RISK FACTORS OF URINARY BLADDER CANCER IN PESHAWAR REGION OF KHYBER PUKHTOONKHAWA

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Background: Urinary Bladder cancer is a fatal disease. No work about its risk factors has been conducted in northern Pakistan. This case control study was conducted in order to investigate the risk factors of the urinary bladder cancer in that area. **Method:** For this study 150 subjects including 50 cases and 100 controls were interviewed from the 2 tertiary care hospitals of Peshawar and the information was collected about the characteristics like gender, age, smoking habits, family history of cancer, etc. Descriptive and inferential statistics were used to explain the risk factors of the disease. Odds ratios and 95% Confidence Intervals were computed by using logistic regression model. **Results:** The odds ratio and 95% confidence interval for chemical exposure are 4.637 and (1.022–21.053), for cigarette smoking 19.526 and (4.688–81.329), for lifestyle 0.171 and (0.031–0.943), for fluid consumption 0.025 and (0.005–0.115), for fried items 5.934 and (1.429–24.648), and for fruits are 0.173 (0.045–0.660), respectively. **Conclusions:** Chemical exposure, cigarette smoking, and high use of fried items increase the risk of urinary bladder cancer. Moderate lifestyle, high fluid consumption and use of fruits are protective against the disease.

Keywords: Bladder cancer, Controls, Odds ratio, Questionnaire, Risk factors

INTRODUCTION

Urinary Bladder cancer is the 9th most common malignancy in men and is accounted for about 330,000 new cases and 130,000 deaths per annum worldwide.[1] Cancer is a fatal disease that causes death of several people in every year. More than 12 million cancer cases and 7.6 million deaths were estimated annually in all over the world in 2007 (American Cancer Society, 2007).

In the Netherlands, Belgium and the United States, the bladder cancer is ranked among the top 5 of most common malignancies in males.[1–3] Bladder tumours occur rarely before the age of 40 but are most commonly observed in the age of 70 and above.[3] The frequency of bladder cancer differs very much from country to country.[3,4] In general, higher incidence rates of bladder cancer are seen in the developed countries of Western Europe, North America and Australia but comparatively low incident rates are observed in the Far Eastern countries.[1] Only in United States, 51,200 bladder cancer cases and more than 10,600 deaths were predicted yearly.[5] Bladder cancer is more common in men than women, with a worldwide male/female ratio of 10:3.[6] In Pakistan, the number of bladder cancer cases and deaths are still unknown.

Smoking is considered as the main risk factor for urinary bladder cancer and about 50% of the bladder cancer cases have been assessed due to smoking tobacco.[7] From several studies, about 4 times more risk was observed in the cigarette smokers as compared to the non-smokers.[8–10] The risk of bladder cancer reduces in ex-smokers as compared to the current smokers.[11]

Occupation exposure was associated with the risk of bladder cancer, especially the workers including dyes or paints factories, chemical factories and in pharmaceutical industries had 3 times more risk of urinary bladder cancer.[12] The industrial workers, petroleum workers, working with oil and chemicals materials had a significantly increased risk of developing bladder cancer.[13]

High intake of coffee (more than 4 cups/day) was observed to increase bladder cancer risk.[14] Relationship of consumption of tea was not established with the risk of bladder cancer.[15] A poor inverse association was observed between tea consumption and urinary bladder cancer risk.[16–17] A high fluid intake is associated with a decreased incidence of bladder cancer in men, and lesser intake of daily fluids proportionally increases the risk of bladder cancer.[18]

High consumption of fats, especially animal fats, can increase the risk of urinary bladder cancer.[19–22] The risk of urinary bladder cancer was inversely associated with the high consumption of fruits and vegetables.[23]

This case control study was conducted in order to investigate the risk factors of the urinary bladder cancer in Peshawar and Khyber Pukhtoonkhawa.

MATERIAL AND METHOD

It was a hospital-based, case-control study which was conducted for descriptive and inferential purposes. This study was conducted in 2 hospitals, Lady Reading Hospital, and Institute of Kidney Diseases, Hayatabad, Peshawar. The sample was taken from the selected hospitals in the month of September to November, 2009 and all patients (cases) of urinary bladder cancer admitted in the urology wards were

interviewed. A self-designed questionnaire was used to collect the requisite information from the individuals about the characteristics like age, income, family history of cancer, cigarette smoking, etc. Cronbach's Alpha was used to measure the reliability of the questionnaire which was found to be 0.78. All information was obtained from the cases and controls by face to face interview. Both males and females of all ages admitted in the urology/cancer wards of the selected hospitals for treatment of urinary bladder cancer were included in this study. The 50 cases (patients) and 100 controls (healthy persons) were taken in the sample. The dependent variable was a binary while the independent variables were nominal, ordinal and quantitative type. Descriptive and analytical measures, the logistic regression model, were used to explain the variables under study. Odds ratio and the 95% confidence intervals for the Odds ratios were estimated using the binary logistic regression model. SPSS-16 was used for the purpose of data analysis.

