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The association between dietary acid load and odds of prostate cancer: a case-control study

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Abstract

Background and objective Conflicting results exist regarding the associations between dietary acid load (DAL) and cancer risk. This study aimed to investigate the association between DAL and the odds of prostate cancer (PC) in the Iranian population.

Methods One hundred and twenty participants (60 controls and 60 newly diagnosed PC patients) engaged in a hospital-based case-control study conducted from April to September 2015. A validated, 160-item semi-quantitative food frequency questionnaire (FFQ) was used to assess usual dietary intakes. DAL was calculated using potential renal acid load (PRAL) and net endogenous acid production (NEAP). Multivariate logistic regression was performed to estimate odds ratios (ORs).

Results Both PRAL (OR = 5.44; 95% CI = 2.09–14.17) and NEAP (OR = 4.88; 95% CI = 2.22–13.41) were associated with increased odds of PC in the crude model. After adjusting for potential confounders (energy intake, smoking, physical activity, ethnicity, job, education, and medication use), being in the third category of PRAL (OR = 3.42; 95% CI = 1.11–8.65) and NEAP (OR = 3.88; 95% CI = 1.26–9.55) were significantly associated with increased odds of PC.

Conclusion Our findings suggest that dietary acid load may be linked to an increased risk of PC; however, further prospective studies with larger sample sizes and longer durations are necessary to validate these findings.

Keywords Dietary acid load, Associated factors, NEAP, PRAL, Prostate cancer, Case-control

Introduction

Prostate cancer (PC) is a major health concern among the global male population [1]. It is the second most frequently diagnosed cancer and the sixth most common cause of cancer death among males worldwide [2–5]. In Iranian males, PC is the third most common cancer and the sixth leading cause of cancer-related deaths [6, 7]. Current data indicate that the incidence rate of PC in Iran is 7.1 cases per 100,000 individuals and it has also show that the rate of disease incidence has increased from 1996 to 2012 [8]. An individual's age, ethnicity, and family history are well-known risk factors for PC; however, the pathogenesis of the disease might also be affected by

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other odds factors such as ultraviolet radiation, chronic inflammation, diet, alcohol consumption, and occupational exposure [9].

The association between dietary patterns and the risk of PC has been investigated in several studies, but has yielded inconsistent results [10]. Indeed, some studies showed that adherence to a Western dietary pattern could increase the odds of PC [11–13], but others did not find any associations [14, 15]. Additionally, research on the Mediterranean diet and the healthy eating index has produced mixed findings regarding their relationship with PC risk [11, 13, 15–19]. Recently, the importance of dietary acid load (DAL) has gained attention, with evidence suggesting that diet plays a significant role in maintaining acid-base balance in the body [20, 21]. Accordingly, it seems that adherence to western diets (with higher meat consumption) and healthy diets (with higher fruits and vegetables consumption and lower meat and processed grain intake), are associated with the acidic and alkali status of the diets, respectively [22]. In order to estimate dietary acid load, the potential renal acid load (PRAL) and the net endogenous acid production (NEAP) can be calculated from dietary intake [23]. The association between the DAL and risk of some cancers have been investigated in few case-control studies with inconsistent findings [24–27]. Accordingly, most of those studies showed no association between dietary acid load and odds of glioma [24], colorectal cancer [27], and breast cancer [25]. However, in a study, while the PRAL was not associated with lung cancer, the NEAP was associated with increased odds of lung cancer [26]. Regarding PC, result from a case-control study showed that a high dietary acid load (both high PRAL and NEAP) may link with increased odds of PC [28].

In summary, while some studies have explored the relationship between DAL and various cancers, there is a lack of focused research on prostate cancer. Also, there is a need for more localized research that considers cultural dietary habits. Iranian diets may differ significantly from those studied in Western contexts, and understanding how these dietary patterns affect cancer risk in this population is crucial. Moreover, by focusing on newly diagnosed PC patients we aimed to provide more reliable data on the association between diet-dependent acid load and odds of PC in an Iranian population.

Methods and materials

Subjects

The methodological framework for this secondary analysis is adapted from our prior original publication study [29]. Briefly, this hospital-based case-control study included 125 participants (62 cases and 63 controls) who were referred to hospital centers in Shiraz city from April to September 2015. The study sample size calculated based on the study by Askari et al. using α error = 0.05, β error = 0.3, and anticipated odds ratio (OR) of 0.4 [13]. Accordingly, a total of 125 individuals (62 cases and 63 controls) were included in this study. During the data collection, five participants (two cases and three controls) failed to respond to the FFQ, so they were excluded from the analyses. So, 120 participants (60 cases and 60 controls) were included in the final analysis. To collect required information such as general characteristics and dietary intakes, the patients were interviewed by trained nutritionists. We enrolled PC patients who were candidates for radical or open prostatectomy during their hospital stay according to the following inclusion criteria: Their disease was diagnosed within one month of diagnosis, and they were free from chronic diseases, diabetes, and any other type of cancer. Meanwhile, control patients from the same hospitals who had non-neoplastic, non-diabetic conditions, such as eye, gastrointestinal, ear, nose, and throat (ENT), kidney, and nerve diseases, were selected. Also, the controls did not follow any chronic disease-specific diets. The two groups were matched for body mass index (< 19, 19–25, 25–30, 30 < kg/m^2) and age (within strata of 5-year age groups). Total energy intakes of < 800 or > 4200 kcal/day and poor/inadequate response to the food frequency questionnaire were considered as exclusion criteria. All participants provided informed consent and the study was approved by the ethics committee at Shiraz University of Medical Sciences (93-01-21-9059). The Helsinki declaration was followed for all methods.

