RESEARCH ARTICLE

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Dietary Factors Associated with Pancreatic Cancer Risk in Minia, Egypt: Principal Component Analysis

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Abstract

Background: Pancreatic cancer (PC) is a serious and rapidly progressing malignancy. Identifying risk factors including dietary elements is important to develop preventive strategies. This study focused on possible links between diet and PC. **Methods:** We conducted a case-control study including all PC patients diagnosed at Minia Cancer Center and controls from general population from June 2014 to December 2015. Dietary data were collected directly through personal interviews. Principal component analysis (PCA) was performed to identify dietary groups. The data were analyzed using crude odds ratios (ORs) and multivariable logistic regression with adjusted ORs and 95% confidence intervals (CIs). **Results:** A total of 75 cases and 149 controls were included in the study. PCA identified six dietary groups, labeled as cereals and grains, vegetables, proteins, dairy products, fruits, and sugars. Bivariate analysis showed that consumption of vegetables, fruits, sugars, and total energy intake were associated with change in PC risk. In multivariable-adjusted models comparing highest versus lowest levels of intake, we observed significant lower odds of PC in association with vegetable intake (OR 0.24; 95% CI, 0.07-0.85, P=0.012) and a higher likelihood with the total energy intake (OR 9.88; 95% CI, 2.56-38.09, P<0.0001). There was also a suggested link between high fruit consumption and reduced odds of PC. **Conclusions:** The study supports the association between dietary factors and the odds of PC development in Egypt. It was found that higher energy intake is associated with an increase in likelihood of PC, while increased vegetable consumption is associated with a lower odds ratio.

Keywords: Pancreatic cancer- dietary- principal component analysis- Egypt

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Introduction

Pancreatic cancer (PC) is one of the most lethal malignant neoplasms across the world, ranking as the seventh cause of cancer mortality in both sexes together (Ferlay et al., 2015). It was reported that PC was more likely to happen in the developed countries and part of the variation in the incidence worldwide may relate to under-diagnosis, under-reporting and imperfect mortality data in the less developed countries (Ferlay et al., 2015). However, in the recent years, with lifestyle and eating habits changing, the incidence of PC in developing countries is on the rise. The estimated number of PC cases in Egypt in 2013 was 2,226, and it is projected to increase and be 2,836 and 6,883 in 2020 and 2050 respectively (Ibrahim et al., 2014). The overall age-adjusted PC mortality rate in Egypt was 1.47/100,000 population and analysis of the regional distribution showed significant variations in rates among provinces with Northern provinces having higher rates than Southern regions (Soliman et al., 2006).

PC is considered a scary malignancy in developing countries where all the limitations are gathered such as unequipped health centers, underutilization of effective health care, patients' unawareness, delayed diagnosis, and insufficient funds for research (O'Donnell, 2007). Moreover, there are no current cost-effective screening recommendations for PC. Therefore, a better understanding of the etiology is essential for the development of preventive strategies including dietary recommendations (Casari and Falasca, 2015).

This is the first study that evaluates the association between dietary factors and PC risk in Egypt, and in the Arab world. Most previous studies reported the results of developed countries research, and there is lack of data from the Middle East region and low-income countries.

Accumulating data from research support the study of dietary groups to help clarify whether and how food types influence the disease risk. Food group analyses allow to consider the overall impact of food group, rather than the individual effects of single nutrients and also facilitate dietary guidance and education of the population

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(WHO, 1998). The principal component analysis was used for dimensionality reduction of dietary variables to identify few food group components.

Materials and methods

Study population

This study was conducted at Minia Cancer Center during the period from June 2014 to December 2015. Cases with a primary PC confirmed by the treating physicians were identified and enrolled in the study within 30 days of diagnosis. Controls were selected randomly from the base population during field visits conducted during the same period of the study. The field visits were conducted for health education purposes from the public health department of Faculty of Medicine. Eligible controls were men and women 40 years or more, residing in Minia, and with no personal history of cancer. The controls were selected to represent the exposure distribution in the base population.

