RESEARCH ARTICLE

Dietary Resistant Starch Contained Foods and Breast Cancer Risk: a Case-Control Study in Northwest of Iran

Aynaz Tajaddini[1], Ali Pourzand[2], Zohreh Sanaat[3], Saeed Pirouzpanah[4]*

Abstract

Background: A protective effect of resistant starch (RS) containing foods on carcinogenesis has been shown from several lines of experimental evidence for gastrointestinal cancers. Therefore, we aimed to investigate the association between RS contained foods and breast cancer (BC) risk in a hospital-based, age- and origin-matched, case-control study. Materials and Methods: A validated, semi-quantitative, food frequency questionnaire (FFQ) was completed by 306 women newly diagnosed with BC aged 25 to 65 years, and 309 healthy women as matched controls. Odds ratios (ORs) and 95% confidence intervals (95%CI) were estimated using conditional logistic regression models. Results: Reduced BC risk was associated with the highest tertile of whole-wheat bread and boiled potato consumption with adjusted ORs at 0.34 (95%CI: 0.19-0.59) and 0.61 (95%CI: 0.37-0.99), respectively. Among consumers of whole-wheat bread, the protective role of cereals remained relatively apparent at higher intakes level of fiber rich breads at adjusted models (OR=0.53, 95%CI: 0.28-1.01). Moreover, high intake of legumes was found out to be a significant protective dietary factor against risk of BC development with an OR of 0.01 (95%CI: 0.03-0.13). However, consumption of white bread and biscuits was positively related to BC risk. Conclusions: Our results show that certain RS containing foods, in particular whole wheat bread, legumes and boiled potato may reduce BC risk, whereas higher intake of white bread and biscuits may be related to increased BC risk.

Keywords: Breast cancer - prebiotics - fiber - resistant starch - whole grains - refined grains

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Introduction

Life-style related factors are object to study consistently as an impressive modifiable element in the etiology of many solid tumors (Sulaiman et al., 2014; Yaw et al., 2014). It has been recently speculated that despite intimate physiologic effect of individual nutrient outlined per se in experimental studies in different episodes of carcinogenesis, it is still remained the topic of active speculations to see whether some plant-derived staple foods which include certain integrative combination of vitamins, minerals, fibers and phytochemical components have cumulative effects on carcinogenesis (Pirouzpanah et al., 2010; Sulaiman et al., 2014). However, their dietary ingredients such as dietary fiber and indigestible carbohydrates implicated to provide health benefits through gut fermentation-related byproducts (Wen et al., 2009; Woo et al., 2013; Kruk, 2014). Although the contribution of dietary fiber resources on prevention of chronic disorders received sufficient attentions by investigators so far, evidence to support the main effect of relationship between dietary resources of indigestible carbohydrates to reveal BC risk are scarce.

Recently, it is well-established that fiber-rich foods are important dietary factors in cancer prevention. Such a dietary source is whole grain products include whole-wheat bread and biscuits, legumes and potatoes vs. refined grains including white bread, rice, pasta and cakes. Whole grain contains numerous substantial phytochemicals other than fiber such as vitamins, minerals and lignans that have anticancer properties and may affect BC risk by several potential mechanisms (Jacobs et al., 1998a). However, refining removes the bran and germ, leaving the endosperm which is rich in starch and protein, so reduced the nutrient contents of grain. Nutrition transition during the past decades leads to higher consumption of refined grains and simple carbohydrates as well as other Western-related dietary habits that in turn result in greater calorie intake and subsequently enhanced prevalence of chronic diseases such as insulin resistance, diabetes, and many types of cancer (Fontana et al., 2006). Despite the accumulating findings showed inverse association of whole grain intake, as a major contributor of Iranian diet, with cancer risk, no studies have assessed the protective effect on BC risk to date.

Although whole grains intake was found to be fairly

*[1]Nutrition Research Center, [2]Department of General Surgery, Faculty of Medicine, [3]Hematology and Oncology Research Center, [4]Department of Biochemistry and Dietetics, Faculty of Nutrition, Tabriz University of Medical Sciences, Tabriz, Iran *For correspondence: pirouzpanah@gmail.com, pirouzpanahs@tbzmed.ac.ir*

protective against cancer, results were not consistent and statistically significant (Aune et al., 2011; Bahadoran et al., 2013; Yaw et al., 2014). Previous lines of evidence have shown the protective effect of whole grain products in several cancer types, including gastrointestinal cancers (Kyro et al., 2013), upper aerodigestive cancers (Turkoz et al., 2011), hepatocellular carcinoma (Al-Fatlawi et al., 2014), and also hormone-related neoplasm's such as prostate (Egeberg et al., 2011), and endometrial cancer (Kasum et al., 2001). Among hormone dependent cancers, Danish Diet, Cancer and Health cohort study reported no association between total intake of whole grain and prostate cancer risk as well as specific whole grain products consumption such as whole-grain bread and risk of prostate cancer (Egeberg et al., 2011). In contrast, a cohort study conducted in US showed a significant elevated risk of prostate cancer with increasing intake of whole grain (Nimptsch et al., 2011).