Demographic and anthropometric assessment

Participant demographic data, including smoking habit (smokers/nonsmokers), physical activity level (little or never /moderate/high), ethnicity (fars/non-fars), employment status (unemployed/employed), education status (illiterate & primary/diploma & academic), and medication use (anti-hyperlipidemic, antihypertensive pharmaceuticals, and aspirin) were collected via a face-to-face interview. Weight was measured by a digital scale, with a precision of 0.1 kg (Glamor BS-801, Hitachi, China), while individuals wore light clothing and unshod. Height was measured at 0.1 cm precision, with participants in a standing position and unshod, using a non-stretchable tape. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared.

Dietary intake assessment and estimation of the DAL

An assessment of dietary intake was performed by using a semi-quantitative food frequency questionnaire (FFQ) [30–32]. In this questionnaire, we asked about 160 common food items common to Iranians. We categorized the frequency of consumption of each food item into nine categories: never or less than once a month, once

a month, once a week, 2–4 times a week, 5–6 times a week, once a day, 2–3 times a day, 4–5 times a day, and ≥ 6 times a day. The portion sizes were categorized as follows: small portions (equal to half of the average serving size or less), medium portions (equal to the average serving size), and large portions (one and a half times the average serving size or more). The FFQs were analyzed using a specific multifunction software which developed by Borland Delphi 7 (https://borland-delphi.software.informer.com/7.0/) and Visual Basic 2008 (VB 9.0) (https://download.cnet.com/visual-basic-2008-express-edition/3000-windows-visual-basic-2008-express-edition.html). Daily intakes of energy, macronutrients, and micronutrients were derived using the Nutritionist 4 (https://nutritionist-pro.software.informer.com/4.3/#google_vignette) software. We used the PRAL and NEAP (indicators of the DAL) for estimation of the DAL. These indexes were calculated based on the previous published equation: NEAP (mEq/day) = 54.5 × protein (g/day)/potassium (mEq/day) – 10.2 [10]. PRAL (mEq/day) = 0.4888 × protein intake (g/day) + 0.0366 × phosphorus (mg/day) – 0.0205 × potassium (mg/day) – 0.0125 × calcium (mg/day) – 0.0263 × magnesium (mg/day) [33].

Statistical analysis

The normality of the data was assessed using Kolmogorov-Smirnov test. Categorical variables were presented as percent, and continuous variables presented as mean ± SD. For comparing quantitative and qualitative variables across tertiles of PRAL and NEAP scores, one-way analysis of variance (ANOVA) and Chi-square or Fischer exact tests were used, respectively. Dietary intakes of participants across tertiles of PRAL and NEAP scores were compared using analysis of covariance (ANCOVA) test and presented as mean ± SE. Using multivariate logistic regression, we evaluated prostate cancer odds using PRAL and NEAP. A number of potential confounders were controlled in adjusted models, including age, body mass index, energy intake, smoking, physical activity, ethnicity, job, education, and drug use. Literature review of previously published articles, including PC as an outcome, led to the selection of these confounders. Statistical analyses were performed using SPSS software (version 23, SPSS Inc., Chicago, IL, USA), whilst $P < 0.05$ was, a priori, considered statistically significant.

Results

Sociodemographic characteristics, anthropometric measures, and energy intakes of participants are shown in Table 1. The results showed that controls were more physically active than cases ($P = 0.02$) and had lower PRAL ($P = 0.01$) and NEAP ($P = 0.01$) scores. Other characteristics didn't differ between the cases and controls ($P > 0.05$).

Major dietary intakes of study participants are shown in Table 2. As seen, there is differences between the cases and the controls in terms of dietary intakes of some food groups. Accordingly, the cases had lower intakes of fruits ($P = 0.001$) and vegetables ($P = 0.01$) and greater intakes of red/processed meats ($P < 0.001$) and sweets ($P = 0.01$) compared to the controls.

The participant characteristics across the tertiles of PRAL and NEAP in cases and controls are shown in Table 3. It was observed that with increment of PRAL score, BMI of individuals in control group decreased ($P = 0.04$). Moreover, through tertiles of NEAP, the number of antihypertensive drug users were significantly increased in cases ($P = 0.02$). The results for other variables were not significant in both cases and controls ($P > 0.05$).