Data collection

All participants were interviewed by a trained investigator to complete the same standardized questionnaire including information on socio-demographic characteristics, tobacco smoking, personal medical history, and dietary habits. Physical activity index (PAI) was evaluated according to The General Practice Physical Activity Questionnaire (National Collaborating Centre for Nursing and Supportive Care (UK), 2008) which calculated the 4-level PAI. Following the guidelines for human subject research, approvals to conduct the study were obtained from Scientific and Ethical Committees of Directorate of Research and Health Development of Ministry of Health and Population and also from Faculty of Medicine of Minia University.

Diet assessment

Dietary data were collected using Diet History Questionnaire II (DHQII) (Diet History Questionnaire Version 2.0., 2010). Participants in the study reported their average intake of various foods, including frequency and portion size, during the two years before diagnosis with PC for cases or before the interview for controls. Responses to the questionnaire were linked to the NCI nutrient database via the Diet*Calc® software (Diet*Calc Analysis Program Version 1.5.0., 2012) which was used to analyze data files and calculate each participant's usual daily nutrient intake.

Statistical analysis

Statistical analyses were conducted using SAS software V9.4 (SAS Institute, Inc., Cary, NC). All statistical tests were two-sided and were considered statistically significant at P-value <0.05.

Principal component analysis (PCA), a data reduction method, was used to identify dietary groups separately. PCA determined the set of components that best explain the variation in the data. We used 33 food nutrient variables that were extracted from DHQII analysis (Table 2). We used PROC FACTOR procedure in SAS to conduct the PCA analysis, using an oblique transformation that facilitates interpretability since components were correlated. Criteria that were used to determine the optimal number of components included scree plots, eigenvalues (>1), the proportion of variance accounted for, and component interpretability. Optimal components' scores were computed for each study participant by summing the intake of each food variable weighted by its component loading value. The higher the component loading value, the stronger the association was between the particular food item and the dietary group. We also computed the communality (h^2) which is the percent of the variance in an observed nutrient/food group variable that is accounted for by retained components.

Dietary groups and other food nutrient variables that were not used in PCA were categorized into quartiles. Cases were grouped based on the distribution of controls values. Unconditional logistic regression models were used to estimate the odds ratios (OR) and 95% confidence intervals (CI) for the association between PC risk and dietary risk factors. Initially, multivariable models were adjusted for confounders and known risk factors for PC (Table 3). Subsequently, a full predictive multivariable model included all of the significant (P-value <0.05) dietary factors. Working backward from the full model variables were manually removed one at a time to create the most parsimonious final model. The final multivariable model contained the same variables as a model constructed using an automated stepwise procedure in SAS (P-value set at 0.15 to enter and 0.05 to stay in the model). The tests for linear trend were based on the effect estimates for the component of interest when included as an ordinal variable in the adjusted logistic regression model.

Results

Data for this study were available from 75 cases and 149 controls. The mean age (years) of cases and controls was 60.7 (SD=9.9), and 59.5 (SD=6.7) respectively. About 57.3% of cases had PC affecting the head and 20.3% diagnosed with distant metastases. Table 1 presents the characteristics of the study participants. Higher odds of PC was associated with old age, male gender, diabetes, heavy smoking, HCV infection, lower physical activity, and mental stress (Table 1).

PCA identified six food groups based on; eigenvalues >1 in the first seven components, each of the first five components account for at least 5% of the variance, and the results of the scree test and interpretability of components; suggesting that only the first six components were meaningful. Therefore, six components were retained from PCA accounting for 83% of the total variance, and we labeled them as cereals and grains, vegetables, proteins, dairy products, fruits, and sugars. The rotated component loadings for the individual food variables and the dietary groups are shown in Table 2. Cereals and grains included the intake of dietary fibers, whole grains, refined grains, selenium, folic acid, thiamin, iron, and magnesium. Vegetables had total vegetables, dark green vegetables, non-starchy vegetables, vitamin A, vitamin C, vitamin E, vitamin K, and beta-carotene.

