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Effect of Age, Geographical Affiliation and Environmental Factors on the Development of Prostate Cancer among Sudanese Patients

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Abstract

Background: Prostate cancer (PCa) is a biologically homogeneous tumor that is one of the leading causes of cancer deaths in men. The reasons behind PCa are not fully understood but are likely to occur due to a range of factors such as aging, family history, and dietary factors. This study aimed at determining the relationship between age, geographical affiliation, environmental factors, and PCa development.

Methods: All patients (55 cases with PCa and 55 control with BPH) were referred to central hospitals in Khartoum. We used an interviewer-administered questionnaire to ask participants about their demographic, socioeconomic, and geographical afflation, cadmium contact, alcohol consumption, as well as Clinical data including duration of disease, grade and family history of PCa. Statistical analysis was performed by using SPSS version 20 to judge the existence of the correlation.

Results: The average age for cases was higher than controls average. However, the difference was insignificant. Population from Central Sudan were the most affected group with PCa followed by Northern, Southern, Western and Eastern. Our result has shown that cases were observed to have cadmium contact much more frequently than controls with p-value of 0.031 and odd ratio of 3.55. While, alcohol consumption, working in a tire plant, a diet high in fat, working in farmer and family history of cancer appeared to have an insignificant role in prostate cancer development among Sudanese patients with p-value of 0.32, 0.50,1.0, 0.43, 0.24 respectively.

Conclusion: Among the various environmental factors discussed in this study, only cadmium contact has a consistent and strong effect as a risk factor for prostate cancer. While other factors are often observed among the cases group but, the correlation is still unclear. Further studies with the inclusion of more sample size are recommended in the future to get a more generalized result.

Keywords: Prostate cancer; Benign prostatic hyperplasia; Risk factors; Geographical Affiliation

Abbreviations: PCa: Prostate Cancer; BPH: Benign Prostatic Hyperplasia; RICK: Radiation and Isotopes Center of Khartoum

Introduction

The prostate is one of the most essential male's accessory glands. The gland is susceptible to various pathological conditions among which both malignant and benign conditions are the most common [1]. Benign Prostatic Hyperplasia (BPH) which is not cancer and familiar among older men occurs when the prostate gland turns to be larger than normal size and when the gland becomes larger it can 'squeeze' the urethra and this will display several manifestations such as difficulty urinating and frequent needs to urinate during the day [2].

PCa is a biologically heterogeneous tumor and it is one of the leading causes of cancer death in men [3]. With an estimated 241,740 new cases and 28,170 deaths in 2012 [4], it is the second leading cause of cancer-related death in men in the United States [5].

In Africa, Prostate cancer incidence and mortality rates were reported to be 23.2 and 17.0 per 100,000, respectively according to GLOBOCAN reports in 2012 [6]. In Sudan, PCa is now recognized as one of the principal medical problems facing the male population and according to the report form, Radiation and Isotopes Center of Khartoum (RICK) PCa is the most common cancer in Sudanese males (3.3%) [7].

About 600 Sudanese men have diagnosed with PCa annually [1], and mortality is 8.7 per 100,000 populations [8]. In addition, the incidence of prostate cancer has increased dramatically in the past 20 years and the disease has gained increased attention from Sudanese urologists [9].

PCa is generally a slow-growing and the majority of men can live with it for a long time without painful symptoms or spread. Early PCa usually causes no symptoms. However, prostate cancer causes symptoms often similar to those of diseases such as BPH.

In the early stage of prostate cancer, there are usually no symptoms, but later stages can cause symptoms that include frequent or sudden need to urinate, difficulty to urinate, blood in urine and pain in various bones if cancer has spread to them [2].

PCa is a major public health problem. Therefore, questions have been raised about the PCa risk factor for a long time. To date, there are

several risk factors to develop prostate cancer which include ages, races, ethnicity, alcohol consumption, genetic factors, farmers, a diet high in fat, tire plant workers and men who been around cadmium in addition to infections with certain viruses [9]. However, the underlying causes of PCa are not completely understood, but it may likely occur due to a combination of factors such as aging, family history and dietary factors in addition to infectious agents [10].