Table 4 presents the mean intakes of macronutrients and micronutrients across the tertiles of PRAL and NEAP in cases and controls. In cases, it shows that higher PRAL was significantly associated with higher dietary protein intake ($P < 0.001$). However, the results showed that dietary fiber ($P < 0.001$), Vitamin E ($P = 0.05$), Vitamin C ($P = 0.03$), Vitamin B6 ($P = 0.04$), potassium ($P < 0.001$), calcium ($P = 0.04$) and magnesium ($P < 0.001$), decreased across tertiles of PRAL. In controls, higher PRAL score were significantly associated with greater protein ($P = 0.01$), total fat ($P = 0.01$), Vitamin B12 ($P = 0.01$). In contrast, increased PRAL was significantly associated with lower dietary fiber ($P < 0.001$), Vitamin A ($P < 0.001$), Vitamin E ($P < 0.001$), Vitamin K ($P < 0.001$), Vitamin C ($P < 0.001$), Vitamin B5 ($P = 0.05$), Vitamin B6 ($P < 0.001$), Vitamin B9 ($P < 0.001$), potassium ($P < 0.001$), phosphorous ($P = 0.05$), calcium ($P = 0.02$), magnesium ($P < 0.001$), and zinc ($P = 0.05$).

Regarding the NEAP score, the higher score was significantly related with greater protein ($P < 0.001$) and zinc ($P = 0.05$) while lower intake of dietary fiber ($P < 0.001$), Vitamin E ($P = 0.02$), Vitamin C ($P = 0.04$), Vitamin B6 ($P = 0.05$), potassium ($P < 0.001$), calcium ($P = 0.02$), and magnesium ($P = 0.01$) in cases. Such assessments in controls showed that higher NEAP scores were linked with less dietary fiber ($P < 0.001$), Vitamin A ($P = 0.01$), Vitamin E ($P < 0.001$), Vitamin K ($P = 0.01$), Vitamin C ($P < 0.001$), Vitamin B6 ($P < 0.001$), Vitamin B9 ($P < 0.001$), potassium ($P < 0.001$), calcium ($P = 0.03$), magnesium ($P < 0.001$) and higher Vitamin B12 ($P = 0.02$).

The odds ratios (OR) of PC according to tertiles of PRAL and NEAP are presented in Table 5. Our crude results suggested that being in the third, compared to the first, tertiles of PRAL (OR = 5.44; 95% CI= (2.09–14.17)) or NEAP (OR = 4.88; 95% CI= (2.22–13.41)) increased the odds of PC. Moreover, after adjusting for potential confounders (energy intake, smoking, physical activity, ethnicity, job, education, anti-hyperlipidemic drugs,

Table 1 Socio-demographic characteristics, anthropometric measures, and energy intakes among 60 prostatic cancer cases and 60 hospital-based controls

Variables	Total	Case	control	*p*-value
Age (year)				0.38
< 50	12 (10.0)	6 (10.0)	6 (10.0)	
50–60	24 (20.0)	15 (25.0)	9 (15.0)	
≥ 60	84 (70.0)	39 (65.0)	45 (75.0)	
Total energy intake (kcal/d)	2654.18 ± 655.68	2712.24 ± 593.48	2596.10 ± 712.77	0.33
BMI (kg/m2)	25.35 ± 3.57	24.84 ± 3.64	25.85 ± 3.46	0.12
PRAL (mEq/d)	-8.44 ± 25.69	-2.67 ± 29.63	-14.21 ± 19.64	0.01
NEAP (mEq/d)	45.65 ± 14.55	49.06 ± 13.22	42.24 ± 15.13	0.01
Ethnicity				0.65
Fars	94 (78.3)	48 (80.0)	46 (76.7)	
Non-Fars	26 (21.7)	12 (20.0)	14 (23.3)	
Job				0.58
Employment	71 (59.2)	34 (56.7)	37 (61.7)	
Unemployment	49 (40.8)	26 (43.3)	23 (38.3)	
Smoking status				0.67
Yes *	16 (26.7)	14 (23.3)	16 (27)	
No	44 (73.3)	46 (76.7)	16 (27)	
Education levels				0.09
Under diploma and illiterate	73 (60.8)	41 (68.3)	32 (53.3)	
Diploma and academic	47 (39.2)	19 (31.7)	28 (46.7)	
Physical activity levels				0.02
Little or never	35 (29.2)	23 (38.3)	12 (20.0)	
Moderate	49 (40.8)	25 (41.7)	24 (40.0)	
High	36 (30.0)	12 (20.0)	24 (40.0)	
Antihyperlipidemic drug user				1.00
Yes	32 (26.7)	6 (10.0)	6 (10.0)	
No	88 (73.3)	54 (90.0)	54 (90.0)	
Antihypertensive drug user				0.21
Yes	12 (10.0)	19 (31.7)	13 (21.7)	
No	108 (90.0)	41 (68.3)	47 (78.3)	
Aspirin user				0.26
Yes	25 (20.8)	10 (16.7)	15 (25.0)	
No	95 (79.2)	50 (83.3)	45 (75.0)	

A) PRAL, potential renal acid load; NEAP, net endogenous acid production; BMI, body mass index

B) Data are presented as mean ± standard deviation or Number (%)

C) *Current smokers and ex-smokers

D) Independent sample t-test or Mann-Whitney U-test were used for comparison of quantitative variables

E) Chi-square test or Fisher's exact test were used for comparison of qualitative variables

antihypertensive drugs, and aspirin), being in the third, compared to the first, tertiles of PRAL (OR = 3.42; 95% CI= (1.11–8.65)) or NEAP (OR = 3.88; 95% CI= (1.26–9.55)) remained significantly associated with an increased odd of PC.