RESULTS

This study contains 50 (33.3%) cases and 100 (66.7%) controls having 150 total subjects from the 2 hospitals. This study consisted on 33 (22.0%) females and 117 (78.0%) males of which 53 (35.33%) belonged to urban and 93 (64.67%) to rural areas. The literate patients were 9 (18.0%) and illiterate were 41 (82.0%), respectively in the sample. Similarly, 34 (34.0%) controls were literate and 66 (66.0%) were illiterate. It employs that the percentage of illiterate in patients is much higher than in controls.

The income was taken in Pak Rupees. The social status was captured from the income and divided into 3 categories, i.e., low (Income<10,000), medium (10,001–20,000) and high (Income>20,000). The low, medium, and high social status patients were 35 (70%), 13 (26%) and 2 (4.0%) respectively. Similarly, low, medium, and high status controls were 55 (55%), 41 (41%) and 4 (4.0%), respectively. The percentages of cases and controls in the low status were 70% and 55% respectively. The higher percentage of cases falls in the category of low status compared to the controls.

Lifestyle was captured from the exercise and taken in 3 categories, i.e., sedentary, normal and active. None of the cases or controls reported about the 3rd category in the overall sample. Hence, 2 categories including sedentary (no exercise) and normal (about 30 minute exercise daily) are observed and used for analysis. The cases and controls having sedentary lifestyle were 46 (92%) and 59 (59%), respectively. The higher percentage of the patients was living a sedentary life than in controls.

None of the case or control reported the cancer in his family history.

Table-1: Classification of cases/controls with different risk factors in Khyber Pukhtoonkhawa

Factors	Categories	Cancer Bladder		
		No	Yes	Total
Gender	Female	22	11	33
	Male	78	39	117
Industrial Area	Non-industrial	100	50	150
	Industrial	0	0	0
Rural Area	Urban	36	17	53
	Rural	64	33	97
Marital Status	Unmarried	0	0	0
	Married	100	50	150
Education	No	66	41	107
	Yes	34	9	43
Family history of cancer	No	100	50	150
	Yes	0	0	0
Lifestyle	Sedentary	59	46	105
	Normal	41	4	45
Social Status Income in PKR	<10,000	55	35	90
	10,001–20,000	41	13	54
	≥Rs. 20,000	4	2	6
Chemical Exposure	No	69	25	94
	Yes	31	25	56
Chew pan	No	100	50	150
	Yes	0	0	0
Use of tea	No	12	6	18
	Yes	88	44	132
Fluid taken(Glasses)	<10 glasses	11	31	42
	≥10 glasses	89	19	108
Source of water (drinking)	Tap	71	36	107
	Govt. Provided	29	14	43
Use of tea	No	12	6	18
	Yes	88	44	132
Hair dye	No	100	37	137
	Yes	0	13	13
Fluid taken Glasses)	<10 glasses	11	31	42
	≥10 glasses	89	19	108
Source of drinking water	Tap	71	36	107
	Govt. Provided	29	14	43
Fried item	Low	78	28	106
	Normal	22	22	44
	High	0	0	0
Fats item	Low	79	35	114
	Normal	21	15	36
	High	0	0	0
Fast food	Low	100	50	150
	Normal	0	0	0
	High	0	0	0
Fruits	Low	35	40	75
	Normal	65	10	75
	High	0	0	0
Cigarette Smoking	No	90	22	112
	Yes	10	28	38

Patients and controls having chemical exposure were 50% and 31%, respectively. The percentage of chemical exposure in patients was higher than in controls. The percentage of the tea drinkers in cases and controls was equal, i.e., 88%. Cases and controls consuming less than 10 glasses of total fluid were 62% and 11%, respectively. The higher percentage of cases was using the less than 10 glasses of water as compared to the controls. Cases and controls consuming tap water were 72% and 71%, respectively. Similarly,

28% of the cases and 29% of the controls in the sample were consuming the government provided water. Eighty percent and 35% cases and controls took fruits 2 or less than 2 days per week respectively, and those using fruits 3 or 4 days per week were 20% and 65%, respectively. The higher percentage of controls was using the fruits 3 or 4 days per week as compared to the cases.

For the purpose of analytical analysis, the binary logistic regression model was run and the regression coefficients, odds ratio, *p*-value and 95% confidence interval for odds ratio were computed. The *p*-value is compared with the predefined values alpha (5%) for the significance of the variables. Omnibus test and Hosmer and Lemeshow Test (HLT) were used for checking the adequacy of the model. The Omnibus test with χ^2=116.922 was significant at *p*=0.000. The HL test is much better when the sample size is small and some variables are continuous than other traditional χ^2 tests.[24] It is observed that the HL test was insignificant with χ^2=3.156 at *p*=0.924 showing that the model is adequately fitted. In order to observe the goodness of fit, the values of Cox and Snell R^2 and Nagelkerke R^2 were 0.541 and 0.752, respectively.