Table 1. Characteristics of Pancreatic Cancer Patients and Controls at Minia Cancer Center, 2014-2015

Characteristics	Cases NO (%)	Controls NO (%)	P-value [a]
Age			
40-50 years	9 (40.9%)	13 (59.1%)	
50-60 years	23 (29.1%)	56 (70.9%)	
60-70 years	29 (29%)	71 (71%)	
>70 year	14 (60.9%)	9 (39.1%)	0.028
Sex			
Female	31 (27%)	84 (73%)	
Male	44 (40.4%)	65 (59.6%)	0.034
Residence			
Urban	25 (37.9%)	41 (62.1%)	
Rural	50 (31.6%)	108 (68.4%)	0.368
Marital status			
Single	12 (37.5%)	20 (62.5%)	
Married	63 (32.8%)	129 (67.2%)	0.603
Education			
Illiterate	32 (26%)	91 (74%)	
Read and write	14 (38.9%)	22 (61.1%)	
Secondary	16 (41%)	23 (59%)	
University and above	13 (50%)	13 (50%)	0.056
Occupation			
Non-worker	29 (39.7%)	44 (60.3%)	
Farmer	26 (26.5%)	72 (73.5%)	
Manual	5 (26.3%)	14 (73.7%)	
Clerk	11 (47.8%)	12 (52.2%)	
Professional	4 (36.4%)	7 (63.6%)	0.207
BMI[b]			
< 25	40 (38.8%)	63 (61.2%)	
25-30	19 (23.7%)	61 (76.3%)	
≥ 30	16 (39%)	25 (61%)	0.074
Smoking			
Non smoker	21 (17.5%)	99 (82.5%)	
Moderate Smokersc	12 (31.6%)	26 (68.4%)	
Heavy Smokersd	26 (61.9%)	16 (38.1%)	
Unknown intensity	16 (66.7%)	8 (33.3%)	< 0.0001
Diabetes			
Non-diabetic	48 (26.7%)	132 (73.3%)	
Diabetic	27 (61.4%)	17 (38.6%)	< 0.0001
HCV[e]			
-ve HCV	62 (30.4%)	142 (69.6%)	
+ve HCV	13 (65%)	7 (35%)	0.003
Physical activity			
Inactive	9 (42.9%)	12 (57.1%)	
Moderate inactive	42 (50%)	42 (50%)	
Moderate active	18 (24.7%)	55 (75.3%)	
Active	6 (13%)	40 (87%)	0.0001
History of mental stress			
No	51 (28.6%)	127 (71.4%)	
Yes	24 (52.2%)	22 (47.8%)	0.003

[a], P-value for bivariate logistic regression; [b]BMI, body mass index; [c] Moderate smokers, < 25 pack-years;[d] Heavy smokers, ≥ 25 pack-years; [e] HCV, hepatitis C virus

Proteins included animal proteins, meat (beef, veal, lamb), poultry, cholesterol, vitamin D, and Zinc. Dairy products included milk products (milk and yogurt), cheese, solid fats (butter and margarine), calcium and phosphorus. In addition to fruits that included total fruits, juicy fruits, fruit sugars, vitamin C, and beta-cryptoxanthin. Finally, sugars had total sugars, added sugars, and fruit sugars.

In multivariable analysis, low vegetable intake, and high total energy intake were independently associated with PC risk. More specifically, comparing the highest versus the lowest quartile of consumption, vegetable intake (OR 0.24; 95% CI, 0.07-0.85, P=0.012), and total energy intake (OR 9.88; 95% CI, 2.56-38.09, P<0.0001) were associated with PC risk adjusting for age group, smoking, physical activity, and mental stress (Table 3). There is also a suggested association between high fruit consumption and lower odds of PC, (P=0.034), although the subgroup analyses did not reach significance due to low power (OR of Q3 versus Q1 0.10; 95% CI, 0.02-0.49 and OR of Q4 versus Q1 0.73; 95% CI, 0.22-2.46).

Discussion

The study found that high energy intake and low vegetable consumption were associated with higher odds of PC. There was also a suggested role of low fruit intake to be associated with an increase in PC odds.

Epidemiological and laboratory studies have consistently shown the association between high BMI and obesity and elevated PC risk. As a result, it is logical to suppose that a high caloric intake, predisposing over time to overweight or obesity, lead to increased risk of PC (Albanes, 1987; Casari and Falasca, 2015) which is consistent with our finding. On the contrary, a previous meta-analysis of cohort studies showed no association between energy intake and PC (Yu et al., 2012). But, they extracted the risk estimates that reflected the greatest degree of the control of potential confounders which likely provide results that differ from those based on standardized adjustments (Yu et al., 2012).