Discussion

The results of this case-control study showed that DAL, as assessed by both PRAL and NEAP, was significantly associated with a higher odd of PC. The association between some nutrients and risk of PC have been investigated previously [34–44]; clearly, diet is the primary external or environmental epigenetic factor determining cancer development or maintenance [45]. This study showed a positive association between the DAL and odds of PC. In line with our results, a case-control study showed that dietary acid load (both high PRAL and NEAP) may link with increased odds of PC [26]. Also, few studies have suggested that acidic environments and the DALs might contribute to cancer development [46–48]; however, other studies have not substantiated these observations [47]. Regarding some specific types of cancer, previous research showed direct association between net acid excretion and odds of bladder cancer [25]. Also, in another study, higher acid load in diet was associated with higher odds of breast cancer [49]. Moreover, a lower

Table 2 Major dietary intakes among 60 prostatic cancer cases and 60 hospital-based controls

Variables	Case	control	*p*-value
Fruits (g/day)	324.02 ± 161.38	514.12 ± 380.40	< 0.001
Vegetables (g/day)	352.50 ± 155.35	501.86 ± 255.66	< 0.001
Dairies (g/day)	463.70 ± 235.05	458.95 ± 315.2	0.77
Grains (g/day)	389.19 ± 97.25	418.48 ± 95.14	0.10
White meats (g/day)	122.83 ± 72.15	119.60 ± 84.60	0.84
Read/processed meats (g/day)	114.05 ± 86.40	77.38 ± 44.20	0.01
Nuts (g/day)	7.00 ± 3.64	9.30 ± 4.25	0.11
Legumes (g/day)	47.71 ± 17.18	45.05 ± 16.25	0.59
Tea/coffee (ml/day)	373.36 ± 156.23	322.16 ± 152.32	0.19
Sweets (g/day)	72.88 ± 15.25	48.71 ± 42.32	0.01

A) Data are presented as mean ± standard

B) Independent sample t-test or Mann-Whitney U-test were used for comparison of quantitative variables

serum bicarbonate level has also been associated with higher cancer mortality [50].

It appears that carcinogenesis may occur via intermediary effects associated with metabolic acidosis, as demonstrated in some studies [45]. As a result of dietary acid overload, metabolic acidosis can promote metastasis due to reduced buffering capacity of cancer patients [51–53]. Some studies on patients with cancer also showed changes in pH in the cancerous cells and their microenvironment, such that intracellular pH (pHi) increased compared to normal cells while extracellular pH (pHe) decreased [54]. Other studies have shown that shift towards higher consumption of acid-forming foods (like meats and processed foods), lower consumption of alkaline-forming foods (like fruits and vegetables), or supplementing with bicarbonate or phosphate salt, could affect the pH of urine, but not the pH of blood. It is generally believed that diet can cause metabolic acidosis through disruption of acid-base balance and the production of acid or alkaline precursors, and consuming acidogenic diets could promote higher urinary acid excretion in comparison to alkalizing foods [55–58]. In our study, the amounts of daily fruits and vegetables intakes seems to be high. Our finding is somewhat similar to a study by another study conducted in Iranian population [59]. In contrast, other Iranian studies reported lower fruits and vegetables intakes [60, 61]. Nevertheless, it cannot affect the overall findings because the indices (the PRAL and the NEAP) were estimated using different nutrients such as protein, phosphorus, potassium, calcium, and magnesium. These nutrients of course derives from different food items. For example, plant-based foods like fruits, vegetables, and grains are rich sources for potassium and magnesium and animal-based foods like dairies and meats are rich in protein, calcium, and phosphorus. So, an acid-base imbalance in a diet is under the influence of different nutrients not only one or two ones.

As a consequence, comprehensive mechanistic and clinical trials would be needed to determine the specific associations between the DAL and cancer pathogenesis.

This study had some strengths that should be noted. First, as far as we know this study is among few research investigating the association between the DAL and odds of PC. Second, as a result of using newly diagnosed cases, we were able to lower cancer odds associated with dietary changes in the subjects. Third, the statistical models were adjusted for several confounders, allowing more certainty of the results. However, despite the strengths and novelty of our study, there are some limitations that should be acknowledged. First, although we used a validated semi-quantitative FFQ, response errors, recall bias, and social desirability are inevitable in gathering data using FFQ. Second, it is impossible to avoid selection bias in case-control studies, and the same as all case-control studies, it was impossible to make a causal association between the DAL and PC. Third, while we matched controls and cases by age and body mass index and adjusted for several confounders, there will always be some residual confounders, which may affect our findings. Forth, we included hospital controls that cannot be representative of the population living in Shiraz province. Fifth, while the analysis provides valuable insights, the findings should be interpreted with caution due to the limited sample size. Sixth, further studies with larger sample sizes are needed to validate the associations observed in this study and reduce the risk of erroneous conclusions.