From the Table-2, it is found that out of 100 controls 93 (93.0%) are correctly predicted as controls while out of 50 patients of bladder cancer, 42 (84.0%) are correctly predicted as cases (patients). But 8 (16.0%)

patients and 7 (7.0%) controls are misclassified 8 (16.0%) as controls and 9 (9.0%) as patients, respectively. The overall correctly classified and misclassified subjects were 135 (90.0%) and 15 (10.0%), respectively.

The significant risk factors and their predictive strengths are observed from the Table-3. Six factors namely chemical exposure, lifestyle, cigarette smoking, fluid consumption, fried items and fruit are found to be significant in Peshawar region of Khyber Pukhtoonkhawa. The logistic regression model is presented below:

$$Z = 1.073 + (1.534 \times CE) - (1.769 \times Lifestyle) + (2.972 \times CS) - (3.691 \times FC) + (1.781 \times Fried) - (1.753 \times Fruit)$$

The percentage of the correct classification, Omnibus test, HL test, Cox and Snell R^2 and Nagelkerke R^2 provide the evidence that the model is adequate and best fitted. Hence, the odds ratios and 95% confidence intervals for the odds ratios are also valid.

Table-2: Correct classification and misclassification of subjects

Observed		Predicted		
		Bladder Cancer		%
		No	Yes	
Bladder	No	93	7	93.0
	Yes	8	42	84.0
		Overall Percentage		90.0

Table-3: Model coefficients with odds ratios and 95% CI for odds ratio

Factors	β	SE (β)	Wald	*p*	Exp (β)	95% CI Lower	95% CI Upper
Chemical exposure	1.534	0.772	3.950	0.047	4.637	1.022	21.053
Lifestyle	-1.769	0.873	4.108	0.043	0.171	0.031	0.943
Smoking	2.972	0.728	16.667	0.000	19.526	4.688	81.329
Fluids consumption	-3.691	0.781	22.313	0.000	0.025	0.005	0.115
Fried food	1.781	0.727	6.008	0.014	5.934	1.429	24.648
Fruits	-1.753	0.683	6.594	0.010	0.173	0.045	0.660
Constant	1.073	0.618	3.015	0.082	2.925		

DISCUSSION

The odds ratio and 95% confidence interval for the odds ratio of the chemical exposure are 4.63 and (1.46, 4.607) respectively showing that the effect of chemical exposure is significant because its confidence interval does not include one. It is observed that the subjects having chemical exposure at their work place have 4.63 times higher risk of bladder cancer as compared to other professions. A combined case control study of 6 European countries (Germany, France, Italy, Spain, Greece and Denmark) from 1976 to 1996 found that the occupations including knitters, automobile painters, machinists, automobile mechanics and textile machinery mechanics had higher risk of bladder cancer as compared to the other occupations.[25] Workers of dyes or paint factories, chemical factories and in pharmaceutical industries had 3 times more risk of urinary bladder cancer as compared to workers related to other

occupations showing that chemical exposure was associated with the risk of bladder cancer.[12]

The odds ratio and 95% confidence interval for the moderate lifestyle are 0.171 and (0.031, 0.943), respectively. It is observed that the effect of lifestyle is inversely associated with the bladder cancer and the odds ratio 0.171 means that 82.9% protection against the disease.

Cigarette smoking is found to be the highest risk factor of the bladder cancer compared to other risk factors. Cigarette smoking is a major risk factor that causes urinary bladder cancer in about 50 to 65% male and 20 to 30% female smokers.[26–28] Odds ratio and 95% CI indicate that the cigarette smokers in Peshawar region have 19.5 times more risk of bladder cancer as compared to the non-smokers. In Spain, the odds ratios and 95% confidence intervals for current smoker in males and females were (7.4; 5.3–10.4), and (5.1; 1.6–16.4), respectively showing that 7.4 times and 5.1 times

more risk of bladder cancer were found in males and females, respectively as compared to the nonsmokers.[29]

The fluid consumption is found to be inversely significant with odds ratio 0.025 and 95% CI of odds ratio (0.005–0.115), which means that a person who consumes 10 or more glasses of water per day has 0.025 times chance of getting disease (i.e., 97% protection against the disease) as compared to the person who consumes less than ten glasses of water per day. Hence, consumption of more water is a protection against the disease. Excess of water in the bladder reduces the concentration and stay time of chemicals by frequent urination. A high fluid intake is associated with a decreased incidence of bladder cancer in males, and lesser intake of daily fluids proportionally increases the risk of bladder cancer.[18]

Use of fried items is significantly associated with urinary bladder cancer. Subject who are using fried items more than 2 days per week have 5.9 times more risk of bladder cancer as compared to those who consume fried items 2 or less days per week. Excessive use of fried items and bladder cancer are directly associated with the increased risk of bladder cancer.

Consumption of fruits more than 2 days per week has 0.173 times risk of bladder cancer, i.e., 83% protection against bladder cancer as compared to those who consume fruits 2 or less than 2 days per week. The risk of bladder cancer was inversely associated with the high consumption of fruits and vegetables.[23]

CONCLUSION

Chemical exposure, cigarette smoking, and high use of fried items increase the risk of urinary bladder cancer. Moderate lifestyle, high fluid consumption and use of fruits are protective against the disease.

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