Vegetables and fruits are among the most widely studied dietary risk factors for cancer. We found that high vegetable intake and high fruit consumption were associated with decreased PC risk. Our findings are consistent with previous reports and reviews (Alsamarrai et al., 2014; Liu et al., 2014; Casari and Falasca, 2015; Wu et al., 2016), but not all of them (Vrieling et al., 2009; Heinen et al., 2012; Koushik et al., 2012; Shigihara et al., 2014).

The results of some earlier studies that examined the associations between PC and individual nutrients support our finding. Nutrients that are mainly provided by vegetables and fruits and highly loaded with them in our data were associated with PC such as vitamin A (Huang et al., 2016; Zhang et al., 2016), vitamin C (Chen et al., 2016), vitamin E (Jeurnink et al., 2015; Chen et al., 2016; Zhang et al., 2016), β-carotene (Jeurnink et al., 2015; Chen et al., 2016; Huang et al., 2016), and β-cryptoxanthin (Chen et al., 2016).

The inverse association between vegetables and fruits and PC risk is biologically plausible because of their

Table 2. Factor Structure for the Six Dietary Groups in Pancreatic Cancer Case- Control Study at Minia Cancer Center, 2014-2015[a]

		Reference structure [c] (semi-partial correlation)						Factor structure [d] (correlation)					
Variables	h^2 [b]	Cereals and grains	Vegetables	Proteins	Dairy products	Fruits	Sugars	Cereals and grains	Vegetables	Proteins	Dairy products	Fruits	Sugars
Dietary fibers	0.90	0.65	-	-	-	-	-	0.93	0.46	0.50	0.47	0.39	0.53
Solid fat margarine, butter)	0.93	-	-	-	0.62	-	-	0.58	-	0.68	0.91	0.43	0.46
Total sugars	0.93	-	-	-	-		0.76	0.53	-	0.36	0.43	0.41	0.96
Animal proteins	0.90	-	-	0.81	-	-	-	0.40	-	0.91	-	0.40	-
Whole grains	0.80	0.84	-	-	-	-	-	0.76	-	-	-	-	-
Refined grains	0.93	0.76	-	-	-	-	-	0.95	-	0.52	0.37	-	0.47
Meat (beef, veal, lamb)	0.73	-	-	0.72	-	-	-	-	-	0.75	-	0.34	-
Poultry	0.40	-	-	0.52	-	-	-	-	-	0.61	-	-	-
Total fruits	0.86	-	-	-	-	0.70	-	0.38	-	0.48	0.41	0.90	0.51
Juicy fruits	0.87	-	-	-	-	0.78	-	0.31	-	0.40	0.32	0.91	0.45
Fruit sugars	0.80	-	-	-	-	0.36	0.61	0.45	-	0.35	0.34	0.60	0.82
Added sugars	0.86	-	-	-	-	-	0.81	0.44	-	-	0.32	-	0.90
Total vegetables	0.83	-	0.77	-	-	-	-	0.35	0.89	0.43	-	0.32	-
Dark green vegetables	0.82	-	0.90	-	-	-	-	-	0.83	-	-	-	-
Nonstarchy vegetables	0.35	-	0.39	-	-	-	-	-	0.51	0.37	-	0.35	-
Milk and other milk products	0.96	-	-	-	0.86	-	-	0.36	-	-	0.97	0.33	0.42
Cheese	0.92	-	-	-	0.93	-	-	-	-	-	0.89	-	-
Cholesterol	0.67	-	-	0.50	-	-	-	0.46	0.40	0.74	0.50	-	0.53
Vitamin A	0.72	-	0.55	-	-	-	-	0.45	0.73	0.47	0.48	0.37	0.55
Vitamin C	0.85	-	0.40	-	-	0.64	-	0.35	0.60	0.46	-	0.82	-
Vitamin D	0.67	-	-	0.38	-	-	-	0.51	0.36	0.72	0.55	0.46	0.62
Vitamin E	0.87	-	0.43	-	-	-	-	0.72	0.71	0.72	0.46	0.47	0.54
Vitamin K	0.86	-	0.92	-	-	-	-	-	0.90	-	-	-	-
Beta carotene	0.75	-	0.83	-	-	-	-	-	0.86	-	-	-	-
Beta-cryptoxanthin	0.75	-	-	-	-	0.71	-	0.34	-	0.41	0.42	0.85	-
Zinc	0.94	-	-	0.49	-	-	-	0.73	0.33	0.91	0.65	0.53	0.52
Calcium	0.97	-	-	-	0.71	-	-	0.62	-	0.46	0.97	0.41	0.55
Phosphorus	0.98	-	-	-	0.43	-	-	0.78	0.34	0.75	0.86	0.52	0.65
Selenium	0.97	0.51	-	-	-	-	-	0.93	0.32	0.78	0.55	0.39	0.56
Folic acid	0.86	0.60	-	-	-	-	-	0.91	-	0.60	0.38	0.39	0.58
Thiamin	0.98	0.63	-	-	-	-	-	0.98	0.33	0.66	0.50	0.46	0.59
Iron	0.98	0.51	-	-	-	-	-	0.94	0.45	0.76	0.49	0.48	0.61
Magnesium	0.84	0.32	-	-	-	-	-	0.80	0.50	0.59	0.58	0.45	0.74

