the bottom quartile (OR: 0·28; 95 % CI: 0·11, 0·72). No significant association was seen between dTAC and odds of breast cancer in premenopausal women, either before or after controlling for confounders.

Discussion

In the current study, we found that high dTAC, as assessed by FRAP, was associated with a decreased risk of breast cancer in the whole population as well as in postmenopausal women. To our knowledge, the current study is among the first investigations that reported the association between dTAC and odds of breast cancer in a Middle Eastern country.

Several studies have considered dTAC as an exposure to predict risk of chronic conditions[18–20,31]. In addition, dietary intake of individual antioxidants including vitamins A, C, E, folate and carotenoids was examined in relation to risk of several cancers including breast cancer[12,32]. As dTAC considers dietary intake of all antioxidant giving us

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Table 1 Baseline characteristics of participants in case–control study of breast cancer in Iran

	Case (*n* 412)		Control (*n* 456)		
	Mean	SD	Mean	SD	P_{value}
Median LCD score	8·9	2·6	9·0	2·6	0·27
Age (years)	46·3	10·4	44·2	11·3	0·003
BMI (kg/m^2)	28·1	5·2	28·8	6·1	0·03
Physical activity (MET h/weak)	20·1	25·1	26·4	37·1	0·001
Age at menarche (years)	13·0	2·4	12·9	2·6	0·31
Educational level, *n*%					
Un university	83·2		84·3		0·66
University	16·7		15·7		
Married (%)	81·1		84·4		<0·001
Family history of breast cancer (yes) (%)	10·19		1·54		<0·001
Oral contraceptive use (yes) (%)	52·8		61·3		0·02
Postmenopausal hormone use (%)	0·49		1·97		0·05
Current smoking (%)	3·4		4·9		0·21
Alcohol intake (%)	2·43		5·83		0·01
Fertility treatment (%)	4·6		6·4		0·26
Nulligravid (%)	13·3		16·0		0·27
Parity					
Nulliparous/missing	43·4		42·9		0·94
1	8·7		9·2		
2–3	33·0		31·8		
≥4	14·8		16·0		
Whole grains (g/d)	93·2	96·4	91·2	101·2	0·38
Refined grains (g/d)	321·1	179·3	305·1	174·2	0·09
Fruits (g/d)	564·3	384·2	569·1	372·2	0·42
Vegetables (g/d)	301·6	242·1	316·6	211·5	0·16
Legumes (g/d)	47·3	51·8	51·8	81·5	0·16
Red meat (g/d)	13·8	18·9	16·2	21·5	0·04
Energy (kcal)	2572·1	820·2	2522·2	860·9	0·19
Carbohydrate intake (% of energy)	51·5	10·2	51·2	10·0	0·36
Protein intake(% of energy)	12·3	3·2	12·7	3·8	0·04
Fat intake (% of energy)	38·4	11·0	38·3	10·9	0·42
Fibre intake (g/d)	22·1	9·9	22·4	10·4	0·35

χ^2 Test for ordinal qualitative variables and *t*-test for continuous variables.

Table 2 Baseline characteristics according to total antioxidant capacity in participants by quartile and menopausal status

