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ORIGINAL PAPER

Determination of Prostate Cancer Risk Factors in Isfahan, Iran: a Case - control Study

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Background: This study was conducted in order to determine the risk factors of prostate cancer in Isfahan, Iran. **Methods:** In this case-control study 95 cases of incident, pathologically confirmed PC and 95 controls were recruited. Odds ratios (OR) and the corresponding 95% confidence intervals (CIs) were estimated using conditional logistic regression models. **Results:** The risk of prostate cancer increased with increasing age (OR: 1.09, 95% CI: 1.04-1.13; p<0.001). A positive family history of prostate cancer was also a significant risk factor (OR: 2.5, 95% CI: 1.1-2.9; p=0.03). Increased dietary intake tomato sauce was associated with a significantly declined risk of prostate cancer (OR: 0.05, 95% CI: 0.01-0.40; p<0.001). Prostate cancer risk was not affected by Smoking, alcohol consumption, history of vasectomy, diabetes mellitus, sexually transmitted diseases, and dietary garlic and fat intake. **Conclusions:** We found that increased age and positive family history of prostate cancer could be considered as some potential risk factors of prostate cancer in the studied population. Moreover, a higher intake of tomato sauce was found to have a protective effect against prostate cancer. **Key words: Prostate cancer, risk factor, Iran.**

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1. INTRODUCTION

Worldwide, prostate cancer is the second most common cancer in men, with an incidence of 61.6 per 100000 in Western Europe and 124.8 per 100000 in the United States (1) with an estimated 900000 cases and 258000 deaths in 2008 (2). The incidence of PC and its mortality rates are outstandingly different in diverse geographic zones and in different racial/ethnic populations, with by far the highest rate in North America and the lowest in Asia (3, 4)

There are few well-defined risk factors apart from age, ethnicity and family history (5). Environmental exposures probably play a major role (6) and there have also been some uncertain factors including educational level, occupation, dietary meat and lycopene consumption, smoking habit, alcohol use, marital status, vasectomy, sexual behavior, having diabetes mellitus, etc. (7, 8, 9, 10, 11). These risk factors still remain controversial based on different studies within different populations around the world.

The risk factors of prostate cancer in Iranians may be different from those in other populations due to different lifestyle, dietary and environmental factors. Interventions to reduce modifiable risk factors result in decreased morbidity and mortality of prostate cancer as the second frequent malignancy in Iranian males (12). In the present study we investigated the association of age, diabetes, family history of prostate cancer, smoking, alcohol consumption, sexual behavior, vasectomy, some dietary factors and risk of prostate cancer in Isfahan, Iran.

2. PATIENTS AND METHODS

This was a case-control study, which was done between August 2005 and May 2009 in Isfahan, Iran. Ninety-five men with incident, pathologically confirmed, no metastatic prostate cancer were recruited. Based on their medical records and history taking, they had no other malignancy. We also included 95 men as the control group. They were residing in the same geographical. In these subjects prostate cancer was ruled out based on normal digital rectal examination and prostate specific antigen levels. Similar to prostate cancer patients, they had no other malignancy according to their medical records and history taking. Exclusion criteria were history of metabolic disease, immune deficiency disorders or previous intervention on the prostate including surgery, hormonal therapy, or radiation therapy. All subjects signed an informed consent form.

Information on socio-demographic characteristics, general lifestyle habits including smoking, alcohol consumption, sexual behavior, intake of selected food items, medical history, and family

P-value	Cancer group [n=95] (%)	Control group [n=95] (%)	Characteristic
<0.001*	73.1±7.5	67.9±8.3	Mean age ±SD(yrs)
0.01‡	25(26.3) 51(53.7) 19(20)	10(10.5) 64(67.4) 21(22.1)	Education Illiterate Diploma University Degree
0.32‡	3(3.2) 47(49.5) 5(5.3) 40(41.1)	5(5.3) 35(36.8) 7(7.4) 48(50)	Occupation Farmer Clerical worker Industrial worker Other
0.75†	6(6.3) 89(93.7)	5(5.3) 90(94.7)	Location of birth Urban Rural
0.31†	92(96.8) 3(3.2)	94(98.9) 1(1.1)	Location of living Urban Rural
0.39‡	90(94.7) 1(1.1) 1(1.1) 3(3.1)	87(91.6) 3(3.2) 1(1.1) 4(4.1)	Ethnicity Fars Turk Lor Other (Kurd, Arab, etc.)
1†	94(98.9)	94(98.9)	Marital status Married
0.047†	13(13.7)	5(5.3)	Family history of prostate cancer
0.28†	22(23.2)	16(16.8)	Smoking
0.15†	4(4.2)	9(9.5)	Alcohol consumption
0.36†	9(9.5)	13(13.7)	Vasectomy
0.86†	18(18.9)	19(20)	Diabetes mellitus
0.37†	1(1.1)	4(4.2)	History of sexually transmitted diseases
0.31†	48(50.5)	41(43.2)	History of urinary tract irritation signs
0.001*	47.1±10.7	42.1±9.3	Mean years of sexual activity ±SD
0.048†	14(14.7)	25(26.3)	Pre-marital sexual activity
1†	95 (100)	95 (100)	Frequency of intercourse (per week)2≥