Resistant starch (RS) is a kind of starch escape from enzymatic digestion normally occurred in small intestine of healthy individual (Brouns et al., 2002). It is largely found in several plant-derived food items including whole grains, seeds, legumes, raw potato and unripe banana. There is an increasing interest in prebiotic potential of RS (Topping and et, 2001; Topping et al., 2003). Kleessen et al. (Kleessen et al., 1997) have reported increased levels of faecal lactobacillus counts in rats fed by retrograded potato starch (RS3), but not RS2. Another preliminary study on volunteers with the consumption of high amylose starch containing foods reported higher butyrate levels, in spite of lower faecal counts of bifidobacterium, compared to a cornflake control diet (Zhang et al., 2013). Moreover, butyrate plays potent roles in cell growth-related mechanisms including promotion of DNA repair, differentiation and apoptosis in tumor cells that result in inhibited malignant cell growth despite enhanced that of normal ones (Roy et al., 2006). Growing body of in vivo evidence has suggested that butyrate may not only protect against colon cancer development but also important in breast tumorigenesis (Zhu et al., 2014). However, it is suggested that dietary intake of approximately 18 g/d non-starch polysaccharides (NSP) and 20 g/d of RS are necessary to provide relevant beneficial effects (Cummings and Englyst, 1995). Since RS is a dietary starch component capable to exert physiologically almost the same as soluble, fermentable fiber (Aune et al., 2011). Nevertheless, there is no evidence available on whether RS-contained prebiotics can prevent either the initiation or promotion of BC, the aim of this hospital-based matched case-control study was to assess the association of dietary status of RS containing foods with BC risk among Iranian women residing in North-West of Iran.

Materials and Methods

Study subjects

In a consecutive case-series with simple convenience sampling method, 306 eligible BC cases were recruited between January 2012 and June 2013 at Shams private hospital in Tabriz, North-West of I.R. of Iran. The eligibility criteria included patients who had histological confirmation of BC, aged 25 to 65 years without any prior history of previous malignancies, no history of adjuvant therapy (including chemotherapy, hormonal therapy, the targeted drug trastuzumab, radiation therapy, or a combination of these treatments), no history of cystic abnormalities or benign breast disease, not being pregnant, postpartum, and breastfed mother (at the time of inclusion), following special dietary habit (vegetarian), suffering from polycystic ovary syndrome, and chronic inflammatory disorders (colitis, gastritis, multiple sclerosis, lupus erythromatosis, and sever rheumatologic disorders). Chronic use of methotrexate, sulphasalazine, anticonvulsants, and anti-contraception drugs, and assessed to have body mass index (BMI) over 45kg/m2 were also considered as exclusion criteria. The informed consent was obtained from participants before interview. The ethics approval was granted by the institutional board of Tabriz University of Medical Sciences (Ethic no 5/4/644). Moreover, Tabriz is the capital city of Eastern-Azarbaijan and Shams hospital is one of the main referral centers for BC surgery from other neighbor provinces, including Ardabil, Western-Azarbaijan, Hamedan and Kurdistan. Our control group consisted of 309 women hospitalized for non-neoplastic diseases, with no prior history of any malignancy and benign neoplasm. Participants in control group were frequency matched to cases for age at diagnosis (5-year interval) and their residence status (rural/urban and province). When participants included in study, they must not being pregnant, postpartum, and breastfed mother, following vegetarian habit and suffering from chronic inflammatory disorders (colitis, gastritis, multiple sclerosis, lupus erythromatosis, and sever rheumatologic disorders).

Trained interviewers completed a structured questionnaire for all the participants by face-to-face interview to collect information on demographics (age, residence, marital status, education level and occupation), reproductive history, hormone use, family history of BC and physical activity level. Body weight and height were self-reported at the time of the interview. BMI was calculated by dividing weight (kg) by height (m2). Relevant medical information and histological findings were obtained from the hospital medical records.

