ORIGINAL ARTICLE

LIFESTYLE FACTORS ASSOCIATED WITH THE RISK OF PROSTATE CANCER AMONG PAKISTANI MEN

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Background: Age-adjusted incidence of prostate cancer in Pakistan is 5.3 per 100,000 which is relatively low compared to other Asian countries, but increasing numbers of cases are being reported. Data on risk factors associated with prostate cancer risk among Pakistani men are sparse. The objective of this study was to identify lifestyle factors associated with the risk of prostate cancer in Pakistani men. **Methods:** An unmatched case-control study was conducted in Lahore from February to October 2011. The study enrolled 195 histologically confirmed cases of adenocarcinoma of prostate from Shaukat Khanum Memorial Hospital and Institute of Nuclear Medicine and Oncology Lahore (INMOL) and Lady Reading Hospital, Peshawar, using purposive sampling technique. A total of 390 hospital controls were selected using convenient sampling technique from different teaching hospitals of Lahore after screening with prostate specific antigen levels. A semi-structured interview form was used to collect data through face-to-face interviews. Odds ratio was used as a measure of strength of association and was calculated using unconditional logistic regression. **Results:** Farmers were found to be at higher odds of prostate cancer (OR=19.76, 95% CI=5.51–70.80, $p<0.001$). No significant association was found with marital status, ethnic background, religious affiliation and consanguineous marriages. Level of physical activity was inversely associated with prostate cancer risk (OR=0.05, 95% CI=0.01–0.26, $p<0.001$). Positive association was found with increased red meat consumption (OR=11.82, 95% CI=2.88–48.54, $p=0.001$) and dairy products intake (OR=11.76, 95% CI=4.23–32.67, $p<0.001$). **Conclusion:** Red meat consumption, higher dairy products intake and working as farmers are strongly associated with increased odds of prostate cancer among Pakistani men.

Keywords: Prostate, Lifestyle, Risk, Red meat, Dairy product, Farmer, Cancer

INTRODUCTION

Carcinoma of prostate is the most commonly diagnosed non-cutaneous cancer among men in developed countries. Globally, incidence rates of this debilitating condition have increased considerably through early 1990s when screening with prostate specific antigen (PSA) was introduced.[1] Age-adjusted incidence rates of prostate cancer vary a great deal worldwide. Rates among African-Americans are highest (185.4 per 100,000 person-years) in the world followed by Caucasian-Americans (107.8/100,000 person years).[2] Incidence rates in Asian countries are relatively low (3–11 per 100,000 person- years), however, there has been an upward trend in Singapore, Japan and Philippines (22–47 per 100,000 person-years)[3] attributed to growing urbanisation and change in lifestyle from simple rural living to more complex urban life. This rise is proportional to increasing urbanisation and rise in socioeconomic status.[4]

Age-adjusted incidence rate in Pakistan is 5.3 per 100,000 person-years[2], which is slightly lower than India (6.8 per 100,000 person-years), but higher than rates in China (3.1 per 100,000 person-years).[3,5] Pattern of prostate cancer incidence and mortality suggests that both environmental and lifestyle factors, especially trend of urbanisation and change in socioeconomic status may have accrued the prostate cancer risk in developing countries.[6] In Pakistan, population drift towards cities and rising poorly regulated industrialisation for the last two to three decades is likely to add new risk factors or modifying the existing deleterious exposures in the community, which in turn may have contributed in growing number of reported prostate cancer cases in Pakistan.

Despite high morbidity and mortality, aetiology of prostate cancer remains largely unknown. Advancing age, race and family history are the only established risk factors.[7,8] Other risk factors like raised androgen levels, high saturated fat in diet, use of red meat, reduced physical activity and obesity have also been reported,[9–12] but their role in disease causation remains to be explained.

Epidemiological studies are consistently documenting that farmers have around 10% excess risk of developing prostate cancer. This may be due to exposure to insecticides and pesticides.[13] Long term physical activity has been found to be protective against prostate cancer because of its role in lowering levels of free and total testosterone, reducing obesity, and enhancing immune system, all of which

contribute in protecting individuals from prostate cancer.[14–16]

Data on risk factors associated with development of carcinoma of prostate in Pakistan is sparse. A few studies describe only the preliminary information about the demographic features of individuals registered in cancer registries of Karachi and Lahore. It is hypothesised that in high socio-economic status, sedentary lifestyle, obesity and consumption of high saturated fats in diet, after adjusting for age and family history of disease, have increased the risk of developing prostate cancer in Pakistani men.

The aim of this study was to identify lifestyle factors associated with prostate cancer risk among Pakistani men. This study not only provided new knowledge about the determinants of prostate cancer in Pakistan but also presented a model to predict risk of prostate cancer among high risk population.