	Premenopause (*n* 568)					Postmenopause (*n* 291)				
	Q1	Q2	Q3	Q4		Q1	Q2	Q3	Q4	
Characteristic	*n* 142	*n* 142	*n* 142	*n* 142	P_{value}	*n* 73	*n* 73	*n* 73	*n* 72	P_{value}
Median score	5·62	9·26	12·03	19·66	<0·001	6·47	9·73	12·68	19·16	<0·001
Age (years)	37·09	41·19	41·24	41·30	<0·001	52·95	53·56	56·34	56·80	0·07
BMI (kg/m^2)	26·81	27·30	28·80	28·69	0·02	29·46	28·74	29·37	30·52	0·07
Physical activity (MET h/weak)	24·99	20·00	23·15	26·93	0·26	22·34	21·96	19·55	29·75	0·33
Age at menarche (years)	13·21	13·23	13·07	12·98	0·71	13·02	12·87	13·05	13·30	0·78
Educational level, *n*%										
Un university	77·5	80·3	83·8	84·5	0·38	90·4	82·2	91·8	88·9	0·28
University	22·5	19·7	16·2	15·5		9·6	17·8	8·2	11·1	
Married (%)	85·21	85·21	85·21	85·92	0·54	82·19	84·93	76·71	77·78	0·89
Family history of breast cancer (yes) (%)	5·63	3·52	6·34	5·63	0·73	9·59	6·85	5·48	4·17	0·58
Oral contraceptive use (yes) (%)	54·47	58·21	61·36	58·27	0·63	47·89	54·93	59·15	60·61	0·43
Postmenopausal hormone use (%)	0·70	0	1·41	0	0·29	2·74	0	5·48	2·78	0·25
Current smoking (%)	5·63	0·70	0	4·93	0·005	2·74	1·37	6·85	16·67	0·006
Alcohol intake (%)	6·34	4·23	2·13	4·93	0·37	2·74	4·11	1·37	6·94	0·33
Fertility treatment (%)	4·93	3·52	5·63	5·63	0·82	8·22	2·74	5·48	8·33	0·44
Nulligravid (%)	19·72	17·61	14·79	14·08	0·55	4·11	6·85	13·70	9·72	0·19
Parity										
Nulliparous/missing	40·85	44·37	42·25	37·32	0·04	34·25	42·47	50·68	54·17	0·11
1	18·31	8·45	10·56	9·15		5·48	5·48	1·37	4·17	
2–3	37·32	34·51	36·62	42·25		23·29	30·14	16·44	22·22	
≥4	3·52	12·68	10·56	11·27		36·99	21·92	31·51	19·44	

Values are mean (SD) or percentages.
χ^2 Test for ordinal qualitative variables and ANOVA for continuous variables.

Table 3 Dietary intakes across categories of the total antioxidant capacity score with stratification by menopausal status