Dietary assessment

An interviewer-administered quantitative food frequency questionnaire (FFQ) was used to assess dietary intake of 136 food items, validated in our previous reports for certain nutrients (Pirouzpanah et al., 2012; Pirouzpanah et al., 2013; Pirouzpanah et al., 2014). The average frequency responses asked in a previous year was multiplied in the amount of individual foods. Certain portion size of each food item was used to make a better conceiving concept. Besides, the customary household utensils were shown to represent average portion size for the other food items to minimize inter-individual variations. At last, standard reference values was used to convert household portions to unique unit in grams for each food (Ghaffarpour et al., 1999). Regarding two main classes of grains based on the study of Jacobs et al.(Jacobs et al., 1998b); whole-wheat bread includes Sangak, Taftoon, Barbari, barley, corn flakes and sprouts, whereas white bread comprises Lavash, baguette, sweetened bread and white flour, in addition biscuit, pasta and rice are as a component of refined grains. With respect to the definition of whole grains in this study, each product that contains ≥25% whole grain or bran by weight, categorized as whole grain otherwise considered as refined grain. Dietary data were analyzed with using Nutritionist software IV for each participant (version 3.5.2; 1994, N-Squared Computing, San Bruno, CA).

Statistical analysis

Normality of continuous quantitative variables distribution were examined with Kolmogrov-Smirnov test and histogram, and box-plot was performed to remove outliers. When the data distribution was not normal, logarithm transformation of the data was conducted. If the data was still not normal-distributed, Mann Whitney U test was also applied just in case. Otherwise, independent sample t-test was used to compare continuous variables between case and control groups. Chi-squared test was performed for categorical variables in association with BC development. The tertile stratification of dietary variables was undertaken based on the distribution of the control population. Conditional logistic regression analysis was performed to calculate odds ratios (OR) and corresponding 95% confidence intervals (95% CI) using the lowest quartile group as the reference. Multivariate unconditional logistic regression analysis was performed to include related potential confounding factors such as age at diagnosis, menopausal status, parity, total calorie and BMI in adjusted models. A p-value of 0.05 or less, double-tailed, was considered to indicate a statistically significant outcome. SPSS software (Version 13.0, Chicago, IL) was used in statistical analysis.

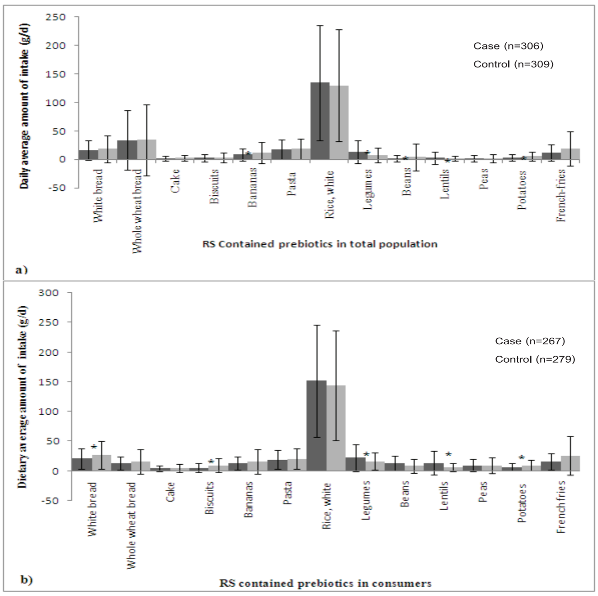

Figure 1. Comparing the Intake Levels of RS Contained Prebiotics between Controls and Cases among Total Population (A) and Consumers (B). Data are presented in mean ± standard deviation (S.D.) and the estimated unit of food was in gram per day (g/d). Data were compared using t-test or Mann Whitney t-test. *p<0.05

Results

The average intake levels of RS contained prebiotic foods between cases and controls were shown in Figure 1. Legume consumption was significantly high in cases around 13.0±20.5 g/d compared to 8.0±12.9 g/d in controls (P<0.01) of total population (combination of consumers and non-consumers). Figure 1 shows that either variable of boiled or fried potato was consumed greater in cases while compared to controls in total population (p<0.01). Mean daily amount of white bread and biscuit consumptions were also estimated high in control group rather than cases (p<0.01). No significant differences were observed for whole-wheat bread.

Tamong only consumers (OR=0.53, 95%CI: 0.28-1.01), but could not pertain statistical significant results (Table 3).