SUBJECTS AND METHODS

This unmatched case control study was conducted from February 2011 to October 2011 in Lahore. A sample of 585 men (195 cases & 390 controls with 1:2) was selected. Cases with histologically confirmed adenocarcinoma of prostate were recruited from cancer registry of Shaukat Khanum Memorial Hospital Lahore and Institute of Nuclear Medicine and Oncology (INMOL) Lahore using purposive sampling technique. On the other hand, hospital controls (individuals without adenocarcinoma of prostate screened clinically by a qualified surgeon and having prostate specific antigen (PSA) at 2.5 ηg/ml or below) were selected from medicine, surgery and eye departments of Mayo, Jinnah Hospital, Services and Fatima Memorial Hospitals Lahore. Since an appreciable size of cases in Cancer Registry belonged to Khyber Pakhtunkhwa province, therefore in order to improve comparability, a set of controls from Lady Reading Hospital Peshawar were also included.

Data were collected through semi-structured face to face interviews both from cases and controls in hospital settings. Fully informed verbal informed consent was taken from the patient and confidentiality of the information was ensured. Pre-testing of the questionnaire was done in a pilot study to establish its validity and reliability. Combined effect of level of education achieved, monthly income and occupation was computed in the form of socioeconomic score, giving more weight to higher categories. Aggregated score was then classified into three classes: low socio-economic status (<30%), middle socioeconomic status (30-60%) and high socio-economic status (>60%). Similarly, physical activity score was also calculated using leisure time exercise levels (mild, moderate, strenuous), whether active at work place and at household level, using a five point scale, giving greater scores to individuals following regular exercise routine, participating in household work and being active at work place. Participants were then classified into three equal groups: mildly active, moderately active and highly active. In the food survey, frequency of food was multiplied with serving size to compute amount of that particular diet consumed per week. This consumption was then entered into NutriSurvey software 2007, to calculate amount of nutrients consumed per week, using food composition table for Pakistani food developed by Human Nutrition Department, Agriculture University Peshawar, published by Nutrition Cell of Planning Commission of Pakistan.

The data were analysed using SPSS-10. Difference between means of two continuous variables was tested using two sample *t*-test. Pearson Chi-Square and Fisher exact test (where appropriate) were applied to observe the association between qualitative variables, and $p<0.05$ was taken as significant. Unconditional Logistic Regression Models were used to compute unadjusted odds ratio followed by multivariate analysis adding more exposures in regression models in step-wise fashion to observe change in unadjusted odds ratio. A change of 10% from unadjusted estimate was used as criteria for confounding effect. Interactions of important factors in the association were also tested using likelihood ratio test.

RESULTS

Mean age of cases and controls was 69.77±4.9 years and 68.09±5.5 years respectively. This difference of means was statistically significant ($p<0.001$). Unadjusted odds ratio (OR 1.06, 95% CI=1.02–1.09) comparing odds of prostate cancer among cases as compared to controls indicates that by one year increase in age, odds of outcome increases by 1.06 times. However, when adjusted with ethnicity, socio-economic status, smoking status, family history of prostate cancer, height and physical activity, the odds ratio was reduced to 1.02 (95% CI=2.32–6.48). Majority (122, 62.6%) of cases were living in rural areas as compared to control population (179, 45.9%). The observed difference was statistically significant ($\chi^2=14.45$ at 1 df, $p<0.001$).

Adjusted estimates show that people living in rural areas had 3.88 times the odds of prostate cancer than individuals living in urban areas (95% CI=2.32–6.48, $p<0.001$).

Association of socio-demographic and economic factors with risk of prostate cancer is shown in Table-1, whereas Table-2 describes the relationship of lifestyle factors with the risk of prostate cancer.

Table–1: Risk of prostate cancer in relation to socio-demographic and economic characteristics