	Premenopause									Postmenopause								
	Quartile 1		Quartile 2		Quartile 3		Quartile 4			Quartile 1		Quartile 2		Quartile 3		Quartile 4		
Variable	Mean	SD	Mean	SD	Mean	SD	Mean	SD	*P* value	Mean	SD	Mean	SD	Mean	SD	Mean	SD	*P* value
n	142		142		142		142			73		73		73		72		
Food groups																		
Whole grains (g/d)	99·7	113·5	88·4	118·7	87·0	85·0	81·9	77·9	0·49	108·5	113·8	88·37	69·0	100·9	117·2	100·1	77·9	0·65
Refined grains (g/d)	383·2	197·2	312·5	155·9	288·9	140·1	321·5	214·3	<0·001	346·2	170·5	281·8	160·4	247·2	149·6	260·9	147·4	<0·001
Fruits (g/d)	366·2	231·7	476·8	244·5	573·9	305·0	813·1	510·7	<0·001	383·0	265·3	527·4	333·3	631·8	338·1	796·8	434·6	<0·001
Vegetables (g/d)	269·4	192·9	322·9	197·7	308·2	201·6	450·4	300·7	<0·001	277·5	187·8	321·8	181·7	373·4	240·0	449·5	315·0	<0·001
Legumes (g/d)	44·7	40·8	48·4	69·2	47·9	47·3	57·8	115·1	0·47	45·4	49·5	49·6	55·6	48·4	66·5	53·8	61·5	0·85
Red meat (g/d)	18·8	32·0	15·8	16·1	14·1	13·8	14·6	15·9	0·22	13·9	33·4	13·3	13·4	12·6	9·9	13·3	11·1	0·98
Low fat dairy (g/d)	47·8	107·4	68·2	146·7	64·8	118·1	72·3	154·8	0·42	55·7	100·4	80·2	150·3	55·4	93·6	76·5	156·6	0·50
High-fat dairy (g/d)	349·5	263·1	375·5	284·1	389·3	288·3	394·6	275·3	0·52	334·6	259·7	343·7	269·1	391·6	238·6	424·3	312·3	0·15
Nutrients																		
Energy (kcal)	2870·5		2482·7		2366·1		2671·9		<0·001	2699·3		2285·2		2322·9		2419·5		0·01
Carbohydrate intake (g/d)	336·8	129·0	307·0	103·4	307·8	104·3	363·3	132·4	<0·001	313·4	109·3	294·7	118·0	300·2	115·0	336·4	115·9	0·13
Protein intake (g/d)	78·0	32·3	77·1	39·4	72·6	24·6	85·1	37·7	0·02	76·0	30·3	72·9	26·8	76·1	34·4	80·9	29·2	0·45
Fat intake (g/d)	140·3	68·4	110·7	49·4	99·6	49·4	105·2	49·1	<0·001	132·0	71·9	95·8	47·6	96·5	45·1	90·3	37·5	<0·001
Saturated fat (g/d)	51·5	32·6	34·5	21·2	31·9	22·5	32·6	21·7	<0·001	50·5	33·7	31·5	20·5	32·8	21·2	25·9	14·4	<0·001
Fibre intake (g/d)	19·6	8·4	20·5	7·7	21·4	8·3	27·8	13·7	<0·001	18·2	7·5	20·7	8·9	22·3	9·8	26·6	11·1	<0·001
Iron (mg)	20·7	10·1	18·9	8·3	19·1	7·9	22·4	9·7	0·004	20·0	8·7	19·0	9·2	19·4	9·3	21·8	8·7	0·24
Folic acid (μg)	226·2	109·5	245·7	86·8	251·1	86·6	337·6	145·3	<0·001	221·4	97·6	245·1	93·1	280·4	111·4	347·8	157·4	<0·001
Vitamin B6 (mg)	1·53	0·65	1·62	0·71	1·59	0·53	2·13	0·92	<0·001	1·46	0·56	1·62	0·64	1·80	0·77	2·03	0·75	<0·001
Vitamin B12	2·57	1·85	2·60	1·77	2·41	1·60	2·85	1·83	0·21	2·47	1·62	2·53	1·91	2·66	2·21	2·56	2·42	0·95
Vitamin E (mg)	23·6	13·4	23·1	13·2	20·8	11·4	23·2	12·2	0·23	20·6	11·4	18·8	12·1	17·8	9·3	18·7	11·4	0·50

P values were determined by the ANOVA test.

Table 4 Risk for breast cancer according to quartiles of the total antioxidant capacity score with stratification by menopausal status

	OR							
	Quartile 1	Quartile 2	95 % CI	Quartile 3	95 % CI	Quartile 4	95 % CI	P_{Trend}*
Total								
No. of cases/controls (412/456)	109/108	105/112		102/115		96/121		
Model 1	1	0·87	0·59, 1·30	0·81	0·55, 1·20	0·68	0·46, 1·01	0·05
Model 2	1	0·69	0·44, 1·06	0·66	0·42, 1·03	0·61	0·38, 0·99	0·06
Premenopause								
No. of cases/controls (267/300)	69/73	69/73		69/73		60/81		
Model 1	1	0·87	0·53, 1·42	0·89	0·54, 1·46	0·67	0·41, 1·10	0·12
Model 2	1	0·75	0·43, 1·29	0·84	0·48, 1·47	0·66	0·36, 1·20	0·29
Postmenopause								
No. of cases/controls (145/147)	45/28	33/40		35/38		32/41		
Model 1	1	0·51	0·26, 1·00	0·51	0·26, 1·01	0·47	0·24, 0·93	0·05
Model 2	1	0·28	0·12, 0·62	0·30	0·13, 0·70	0·28	0·11, 0·72	0·02

