

ASSOCIATION BETWEEN SOME RISK FACTORS AND PROSTATE CANCER PROGRESSION IN BASRAH, IRAQ

Rasha A. Al-Badran^{*}, Adnan Issa Al-Badran^{*}, Majed Azkar^{**},

Loma Al-Mansouri^{***}

^{*}Department of Biology, College of Science, University of Basrah, Basrah, Iraq

^{**}Department of surgery, College of Medicine, University of Basrah, Iraq

^{***}Department of Internal Medicine and Oncology, College of Medicine, University of Basrah,
Iraq

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**Corresponding Author:* Adnan.albadran@uobasrah.edu.iq

ABSTRACT

Prostate cancer is a complex disease in which both genetic and environmental influences led to the development and growth of tumors. At the recent time, it is considered the second most common malignancy after lung cancer in men and the sixth leading cause of cancer-related death worldwide. Sixty-seven blood samples of prostate cancer patients collected from Basrah oncology and Hematology center aging between (45-90). On the other hand, seventy blood samples of men without cancer were collected as control group aging between (45-90). Two ml of peripheral blood were drawn by sterilized syringe from the two groups and kept in the EDTA tube for DNA extraction for molecular study (not included). Both study groups have answered questions about personal information such as age, address, cigarette smoking, occupation, and family history. The present study found evidence that the aging was a significant risk factor for developing prostate cancer, as well as family history increased the risk of disease about eighteenfold (OR=18.8). Type of work people do related to the development of prostate cancer, free business increase the risk about eightfold (OR=8.18), and military increase the risk for fold (OR=4.09) while men deal with chemical material increase the risk about threefold (OR=2.5). In our study, the place of living was divided into three regions (South, North, and the center of Basra) the risk of disease increases about threefold for both South and North of Basra compared with the Centre of Basra. Cigarette smoking also increases the risk of twofold compared with non-smokers.

INTRODUCTION

Prostate cancer was the most common cancer among men, there are three non-modifiable risk factors for prostate cancer: age, race, and a positive family history of prostate cancer. Furthermore, it was found that a variety of modifiable or behavioral causes are associated with the risk of prostate cancer. Although not firmly established, protective behavioral factors can include physical activity and frequent tomato consumption, cruciferous vegetables, and soy foods. In contrast, high dietary intake of dairy products and meat may increase prostate cancer risk. On the other hand, factors such as smoking and obesity were weakly associated with prostate cancer incidents and mortality (1). Prostate cancer is an example of the age –depending disease. This affects predominantly men older than 40 years. The average age is about (65-70) years. It is rare before 40 years old, but the rate increases with age in constant to other types of cancer. Tumor at this site occurs with insignificant frequency in men that are less than 55 years old, the vast majority of the cases (86%) occur over the age of 66 (2).

The disease is most common among Australian, New Zealand, and African American men, followed by Western and Northern Europeans, in these countries, the high incidence is partly due to the high detection rate resulting from routine screening and diagnostics. Prostate cancer is also relatively common in the Caribbean, Southern Africa, and South America. In contrast, Prostate cancer is less incidence in Eastern and South-Central Asia (3). Prostate cancer as many common cancers tend to cluster in families, 5-10% of prostate cancer cases describe as familial cancer which is considered to result from heritable risk genetic factors. The risk of prostate cancer increases with the increasing number of affected relatives, especially those diagnosed at a young age. Men with an inherited predisposition are more likely to be affected at a younger age than 55 years (4). Athletes and men with high physical activity are less likely to develop prostate cancer and urinary tumor (5). Physical activity can reduce fatigue, elevate mood, reduce physical limitations, decrease falls, attenuate bone loss, and promote weight (6).The purpose of this work was to determine the association between some risk factors and prostate cancer progression.

MATERIALS AND METHODS

In the present study sixty-seven of blood samples were collected from prostate cancer patients from Al-Sadder teaching Hospital – Basra center for Oncology and Hematological disease their ages range between (45-90) years old. On the other hand, seventy blood samples of males without cancer were collected as a control group their ages range between (45-90) years old. Two ml of peripheral blood was drawn by sterilized syringe from the two groups than they have been kept in sterilized EDTA tubes for DNA extraction using Genomic DNA Mini Kit (Geneaid, Taiwan) and molecular study (not included) was done to amplifying segment of the gene *HOXB13* by PCR technique using pair of specific primers.