[a] Component patterns matrix include rows representing the variables being analyzed, and columns representing the retained components and the entries in the matrix are variable loadings. For simplicity, variable loadings < 0.30 in absolute are indicated by a dash; [b] h2, final communality is the percent of the variance in an observed variable that is accounted for by the retained components; [c] Reference structure, component loadings are equivalent to semi-partial correlations between the observed variables and the components accounting for correlation with other components; [d] Component structure, component loadings are equal to bivariate correlations between the observed variables and the components.

beneficial constituents. Vegetables and fruits provide a range of nutrients and bioactive compounds including phytochemicals as carotenoids, vitamins as vitamin C and A, minerals, and fibers (Liu, 2013). Phytochemicals have complementary and overlapping mechanisms of action for cancer prevention including and not limited to reducing oxidative stress, induction of tumor suppressor gene expression, regulation of cell cycle and induction of apoptosis (Liu, 2013). Moreover, dietary fibers provided by fruits and vegetables, have been found to have an inverse correlation with PC risk (Bidoli et al., 2012). Of note, the evidence for the health benefits of fruits and vegetables is linked to the consumption of whole foods as the potent antioxidant, and anticancer activities of fruits and vegetables are attributed to the additive and synergistic effects of their constituents of phytochemicals and vitamins (Liu, 2013).

Our results did not support the conclusions of the World Cancer Research Fund report (World Cancer Research Fund/American Institute for Cancer

Table 3. Associations between Dietary Factors and Pancreatic Cancer Risk at Minia Cancer Center, 2014-2015