Conclusion

The results of this study suggest that the DAL could increase the odds of PC. Furthermore, the study revealed higher consumption of animal-based nutrients and lower consumption of plant-based nutrients after DAL scores were increased. The study's findings suggest a significant association between dietary acid load and increased odds of PC, indicating that dietary modifications could play a crucial role in cancer prevention and management. Integrating these dietary considerations into clinical practice and healthcare providers can enhance patient care and potentially improve outcomes for individuals. These findings, however, need to be verified in further prospective studies with larger sample sizes and lengthier follow-up times.

Table 3 General characteristics of participants across tertiles of PRAL and NEAP scores among 60 prostatic cancer cases and 60 hospital-based controls

Variable	PRAL								NEAP							
	Cases				Controls				Cases				Controls			
	Tertile 1	Tertile 2	Tertile 3	*P* trend	Tertile 1	Tertile 2	Tertile 3	*P* trend	Tertile 1	Tertile 2	Tertile 3	*P* trend	Tertile 1	Tertile 2	Tertile 3	*P* trend
Age (y)	63.33 ± 12.24	66.2 ± 8.43	67 ± 9.53	0.28	58.25 ± 7.4	64.15 ± 9.7	64.08 ± 11.62	0.07	63.67 ± 12.35	67 ± 8.51	66.29 ± 9.47	0.44	58.79 ± 7.12	63.1 ± 10.44	64.58 ± 11.51	0.08
BMI (kg/m2)	25.34 ± 3.37	24.3 ± 3.59	25.02 ± 3.86	0.80	27.26 ± 3.39	24.45 ± 3.12	24.92 ± 3.12	0.04	25.38 ± 3.32	23.59 ± 3.44	25.51 ± 3.79	0.92	27.02 ± 3.36	24.88 ± 3.43	24.77 ± 3.15	0.06
Energy intake (Kcal/day)	2930.82 ± 694.02	2599.89 ± 615.25	2698.83 ± 525.63	0.26	2783.6 ± 692.51	2443.68 ± 668.88	2412.67 ± 778.89	0.13	2855.8 ± 655.02	2744.88 ± 663.35	2627.42 ± 517.5	0.27	2726.99 ± 682.52	2603.26 ± 754.17	2278.78 ± 667.53	0.07
Ethnicity				0.66				0.91				0.66				0.83
Fars	10 (83.3)	17 (85)	21 (75)		21 (75)	16 (80)	9 (75)		10 (83.3)	17 (85)	21 (75)		21 (75)	15 (75)	10 (83.3)	
Non Fars	2 (16.7)	3 (15)	7 (25)		7 (25)	4 (20)	3 (25)		2 (16.7)	3 (15)	7 (25)		7 (25)	5 (25)	2 (16.7)	
job				0.73				0.56				0.98				0.17
Employment	8 (66.7)	11 (55)	15 (53.6)		16 (57.1)	12 (60)	9 (75)		7 (58.3)	11 (55)	16 (57.1)		17 (60.7)	10 (50)	10 (83.3)	
Unemployment **	4 (33.3)	9 (45)	13 (46.4)		12 (42.9)	8 (40)	3 (25)		5 (41.7)	9 (45)	12 (42.9)		11 (39.3)	10 (50)	2 (16.7)	
Education				0.89				0.09				0.70				0.06
Illiterate & primary	8 (66.7)	13 (65)	20 (71.4)		11 (39.3)	12 (60)	9 (75)		7 (58.3)	14 (70)	20 (71.4)		12 (42.9)	10 (50)	10 (83.3)	
Diploma & academic	4 (33.3)	7 (35)	8 (28.6)		17 (60.7)	8 (40)	3 (25)		5 (41.7)	6 (30)	8 (28.6)		16 (57.1)	10 (50)	2 (16.7)	
Smokers				0.32				0.59				0.32				0.27
Non-Smokers	10 (83.3)	13 (65)	23 (82.1)		19 (67.9)	15 (75)	10 (83.3)		10 (83.3)	13 (65)	23 (82.1)		19 (67.9)	14 (70)	11 (91.7)	
Smokers	2 (16.7)	7 (35)	5 (17.9)		9 (32.1)	5 (25)	2 (16.7)		2 (16.7)	7 (35)	5 (17.9)		9 (32.1)	6 (30)	1 (8.3)	
Physical activity				0.70				0.07				0.52				0.26
less or never	4 (33.3)	8 (40)	11 (39.3)		5 (17.9)	3 (15)	4 (33.3)		4 (33.3)	7 (35)	12 (42.9)		5 (17.9)	4 (20)	3 (25)	
moderate	5 (41.7)	10 (50)	10 (35.7)		7 (25)	11 (55)	6 (50)		5 (41.7)	11 (55)	9 (32.1)		8 (28.6)	9 (45)	7 (58.3)	
high	3 (25)	2 (10)	7 (25)		16 (57.1)	6 (30)	2 (16.7)		3 (25)	2 (10)	7 (25)		15 (53.6)	7 (35)	2 (16.7)	
Antihyperlipidemic drug user				0.56				0.56				0.18				0.56
No	10 (83.3)	19 (95)	25 (89.3)		25 (89.3)	19 (95)	10 (83.3)		10 (83.3)	20 (100)	24 (85.7)		25 (89.3)	19 (95)	10 (83.3)	
Yes	2 (16.7)	1 (5)	3 (10.7)		3 (10.7)	1 (5)	2 (16.7)		2 (16.7)	0 (0)	4 (14.3)		3 (10.7)	1 (5)	2 (16.7)	
Antihypertensive drug user (%)				0.19				0.95				0.02				0.68
No	10 (83.3)	15 (75)	16 (57.1)		22 (78.6)	16 (80)	9 (75)		10 (83.3)	17 (85)	14 (50)		21 (75)	17 (85)	9 (75)	
Yes	2 (16.7)	5 (25)	12 (42.9)		6 (21.4)	4 (20)	3 (25)		2 (16.7)	3 (15)	14 (50)		7 (25)	3 (15)	3 (25)	
Aspirin user (%)				0.42				0.80				0.97				1.00
No	10 (83.3)	15 (75)	25 (89.3)		22 (78.6)	14 (70)	9 (75)		10 (83.3)	17 (85)	23 (82.1)		21 (75)	15 (75)	9 (75)	
Yes	2 (16.7)	5 (25)	3 (10.7)		6 (21.4)	6 (30)	3 (25)		2 (16.7)	3 (15)	5 (17.9)		7 (25)	5 (25)	3 (25)	