Questions were asked to both patients and healthy groups about age, place of residence, family history of cancer, type of work, and smoking. Descriptive statistics were applied to describe patients and controls characteristic according to use percentage. ORs and 95%CLs were calculated by using the SPSS program. OR were considered significant if $OR \geq 1.5$.

RESULTS

Demographic Variables

All study subjects, prostate cancer patients (n=67) and control group (n=70) have answered questions in the questionnaire form as in appendix. Different parameters from both groups were obtained from questionnaire form; some of them are shown in table (1)

Table (1): Distribution of demographic variables between patients and control group.

Variable	Control (n=70)	Patient (n=67)
Age (years)		
Mean age(+SD)	60 (± 9)	71 (± 8)
Range	45-90	45-90
Obesity		
Normal	5 (7%)	4 (6%)
Thin	34 (49%)	37 (55%)
Obesity	31 (44%)	26 (39%)

Family history

Table (2) shows the family history as a strong significant factor in development of prostate cancer for eighteen folds comparing with no family history.

Table (2): distribution of patients and controls according to family history

Family history	control	Patient	OR	95/CI	P value
No	69(98.57%)	52(78%)	1.0	-----	-----
Yes	1(1.43%)	15(22%)	18.8	1.101-1.423	0.0002

Age

The age distribution of patients and control groups showed in table (3) which explain that the maximum number of patients were in the age group of 66-75 year (49.3%) followed by the age group of 56-65 year (21%), followed by 76-85 year(22.3%), 45-55year (4.4%), and the minimum number was in age group 86-95 year (3%). In other hand the age group 56-65year (41%) from the control group was the highest, followed by the age group of 45-55year (39%), followed by 66-75year (14%), 3% for both age groups (76-85), and (86-95) respectively. The present study showed that the age was a significant risk factor for developing the disease with age progress

Table (3): Distribution of age among patients and control groups.

Age (years)	control	patient	OR	95% CI	P Value
45-55	27 (39%)	3 (4.4%)	-----	-----	----
56-65	29 (41%)	14 (21%)	4.34	1.123-16.804	0.02
66-75	10 (14%)	33 (49.3%)	29.7	7.421-118.865	0.65
76-85	2 (3%)	15(22.3%)	67.5	10.124- 450.064	0.77
86-95	2 (3%)	2 (3%)	9	0.907- 89.266	0.03

Address

The majority of patients with prostate cancer were from south of Basrah 16.3%, followed by north of Basrah 14.2% then by center of Basrah 15.6% as shown in table (4). The risks of prostate cancer increased about three folds in south of Basrah compared with center of Basrah OR=2.73 (95%CI=1.3-6.0925) and P value= 0.008 as shown in Table (4-4).

Table (4): Distribution of study subjects according to their address

Address	control	patient	OR	95% CI	P value
Center of Basra	42 (70%)	23 (34%)	1.0	-----	-----
North of Basra	14 (20%)	20 (30%)	2.73	1.175-6.383	0.012
South of Basra	14 (20%)	24 (36%)	3	1.3-6.925	0.008

OR= Odds ratio, 95%CI=95% confidence interval

Occupation

Table (5) shows that patient's exposure to chemical material in their job were large number than other group, these group had odds ratio about 2.5, military group formed 4.09 odds ratio, and free job group had highest odds ratio 8.18. In other hand large group of control work in business office followed by chemical group then by military group, finally group of free business. It has been noticed that significant risk factor increased development of prostate cancer in patients who work in free business to about eight folds OR=8.18 than group of business office, followed by military group, then by chemical works group.

Table (5): Distribution of occupation among patients and control groups

Occupation	control	Patient	OR	95% CI	P value
Business office	30(43%)	11(16.4%)	1.0	-----	-----
Chemical works	25(36%)	23(34.3%)	2.5	1.027-6.13	0.041
Free business	7(10%)	21(31.3%)	8.18	2.725-24.568	8.1E-5
Military	8(11%)	12(18%)	4.09	1.321-12.668	0.012

OR= Odds ratio, 95%CI=95% confidence interval

Cigarette Smoking

As shown in table (6), heavy smoking was significantly associated with risk of prostate cancer OR=1.69(95%CI=0.387-2.507).