In Sudan, only few researchers have addressed PCa risk factors. Hence, The key research question of this study was to determine whether the age, geographical affiliation, and environmental factors correlated with PCa. Another question is to determine the strings of the correlation if existed.

Methods

All patients (55 cases with PCa and 55 control with BPH) were referred to central hospitals in Khartoum during the period from January to November 2018. We used an interviewer-administered questionnaire to ask participants about their demographic, socioeconomic, and geographical afflation, cadmium contact, alcohol consumption, cancer grade along with extensive contact information for result communication and subsequent treatment if necessary. Prior to commencing the study, the proposal was ethically approved by the ethical committee of Omdurman Islamic University. Then, informed consent from each patient and permission from the general managers of hospitals was obtained.

Demonstration of the effect of age, geographical affiliation and different statistical analysis

Statistical analysis was performed by using SPSS version 20 (Statistical Package for the Social Sciences). And the result was presented through various graphics and tabulated modules. In addition, a special statistical test like chi-square was performed to detect the presence of any correlation and odd ratio and to illustrate the contribution of each risk factor. This result is significant at the $p \leq 0.05$ level.

Results

Demographic characteristics and prostate cancer risk factors

Of the study population, all subjects completed and returned the questionnaire. A common view amongst interviewees was that the mean of age and duration of disease for both cases and controls were 70.7 ± 8.0 years and 9.2 ± 3.39 month respectively (Table 1).

Statistics		Age/years	Duration of early symptoms recognition/month
N	Valid	110	110
	Missing	0	0
Mean		70.74	9.24
Median		70	9
Mode		70	9
Std. Deviation		8.045	3.392
Minimum		49	2
Maximum		89	24

Table 1: Mean, Median, Mode, Std. Deviation, Minimum and Maximum of Age and Duration of early symptoms recognition of both cases and control collectively.

However, the cases had an average age of 70.98 ± 7.4 years, which is the slightly higher than the control age mean of 70.49 ± 8.6 years, but this difference when analyzed by SPSS was found to be insignificant with p-value 0.771 (Table 2).

Also, the result finds that the cases had a duration of disease mean of 8.47 ± 2.6 month which is lower significantly than controls duration of disease mean 10.0 ± 3.8 months with p-value (0.018) (Table 2).

	Type of patients	Number	Mean	Standard deviation	p-value
Age/years	Case	55	70.98	7.485	0.751
	Control	55	70.49	8.632	
Duration of early symptoms recognition/month	Case	55	8.47	2.638	0.018
	Control	55	10	3.883	

Table 2: Independent T test result shows a comparison between cases and control in the age means and duration of early symptoms recognition [p-value is significant at a level equal to or less than 0.05].

Among cases group, the Gleason score 7 (3+4) was the most identified prostate cancer grade followed by score 6 (3+3), 9(4+5), 8(4+4) and 10 (5+5) with percentage of 34.5%, 21.8%, 20.0%, 18.2%, 5.5% respectively (Table 3).

Cancer Grade	Frequency	Percentage
3+4 (7)	19	34.50%
3+3 (6)	12	21.80%
4+4 (8)	10	18.20%
4+5 (9)	11	20.00%
5+5 (10)	3	5.50%
Total	55	100.00%

Table 3: Describe the frequency and percentage of different cancer Grades among cases group.

Gleason score 9 patients were showed the highest average of age 74.18 years followed by scores 8, 6, 7 and 10 with age mean of 73.9, 69.42, 69.0 and 68.33 years respectively (Figure 1).

On the other hand, the result showed that Gleason score 10 patients were associated with the lowest average of duration of the disease 4 months, while the highest mean duration of disease was seen among patients from Gleason Score 6 followed by 9.7 and 8 with 9.5, 8.73, 8.53, 8.2 months respectively (Figure 2).

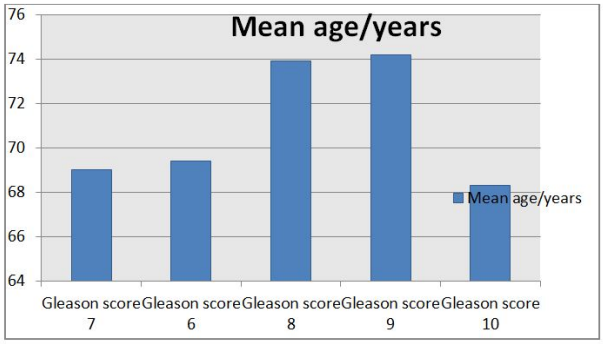

Figure 1: Shows age mean vs. different prostate cancer grades of cases.