The association of RS contained prebiotic foods (categorized variables based upon tertiles) and BC risk among cases versus controls were shown in Table 2 for total population and Table 3 for merely consumers of each prebiotic food. Higher intake of white bread was

Table 1. General Characteristics of Womenparticipants in Case and Control Groups

	Case (n=306)	Control (n=309)	p-value*
Age at diagnosis (years)			
Mean±SD	46.4±10.2	41.4±9.6	<0.001
≤44	133 (44.8)	182 (61.9)	<0.001
>44	164 (55.2)	133 (44.8)	
BMI (kg/m²)			
Mean±SD	27.9±4.8	27.8±5.1	0.967
<25	85 (30.6)	99 (35.2)	0.452
25-30	94 (33.8)	93 (33.1)	
≥30	99 (35.6)	89 (31.7)	
Frequency of pregnancy (n)			
<2	148 (54.0)	166 (62.9)	0.008
2-Mar	71 (25.9)	40 (15.2)	
≥3	55 (20.1)	58 (22.0)	
The number of lactation (n)			
<2	151 (57.9)	120 (65.2)	0.058
2-Mar	64 (24.5)	28 (15.2)	
≥3	46 (17.6)	36 (19.6)	
Menopause			
Premenopause	180 (58.6)	232 (74.8)	<0.001
Postmenopause	127 (41.40)	78 (25.20)	
Education			<0.001
Illiterate	40 (16.7)	11 (5.6)	
Primary school	93 (38.9)	79 (40.3)	
High school	1 (0.4)	17 (8.7)	
Diploma	52 (21.8)	50 (25.5)	
University graduate	53 (22.2)	39 (19.9)	
Occupation			0.005
Sun exposed occupation	2 (0.7)	0 (0.0)	
House keeping	225 (80.6)	149 (72.7)	
Employee	51 (18.3)	47 (22.9)	
Student	1 (0.4)	9 (4.4)	
PAL			<0.001
Sedentary	8 (3.1)	29 (13.8)	
Moderate	30 (11.6)	32 (15.2)	
Active	132 (51.0)	55 (26.2)	
Very active	89 (34.4)	94 (44.8)	

BMI, body mass index; PAL, physical activity level; S.D., standard deviation; *Chi-square test was performed

Table 2. The Relative Frequency and OR (95%CI) of Breast Cancer Risk in Association with RS Containing Foods (Total-population*)

Variables†		Case (n=306)	Control (n=309)	P -value†	OR (95%CI)	Adjusted OR (95%CI)‡
Bread (g/day)						
White-bread	<0.7	72 (23.5)**	115 (37.2)	<0.001	1	1
	0.7-21.0	108 (35.3)	83 (26.9)		2.07 (1.37-3.13)	1.71 (1.02-2.85)
	>21.0	126 (41.2)	111 (35.9)		1.81 (1.22-2.67)	1.40 (0.87-2.26)
Whole-wheat bread	<1.0	142 (45.7)	155 (53.4)	0.095	1	1
	1.0-23.0	45 (14.5)	29 (10)		1.69 (1.00-2.84)	1.39 (0.68-2.83)
	>23.0	124 (39.8)	106 (36.6)		1.27 (0.90-1.80)	0.61 (0.37-0.99)
Cake (g/day)	<1	151 (50.2)	143 (46.3)	0.383	1	1
	1-1.3	30 (10.0)	41 (13.3)		0.70 (0.40-1.20)	0.48 (0.26-0.91)
	>1.3	120 (39.8)	125 (40.4)		0.90 (0.60-1.30)	0.85 (0.56-1.29)
Biscuits (g/day)	<0.1	134 (44.5)	198 (64.1)	<0.001	1	1
	0.1-0.3	5 (1.7)	3 (1.0)		2.46 (0.57-10.47)	1.95 (0.39-9.65)
	>0.3	162 (53.8)	108 (34.9)		2.21 (1.59- 3.07)	2.00 (1.35-2.99)
Bananas (g/day)	<2.3	117 (38.8)	90 (29.1)	0.081	1	1
	2.3-10	100 (33.2)	121 (39.2)		0.70 (0.50-1.00)	0.65 (0.41-1.04)
	>10	84 (27.9)	98 (31.7)		0.70 (0.40-1.00)	0.70 (0.48-1.30)
Cooked cereals/pastas (g/day)						
Pasta(macaroni/spaghetti)	<8.3	136 (44.5)	123 (39.8)	0.112	1	1
	8.3-20	64 (20.9)	87 (28.2)		0.66 (0.44-0.99)	0.65 (0.40-1.06)
	>20	106 (34.6)	99 (32)		0.96 (0.67-1.39)	0.82 (0.52-1.29)
Rice, white	<78.6	98 (32.6)	110 (35.6)	0.678	1	1
	78.6-165	93 (30.9)	95 (30.7)		1.09 (0.74-1.63)	0.95 (0.59-1.53)
	>165	110 (36.5)	104 (33.7)		1.18 (0.81-1.74)	1.04 (0.65-1.65)
Legumes (g/day)	<1	114 (52.5)	212 (81.9)	<0.001	1	1
	1-7.3	31 (14.3)	6 (2.3)		0.104 (0.04-0.26)	0.012 (0.01-0.05)
	>7.3	72 (33.2)	41 (15.8)		0.306 (0.20-0.48)	0.011 (0.03-0.13)
Vegetables (g/day)						
Potatoes (baked/boiled)	<1.0	146 (48.5)	140 (45.3)	<0.001	1	1
	1.0-5.0	87 (28.9)	53 (17.2)		1.57 (1.04-2.37)	1.41 (0.80-2.34)
	>5.0	68 (22.6)	116 (37.5)		0.56 (0.38-0.82)	0.45 (0.28-0.71)
Potatoes (fried)	<1.8	96 (31.9)	103 (33.3)	0.005	1	1
	1.8-17.1	123 (40.9)	91 (29.4)		1.45 (0.98-2.13)	1.24 (0.77-2.00)
	>17.1	82 (27.2)	115 (37.3)		0.76 (0.51-1.13)	0.64 (0.39-1.05)

