Dietary Nutrient Patterns and Prostate Cancer Risk: A Case-Control Study from Iran

Alireza Bahrami¹, Mehdi Movahed², Farshad Teymoori¹, Mohammad Reza Mazandaranian¹, Bahram Rashidkhani², Azita Hekmatdoost³, Ehsan Hejazi*³

Abstract

Background: Prostate cancer is the second common cancer in the world. Although some associations between dietary intakes and prostate cancer have been found, the effects of dietary nutrients interactions have not yet evaluated. The aim of this study is to assess the association between nutrient patterns and risk of prostate cancer. Methods and Materials: Ninety-seven patients with prostate cancer and 205 controls were asked about their demographic and dietary intakes using validated questionnaires. To extract nutrient patterns, Principal Component Analysis (PCA) based on the 35 nutrient items were applied. Varimax rotation was used for improving interpretation and minimizing correlation between the factors. Logistic regression was used to determine the odds ratio (OR) with 95% confidence interval (CI) of prostate cancer by higher scores on the nutrient patterns. Results: High adherence to the “plant source” pattern was negatively associated with prostate cancer risk (OR 0.29 for the highest vs. the lowest score tertile; 95% CI= 0.13 – 0.65; P value for trend:<0.003). Similarly, the “antioxidant and fiber” pattern was associated with decreasing risk of prostate cancer (OR 0.06 for the highest vs. the lowest score tertile;95% CI=0.02 – 0.19; P value for trend:<0.001). There was no significant association for the “mixed” and “vitamin and minerals” pattern with risk of prostate cancer. Conclusion: This study confirms the potential and important role of nutrients on prostate cancer risk. Our finding revealed that “antioxidant and fiber” and “plant source” pattern is inversely associated with prostate cancer risk; however, further longitudinal and trial studies are needed to make a firm conclusion.

Keywords: Factor analysis- prostate cancer- nutrient patterns

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Introduction

Prostate cancer (PC) is the second common cancer in the world (Mwangi and Zhang, 2013). Compared to other countries in Asia the incidence of PC is higher in Iran and it is the third common cancer in men and the six common cancer in Iranian population (Radmard, 2010; Pakzad et al., 2016). Generally the incidence of PC in developing countries is lower than developed countries (Pishgar et al., 2017; Hassanipour et al., 2018). This could be explained by numerous factors such as screening methods, genetic factors, younger age structure, life style and diet (Center et al., 2012; Mottet et al., 2017).

Studies on dietary patterns have reported that high healthy eating index (HEI) or adherence to Mediterranean diet characterized by fruits, grain, vegetable, and nuts are associated with lower risk of prostate cancer (Bosire et al., 2013; Möller et al., 2013; Hashemian et al., 2015; Eslamparast et al., 2017). By contrast, unhealthy dietary patterns like western diet, where red and processed meat and saturated fatty acids are highly consumed, are associated with higher risk of prostate cancer (Askari et al., 2014; Bagheri et al., 2018).

Investigating nutrient interactions through creating nutrient patterns could be proper alternative approach for evaluating the effects of diet on risk of disorder development (Allès et al., 2016). Numerous studies have found the effect of single nutrient on PC risk (Butler et al., 2010; Van Poppel and Tombal, 2011). Since nutrients are consumed in combination, they can be effective in bioavailability and absorbing of each other (Hu, 2002). Therefore, their individual effects cannot be identified.

Until now, there is no study evaluating the association between nutrient patterns and risk of PC in Iranian men. So, the aim of this study is to examine the relationship between nutrient patterns and PC among Iranian men.
Materials and Methods

Subjects

This hospital based case-control study carried out in Tehran (the capital of Iran). A hundred forty men with a histological confirmed diagnosis of PC in the preceding six months, who were referred to Shahid Labafi and Modarres hospitals (teaching and referral hospitals), were recruited. One hundred and thirty individuals showed their willingness to participate in the study. The study inclusion criteria were: 1) age between 40 and 80 years; 2) no change in the diet since diagnosis of PC.

According to the adherence of about 73% of Tehran’s adult population of an unhealthy dietary pattern (P2 = 0.53) (Azadbakht et al., 2005) and taking odds ratio (OR<2.75) (Walker et al., 2005), the ratio of case to control 1 to 2 (C =2), 95% confidence interval (α = 0.05) and 80% power (β = 0.20) The sample size was calculated. Using this formula, 79 cases and 158 controls were calculated. However, in order to increase the Precision of study, 100 patients in the case group and 200 subjects in the control group were selected.