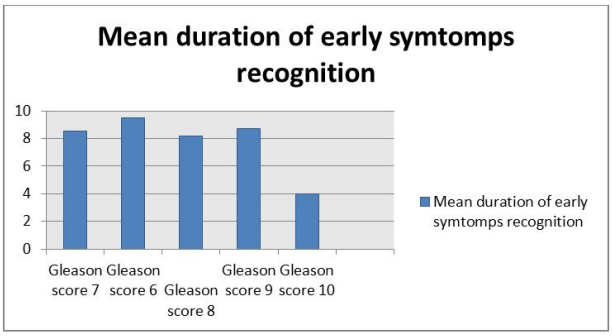

Figure 2: Shows the average of early symptoms recognition/ month vs. different prostate cancer grades of case.

There are two very important epidemiological findings. The first one, Central Sudan was the most affected area with both PCa 58.1% and BPH 50.9%. In addition, among cases group, the second most affected Sudanese population were Northern Sudanese 12.7% followed by Western and Southern with percentage of 10.9% for both, while the least affected area was Eastern Sudan with only 7.4% (Table 4 Instead, Western Sudan was the second most affected region among the control group, with 25.5% followed by Northern Sudan (20%), and East and Southern Sudan (1.8%) respectively.

Another important finding, score 10 (5+5) was only seen among central Sudanese, while other Cancer Grades were distributed mostly among the population from Central Sudan followed by North (Table 5).

Participants	Geographical affiliation					Total	p-value
	East	West	Center	South	North		
Case	4 (7.4%)	6 (10.9%)	32 (58.1%)	6 (10.9%)	7 (12.7%)	55(100%)	
Control	1 (1.8%)	14(25.5%)	28 (50.9%)	1 (1.8%)	11 (20%)	55(100%)	0.045
Total	5	20	60	7	18	110	

Table 4: Distribution of cases and controls according to their geographical affiliation (p-value is significant at a level equal to or less than 0.05).

Geographical affiliation	Cancer Grade (Gleason score)					Total
	3+4	3+3	4+4	4+5	5+5	
East	2	1	0	1	0	4
West	3	0	3	0	0	6
Center	11	6	4	8	3	32
South	2	2	1	1	0	6
North	1	3	2	1	0	7
Total	19	12	10	11	3	35

Table 5: Cancer Gradesvs. geographical affiliation (p-value is significant at a level equal to or less than 0.05).

The most surprising aspect of the data is that alcohol consumption, working in tire plant were more frequently identified among cases with percentage of 21.8%, 10.9% respectively while controls were slightly less frequently associated with alcohol consumption and tire plant working with a percentage of 14.5%, 7.3% respectively and by using chi-square cross tabulation test we didn't find any significant difference between cases and controls in consumption of Alcohol or working in a tire plant with a p-value of 0.323 and 0.507 respectively (Table 6). Moreover, our study finds that working in farmer and positive family history of the disease was less frequently identified among cases with a percentage of 36.4% and 38.1% for each. In contrast, farmer occupations and positive family history of disease were observed more predominantly among controls with a percentage of 43.6%, 49.1% respectively and this discrepancy between cases and controls in the proportion of patients who associated with farmer working and positive family history of the disease was analyzed by chi-square test which demonstrates an insignificant difference between the

cases and controls in the presence of the above mentioned cofactors with p-value of 0.436 and 0.249 respectively (Table 6).

Participant	Count		p-value
Alcohol consumption			
	Yes	No	
Case	12 (21.8%)	43 (78.2%)	
Control	8 (14.5%)	47 (86.4%)	0.323
Working in farmer			
	Yes	No	
Case	20(36.4%)	35(63.6%)	
Control	24(43.6%)	31(56.4%)	0.436
Diet high in Fat			
	Yes	No	
Case	16(29.1%)	39(70.9%)	
Control	16(29.1%)	39(70.9%)	1
Tire Plant Working			
	Yes	No	
Case	6(10.9%)	49(89.1%)	
Control	4(7.3%)	51(92.7%)	0.507
Family history of disease			
	Yes	No	
Case	21(38.1%)	34(61.9%)	
Control	27 (49.1%)	28(50.9%)	0.249
Cadmium contact			
	Yes	No	
Case	12 (21.8%)	43 (78.2%)	
Control	4 (7.3%)	51 (92.7%)	0.031

Table 6: Prostate cancer risk factorsvs. cases and controls (p-value is significant at a level equal to or less than 0.05).