*Total population is a term referred to both consumers and non-consumers; **Data were shown in number (relative frequency); †Chi-square test was performed; ‡Adjusted for confounders included age at diagnosis (≤48, >48 years), menopause (yes or no), total calorie (≤2148, >2148 kcal), parity (≤2, >2), and BMI (≤24.9, 25-29.9, and >30). Results highlighted in bold form are statistical significant

significantly observed in case group (41.2%) rather than controls (35.9%) in total population (p<0.01), and associated with increased BC risk at OR equal to 1.81(95%CI: 1.22-2.67; Table 2). Likewise the results obtained in total population, consumers of while bread versus non-consumers was placed at higher BC risk category (OR= 1.9, 95% CI: 1.4-2.8). The highest tertile of whole wheat bread was associated significantly with protective rate of OR at 0.61 (95%CI: 0.37-0.99) to BC risk among total population. This finding was also observed to be protective at relative 50% lower risk of BC

High intake of legumes was found out to be a significant protective dietary factor against risk of BC development with an adjusted OR of 0.01 (95%CI: 0.03-0.13; Table 2). Consumers versus non-consumers of legumes were also at lower risk of BC development (OR=0.05, 95%CI: 0.02-0.09; Table 3). Among solely legume consumers, the modest level of intake was associated with lower BC risk (OR=0.06, 95%CI: 0.02- 0.17; Table 3).

Decreased BC risk for the highest tertile of boiled potato intake was evident with an OR equal to 0.45(95%CI: 0.28-0.71) among total population. In consumers, boiled potato consumption was associated with reduced risk of BC development 0.38 (95%CI: 0.19-0.76) while compared to the lowest intake category (Table 3). Higher intake of biscuits among cases (53.8%) was notable in comparison to controls (35%) among total population (p<0.01). The highest intake tertile of biscuits was associated with virtually twice BC risk among total population, after adjusting for covariates. However, we observed a significant trend of decreasing ORs in line with increasing intake of biscuits in consumers.

Discussion

The results of our study showed a favorable inverse association between consumption of whole grain bread and legume and BC risk, whereas intake of white bread as a predominant part of consumed refined cereals and one of staple food items among Iranian population might associate with elevated risk of BC. However, we did not observe any significant relation of other refined foods and BC. Similarly, in a cohort of Iowa Women's Health Study, Kasum et al. indicated an inverse association

Table 3. The relative frequency and OR (95%CI) of breast cancer risk in association with RS containing food between controls and cases (Consumers)