Based on inclusion criteria, 100 men with PC included in this study (participation rate=71%). Furthermore, 205 patients admitted to the same hospitals (due to ear, nose or eye problems, appendicitis or general surgery) without any special diet were selected as control group. Individuals in case and control groups were matched based on age (with a ten-year interval) and the number of controls was twice as cases.

All participants were interviewed by trained interviewers during their hospital stay to obtain necessary information including history of diabetes, hypertension, smoking status, family history of cancer, life style habits including smoking, marital status and physical activity. The weight of each individual with the least amount of clothing and a sensitivity of 100 grams by digital scale and height without shoes with a sensitivity of 0.1 cm were measured. The study was approved by ethics committee at Shahid Beheshti University of medical sciences.

Dietary assessment: Usual dietary intake of the cases (1 year before diagnosis) and the controls (1 year before interview) was assessed using a valid and reliable semi-quantitative food frequency questionnaire (FFQ) that consists of 148 food items with standard serving size commonly consumed by Iranian people (Mirmiran et al., 2009). The frequency of consumption of given serving of each food item was questioned on a daily (e.g fruit), weekly (e.g meat) or monthly (e.g fish) basis and converted to daily intakes, assuming one month equal 30 days. The portion sizes were then converted to grams by using the household scales (Ghaffarpour et al., 1999). Consumption of food items in grams were then calculated by multiplying the portion size by daily intake frequency. Daily energy, macronutrients and micronutrients consumption for participants was computed by Nutritionist IV software. Since the Iranian food composition table (FCT) is not complete and comprehensive, analyzes of energy and nutrients were done by using the United States Department of Agriculture (USDA).

Results

After calculating the energy intakes of participants, 3 individuals of case group who’s their log scale of total energy intake was either >3SD or <3SD from the mean were excluded from the study. So, the data of 97 cases and 205 controls were analyzed. The General characteristics and dietary intakes of participants are shown in table 1. Cases were more likely to be smoker, married status and had higher family history of prostate cancer. Controls had higher dietary intakes.

Table 2 shows factor loading matrix for the four retained factors. These factors explained 67.2% of total variance of nutrient intake. The first pattern characterized by high consumption of manganese, selenium, thiamine, starch, niacin and iron, labeled “vitamin and mineral” pattern. The second Pattern was characterized by high intake of lutein, Vitamin K, total folate, beta-carotene and potassium, named “plant source” pattern. The Third Pattern reflected high intake of insoluble fiber, soluble fiber, Alpha-tocopherol, vitamin E, Beta-cryptoxanthin and vitamin C, called “antioxidant and fiber” pattern, and
The fourth pattern had the greatest loading on vitamin B12, riboflavin and vitamin A named “mixed” pattern.

Table 2 presents the odds ratio (OR) and corresponding confidence interval (CI) for prostate cancer according to tertile of factor scores for the retained nutrients pattern. After adjusting the effects of potential confounders, there was no significant association between “vitamin and mineral” pattern and prostate cancer. High adherence to the “plant source” pattern was negatively associated with prostate cancer risk (OR 0.29 for the highest vs. the lowest score tertile; 95% CI= 0.13 – 0.65; P value for trend:<0.003). Similarly, the “antioxidant and fiber” pattern was associated with decreasing risk of prostate cancer (OR 0.06 for the highest vs. the lowest score tertile;95% CI=0.02 – 0.19; P value for trend:<0.001). There was no significant association for the “mixed” pattern with risk of prostate cancer.

Discussion

In this study, four nutrient patterns were identified. The “antioxidant and fiber” and “plant source” patterns were inversely associated with prostate cancer whereas no significant association were found with “vitamin and mineral” and “mixed” patterns. The “antioxidant

Table 1. Baseline Characteristics of Study Participants

| Nutrients                        | Cases (n=97)     | Controls (n=205) | P-value* |
|----------------------------------|------------------|------------------|----------|
| Age (mean±SD)                    | 59.82± 9.55      | 59.59± 9.32      | 0.85     |
| BMI (mean±SD)                    | 25.09± 2.51      | 25.1± 3.00       | 0.98     |
| Smoking (yes) n (%)              | 33 (34)          | 24 (11.7)        | <0.001   |
| Prostate cancer family history (yes) n (%) | 16 (16)         | 13 (6.3)         | <0.001   |
| Marital status (married) n (%)   | 95 (95)          | 164 (81.6)       | 0.008    |
| Physical activity(mean±SD)       | 35.55±6.37       | 35.79±5.58       | 0.52     |