Table 1. Demographic information of patients with prostate cancer and subjects in the control group. SD: standard deviation; * Independent samples t test, † Fisher's Exact test, ‡ Chi-square test

history of prostate cancer was gathered by trained interviewers using a structured questionnaire. Information on diet included the consumption of red meat, fish, poultry, liver, eggs, cream, milk, and tomato sauce.

Statistical analysis was performed using SPSS version 17 (SPSS Corp, Chicago, IL, USA). Normality of data distribution was assessed with Kolmogorov–Smirnov test. Independent sample t-test was used to compare normally distributed measurements in different groups. Chi-square test or Fisher's exact test were used for comparison of categorical variables between the two groups. The effect of different parameters on the risk of prostate cancer was estimated by odds ratios (OR) and corresponding 95% confidence intervals (95% CI), which were derived from conditional logistic regression models while potential confounders were included as covariates in the models. P value less than 0.05 was considered statistically significant.

3. RESULTS

We recruited 190 subjects (95 patients with prostate cancer and 95 healthy controls). Demographic information of all subjects is presented in Table 1. The mean age (range) of subjects with prostate cancer and healthy controls was 73.1 (54-88) and 67.9 years (52-92), respectively. Patients with prostate cancer had significantly lower levels of education, and the proportion of men with a family history of prostate cancer was higher in prostate cancer patients. However, type of occupation, smoking or history of diabetes mellitus did not have a statistically significant association with prostate cancer risk (Table 1).

The mean years of sexual activity were significantly higher in prostate cancer patients. However, patients were less likely to have a history of premarital sex in comparison to healthy subjects (OR: 0.86, 95% CI: 0.75-1.00; P=0.05).

Dietary red meat consumption did not differ significantly in prostate cancer patients and the control group (231.42±94.80 vs. 229.79±103.66 gr/week, P=0.9). Increased dietary intake tomato sauce was associated with a significantly declined risk of prostate cancer (OR: 0.05, 95% CI: 0.01-0.40; p<0.001) (Table 2).

On multivariate analysis, age and a positive family history for prostate cancer were significantly related with an increased risk of prostate cancer (OR: 1.09, 95% CI: 1.04-1.13; P<0.001, and OR: 2.5, 95%CI: 1.1-2.9; P= 0.03, respectively). In this analysis tomato dressing intake of less than 10 grams per week was associated with a significant risk of prostate cancer (Table 3).

4. DISCUSSION

The incidence of prostate cancer in Iran is similar to those in Eastern Mediterranean regions but it is significantly less than that in developed countries (13). After stomach cancer, prostate cancer is the most common malignancy in Iranian males (12). The incidence rate of prostate cancer varies from 3.2 to 16.0 per 100,000 in different regions (13). Iranian men are ethnically and racially different from most of Asian men. Therefore, it seems crucial to investigate possible risk factors in this population. In the present study, we evaluated the role of some common risk factors of prostate cancer in Isfahan, the third largest city of Iran.

Older age is a well-known risk factor of prostate cancer (14). Prostate cancer has a low overall incidence in men younger than 50 years of age, who represent less than 0.1% of all affected patients. Approximately 85% of cases of

P-value	Cancer group [n=95] (%)	Control group [n=95] (%)	
0.03†	22(23.2) 49(51.6) 24(25.3)	30(31.6) 31(32.6) 34(35.8)	Meat (gr/week) 150≥ 151-300 > 300
0.54†	13(13.7)	16(16.8)	Fat (gr/week) >50
<0.001 †	94(98.9) 1(1.1)	79(83.2)	Tomato sauce (gr/week) 10>
0.31†	83(87.4)	78(82.1)	Garlic Yes

Table 2. Comparison of dietary habit between prostate cancer patients and control group † Chi-square test.