Variables†		Case (n=267)	Control (n=279)	P-value**	OR (95%CI)†	Adjusted OR (95%CI)‡
Bread (g/day)						
White-bread	Non-consumers	70 (22.9)*	113 (36.6)	<0.001	Ref.	Ref.
	Consumers	236 (77.1)	196 (63.4)		1.90 (1.40-2.80)	1.46 (0.94-2.26)
	<11.5	89 (37.7)	65 (33.2)	0.029	1	1
	11.5-28	89 (37.7)	60 (30.6)		1.00 (0.70-1.70)	1.03 (0.59-1.79)
	>28	58 (24.6)	71 (36.2)		0.60 (0.40-0.90)	0.56 (0.32-1.00)
Whole-wheat bread	Non-consumers	142 (45.7)	155 (53.4)	0.056	Ref.	Ref.
	Consumers	169 (54.3)	135 (46.6)		1.40 (1.00-1.90)	0.74 (0.47-1.16)
	<35.5	63 (37.2)	45 (33.3)	0.695	1	1
	35.5-80.5	53 (31.4)	42 (31.1)		0.90 (0.50-1.60)	0.67 (0.36-1.23)
	>80.5	53 (31.4)	48 (35.6)		0.80 (0.40-1.40)	0.53 (0.28-1.01)
Cake (g/day)	Non-consumers	151 (50.2)	143 (46.3)	0.561	Ref.	Ref.
	Consumers	150 (49.8)	166 (53.7)		0.80 (0.60-1.20)	0.74 (0.50-1.09)
	<1.3	30 (20.0)	41 (24.7)	0.606	1	1
	1.3-4	62 (41.3)	65 (39.2)		1.30 (0.72-2.34)	1.46 (0.71-2.99)
	>4	58 (38.7)	60 (36.1)		1.32 (0.73-2.39)	2.02 (0.99-4.12)
Biscuits (g/day)	Non-consumers	134 (44.5)	198 (64.1)	<0.001	Ref.	Ref.
	Consumers	167 (55.5)	111 (35.9)		2.20 (1.60-3.00)	2.00 (1.34-2.98)
	<2.8	86 (51.5)	37 (33.3)	0.009	1	1
	2.8-8.6	48 (28.7)	40 (36.1)		0.50 (0.30-0.90)	0.62 (0.31-1.23)
	>8.6	33 (19.8)	34 (30.6)		0.40 (0.20-0.80)	0.50 (0.23-1.07)
Bananas (g/day)	Non-consumers	109 (35.0)	77 (24.9)	0.006	Ref.	Ref.
	Consumers	202 (65.0)	232 (75.1)		0.60 (0.40-0.90)	0.60 (0.39-0.93)
	<4.7	40 (19.8)	49 (21.1)	0.943	1	1
	4.7-20	89 (44.1)	100 (43.1)		1.09 (0.65-1.80)	0.97 (0.51-1.85)
	>20	73 (36.1)	83 (35.8)		1.07 (0.63-1.81)	1.16 (0.60-2.25)
Cooked cereals/pastas (g/day)						
Pasta (macaroni/spaghetti)	Non-consumers	29 (10.5)	27 (9.7)	0.953	Ref.	Ref.
	Consumers	247 (89.5)	250 (90.3)		0.90 (0.50-1.60)	0.88 (0.45-1.70)
	<10	99 (40.1)	88 (35.2)	0.219	1	1
	10.0-22.0	61 (24.7)	79 (31.6)		0.70 (0.40-1.00)	0.89 (0.53-1.51)
	>22	87 (35.2)	83 (33.2)		0.90 (0.60-1.40)	1.00 (0.61-1.65)
Rice, white	Non-consumers	34 (11.3)	30 (9.7)	0.238	Ref.	Ref.
	Consumers	267 (88.7)	279 (90.3)		0.80 (0.50-1.40)	0.52 (0.26-1.020)
	<94.3	100 (37.5)	105 (37.6)	0.507	1	1
	94.3-165	57 (21.3)	70 (25.1)		0.80 (0.50-1.30)	0.83 (0.48-1.41)
	>165	110 (41.2)	104 (37.3)		1.10 (0.70-1.60)	1.11 (0.69-1.78)
Legumes (g/day)	Non-consumers	114 (52.5)	212 (81.9)	<0.001	Ref.	Ref.
	Consumers	163 (47.5)	47 (18.9)		0.24 (0.16-0.37)	0.05(0.02-0.09)
	<7.3	147 (67.6)	219 (84.7)	0.119	1	1
	7.3-17.6	35 (16.1)	7 (2.7)		0.13 (0.06-0.31)	0.06 (0.02-0.17)
	>17.6	35 (16.1)	33 (12.7)		0.63 (0.37-1.06)	0.26 (0.13-0.51)
Vegetables (g/day)						
Potatoes (baked/boiled)	Non-consumers	146 (48.5)	140 (45.3)	0.009	Ref.	Ref.
	Consumers	155 (51.5)	169 (54.7)		0.90 (0.60-1.20)	0.73 (0.49-1.08)
	<5	87 (56.1)	70 (41.4)	0.021	1	1
	5-8.6	37 (23.9)	47 (27.8)		0.60 (0.40-1.00)	0.56 (0.30-1.06)
	>8.6	31 (20.0)	52 (30.8)		0.50 (0.30-0.80)	0.38 (0.19-0.76)
Potatoes (fried)	Non-consumers	74 (24.6)	85 (27.5)	0.062	Ref.	Ref.
	Consumers	227 (75.4)	224 (72.5)		1.20 (0.80-1.70)	0.95 (0.60-1.48)
	<8.9	89 (39.2)	74 (33.1)	0.02	1	1
	8.9-25	86 (37.9)	72 (32.1)		0.99 (0.64-1.54)	1.56 (0.90-2.70)
	>25	52 (22.9)	78 (34.8)		0.55 (0.34-0.88)	0.69 (0.39-1.23)