Table 2. Factor Loading Matrix and Explained Variances for the Four Major Nutrient Patterns Identified by Factor Analysis

| Nutrients                        | Nutrient patterns |
|----------------------------------|-------------------|
|                                 | 1     | 2     | 3     | 4     |
| Mn (mg)                          | 0.89  |       |       |       |
| selenium (mg)                    | 0.89  |       |       |       |
| thiamin (mg)                     | 0.86  |       |       |       |
| niacin (mg)                      | 0.8   | 0.32  |       |       |
| Fe (mg)                          | 0.78  | 0.45  |       |       |
| Cr (mg)                          | 0.77  |       |       |       |
| Starch (gr)                      | 0.76  |       |       |       |
| Mg (mg)                          | 0.72  | 0.5   |       |       |
| Zn (mg)                          | 0.71  | 0.44  | 0.41  |       |
| P (mg)                           | 0.63  | 0.41  | 0.5   |       |
| Fiber.Total (gr)                 | 0.6   | 0.36  | 0.35  |       |
| Cu (mg)                          | 0.59  | 0.34  | 0.35  |       |
| vitB6 (mg)                       | 0.52  | 0.44  | 0.5   |       |
| protein (gr)                     | 0.51  | 0.31  | 0.33  |       |
| lutein (mg)                      | 0.93  |       |       |       |
| vitK (mg)                        | 0.9   |       |       |       |
| folate (mg)                      | 0.35  | 0.81  |       |       |
| beta_carotene (mg)               | 0.73  | 0.38  | 0.34  |       |
| K (mg)                           | 0.31  | 0.69  | 0.43  | 0.35  |
| caffeine (mg)                    |       |       |       |       |
| Na (mg)                          |       |       |       |       |
| Fiber.insoluble (gr)             | 0.74  |       |       |       |
| fiber.soluble (gr)               | 0.7   |       |       |       |
| alpha_toco (mg)                  | 0.69  |       |       |       |
| vitE (mg)                        | 0.67  |       |       |       |
| beta_cryptoxantin (mg)           | 0.62  |       |       |       |
| vitC (mg)                        | 0.46  | 0.61  |       |       |
| alpha_carotene (mg)              | 0.51  | 0.39  |       |       |
| lycopene (mg)                    | 0.47  |       |       |       |
| vitB12 (mg)                      |       |       |       | 0.78  |
Table 3. Odds Ratios (OR) of Prostate Cancer and 95% Confidence Intervals (CI) According to Tertile Scores on The Nutrient Patterns

| Nutrient pattern | Cases/Controls | ORa | 95% CI | P for trend* | ORb | 95% CI | P for trend* |
|------------------|----------------|-----|--------|-------------|-----|--------|-------------|
| First pattern    |                |     |        |             |     |        |             |
| T1               | 51/50          | 1   | reference | <0.001     | 1   | reference | 0.72        |
| T2               | 26/76          | 0.33 | 0.18 – 0.60 | 0.55      | 0.52 – 1.17 |
| T3               | 23/79          | 0.27 | 0.14 – 0.50 | 0.91      | 0.36 – 2.24 |
| Second pattern   |                |     |        |             |     |        |             |
| T1               | 41/60          | 1   | reference | 0.001     | 1   | reference | 0.003        |
| T2               | 40/62          | 0.92 | 0.52 – 1.62 | 0.61      | 0.30 – 1.25 |
| T3               | 19/83          | 0.32 | 0.17 – 0.61 | 0.29      | 0.13 – 0.65 |
| Third pattern    |                |     |        |             |     |        |             |
| T1               | 65/36          | 1   | reference | <0.001     | 1   | reference | <0.001       |
| T2               | 25/77          | 0.17 | 0.09 – 0.32 | 0.16      | 0.07 – 0.34 |
| T3               | Oct-92         | 0.05 | 0.02 - 0.12 | 0.06      | 0.02 – 0.19 |
| Fourth pattern   |                |     |        |             |     |        |             |
| T1               | 31/70          | 1   | reference | 0.24      | 1   | reference | 0.86        |
| T2               | 42/60          | 1.56 | 0.87 – 2.79 | 1.06      | 0.52 – 2.16 |
| T3               | 27/75          | 0.81 | 0.44 – 1.49 | 0.93      | 0.43 – 1.98 |

* Significant trend (Linear regression analysis, p-trend value <0.05); Logistic regression was performed to obtain the odds ratio (95% CI) of prostate cancer; a, Age adjusted model; b, Adjusted additionally for prostate cancer family history (yes, no), body mass index, smoking (yes or no), marital status (single or married), dietary energy intake and physical activity.