Characteristics	Unadjusted estimates			Adjusted estimates		
	Odds ratio	95% CI	*p*	Adjusted Odd ratio	95% CI	*p*
Age (years)	1.06	1.02–1.09	<0.001	1.02	0.97–1.06	0.32
Area of Residence						
Urban	1	Reference		1	Reference	
Rural	1.97	1.38–2.80	<0.001	3.88	2.32–6.48	<0.001
Ethnic/Language Groups						
Hindko	1	Reference		1	Reference	
Muhajir	0.41	0.12–1.36	0.15	0.17	0.04–0.78	0.02
Punjabi	0.25	0.09–0.70	0.17	0.12	0.02–0.59	0.009
Pashtun	0.24	0.08–0.71	0.14	0.33	0.06–1.84	0.20
Level of Education						
No formal schooling	1	Reference		1	Reference	
Up to Primary level	0.44	0.26–0.74	0.002	0.58	0.29–1.15	0.12
Secondary level	0.53	0.34–0.80	0.003	1.43	0.73–2.78	0.28
Higher Secondary	0.26	0.12–0.54	<0.001	1.19	0.43–3.27	0.70
Graduation / Professional	0.24	0.10–0.57	0.001	4.23	1.10–16.25	0.03
Level of Monthly Income (Rs)						
No Source of Income	1	Reference		1	Reference	
Low level Income	1.47	0.65–3.29	0.34	1.10	0.60–2.02	0.75
Middle level Income	0.49	0.19–1.24	0.13	0.52	0.22–1.26	0.15
Higher level Income	2.34	1.04–5.26	0.03	1.17	0.29–4.67	0.81
Worked as farmer						
No	1	Reference		1	Reference	
Yes	9.31	5.37–16.15	<0.001	19.76	5.51–70.80	< 0.001
Socio-economic Status (SES)						
Low	1	Reference		1	Reference	
Middle	0.35	0.24–0.52	<0.001	0.93	0.49–1.79	0.84
High	0.10	0.05–0.21	<0.001	0.24	0.07–0.76	0.01
Consanguineous marriages						
Not Frequent	1	Reference		1	Reference	
Less Frequent	0.68	0.31–1.47	0.33	1.43	0.51–4.01	0.49
Very Frequent	1.46	0.67–3.19	0.33	0.63	0.22–1.79	0.39

Table-2: **Risk of prostate cancer in relation to lifestyle factors**

CHARACTERISTICS	UNADJUSTED ESTIMATES			ADJUSTED ESTIMATES		
	Odds ratio	95% CI	*p*	Adjusted Odd ratio	95% CI	*p*
Cigarette Smoking						
Never Smoked	1	Reference		1	Reference	
Currently Smoking	0.79	0.47–1.32	0.37	0.79	0.41–1.55	0.51
Previously Smoked	3.24	1.95–5.36	< 0.001	3.86	1.99 –7.48	<0.001
Alcohol Drinking status						
Never ever drink	1	Reference		1	Reference	
Currently drinking	0.77	0.20–2.94	0.70	0.56	0.13–2.34	0.43
Previously drinking	1.71	0.84–3.48	0.13	2.17	0.97–4.83	0.06
Physical activity Index						
Mild	1	Reference		1	Reference	
Moderate	0.61	0.42–0.88	0.009	0.28	0.11–0.72	0.008
High	0.11	0.05–0.24	<0.001	0.05	0.01–0.26	0.001
Red Meat Consumption						
No Red meat in a week	1	Reference		1	Reference	
Once a week	1.81	1.21–2.71	0.004	2.23	1.27–3.87	0.005
Twice a week	10.38	5.15–20.90	<0.001	10.67	4.05–28.10	<0.001
Thrice a week	6.89	2.90–16.32	<0.001	11.82	2.88–48.54	0.001
Daily	2.73	0.91–8.22	0.073	14.53	2.58–58.87	<0.001
Chicken Meat Consumption						
No Chicken in a week	1	Reference		1	Reference	
Once a week	0.29	0.19– 0.43	<0.001	0.25	0.14–0.44	<0.001
Twice a week	0.81	0.45–1.46	0.49	0.72	0.31–1.68	0.45
Thrice a week	0.54	0.22–1.31	0.17	0.20	0.05–0.67	0.01
Daily	1.92	0.44–8.25	0.37	0.54	0.08–3.33	0.50
Fats (gm/day)						
<50	1	Reference		1	Reference	
50–64	2.87	1.67–4.93	<0.001	3.23	1.67–6.23	< 0.001
65–79	4.24	2.62–6.84	<0.001	5.08	2.86–9.02	<0.001
≥ 80	8.63	5.14–14.5	<0.001	7.95	4.38–14.43	<0.001
Height (Cm)						
150–164	1	Reference		1	Reference	
165–174	2.36	1.33–4.19	0.003	2.87	1.32–6.22	0.007
175–184	3.60	1.95–6.67	<0.001	6.17	2.68–14.20	<0.001
≥185	1.32	0.38–4.53	0.65	2.75	0.67–11.19	0.156