*Data were shown in number (relative frequency).
**Chi-square test was performed to assess the frequency of consumers and non-consumers of prebiotic foods (independent variables) across case and control groups. †Unconditional logistic regression analyses was also performed to assess the risk breast development through exposure to either independent variables, i.e., the condition of prebiotic food usage (dichotomous variable) or tertile of usage. ‡ Unconditional multivariate logistic regression analysis adjusted for confounders included age at diagnosis (≤48, >48 years), menopause (yes or no), total calorie intake (≤2148, >2148 kcal/d), parity (≤2, >2 childbirth), and BMI (≤24.9, 25-29.9, and >30).

between whole grain consumption and endometrial cancer, whereas there was no statistical relations between refined grain intake and cancer risk (Kasum et al., 2001). Another study of 274 endometrial cancer cases and 572 controls in Switzerland reported consistent but non-significant result suggesting increased risk of cancer in the status of highest tertiles of white bread, pasta and rice intakes (Levi et al., 1993). It is also possible that more frequent intake of whole grain might lead to a lower intake of refined grains which likely has to do with reduced risk of breast carcinogenesis (Dong et al., 2012). Likewise to our data, a large case-control study in Northern Italy found out a significant 10 percent protective effects of regular and habitual consumption of whole grain against BC risk while compared to those who rarely or never ate whole grain (Chatenoud et al., 1998). Other case-control studies over different sample populations in Italy have shown significant trend of increasing BC risk across higher intake categories of refined bread and cereal dishes, whereas they showed high intake of potatoes could associate with lower BC risk which are also found out in present study (Franceschi et al., 1997).

To explain this discrepancy about cereals, one could notice that these studies did not classify and separate data of whole from refined grains. Another possible explanation can be underlined in the light of associations between starch and energy intake, which is mediated in part through adiposity in susceptibility to BC development (Kaaks and Lukanova, 2001). A case-control study in US showed that the risk of postmenopausal BC among American women was 20% greater in the highest quintile of whole grain intake compared to those in the lowest quintile of consumption, when only cases treated with hormone replacement therapy was included (Nicodemus et al., 2001). It is not clear, whether antioxidative components such as vitamin E, zinc and selenium in whole grains account for the underlying mechanism of protections against BC or other metabolites might be involved. Additionally, dietary fiber and resistant starch are major functionally active biological constituents of whole grain which increases circulation levels of short chain fatty acid (SCFA) which is penetrated across colon membranes (Salvin, 2004). In addition, RS in gut raises the transient time and peristaltic activities in alimentary lumen. These collectively have addressed to be likely involved in mechanisms related to reduction in circulating estrogen and androstenedione levels (Dong et al., 2012). Moreover, the beneficial effects of whole grain cereals consumption in regular diet have been linked to lessen glycemic load and changes in dynamic of insulin in circulation and insulin-like growth factor-1, which are candidate for being metabolic promoters of carcinogenesis (Woo et al., 2013). Whole grains are also major source of plant lignans, phytoestrogens with estrogen antagonistic effects, that can stimulates the production of enterolactone and subsequently increased formation of butyric acid with anticancer activity (Zaineddin et al., 2012). Bread as a staple food item among Iranian dietary habits (consumed in the magnitude range of 410 g/d) provide an exclusive evidence to meet resource of RS in whole grains and refined cereals with BC risk in appropriate ranges of intakes. Together, it could be speculated that the protective role of bread as RS contained food against BC risk, may be remarkably beneficial when whole grains which contained fiber in addition to RS taken into account in regular dietary habits.

Several studies have indicated that highly refined foods as major parts of Western diet may affect the risk of non-communicable chronic disease for instance in certain sorts of malignancies (Pirouzpanah et al., 2010; Aune et al., 2011; Egeberg et al., 2011; Pirouzpanah et al., 2014). Our findings supported the speculation that higher consumption of refined starchy foods (such as white bread, and biscuit) is positively associated with increased BC risk. In concordance, a case-control study conducted in Polish population reported direct correlation between intake of cereal, rice and pasta with gastric cancer risk, there was not any protective effect of whole grains consumption though (Lissowska et al., 2004). Satia-Abouta et al. found out a positive association between dietary intakes of refined cereals and colon cancer risk in a case- control study of African-Americans and Caucasians (Satia-Abouta et al., 2004). Another population based case-control study reported an inverse association between whole grains consumption and rectal cancer, whereas; high intake of refined carbohydrates was positively associated with rectal cancer risk (Slattery et al., 2004). Overall, positive effect of refined grains consumption irrespective to RS content on cancer risk may be attributable to higher digestibility that followed by increased insulin and insulin-like growth factors plasma levels as crucial mutagens in cancer initiation.