Table (6): Association of cigarette smoking with prostate cancer

Type of smoking	control	patient	OR	95% CI	P value
Non	55 (79%)	51 (76.1%)	1.0	-----	-----
Light smoking	12 (17%)	11 (16.4%)	0.93	0.38-2.297	0.881
Heavy smoking	3 (4%)	5 (7.5%)	1.69	0.387-2.507	0.479

OR= Odds ratio, 95%CI=95% confidence interval

DISCUSSION

The most common disease among men is prostate cancer, the incidence and mortality of prostate cancer vary widely. While some of these differences can be attributed to variation in diagnostic intensity, the considerable heterogeneity in prostate cancer mortality across countries indicates that behavioral factors play an important role. The sizeable rise in the incidence and mortality of prostate cancer following migration from low-risk to high-risk countries, as well as changing lifestyle like changing dietary habits, some behaviors such as smoking and direct contact with chemical substances are major contributors to the risk factors. (1)

In our study, it was found that the mean age for prostate cancer is 71 with standard deviation (± 8) as shown in table (1), table (3) cleared that incident of prostate cancer increased with age and the age group of (66-75) recorded high percentage 48% which agreed with previous research which consider age As a risk factor for prostate cancer (7). Aging exhibits an increase to various autoimmune, led to a decline in the immune response, and triggers the inflammatory pathways causing the development of prostate cancer (8). on the other hand, high levels of blood cholesterol in advanced age, progressing incident of prostate cancer because the metabolism of this fatty acid affected cellular activity including cell division (9). Prostate cancer in high age may increase due to an irregular level of testosterone (10).

On the other hand, the Body Mass Index (BMI) and prostate cancer relationship result was not clear, a study by (11) detected that high BMI may be related to an increased risk of

aggressive prostate cancer. while the inverse relationship was observed between high BMI and nonaggressive prostate cancer. Another study by (12) suggests that BMI was strongly correlated with prostate cancer mortality and that men with high BMI (overweight or obese) who had aggressive prostate cancer would have markedly greater odds of death. Body Mass Index (BMI) was not significant in our study. Moreover in our study, the family history as shown in table (2) was associated with a significant increase in the risk of prostate cancer about eighteen –fold. Family history is widely recognized as a risk factor for prostate cancer with an estimated heritability of 58%, while the other 42% explained by other common causes. low penetrance variants, a study by Mancuso estimates that as much as 42% of ‘missing’ heritability is likely to be explained by rare variants (13).

Ewing and colleagues observed that the case carrier frequency was higher in a familial cohort (14). Several studies have since replicated this finding in the Caucasian family and case-control populations and estimated that the variant is associated with a 4- to 8-fold increase in the risk of prostate cancer and early disease (15) We agreed with the study by (16) which explained the role of hereditary of family history with prostate cancer.

Table (4) shows the distribution of patient and control group at different parts of Basrah, the risk of prostate cancer increased in south and north of Basrah (OR=3,59, 2.7) respectively comparing to the center of Basrah, this may due to accumulation of high level of carcinogens in these reigns such as depleted uranium and other chemical materials which used in previous wars. In addition, these areas lay near oil fields which throws many kinds of pollutants especially hydrocarbons, also the pollution from fumes and wastes of many industrial factories present in or near south and north of Basrah. The annual report of the Iraqi Cancer Registry (2015) confirms this fact. this result also agreed with other researches consider chemicals and radiation material as carcinogens for cancer incidents and mortality (17,18).

In addition to working around dust, the fibers, chemicals, and fumes can also increase the risk for developing an occupational disease such as cancer. Our study found that the risk of prostate cancer increases the risk of cancer eight-fold (OR=8, 95%CI= 2.7-24.5) in free business included workers in construction, drivers, shop owners, farmers, and Oil stations. Military and chemical workers were also at high risk to develop prostate cancer (OR=4,59, 2.5) respectively. Previous studies have reported elevated risks associated with employment in construction and transportation, with some evidence linked to whole□body vibrations, diesel exhaust, and

polycyclic aromatic hydrocarbons (PAH). (19). On the other hand, men who deal with pesticides and diesel engine exhaust from farm equipment or have a store of agriculture material and machinery are suspected of contributing risk factors. Exposure to pesticides may affect hormone levels and function by disrupting endocrine activity and increasing estrogen levels leading to tumor promotion (20).