Food group	Cases NO (%)	Controls NO (%)	Model[a] OR (95% CI) P-value P for trend	Model[b] OR (95% CI) P-value P for trend	Model[c] OR (95% CI) P-value P for trend
Cereals and grains					
Q1	10 (20.8%)	38 (79.2%)	1	1	
Q2	8 (17.8%)	37 (82.2%)	0.44 (0.12-1.67)	0.38 (0.06-2.26)	
Q3	14 (28%)	36 (72%)	0.59 (0.15-2.37)	1.32 (0.20-8.59)	
Q4	43 (53.1%)	38 (46.9%)	0.89 (0.21-3.71)	1.18 (0.18-7.86)	
			0.467	0.435	
			0.671	0.511	
Vegetables					
Q1	34 (47.9%)	37 (52.1%)	1	1	1
Q2	8 (17.8%)	37 (82.2%)	0.25 (0.08-0.73)	0.15 (0.04-0.61)	0.13 (0.03-0.57)
Q3	17 (31.5%)	37 (68.5%)	0.37 (0.15-0.90)	0.18 (0.05-0.72)	0.17 (0.04-0.67)
Q4	16 (29.6%)	38 (70.4%)	0.25 (0.10-0.62)	0.18 (0.05-0.67)	0.24 (0.07-0.85)
			0.007	0.011	0.012
			0.003	0.006	0.001
Proteins					
Q1	17 (31.5%)	37 (68.5%)	1	1	
Q2	18 (32.7%)	37 (67.3%)	0.50 (0.18-1.43)	0.65 (0.17-2.49)	
Q3	10 (20.8%)	38 (79.2%)	0.21 (0.06-0.68)	0.25 (0.05-1.21)	
Q4	30 (44.8%)	37 (55.2%)	0.42 (0.14-1.28)	0.57 (0.14-2.38)	
			0.079	0.356	
			0.141	0.413	
Dairy products					
Q1	9 (19.2%)	38 (80.8%)	1	1	
Q2	7 (16.3%)	36 (83.7%)	0.54 (0.14-2.11)	0.37 (0.06-2.19)	
Q3	12 (24%)	38 (76%)	0.59 (0.16-2.10)	0.43 (0.08-2.25)	
Q4	47 (56%)	37 (44 %)	1.73 (0.49-6.03)	0.69 (0.12-3.91)	
			0.051	0.559	
			0.092	0.876	
Fruits					
Q1	27 (42.2%)	37 (57.8%)	1	1	1
Q2	17 (30.9%)	38 (69.1%)	0.63 (0.26-1.54)	0.46 (0.14-1.56)	0.65 (0.19-2.17)
Q3	7 (16%)	37 (84%)	0.20 (0.07-0.56)	0.11 (0.02-0.51)	0.10 (0.02-0.49)
Q4	24 (39.3%)	37 (60.7%)	0.66 (0.28-1.55)	0.89 (0.27-2.91)	0.73 (0.22-2.46)
			0.026	0.026	0.034
			0.136	0.601	0.315
Sugars					
Q1	6 (14%)	37 (86%)	1	1	
Q2	5 (11.9%)	37 (88.1%)	0.78 (0.20-3.02)	0.76 (0.15-3.82)	
Q3	14 (26.9%)	38 (73.1%)	1.94 (0.55-6.83)	1.59 (0.34-7.54)	
Q4	50 (57.5%)	37 (42.5%)	6.04 (1.74-20.94)	2.58 (0.51-12.98)	
			0.002	0.438	
			0.0005	0.150	
Energy (kcal/day)					
Q1	10 (20.8%)	38 (79.2%)	1	1	1
Q2	3 (7.5%)	37 (92.5%)	0.25 (0.05-1.06)	0.09 (0.01-0.61)	0.09 (0.01-0.71)
Q3	13 (26%)	37 (74%)	1.60 (0.58-4.39)	1.64 (0.44-6.10)	1.91 (0.41-8.79)
Q4	49 (57%)	37 (43%)	5.68 (2.35-13.75)	4.28 (1.37-13.32)	9.88 (2.56-38.09)
			<0.0001	0.0002	<0.0001
			<0.0001	<0.0001	<0.0001
Processed meat					
Q1	15 (29.4%)	36 (70.6%)	1	1	
Q2	15 (28.3%)	38 (71.7%)	0.71 (0.26-1.97)	0.60 (0.14-2.51)	
Q3	10 (22.2%)	35 (77.8%)	0.54 (0.18-1.59)	0.28 (0.04-1.18)	
Q4	35 (46.7%)	40 (53.3%)	1.65 (0.67-4.05)	1.09 (0.32-3.70)	
			0.083	0.164	
			0.159	0.709	
Glycemic load					
Q1	8 (17.4%)	38 (82.6%)	1	1	
Q2	6 (14%)	37 (86%)	0.87 (0.23-3.20)	0.70 (0.13-3.70)	
Q3	12 (24.5%)	37 (75.5%)	1.47 (0.31-7.02)	3.94 (0.43-36.14)	
Q4	49 (57%)	37 (43%)	3.56 (0.69-18.22)	7.95 (0.82-76.84)	
			0.158	0.167	
			0.059	0.073	
Fish intake					
Q1	21 (35%)	39 (65%)	1	1	
Q2	8 (17.8%)	37 (82.2%)	0.46 (0.16-1.35)	0.32 (0.07-1.51)	
Q3	28 (43.1%)	37 (56.9%)	1.67 (0.72-3.88)	3.22 (0.94-10.94)	
Q4	18 (33.3%)	36 (66.7%)	0.86 (0.35-2.09)	0.56 (0.14-2.30)	
			0.096	0.016	
			0.662	0.647	

[a] Adjusted OR for age, sex, and total energy intake;[b] Multivariable adjusted OR for age, sex, BMI, diabetes, HCV, mental stress, physical activity, smoking and total energy intake; [c] Final model adjusted for age, smoking, physical activity, mental stress and total energy intake.