PRAL, potential renal acid load; NEAP, net endogenous acid production; BMI, body mass index

** Unemployed participants were retired or jobless individuals

Data are presented as mean ± SD or number (percent)

P values are from one way analysis of variance (ANOVA) test for quantitative and Chi-square or Fischer exact tests for qualitative variables comparisons across tertiles of dietary acid load, respectively

Table 4 Dietary intakes of participants across tertiles of PRAL and NEAP scores among 60 prostatic cancer cases and 60 hospital-based controls[a]

Variables	PRAL								NEAP							
	Cases				Controls				Cases				Controls			
	Tertile 1 (<-5.12) (*N* = 12)	Tertile 2 (-5.12 _6.11) (*N* = 20)	Tertile 3 (> 6.11) (*N* = 28)	*P*-value[b]	Tertile 1 (<-22.37) (*N* = 28)	Tertile 2 (-22.37_ − 3.87) (*N* = 20)	Tertile 3 (>- 3.87) (*N* = 12)	*P*-value[b]	Tertile 1 (< 43.88) (*N* = 12)	Tertile 2 (43.88_ 53.19) (*N* = 20)	Tertile 3 (> 53.19) (*N* = 28)	*P*-value[b]	Tertile 1 (< 35.22) (*N* = 28)	Tertile 2 (35.22_ 45.24) (*N* = 20)	Tertile 3 (> 45.24) (*N* = 12)	*P*-value[b]
Carbohydrate (gr/day)	399.46 ± 30.13	333.52 ± 23.15	334.04 ± 19.45	0.16	345.8 ± 12.95	299.92 ± 15.18	331.37 ± 19.58	0.08	405.73 ± 29.6	335.03 ± 22.8	330.27 ± 19.36	0.09	342.36 ± 13.13	311.31 ± 15.41	320.41 ± 20.32	0.30
Protein (gr/day)	105.65 ± 6.06	108.3 ± 4.66	130.11 ± 3.91	< 0.001	106.39 ± 3.43	100.74 ± 4.02	120.53 ± 5.19	0.01	104.62 ± 6.01	108.84 ± 4.63	130.18 ± 3.93	< 0.001	104.57 ± 3.51	104.52 ± 4.12	118.49 ± 5.44	0.08
Total fat (gr/day)	67.58 ± 10.8	66.37 ± 8.3	72.29 ± 6.97	0.85	56.31 ± 2.32	47.76 ± 2.72	61 ± 3.51	0.01	68.1 ± 10.48	59.15 ± 8.07	77.23 ± 6.85	0.24	56.31 ± 2.45	50.8 ± 2.88	55.94 ± 3.79	0.31
Dietary fiber (gr/day)	27.03 ± 1.44	21.75 ± 1.11	19.2 ± 0.93	< 0.001	28.19 ± 0.87	20.21 ± 1.02	18.82 ± 1.32	< 0.001	26.94 ± 1.44	21.74 ± 1.11	19.24 ± 0.94	< 0.001	27.79 ± 0.91	20.81 ± 1.07	18.76 ± 1.41	< 0.001
Vitamin A (RAE/day)	2715.59 ± 418.29	2695.48 ± 321.46	3226.53 ± 270.02	0.37	3548.8 ± 202.14	2146.24 ± 237.04	2554.31 ± 305.69	< 0.001	2623.85 ± 410.36	2640.85 ± 316.11	3304.87 ± 268.34	0.20	3395.66 ± 214.88	2352.06 ± 252.13	2568.59 ± 332.37	0.01
Vitamin E (mg/day)	5.17 ± 0.39	4.18 ± 0.3	4.01 ± 0.25	0.05	5.47 ± 0.22	3.93 ± 0.26	3.94 ± 0.34	< 0.001	5.29 ± 0.38	4.09 ± 0.29	4.02 ± 0.25	0.02	5.4 ± 0.23	4.1 ± 0.27	3.81 ± 0.35	< 0.001
Vitamin K (µg/day)	108.22 ± 9.12	98.19 ± 7.01	108.71 ± 5.88	0.49	168.53 ± 9.8	121.11 ± 11.49	118.73 ± 14.82	< 0.001	106.62 ± 9.12	100.99 ± 7.02	107.4 ± 5.96	0.77	166.88 ± 9.8	125.78 ± 11.5	114.81 ± 15.16	0.01