P-value	95% ConfidenceInterval	Odds Ratio	Variable
<0.001	1.04-1.13	1.09	Age (yrs.)
0.03	1.1-2.9	2.5	Positive family history of prostate cancer
<0.001	0.01-0.40	0.05	Tomato sauce consumption ≥10 gr/ week

Table 3. Association of different factors with prostate cancer risk in conditional logistic regression model

prostate cancer are diagnosed after the age of 65 years. At the age of 85 years, the cumulative risk of developing prostate cancer ranges from 0.5% to 20.0%, worldwide (5). We also found an association between older age and prostate cancer. However, in the present study, we could not match subjects in two groups based on their age and prostate cancer patients were 5 years older than healthy subjects. This is amongst the limitations of our study but age was adjusted in other risk factor analysis.

We found a significant association between prostate cancer and a positive family history of prostate cancer. Family history is now an established risk factor for prostate cancer (15). The relative risk for prostate cancer increases in accordance with the number of affected family members and the degree of relatedness, and is inversely related to the age at which family members were affected (14). However, a previous study India did not find such association (16).

Dietary factors might contribute to prostate cancer risk (11). The lower incidence of prostate cancer in Asian countries, such as Iran, compared with Western countries, may be related to a diet of low animal fat and high fiber content (17). Positive energy balance, total fat intake, animal and saturated fat, meat, and dairy products are associated with prostate cancer risk (18).

Dietary fat has been suggested to increase the levels of circulating androgens, thereby increasing the growth of prostate cancer cells. Dietary fat also increases oxidative stress and levels of reactive oxygen species that interfere with cellular processes. Healthy cells are attacked by free radicals, which cause peroxidation and eventually DNA damage (18). In the present study we did not find any association between fat intake and prostate cancer. This is in contrast with the previous study in Iran (17). However, a large cohort study did not demonstrate an association between dietary fat and prostate cancer development (19).

Dietary intake of meat is associated with the risk of prostate cancer (18). Elevated risk of prostate cancer was related to the intake of red and processed meat in the US (20). However, such association might be different based on races (21). In the present study we did not find any relationship between red meat consumption and prostate cancer which is consistent with two previous studies in Iran (17, 22). The evidence of a relation between meat and prostate cancer remains unclear, with various epidemiologic studies reporting null results (23)

Among the potential dietary determinants of this disease, attention has focused on tomato products and a major tomato constituent, lycopene, as possible protective agents (21). In a meta-analysis of case-control and cohort studies, serum lycopene was associated with a greater reduction in prostate cancer risk than dietary lycopene, whereas cooked tomato products were associated with greater risk reduction than raw tomato products, although reductions in risk were modest in all instances (24). Similar to our findings, in a case control study in Malaysia, intake of tomato sauce was related to reduced prostate cancer risk (25). However, a large prospective study in US did not support the hypothesis that greater lycopene/tomato product consumption protects from prostate cancer (26). A recent systematic review which included only randomized clinical trials (three studies), concluded that there was insufficient evidence to either support, or refute, the use of lycopene for the prevention of prostate cancer (27).

Garlic is a vegetable of the Allium genus. The major compounds that are known to contribute to the pharmacologic effect of garlic are sulfur-containing compounds, such as daily (28). Eating more than 2.14g/d of garlic negatively affected the incidence of prostate cancer in China (29). In contrast to our study, in a recent study in Iran a borderline reduction in risk of prostate cancer was observed in relation to garlic consumption (30). However, a systematic review has concluded that it is highly unlikely that garlic intake reduces the risk of prostate cancer (28).

No clear dose-dependent relationship has been demonstrated between smoking and prostate cancer risk. However, smoking is a source of cadmium exposure, increases oxidative stress, and increases circulating androgen levels, all of which represent potential mechanisms of prostate carcinogenesis (14). In the present study we did not find any relationship between smoking status and prostate cancer which is in agreement with previous studies (16). However, a recent large prospective observational study demonstrated an association between smoking at the time of diagnosis and adverse prostate cancer events (31).

Alcohol consumption was not associated to prostate cancer risk in the present study. A prospective cohort study in US demonstrated an increased risk of prostate cancer in men who consumed more than three alcoholic drinks per day (32). In contrast, a recent meta-analysis including a total of 52899 prostate cancer cases provided no evidence of a material association between alcohol drinking and prostate cancer, even at high doses (33).

An inverse relationship between diabetes and prostate cancer has been widely suggested (34). However, like some other studies (16, 35) we did not find such association.

The weight of evidence shows no association overall between vasectomy and prostate cancer (36). Our findings also suggest that prior vasectomy is not associated with a significantly increased risk of prostate cancer.

