



Risk Factors of Urinary Bladder Cancer in Islamabad, Federal Area of Pakistan

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Case Study

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ABSTRACT

It is retrospective and hospital based case control study which was conducted in the federal city of Islamabad in Pakistan in order to assess the risk factors of the urinary bladder cancer. This study was based on the 100 controls and 50 cases comprising 150 subjects which were selected for interview from the two hospitals and required information like gender, age, smoking habits, family history of cancer, etc., was achieved. Both the descriptive and analytical approaches were used to find out the dominating risk factors of the disease. Odds ratios and 95 % Confidence Intervals were obtained for analytical purpose by using the binary logistic regression model. Three factors including cigarette smoking, source of drinking water and fried items were found to be significant having odds ratios and 95% confidence intervals of (17.158, 6.244-47.147), (0.192, 0.061- 0.603) and (12.206, 3.291- 45.275), respectively. The study revealed that cigarette smoking, consumption of tap water and high use of fried items increases the risk of developing bladder cancer. On the other hand, the use of government provided for drinking purpose is a protection against the urinary bladder cancer as compared to tap water.

Keywords: Case study; Urinary Bladder cancer; Controls; Odds ratio; Risk factors;

1. INTRODUCTION

Urinary bladder cancer occurs in all countries around the world, and it is the fifth most common cancer in the United States (Silverman et al., 1996; Ohno et al., 1985). Urinary Bladder cancer is the ninth most common cancer in men and is accounted for about 330,000 new cases and 130,000 deaths per annum worldwide (Steward and Kleinhaus, 2003). In Belgium, Netherlands and United States, the bladder cancer is ranked among the top five of most common malignancies in males (Steward and Kleinhaus, 2003; Lousbergh et al., 2003; Visser et al., 2002). Only in United States, 51200 bladder cancer cases and more than 10600 deaths were predicted yearly (Boring et al., 1994). In USA, the urinary bladder cancer is the fourth most common malignancy in men and 8th in women (Jemal et al., 2003).

The frequency of bladder cancer differs very much from country to country (Schottenfeld and Fraumeni, 1996). Males are mostly affected by bladder cancer, with a male/female ratio of 3:1, showing sex-linked etiological reasons (Rabbani and Cordon, 2000). Bladder tumours occur rarely before the age of 40 but most commonly observed in the age of seventy and above (Visser et al., 2002). Bladder cancer is more common in men than women, with a worldwide male/female ratio of 10:3 (Sylvester et al., 2004). In general, higher incidence rates of bladder cancer are investigated in the developed countries of Western Europe, North America and Australia but comparatively low incidents rates are observed in the Far Eastern countries (Steward and Kleinhaus, 2003). Such figures about the occurrence of bladder cancer are not available in Pakistan.

Cigarette smoking accounts for 50% and 31% of bladder cancers in men and women respectively (Wynder and Goldsmith, 1971). Approximately 4 times higher risk of bladder cancer was investigated in the cigarette smokers as compared to the non-smokers (Burch et al., 1989; Clavel et al., 1989; Morrison, 1984). The higher risk was found in current smokers as compared to the ex-smokers (Augustine, 1988).

High consumption of fats, especially animal fats, can increase the risk of urinary bladder cancer (Riboli et al., 1991; Radosavljevic' et al., 2005). The risk of urinary bladder cancer was inversely associated with the high consumption of fruits and vegetables (Negri and Vecchia, 2001). The use of hair dyes was investigated a risk factor for urinary bladder cancer (Gago et al., 2001). But the meta-analysis of 10 published case control studies did not confirm it in which the combined relative risk and 95 % confidence interval for ever users of hair dyes was 1.01 and (0.89-1.14), respectively (Takkouche et al., 2005).

High intake of coffee (more than 4cups/day) was observed to increase bladder cancer risk (Villanueva, et al., 2006). The relationship of consumption of tea with the risk of bladder cancer was not established (Zeegers et al., 2004). A poor inverse association was observed between tea consumption and urinary bladder cancer risk (Bianchi et al., 2000; Zeegers et al., 2001). 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 (Claus et al., 1996).

In the light of these facts, it is necessary to take steps for controlling such a fatal, life threatening and aggressive disease. No published research is available that can explain the risk factors of the urinary bladder cancer in Islamabad (federal city of Pakistan).

2. MATERIAL AND METHODS

In this section, the study design, software and the statistical methods were used for the analyses of data are discussed.

This case control was conducted to investigate the risk factors of the urinary bladder cancer in Islamabad (federal city of Pakistan). In order to obtain the requisite information, the two hospitals Pakistan Institute of Medical Sciences (PIMS) and Nuclear Medicine of Oncology & radiotherapy Institute (NORI) having urology /oncology ward were selected. The requisite information for the sample was taken in the month of November and December, 2009 and all the patients of urinary bladder cancer admitted in the urology wards were interviewed. A questionnaire was developed to obtain the requisite information from the subjects about the characteristics like age, residential area, family history of cancer, lifestyle, source of drinking water, cigarette smoking, etc. Information was obtained from the cases and controls by interview method. Both males and females of all ages admitted in the urology / cancer wards of the selected hospitals for the treatment of urinary bladder cancer were included in this study. The fifty cases (patients) and one hundred controls (healthy persons) were taken in the sample. The selected cases were diagnosed by the basic symptom of PPP's (Profuse Periodic Painless Heamuturia) and biopsy report. The reliability of the instrument was measured by using the Cronbach's Alpha and was found to be 0.81. The response variable was a binary while the independent variables were nominal, ordinal and quantitative type. For the purpose of descriptive measures, the counts and the percentages were used. The binary logistic regression model was used to explain the risk of the urinary bladder cancer. The analysis of the data was done by using the SPSS (Version-16) as software.