Vitamin D (µg/day)	2.68 ± 0.9	2.02 ± 0.69	1.73 ± 0.58	0.68	1.33 ± 0.18	1.08 ± 0.21	0.96 ± 0.27	0.47	2.69 ± 0.89	1.37 ± 0.68	2.19 ± 0.58	0.46	1.34 ± 0.18	1.07 ± 0.21	0.96 ± 0.28	0.45
Vitamin C (mg/day)	173.4 ± 13.41	160.69 ± 10.31	134.82 ± 8.66	0.03	239.55 ± 9	167.4 ± 10.56	141.58 ± 13.62	< 0.001	178.11 ± 13.36	154.69 ± 10.29	137.09 ± 8.74	0.04	236.28 ± 9.29	172.18 ± 10.89	141.26 ± 14.36	< 0.001
Vitamin B1 (mg/day)	2.47 ± 0.17	2.4 ± 0.13	2.42 ± 0.11	0.94	2.44 ± 0.08	2.19 ± 0.09	2.41 ± 0.12	0.09	2.54 ± 0.17	2.4 ± 0.13	2.39 ± 0.11	0.72	2.39 ± 0.08	2.26 ± 0.09	2.42 ± 0.12	0.45
Vitamin B2 (mg/day)	2.41 ± 0.33	2.36 ± 0.25	2.91 ± 0.21	0.21	2.26 ± 0.11	2 ± 0.13	2.44 ± 0.17	0.10	2.4 ± 0.33	2.44 ± 0.26	2.85 ± 0.22	0.36	2.24 ± 0.11	2.05 ± 0.13	2.42 ± 0.17	0.22
Vitamin B3 (mg/day)	29.39 ± 2.27	30.61 ± 1.75	34.01 ± 1.47	0.16	27.76 ± 1.12	26.68 ± 1.31	31.45 ± 1.69	0.08	29.35 ± 2.25	30.53 ± 1.73	34.08 ± 1.47	0.14	27.43 ± 1.1	26.96 ± 1.3	31.75 ± 1.71	0.07
Vitamin B5 (mg/day)	6.73 ± 0.52	6.49 ± 0.4	7.47 ± 0.34	0.16	7.13 ± 0.22	6.29 ± 0.25	6.66 ± 0.33	0.05	6.78 ± 0.52	6.6 ± 0.4	7.36 ± 0.34	0.33	7.06 ± 0.22	6.4 ± 0.26	6.66 ± 0.34	0.16
Vitamin B6 (mg/day)	3.74 ± 0.43	2.51 ± 0.33	2.49 ± 0.28	0.04	2.61 ± 0.07	2.01 ± 0.08	2 ± 0.11	< 0.001	3.7 ± 0.43	2.52 ± 0.33	2.5 ± 0.28	0.05	2.58 ± 0.07	2.05 ± 0.09	2 ± 0.11	< 0.001
Vitamin B9 (µg/day)	384.18 ± 24.77	322.28 ± 19.03	325.53 ± 15.99	0.11	405.7 ± 13.36	310.77 ± 15.66	305.98 ± 20.2	< 0.001	381.6 ± 24.66	324.23 ± 18.99	325.24 ± 16.12	0.13	400.66 ± 13.72	319.24 ± 16.1	303.63 ± 21.22	< 0.001
Vitamin B12 (µg/day)	7.79 ± 6.23	10.68 ± 4.79	22.65 ± 4.02	0.06	7.29 ± 1.65	6.67 ± 1.93	15.49 ± 2.49	0.01	7.24 ± 6.2	11.3 ± 4.77	22.44 ± 4.05	0.08	6.6 ± 1.64	7.71 ± 1.92	15.38 ± 2.54	0.02
Potassium (mg/day)	5822.34 ± 351.47	4204.76 ± 270.11	3991.92 ± 226.89	< 0.001	5384.82 ± 134.14	3979.81 ± 157.3	3724.82 ± 202.86	< 0.001	5796.6 ± 349.95	4218.64 ± 269.58	3993.04 ± 228.84	< 0.001	5319.77 ± 141.22	4102.04 ± 165.7	3672.89 ± 218.44	< 0.001
Phosphorous (mg/day)	1472.16 ± 70.56	1423.16 ± 54.22	1524.65 ± 45.55	0.36	1512.76 ± 45.38	1335.01 ± 53.19	1401.54 ± 68.59	0.05	1470.92 ± 71.02	1456.63 ± 54.71	1501.28 ± 46.44	0.82	1499.89 ± 45.81	1365.45 ± 53.75	1380.84 ± 70.85	0.13
Calcium (mg/day)	1223.15 ± 52.29	1075.91 ± 40.18	1064.59 ± 33.75	0.04	1290.67 ± 51.13	1089.1 ± 59.95	1090.8 ± 77.32	0.02	1222.73 ± 51.32	1102.89 ± 39.54	1045.5 ± 33.56	0.02	1286.62 ± 50.84	1093.78 ± 59.65	1092.45 ± 78.63	0.03
Iron (mg/day)	24.92 ± 1.93	24.61 ± 1.49	26.46 ± 1.25	0.59	23.89 ± 2.23	20.76 ± 2.61	30.68 ± 3.37	0.07	24.17 ± 1.91	24.98 ± 1.47	26.53 ± 1.25	0.53	23.2 ± 2.22	21.67 ± 2.61	30.77 ± 3.44	0.10