Epidemiological data on sexual activity and prostate cancer are almost entirely limited to case-control studies, which may be particularly prone to methodological bias because information on prediagnosis sexual activity is collected after the diagnosis of cancer. Sexual function may diminish after the diagnosis of prostate cancer and its treatment (37). There is such a limitation in our study in which no association was found. In a large prospec-

tive study, Leitzmann et al found that ejaculation frequency was not related to increased risk of prostate cancer (37).

We realize that our study has some limitations such as small sample size, failure to match for age, and lack of information on prostate cancer stage.

5. CONCLUSION

The present study demonstrates age, positive family history of prostate cancer, and decreased tomato products intake as important determinants of prostate cancer risk in Isfahan, Iran. Adopting appropriate preventive strategies against the modifiable risk factors is necessary to reduce the burden of prostate cancer in Iran.

Conflict of interest: none declared.

REFERENCES

1. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA Cancer J Clin. 2005; 55(2): 74-108.
2. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin. 2011; 61(2): 69-90.
3. Hsing AW, Tsao L, Devesa SS. International trends and patterns of prostate cancer incidence and mortality. Int J Cancer. 2000; 85(1): 60-67.
4. Quinn M, Babb P. Patterns and trends in prostate cancer incidence, survival, prevalence and mortality. Part I: international comparisons. BJU Int. 2002; 90(2): 162-173.
5. Grönberg H.. Prostate cancer epidemiology. Lancet. 2003; 361(9360): 859-864.
6. Lichtenstein P, Holm NV, Verkasalo PK, Iliadou A, Kaprio J, Koskenvuo M, Pukkala E, Skytthe A, Hemminki K. Environmental and heritable factors in the causation of cancer -analyses of cohorts of twins from Sweden, Denmark, and Finland. N Engl J Med. 2000; 343: 78-85.
7. Pienta KJ, Esper PS. Risk factors for prostate cancer. Ann Intern Med. 1993; 118(10): 793-803.
8. Haas GP, Sakr WA. Epidemiology of prostate cancer. CA Cancer J Clin. 1997; 47(5): 273-287.
9. Chan JM, Stampfer MJ, Giovannucci EL. What causes prostate cancer? A brief summary of the epidemiology. Semin Cancer Biol. 1998; 8(4): 263-73.
10. Sasagawa I, Nakada T. Epidemiology of prostatic cancer in East Asia. Arch Androl. 2001; 47(3): 195-201.
11. Bostwick DG, Burke HB, Djakiew D, Euling S, Ho SM, Landolph J, Morrison H, Sonawane B, Shifflett T, Waters DJ, Timms B. Human prostate cancer risk factors. Cancer. 2004; 101(10 Suppl): 2371-490.
12. Moslemi MK, Lotfi F, Tahvildar SA. Evaluation of prostate cancer prevalence in Iranian male population with increased PSA level, a one center experience. Cancer Manag Res. 2011; 3: 227-231.
13. Mousavi SM. Toward prostate cancer early detection in Iran. Asian Pac J Cancer Prev. 2009; 10(3): 413-418.
14. Patel AR, Klein EA. Risk factors for prostate cancer. Nat Clin Pract Urol. 2009; 6(2): 87-95.
15. Eeles RA, Dearnaley DP, Ardern-Jones A, Shearer RJ, Easton DF, Ford D, Edwards S, Dowe A. Familial prostate cancer: the evidence and the Cancer Research Campaign/British Prostate Group (CRC/BPG) UK Familial Prostate Cancer Study. Br J Urol. 1997; 79 Suppl 1: 8-14.
16. Ganesh B, Saoba SL, Sarade MN, Pinjari SV. Risk factors for prostate cancer: An hospital-based case-control study from Mumbai, India. Indian J Urol. 2011; 27(3): 345-350.
17. Pourmand G, Salem S, Mehrsai A, Lotfi M, Amirzargar MA, Mazdak H, Roshani A, Kheirollahi A, Kalantar E, Baradaran N, Saboury B, Allameh F, Karami A, Ahmadi H, Jahani Y. The risk factors of prostate cancer: a multicentric case-control study in Iran. Asian Pac J Cancer Prev. 2007; 8(3): 422-428.
18. Venkateswaran V, Klotz LH. Diet and prostate cancer: mechanisms of action and implications for chemoprevention. Nat Rev Urol. 2010; 7(8): 442-453.