DISCUSSION

Prostate cancer is the most common malignancy among males in Western Europe, Australia and North America. Although its burden in South East Asian countries is comparatively low, however, increasing numbers of cases are being reported which in part may be due to introduction of more sophisticated screening and diagnostic tools. Increase in age is consistently found to have a strong association with prostate cancer risk. This study found the mean age of cases above 65 years. A large number of studies both on population with high prevalence to moderate level burden of disease indicated that this disease was more prevalent among men aged 65 and above (average 70 years) and probability of its occurrence enhances twofold after seventies.[17] It has been suggested that oxidative stress and other endogenous factors related with aging process might expose these individuals to develop the carcinomatous change in presence of other putative agents like strong family history of prostate cancer, exposure to environmental carcinogens and sedentary lifestyle. Ethnic background plays a vital role in explaining the variation in prostate cancer risk. While current study identified men from Hindko ethnic background as having higher odds of prostate cancer, but after adjustment, this effect was lost and ethnic differences in current study were not found as strong predictors of prostate cancer risk. This finding is in consistence with the study of Bhurgri *et al*[18], who investigated a multi-ethnic population in South Karachi. On the other hand, the fact that selection of cases and controls in this study was hospital based, therefore, finding no association between ethnicity and prostate cancer risk lacks external validity; and inference cannot be drawn for the effect of ethnicity on prostate cancer risk for general population.

Socioeconomic factors, though, not directly associated with disease risk may act as a surrogate measure for access to health care, expenditure on food and other activities producing direct or indirect impact on physical and/or mental health of the individuals. The way people live their lives is highly correlated with level of education, income and type of occupation they adopt. In our study, men from low socio-economic background living mainly in rural areas were found to have increasing odds of prostate cancer as compared to men belonging to both middle and higher socio-economic class. This is in contrast to previous studies which identified affluent class at higher risk of prostate cancer.[19,20] This variation can be attributed to disproportionate rural residence in our study settings as compared to more industrialised states and differences in educational status and income levels, which ultimately influence the socioeconomic status. In addition, we found farmers to be at higher odds of prostate cancer (OR=19.7) than men from other professions which might be due to exposures to these individuals to pesticide and herbicides, however attribution of any particular chemical in this regard can be explored in future studies. Similar findings were reported by Sharma-Wagner *et al*[21] in Sweden (7–12% higher risk among farmers) and Nelsen *et al*[11] in a cohort of 22,895 Norwegian men (OR=1.09).

Growing numbers of studies are reporting the beneficial effects of physically active lifestyle in disease prevention. It has been suggested that higher level of physical activity may reduce the quantities of free and total testosterone, reduce obesity and enhance immune mechanism, which collectively would contribute towards prostate cancer protection. This protective effect was also demonstrated in current study which showed that men exercising regularly for at least once a week and also active at their work place had lower odds of prostate cancer than men with more sedentary lifestyle. This effect has also followed a dose-response relationship such that with increasing activity level, odds of prostate cancer reduce. This inverse relationship was also reported by studies in Turkey[22], Canada[23], China[24] and Sweden.[25,26]

Andersson *et al*[27] found a weak association between height and prostate cancer risk (OR=1.2), however, we found a very strong association with height. Odds of prostate cancer increased from height of 165 Cm (2-fold) to 180 Cm (6-fold). This variation may be explained by the effect of modification between height and physical activity level. Furthermore, its effect may not be singly defined since height is a surrogate marker for dietary and hormonal influences. Our finding was also supported by the report of Norrish *et al*[28] who mentioned that height was associated (OR=1.62) with risk of advanced prostate cancer.

Dietary decisions are influenced by cultural norms, values, economics and religious affiliation. The dietary pattern can vary based on area of residence, social class, income level, health and disease status and education. Patterns of diet differ between rural and urban areas and among social classes. For instance, beef consumption is more dominant in rural areas and also urban areas of Pashtun belt. There are wide variations in vegetable and fruit consumption. Cooking methodology and food mix also plays an essential role in final provision or non-availability of nutrients. Current study reached the similar conclusion that odds of prostate cancer increases exponentially with more consumption of red meat and fats, however, relationship with white meat consumption was insignificant. The protective role of vegetables shown in our results is consistent with the findings of Kristal *et al*[11] and Hsing *et al*[29] Moreover, mixing vegetables with meat might provide protection; however this issue was not studied and if explored, could give important clues about disease prevention.

Findings of this study should be interpreted considering its design and methodological limitations. Being a case control design, the study might have limited

power to detect association, especially regarding association with dietary exposures. There may be issues of recall bias in responses about income level, cigarette smoking; nevertheless, every measure was adopted to ensure the quality of data. This study tried to provide an understanding of the risk factors and their strength of association with prostate cancer that has practical importance for public health policy, research, designing preventive strategies and health promotion.

CONCLUSION

Age, height, positive family history of prostate cancer, previous smoking, red meat consumption, farming and rural living are strong predictors for prostate cancer risk among men in studied population. In addition, vegetable consumption, increased dietary fibre intake and physical activity demonstrated a protective role. Socioeconomic indicators did not show significant relationship with prostate cancer risk individually, however, combined effect of education, income and occupation indicates that men from lower socioeconomic class are at higher risk.

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