The most striking result that emerged from our data that the rate of the diet high in fats consummation was equally distributed within both cases and controls with a percentage of 29.1 for both (Table 6). However, cases were observed to have contact with cadmium much more frequently than controls with p-value of 0.031 and odd ratio of 3.55. Interestingly, contact with cadmium appears to have a significant role in PCa development (Table 6).

Another notable finding in our study is that When we analyze the effect of Geographical affiliation, alcohol consumption, working in a tire plant, cadmium contact, diet high in fat, working in farmer and family history of cancer on cases prostate cancer grade we find an insignificant role of the above cofactor on the cancer grade with p-value of 0.61, 0.66,0.31, 0.55, 0.99, 0.26 and 0.15.

Discussion

PCa is a global health problem and it is the sixth most common cancer in the world in the number of new cases and it is the fourth most common cancer in both sexes combined and the second most common cancer in men [11]. A large and growing body of literature has investigated different aspects of PCa including causes, risk factors, and diagnosis and treatment options.

As is well known, the increase in age can pose a significant risk for PCa development. We found that both PCa patients and BPH patients were exceeded 70 years age (70.9 ± 7.4, 70.4 ± 8.6). Another study conducted in 2011 by Hamad et al. In Sudan showed that PCA patients in Sudan had an average age of 72.2 ± 9.25 years [12]. This may be in agreement with our findings.

Sudan is classified among the country with heterogeneous ethnic group and geographical affiliations with 5 main provinces. Despite the fact that PCa ranked first among all cancers among Sudanese men, few publications described disease epidemiology and pathology [13]. Therefore, the study was analyzed the geographical affiliation data of patient who came from a different area in Sudan to the three major hospitals in Khartoum state. Unlike other research carried out in this area, we find that the PCa was more predominant among central Sudanese patients 58.1% while in the other area the cancer was evenly distributed between 12% to 7%. Moreover, the BPH patients were also been more frequent among central Sudanese 50.1% this finding was similar to that concluded by Hamad., in 2011 who reported that more than 70% of patient with PCa were from central Sudan [12]. In addition, the Gleason grade 10 which is the highest score that detected in this study was found only in Sudanese patients in central Sudan. Although there were more than 8 years distance between the two studies there was an agreement in result between our finding and Hamad finding in the geographical distribution of PCa and This may open up a wide range of questions about the large intensification of the disease in central Sudan, The answer is through ongoing research in the field of geographic factors and genetic factors that may be present in central Sudan and make its population more prepared for PCa.

More than half of PCa patients in this study were identified with Gleason score ≤ 7 scores. However, about 40% of cases showed a Gleason score ≥ 8. This might be good news, as the majority of treatable/treated cancers cases are fall between the Gleason scores of 5 to 7, while tumors with Gleason scores 8-10 tend to be advanced neoplasms that are unlikely to be cured.

Exposure to environmental chemicals may cause PCa. Studies show that men who work in certain occupations (e.g., tire plant workers, farmers, painters) are more likely to get PCa. This is believed to be related to their exposure to chemicals such as insecticidal [14]. In this study working a tire plant was more frequently identified among cases than control this finding supported by Delzell et al., in 2003 they reported that in the vehicle manufacturing industry, mortality rates due to PCa are found to be higher than those expected for workers in casting operations [15]. The hypothesis that linked between PCa and the use of pesticides among agricultural workers have been investigated in a number of studies, However, in our study farmer working was less frequently demonstrated among PCa patient (36.4%) and thus, have no statistically significant association with risk for prostate cancer development and this finding was similar to that obtained by Kumar et al., 2010 who find an insignificant association between exposures to pesticides, or a chemical family of pesticides which usually were used in farmer and PCa while Koutros et al. in

2010 were found a significant association [16,17]. Moreover, our finding supported by Australian study conducted by Macfarlane et al. 2009 Whom examined the occupational classification of workers who were exposed to pesticides and concluded that only about 30% of farm workers actually came in contact with pesticides, herbicides or insecticides and, therefore, the level of pesticide exposure for this group of workers may be overestimated [18]. This may explain why the role of the farmer working in the development of PCa has decreased.