19. Severson RK, Nomura AM, Grove JS, Stemmermann GN. A prospective study of demographics, diet, and prostate cancer among men of Japanese ancestry in Hawaii. Cancer Res. 1989; 49(7): 1857-1860.
20. Sinha R, Park Y, Graubard BI, Leitzmann MF, Hollenbeck A, Schatzkin A, Cross AJ. Meat and meat-related compounds and risk of prostate cancer in a large prospective cohort study in the United States. Am J Epidemiol. 2009; 170(9): 1165-1177.
21. Rodriguez C, McCullough ML, Mondul AM, Jacobs EJ, Chao A, Patel AV, Thun MJ, Calle EE. Meat consumption among Black and White men and risk of prostate cancer in the Cancer Prevention Study II Nutrition Cohort. Cancer Epidemiol Biomarkers Prev. 2006; 15(2): 211-216.
22. Hosseini M, SeyedAlinaghi S, Mahmoudi M, McFarland W. A case-control study of risk factors for prostate cancer in Iran. Acta Med Iran. 2010; 48(1): 61-66.
23. Bosetti C, Micelotta S, Dal Maso L, Talamini R, Montella M, Negri E, Conti E, Franceschi S, La Vecchia C. Food groups and risk of prostate cancer in Italy. Int J Cancer. 2004; 110(3): 424-428.
24. Etminan M, Takkouche B, Caamaño-Isorna F. The role of tomato products and lycopene in the prevention of prostate cancer: a meta-analysis of observational studies. Cancer Epidemiol Biomarkers Prev. 2004; 13(3): 340-345.
25. Shahar S, Shafurah S, Hasan Shaari NS, Rajikan R, Rajab NF, Golkhalkhali B, Zainuddin ZM. Roles of diet, lifetime physical activity and oxidative DNA damage in the occurrence of prostate cancer among men in Klang Valley, Malaysia. Asian Pac J Cancer Prev. 2011; 12(3): 605-611.
26. Kirsh VA, Mayne ST, Peters U, Chatterjee N, Leitzmann MF, Dixon LB, Urban DA, Crawford ED, Hayes RB. A prospective study of lycopene and tomato product intake and risk of prostate cancer. Cancer Epidemiol Biomarkers Prev. 2006; 15(1): 92-98.
27. Ilic D, Forbes KM, Hassed C. Lycopene for the prevention of prostate cancer. Cochrane Database Syst Rev. 2011; 11: CD008007.
28. Kim JY, Kwon O. Garlic intake and cancer risk: an analysis using the Food and Drug Administration's evidence-based review system for the scientific evaluation of health claims. Am J Clin Nutr. 2009; 89(1): 257-264.
29. Hsing AW, Chokkalingam AP, Gao YT, Madigan MP, Deng J, Gridley G, Fraumeni JF Jr. Allium vegetables and risk of prostate cancer: a population-based study. J Natl Cancer Inst. 2002; 94(21): 1648-1651.
30. Salem S, Salahi M, Mohseni M, Ahmadi H, Mehrsai A, Jahani Y, Pourmand G. Major dietary factors and prostate cancer risk: a prospective multicenter case-control study. Nutr Cancer. 2011; 63(1): 21-27.
31. Kenfield SA, Stampfer MJ, Chan JM, Giovannucci E. Smoking and prostate cancer survival and recurrence. JAMA. 2011; 305(24): 2548-2555.
32. Sesso HD, Paffenbarger RS Jr, Lee IM. Alcohol consumption and risk of prostate cancer: The Harvard Alumni Health Study. Int J Epidemiol. 2001; 30(4): 749-755.
33. Rota M, Scotti L, Turati F, Tramacere I, Islami F, Bellocco R, Negri E, Corrao G, Boffetta P, La Vecchia C, Bagnardi V. Alcohol consumption and prostate cancer risk: a meta-analysis of the dose-risk relation. Eur J Cancer Prev. 2011 Nov 15. [Epub ahead of print]
34. Kasper JS, Giovannucci E. A meta-analysis of diabetes mellitus and the risk of prostate cancer. Cancer Epidemiol Biomarkers Prev. 2006; 15(11): 2056-2062.
35. Tavani A, Gallus S, Bertuzzi M, Dal Maso L, Zucchetto A, Negri E, Franceschi S, Ramazzotti V, Montella M, La Vecchia C. Diabetes mellitus and the risk of prostate cancer in Italy. Eur Urol. 2005; 47(3): 313-317.
36. Holt SK, Salinas CA, Stanford JL. Vasectomy and the risk of prostate cancer. J Urol. 2008; 180(6): 2565-2567.
37. Leitzmann MF, Platz EA, Stampfer MJ, Willett WC, Giovannucci E. Ejaculation frequency and subsequent risk of prostate cancer. JAMA. 2004; 291(13): 1578-1786..