Table 4 (continued)

Variables	PRAL								NEAP							
	Cases				Controls				Cases				Controls			
	Tertile 1 (<-5.12) (*N* = 12)	Tertile 2 (-5.12 _6.11) (*N* = 20)	Tertile 3 (>6.11) (*N* = 28)	*P*-value[b]	Tertile 1 (<-22.37) (*N* = 28)	Tertile 2 (-22.37_ – 3.87) (*N* = 20)	Tertile 3 (>- 3.87) (*N* = 12)	*P*-value[b]	Tertile 1 (<43.88) (*N* = 12)	Tertile 2 (43.88_ 53.19) (*N* = 20)	Tertile 3 (>53.19) (*N* = 28)	*P*-value[b]	Tertile 1 (< 35.22) (*N* = 28)	Tertile 2 (35.22_ 45.24) (*N* = 20)	Tertile 3 (> 45.24) (*N* = 12)	*P*-value[b]
Magnesium (mg/day)	460.07 ± 26.05	371.88 ± 20.02	348.6 ± 16.82	< 0.001	449.18 ± 13.03	344.72 ± 15.27	332.11 ± 19.7	< 0.001	455.05 ± 26.13	374.13 ± 20.13	349.15 ± 17.09	0.01	442.44 ± 13.66	354.21 ± 16.03	332.03 ± 21.14	< 0.001
Zinc (mg/day)	11.66 ± 0.76	11.74 ± 0.58	13.21 ± 0.49	0.09	11.76 ± 0.38	10.3 ± 0.45	11.55 ± 0.58	0.05	11.42 ± 0.74	11.72 ± 0.57	13.33 ± 0.48	0.04	11.56 ± 0.39	10.6 ± 0.46	11.52 ± 0.6	0.25

PRAL, potential renal acid load; NEAP, net endogenous acid production

[a] Data are presented as mean ± SE

[b] Ancova test was used

Table 5 Odds of prostate cancer in relation to PRAL and NEAP among 60 prostatic cancer cases and 60 hospital-based controls[a]

Patterns	Categories of PRAL and NEAP scores			
	Tertile 1	Tertile 2	Tertile 3	*P* trend
PRAL	(<-14.28 mEq/d)	(-14.28 to 2.57 mEq/d)	(> 2.57 mEq/d)	
No. cases/controls	12/28	20/20	28/12	
Crude	1.00 (Ref)	2.33(0.93–5.84)	4.88(2.22–13.41)	0.001
Model 1	1.00 (Ref)	1.78(0.62–5.12)	3.94(1.37–1131)	0.01
Model 2	1.00 (Ref)	1.72(0.89–5.04)	3.94(1.32–11.71)	0.01
Model 3	1.00 (Ref)	2.07(0.68–6.32)	3.42(1.11–8.65)	0.03
NEAP	(< 38.09 mEq/d)	(38.09 to 49.97 mEq/d)	(> 49.97 mEq/d)	
No. cases/controls	12/28	20/20	28/12	
Crude	1.00 (Ref)	2.33(0.93–5.84)	5.44(2.09–14.17)	0.001
Model 1	1.00 (Ref)	1.64(0.59–4.58)	4.25(1.49–12.10)	0.01
Model 2	1.00 (Ref)	1.55(0.55–4.39)	4.29(1.45–12.71)	0.01
Model 3	1.00 (Ref)	1.63(0.56–4.79)	3.88(1.26–9.55)	0.02

PRAL, potential renal acid load; NEAP, net endogenous acid production

[a] Multivariable logistic regression was used

Data are presented as odds ratio (95% confidence interval)

Model 1: Adjusted for age, body mass index, energy intake, smoking, and physical activity

Model 2: Adjusted for confounders in model 1 plus ethnicity, job, and education

Model 3: Adjusted for confounders in model 2 plus drug usage (Anti-hyperlipidemic drugs, antihypertensive drugs, and aspirin)

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Author contributions
S.M. wrote the manuscript; Y.J. collected the data; A.J. contributed to data analysis; H.R, L.S., and C. C. revised and edited the manuscript; S.F. designed the study and managed and supervised the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
This study was ethically approved by ethics committee of Shiraz University of medical sciences (approval number: IR.SUMS.REC.1394. S 438). Then, written informed consent was obtained from all patients. All methods were performed in accordance with the declaration of Helsinki.

Competing interests
The authors declare no competing interests.

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