Alcohol consumption may increase oxidative stress and alter steroid hormone metabolism. In addition, increased alcohol intake is associated with a moderate risk of several cancers. Despite some recent prospective studies suggesting increased prostate cancer risk among heavy drinkers but they did not establish the association. Our study team find that 21.8% of cases were alcohol drinker compared to only 14.5% of control but this difference was statistically insignificant so, there is no clear association between alcohol consumption and PCa in our study. In the other hand, there are a lot of studies that associated between heavy alcohol consumption and high-grade PCa. Three of the six most recent prospective studies found some evidence of an increased risk of high-grade disease ranging from a 20% increase to a doubling of the risk in the heaviest as compared to light or nondrinkers. Whereas two studies did not find increased risks and another did not report results for heavy drinkers [19]. Furthermore, Evidence of PCa Prevention has been suggested through heavy drinking of alcohol [20]. These controversial results and finding may need more and more work to get a clear cut association between the PCa and Alcohol consumptions.

The absolute lifetime risk of prostate cancer has been estimated to range from 12% for a man with a father affected at ≥60 years compared with an 8% absolute risk in men without a family history of the disease [21]. Despite the fact shown above, our study found that the family history of PCa is positive among 38.1% so more than half of patients have no history of the disease. This may reflect a shared environment and common behaviors for our patients which may play a more significant role in developing prostate cancer than sharing mutagen which may be transferred from the grandparents to their offspring. This supported by Kramer and Siroky study in 2004 who stated that family history is one of the few established risk factors for PCa [22].

Epidemiologic studies suggest a correlation between fat consumption and the risk of developing PCa [23]. However, our study found that the diet high in fats was equally distributed between cases and controls groups and this was disagreed with Schmitz et al finding in 2001 who reported that 11 out of 14 case-control trials yielded a significant correlation between fat consumption and PCa risk [24]. The interpretation of variance in the risk of high-fat diets between our study and the other trails was that most of the previous studies were conducted outside Africa where the lifestyle was extremely different and the up taking of a high fat diet to gather with resting may lead to accumulation of cholesterol which is a precursor for steroid hormone including androgen from which testosterone and Dihydrotestosterone are made and may subsequently lead to prostate enlargement and cancer [23]. This apparent lack of correlation in our country can be attributed to living in Africa (especially sub-Saharan area) where too much fat has overtaken normal daily activities that may reduce the level of cholesterol in the blood. so prostate cancer may result from risk factors other than a diet high in fat.

Metallic cadmium is classified as a human carcinogen and most of the previous study studies have examined the relationship between dietary exposure to cadmium and PCa risk. Our study examines the correlation between the retrospective occupational cadmium contact and the presence of cancer risk and we find that the contact with cadmium showed a significant role in the development of prostate cancer with a P value of 0.031 and the odd ratio of 3.55. Meaning that patients with contact cadmium have 3.55 chances to develop PCa cancer than from others.

Conclusion

Our work has led us to a conclusion that among the various environmental factors which investigated in this research only cadmium contact have a constant and solid impact as a prostate cancer risk factor. While other factors are often observed among cases group but still the correlation is not clear. We are aware that our research may have two limitations. The first is the size of the sample, which appears to be few, another limitation is lacking the normal interviewee in this study. Further studies with more sample size as well as the inclusion of normal participants along with PCa and BPH patients are recommended in the future to get a more generalized result.

Declarations

Before conducting study the proposal of the study was ethically approved by the ethical committee of Omdurman Islamic University and Ministry of Health. Then informed consent from each patient and permission from the general managers of hospitals were obtained.

Conflict of Interest

The authors declare that they have no competing interest

Authors' Contributions

BG collected patients' information and Data. BG, IS and MO analyze the Data and wrote the manuscript. All authors read and approved the final manuscript.

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