and fiber” pattern was greatest loaded on vit E, vit C, Beta-cryptoxantin, Alpha-tocopherol, soluble fiber and insoluble fiber. Previous studies demonstrated that the increased level of oxidative stress (OS) causing prostate cancer, so micronutrient antioxidant could be effective in neutralizing the harmful effect of OS by involving in reactive oxygen species(ROS) elimination (Udensi and Tchounwou, 2016). The present finding seem to be consistent with other researches which found higher intake of dietary and supplementary vit E are inversely associated with risk of prostate cancer (Wright et al., 2007; Bidoli et al., 2009). However, some studies found no association or increased risk of prostate cancer with vitamin E (Gaziano et al., 2009; Klein et al., 2011). This discrepancy in results may be due to differences in baseline levels of OS. Kirsh et al., (2006) revealed that risk of prostate cancer decreased by increasing dose and duration of vitamin E supplementation in current and recent smokers. In line with our results, a meta-analysis reported dietary vitamin C intake associated with reduced prostate cancer risk (Bai et al., 2015), while cohort and trial studies have found no association (Schuurman et al., 2002; Bidoli et al., 2009; Gaziano et al., 2009). It has been supposed that dietary fiber might decrease risk of prostate cancer by improving insulin sensitivity and decrease bioactivity of Insulin-like growth factor-1 IGF-1 (Barnard et al., 2002). Previous cohort and case-control studies have demonstrated that total, insoluble, soluble and legume fiber are inversely associated with prostate cancer risk (Tabung et al., 2012; Deschasaux et al., 2014; Sawada et al., 2014). Similarly, the “plant source” pattern (loaded heavily on potassium, Vitamin K, total folate, beta-carotene and lutein) was negatively associated with risk of prostate cancer. Numerous studies have shown the protective effects of vitamin K and carotenoids consumption on prostate cancer risk (Nimptsch et al., 2008; Nimptsch et al., 2015; Dasari et al., 2017), however there is conflicting evidence regarding folate intake and prostate cancer risk. Some Studies found no association between dietary and total folate intake and prostate cancer risk, while other studies reported that higher blood folate levels increased prostate cancer risk (Figueiredo et al., 2009; Wang et al., 2014). It is possible that synergistic effect of other nutrients in this pattern, cause the significant effect of folate on reducing the risk of prostate cancer, that is completely in line with our hypothesis based on the effect of interactions between nutrients and the predominance of the effect of a higher consumption of nutrients that exhibit behavioural coexistence.

Inverse association between green leafy and cruciferous vegetables (the main source of vitamin K1) and prostate cancer risk have been reported in several studies (Hardin et al., 2011; Dasari et al., 2017). Also, the protective effect of vitamin K2 (another form of vitamin K that found in animal product) reported in one cohort study (Nimptsch et al., 2008). Anticancer effects of vitamin K can be explained by several mechanisms including decreasing ROS production or increase in ROS elimination by active scavenging systems, activating apoptosis pathways and inducing apoptosis by active Caspase dependent apoptosis via the MAP kinase pathway (Showalter et al., 2010; Dasari et al., 2018), inducing autophagy that can regulate living cells to remove damaged or long-lived cytosolic protein (Yokoyama et al., 2008).

Several studies have reported a negative association between intake of carotenoids and risk of PC (Antwi et al., 2016; Van Hoang et al., 2018). Epidemiological studies demonstrated that consumption of fruits and vegetables rich in lutein are inversely related to incidence of prostate cancer (McCann et al., 2005; Zhang et al., 2007). The
anticancer effects of lutein could be due to the function of lutein as an antioxidant, a chemo preventative agent or a regulator of apoptosis, angiogenesis and gap junctional intercellular communication (Ribaya-Mercado and Blumberg, 2004).

This study has some limitations. Case-control studies limitations could affect the result and should be taken into consideration. The probability of selection bias in case-control studies cannot be avoided. Furthermore, possible nutritional problems of control subjects might dilute the association of dietary intake and prostate cancer risk. In this regard, hospital controls (oppose to community controls) were recruited because of higher cooperation and participation rate. To avoid selection bias, and reduce the possibility of recall bias, patients with less than 6 month of diagnosis were enrolled in the recent study.

In conclusion, this study confirms the potential and important role of nutrients on prostate cancer risk. Our findings revealed that “antioxidant and fiber” and “plant source” pattern is inversely associated with prostate cancer risk; however, further longitudinal and trial studies are needed to make a firm conclusion.

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