In addition, RS is naturally found in several other food items including legumes, raw potato and unripe banana. Despite of higher amounts of RS in raw potato, cooling process of boiled potato can help to boost decreased rate of RS, which is due to retrograded amylopectin and amylose.

Some *in vivo* studies have shown increased lactic acid-producing bacteria throughout the caecum and proximal colon of eighteen rats with administration of potato resistant starch diet for 14 days (Paturi et al., 2012). The results of a study in rats with consumption of combined diet containing potato resistant starch or fiber and protein showed lower bacteroides and higher SCFA concentrations in comparison to merely protein consumers (Paturi et al., 2012). Additionally, Hirose et al. (1995) reported decreasing trend of BC risk with potato consumption in premenopausal women, but it was not significant among postmenopausal women.

In this context, legumes are known for their high concentration of dietary fiber, both soluble and insoluble, and RS. Additionally, hydrothermal processing on legumes can cause increase in the fraction of RS. Thus, cooked legumes are prone to retrograded quickly that contain significant amount of RS3 (Ollberding et al., 2012). Moreover, high intake of legumes may replace animal sources of protein in the diet such as red meat, which has been implicated as a substantial risk factor for several cancers. Legume intake is more strongly related to protection against gastrointestinal (GI) cancers which has not being supported in breast, and prostate cancers (Egeberg et al., 2011; Ollberding et al., 2012). It is possible that this is due to direct exposure of GI system to the potential protective constituents of legumes and thus may to a larger extent be affected via diet. However, according to our findings decreased risk of BC is in relation to the modest intake of legumes. Several case-control and longitude cohort studies (Adebamowo et al., 2005; Shannon et al., 2005) have reported noticeable BC risk reduction with legumes consumption. A case-control study among South Asian migrant women indicated strong inverse trends of ORs of BC development along with increasing intake of pulses and dietary fiber (Dos Santos Silva et al., 2002). Women in the highest quartile of pulses showed about half of the odds of those placed in the lowest category (Dos Santos Silva et al., 2002). Similarly, in a study conducted among Shanghai population, legume intake reported to associate with decreased risk of this type malignancy (Tao et al., 2005). However, some previous studies found no association between legumes intake and risk of BC (Witte et al., 1997). Some legumes are not only an excellent source of dietary fiber but also abundant in folate, which is thought to reduce the risk of cancer (Pirouzpanah et al., 2013). Besides, legumes contain several anti nutrient components, such as phytate (inositol hexaphosphate), oligosaccharides, and saponins. It has been postulated that phytic acid may reduce cancer risk, possibly because of its antioxidant effects. There may be some beneficial effects associated with oligosaccharide such as raffinose and stachyose because of their growth-promoting effects on colon microbiota (Tharanathan and Mahadevamma, 2003).

There are some limitations in our study including the limited sample size in some stratum. Subsequent categorizing upon menopausal or pathological status was not carried out. Recall bias involves as an intrinsic nature of retrospective dietary assessments in nutritional epidemiologic studies. But in an attempt to minimize the potential effects of such within random errors we made estimation based on illustrating portion size. Block et al. (Block et al., 1986) have outlined that portion size usage boost the fidelity of the diet estimates. Furthermore, our FFQ was validated for particular related nutrients especially folate that is abundant in many fruits and vegetables (Pirouzpanah et al., 2012; Pirouzpanah et al., 2014).

In conclusion, our findings suggest the inverse correlation between high intakes of RS-contained foods in particular whole grains, legumes and potato with risk of BC. Regarding fermentable properties of RS and its role in increasing the gut microbita and providing the large amount of SCFAs, further insight may be provided by studies on the association of prebiotic-probiotic (synbiotic) models with BC risk. On the other hand, some types of RS containing foods such as whole grains are also a good source of other dietary fibers especially some of oligosaccharides like FOS that can reinforce RS prebiotic and health-benefiting effects. This synergistic interaction of dietary fibers is also an issue that remained to be resolved. Moreover, considering coadministration of dietary fibers with other foods with likely harmful by-products such as red meat could be a practical approach for healthier and balanced diet.

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