Military men have elevated risk for prostate cancer may be the reason is exposure to diesel exhaust, dust and particulate matter, chemical agents, radiation, and other mixed agents, and they can be under constant psychological stress which may impact biological processes leading to the development of cancer(21). Of course, deal with chemical induce forming a tumor, our result agreed with other research (22). In addition to above factor it is clearly that cigarette smoking harms nearly every organ of the body, causes many diseases including cancer, and reduces the health of smokers in general. Heavy smoking increases the risk of prostate cancer two-fold comparing with non-smoking as shown in table (6). Smoking may cause a genetic mutation by affected hormones that exhibit tumor suppressor genes lead to tumor formation. (23) Smoking was associated with a higher risk of dying from prostate cancer as well as other causes of death. In contrast, past smoking was not associated with prostate cancer-specific mortality suggesting that smoking may be a modifiable risk factor (24), study of (25) found an association between tobacco smoking and incident of prostate cancer.

العلاقة بين بعض عوامل الخطورة وزيادة الاصابة بسرطان المثانة في مدينه البصرة – العراق

رشا عبدالامام عبدالرزاق* ، عدنان عيسى البدران* ، ماجد اصغر* ، لمى احمد المنصوري***

* قسم علم الحياة، كلية العلوم، جامعة البصرة ، البصره ،العراق.

**قسم الجراحة، كلية الطب، جامعة البصرة ، البصره ،العراق.

***قسم الباطنية والاورام، كلية الطب، جامعة البصرة ، البصره ،العراق.

الخلاصة

يعد سرطان البروستات مرضًا معقدًا يحدث نتيجة التأثيرات الوراثية والبيئية معا حيث تسبب تكون الأورام ونموها. في الآونة الأخيرة ، يعتبر ثاني أكثر الأورام الخبيثة شيوعًا بعد سرطان الرئة لدى الرجال والسبب الرئيسي السادس للوفاة المرتبطة بالسرطان في جميع أنحاء العالم. سبعة وستون عينة دم لمرضى سرطان البروستات تم جمعها من مستشفى

البصره التعليمي و مركز البصرة للأورام وأمراض الدم تتراوح اعمارهم بين (٤٥-٩٠). و جمع سبعين عينة دم من الرجال الاصحاء كمجموعة ضابطة اعمارهم تتراوح بين (٤٥-٩٠). تم سحب ٢ مل من الدم الوريدي عن طريق حقنة معقمه من المجموعتين ، تم الاحتفاظ بها في أنبوب EDTA لاستخلاص الحمض النووي. تمت الاجابة على بعض الأسئلة حول المعلومات الشخصية مثل العمر والعنوان وتدخين السجائر والوظيفة وتاريخ الأسرة من قبل كلا المجموعتين ووجدت الدراسة الحالية ان العمر عامل خطر كبير لتطور سرطان البروستات ، كما تبين ان تاريخ الأسرة يزيد من خطر المرض حوالي ثمانية عشر ضعفا (OR = 18.8). كما ان نوع العمل الذي يقوم به الافراد المشمولين بالدراسة الحالية له علاقة بتطور سرطان البروستات ، فالأعمال التجارية الحرة زادت من خطر الإصابة بحوالي ثمانية أضعاف (OR=٨.١٨) والعسكرية تزيد من خطر الإصابة (OR=٤.٠٩) بينما الرجال الذين يتعاملون مع المواد الكيميائية ازداد خطر الإصابة لديهم بحوالي ثلاثة أضعاف (OR = 2.5). تم تقسيم مدينة البصره الى ثلاث مناطق (جنوب وشمال ووسط البصرة) ووجد ان خطر الإصابة يزيد بحوالي ثلاثة أضعاف لكل من جنوب وشمال البصرة مقارنة بمركز البصرة. كما وجد ان تدخين السجائر يزيد من خطر الإصابة بعشرين ضعفاً مقارنةً بعدم التدخين.

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