Research, 2012) and other studies that reported the high risk of PC with excess processed meat consumption (Larsson and Wolk, 2012; Zhao et al., 2017) or low fish intake (Ghorbani et al., 2015). However, other studies were consistent with our findings and found no association (Larsson et al., 2006; Rohrmann et al., 2013). The inconsistent literature could have occurred because case-control studies are prone to more biases. In a recent meta-analysis, only case-control but not cohort studies reported the association of red and processed meat consumption with risk of PC (Zhao et al., 2017). Furthermore; some studies reported such association in either men or women only (Larsson et al., 2006; Larsson and Wolk, 2012) indicating that there are gender differences and others concluded that cooking methods also have an important role (Larsson and Wolk, 2012; Ghorbani et al., 2015). The impact of fish consumption on health may also depend on the types of fish consumed and fish preparation methods. Deep-frying of fish may reduce the amount of long-chain polyunsaturated fatty acids (LC-PUFAs) and generates food mutagens (benzo(a)pyrene and heterocyclic amines), that promote carcinogenesis and increase PC risk (Li et al., 2007). It was found that LC-PUFAs, but not shellfish or fried fish, may reduce PC risk (He et al., 2013).

Inconsistent with some previous studies (La Vecchia, 2009; Lei et al., 2016), we found no association between PC risk and cereals and grain consumption which contain elevated amounts of dietary fiber, folate, and various antioxidants, that may play a protective role in pancreatic carcinogenesis (Casari and Falasca, 2015; Chen et al., 2016). However, in studies conducted among Mediterranean colorectal cancer patients (La Vecchia, 2009) and Italian PC patients (Bidoli et al., 2012), both vegetable fibers and fruit fibers were protective while cereal fibers were not. Moreover, the intake of refined grains was associated with an increased risk of stomach, colorectal, breast, upper digestive tract, and thyroid cancers (La Vecchia, 2009). Cereals mainly rice and bread are essential components of the Egyptian diet accounting for 62.3 % of the daily calorie intake (McGill et al., 2015). A previous case-control study demonstrated that increased frequency of bread and rice consumption was associated with increased risk of PC which might be due to high amounts of acrylamide that is supposed to play a role in PC pathogenesis (Ghorbani et al., 2015). However, we cannot entirely exclude the possibility that absence of the association between PC and cereals and grains intake is due to some measurement error or too little contrast in our data.

This study had several strengths and some limitations. Using PCA allowed food group analyses to consider the overall impact of food group, rather than the individual effects of single nutrients. Moreover, the study included both men and women and controls from the general population and not hospital controls whose dietary habits may be affected by their disease conditions. The similar catchment areas and the almost complete participation of cases and controls are reassuring against any selection bias.

On the other side, the study might be unable to detect associations between PC and the less prevalent risk factors due to the relatively small sample size. Also, as with all case-control studies, there is a potential for recall bias, and with the use of food frequency questionnaires, there is a possibility of measurement and misclassification biases. In addition, reverse causality might be an issue. To overcome these problems, we standardized measuring all variables and adjusted for all known covariates and major potential confounders. Specifically, the collection of data was done by the same investigator and using the same questionnaire for cases and controls so it is expected that any potential misclassification would have been nondifferential which tends to bias the findings toward the null. Also, dietary questionnaires were filled by the investigator who clarified, simplified, and repeated the questions to the study participants to help them to recall information. Because PC is a rapidly progressive cancer, we do not anticipate that cancer would have been developed two years before its diagnosis, therefore it is unlikely that PC patients have changed their dietary patterns and thus reverse causality might not be a major issue. In conclusion, the study provides further support to the associations between dietary factors and PC risk. High energy intake and low vegetable consumption in Egypt may have a role to increase PC risk.

Conflict of interest:

The authors declare no conflict of interest.

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