Model 1: Adjusted for age and energy.
Model 2: further adjusted for physical activity, family history of breast cancer, menopausal hormone use, education, parity, oral contraceptive use, cigar smoking, alcohol consumption, fertility treatment, marital status, folic acid, B6 and BMI.
*Trend based on median values of each quartile.

the possibility to evaluate the overall antioxidants from a wide source of foods in the diet, it seems that its assessment in the diet has several preferences over individual antioxidants. Several methods have been used to assess dTAC including total radical trapping antioxidant parameters (TRAP), oxygen radical absorbance capacity (ORAC), trolox equivalent antioxidant capacity (TEAC) and FRAP[33]. Despite some differences, assessment by FRAP seems to have several advantages over others[34]. This is why we used FRAP method in the current study to examine dTAC.

We found a significant inverse association between dTAC and risk of breast cancer among whole participants. This finding was in line with some previously published reports. In the Rotterdam study, high dietary FRAP score was prospectively associated with a lower risk of incident breast cancer[21]. However, Karimi *et al.* in a case–control study on 275 women found no significant association between dietary TAC and odds of breast cancer[22]. That study had limited sample size, used ORAC method and did not perform the analysis by menopausal status. In addition, they did not control the analysis for several important confounders. Our findings were in line with studies that examined individual antioxidants or plasma antioxidant levels and risk of breast cancer[11,14,35]. Different dietary habits, cooking methods and health status of study participants might provide some reasons for discrepant findings.

After stratifying by menopausal status, we found an inverse significant association between dTAC and odds of breast cancer among postmenopausal women, but not in premenopausal women. It seems that hormonal status is involved in the association of dTAC and odds of breast cancer. The metabolism of sex steroids such as oestrogen, testosterone and progesterone changes with age[36]. In line with our findings, results of Nurses' Health Study II revealed no association between dietary intake of vitamins A, C, and E, folate and carotenoids with risk of breast cancer among premenopausal women[37]. The etiologic factors for premenopausal breast cancer seem to be different from those in postmenopausal breast cancer. It seems that genetic and early life events play an important role in breast cancer in premenopausal women, while environmental factors including dietary intakes are important in postmenopausal women.

Breast cancer cells are exposed to greater levels of oxidative stress and increased production of free radicals which can in turn further stimulate malignant processes resulting in DNA damage, activation of several proto-oncogenes and mutation of tumor suppressor genes and subsequent genetic mutations[38]. Some non-enzymatic factors such as antioxidants have protective effects against these detrimental events[39].

The current study has several strengths. Large sample size, the use of validated questionnaires for dietary assessment, considering total antioxidant capacity of the whole diet rather than single antioxidants, doing stratified analysis by menopausal status and controlling for a wide range of confounders are among strengths. Our study had some limitations that need to be considered. Findings from case–control studies have inherent limitations of recall and selection bias, which can prohibit us inferring causality. In addition, current dietary intakes might influence the reports of the diet in the previous year. However, we asked patients to report their dietary intakes before the diagnosis of cancer. Because we used frequency matching method to match the cases and controls for age, the average age was slightly lower in the controls compared with the cases and the difference was statically significant. To allay the concerns about confounding effects of the age, we included the age in all regression models. We did not collect information on dietary supplement use, which may contribute to overall FRAP score. To compute dTAC, we applied FRAP assay, while this method might underestimate true antioxidant capacity of the diet due to not considering lipophilic antioxidants. In addition, FRAP mainly measures

in vitro antioxidant activity, and it might not accurately represent *in vivo* antioxidant activity because the bioavailability of antioxidants is highly variable[26]. For food items without any TAC value in the published papers, we used similar ones to compute FRAP score. This might further influence our findings. We did not collect data on hormone receptor status, which might intermediate the risk of breast cancer.

In conclusion, we found an inverse significant association between total dietary antioxidant capacity and odds of breast cancer in postmenopausal women. Additional studies are required to prospectively examine the association of total dietary antioxidant capacity and risk of breast cancer considering the specific subgroups of oestrogen receptor.

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