3. RESULTS

This analysis contains both the descriptive and inferential parts which are necessary for explaining the risk factors of the disease.

Table 1 stated that this study was consisted on 24 (16%) females and 126 (84%) males of which 85 (56.67%) belong to the urban and 65 (43.33%) rural areas. The counts (percentages) of literate and illiterate patients were 14 (28.0 %) and 36 (72.0%), respectively in the sample of 50 (33.3%) cases and 100 (66.7%) controls having 150 total subjects. Similarly, counts (percentages) of literate and illiterate controls were 30 (30 %) and 70 (70%), respectively. The social status was captured from the income (Rupees) and divided into three categories that is low (Income <10,000), medium (10,001<Income<20,000) and high (Income >20,000). The counts (percentages) of the low, medium and high in patients were 31(62%), 18 (36%) and 1 (2%), respectively. Similarly, the counts (percentages) of the low, medium and high in controls were 45(45%), 47 (47%) and 8 (8%), respectively. The percentage of the cases in the category of low status is much higher as compared to the controls. The percentages of the patients and controls consuming tap water were 74% and 56%, respectively.

Similarly, 26% of the cases and 44% of the controls in the sample were consuming the government provided water. The percentages of the cases and controls consuming less than 10 glasses of total fluid were 50% and 30%, respectively. The higher percentage of cases was using the less than 10 glasses of water as compared to the controls. The percentages of the cases and controls using fruits 2 or less than 2 days per week were 80% and 61%, respectively. Similarly, the percentages of the cases and controls using fruits 3 or 4 days per

week were 20% and 39%, respectively. The higher percentage of controls was using the fruits 3 or 4 days per week as compared to the cases.

Table1. Classification of cases/controls with different risk factors

Factors	Categories	Bladder Cancer		
		No	yes	Total
Gender	Female	16	8	24
	Male	84	42	126
Rural Area	Urban	60	25	85
	Rural	40	25	65
Education	No	70	36	106
	yes	30	14	44
Family history of cancer	No	100	50	150
	yes	0	0	0
Lifestyle	Sedentary	90	40	130
	Normal	10	10	20
Social Status	< Rs. 10000	45	31	76
	Rs.10000-20000	47	18	65
	≥ Rs.20000	8	1	9
Use of tea	No	5	2	7
	yes	95	48	143
Hair dye	No	99	41	140
	yes	1	9	10
Fluid taken (Glasses)	< 10 glasses	30	25	55
	≥ 10 glasses	70	25	95
Source of Drinking Water	Tap	56	37	93
	Govt. Provided	44	13	57
Fried item	Low	96	29	125
	Normal	4	21	25
	High	0	0	0
Fats item	Low	98	35	133
	Normal	2	15	17
	High	0	0	0
Fast food	Low	100	50	150
	Normal	0	0	0
	High	0	0	0
Fruits	Low	61	40	101
	Normal	39	10	49
	High	0	0	0
Cigarette Smoking	No	87	14	101
	yes	13	36	49

For the inferential purpose, the binary logistic regression was run and the regression coefficients, odds ratio, p-values and 95% confidence intervals for odds ratios were obtained. The p-value was compared with the alpha (5%) for the significance of the variables. If the p-value is less than 0.05 then factor is significant other wise insignificant. The discussions of the significant results about the risk factors were made on the basis of odds ratios and 95% confidence intervals of the odds ratio. Adequacy of the model was observed by using the Omnibus test and Hosmer and Lemeshow Test (HL test). According to the omnibus test, $\chi^2 = 78.08$ which was significant at P-value = 0.000 indicating that at least one of the factor was significantly affecting the response variable. The same purpose is also served by an other test called the HL test which is an alternate of the omnibus test. HL test was found to be insignificant with $\chi^2 = 0.628$ p-value = 0.890 showing that the model was adequately fitted. In order to observe the goodness of fit, the values of Cox and Snell R^2 and Nagelkerke R^2 were 0.406 and 0.564, respectively. In logistic regression, the value of R^2 is an attempt to measure the amount of association of the factors with the response variable.

From Table 2, it was found that out of 100 controls 91 (91.0%) were correctly predicted as controls while out of 50 patients of bladder cancer, 36 (72.0%) were correctly predicted as cases (patients). But 14 (28.0%) patients and 9 (9.0%) controls were misclassified, 14(28.0%) as controls and 9 (9.0%) as patients, respectively. The overall numbers (percentages) of correctly classified and misclassified of subjects were 127 (84.7%) and 23 (16.0%), respectively.

Table 2. Correct classification and misclassification of subjects

Observed		Predicted		
		Bladder Cancer		Percentage Correct
		No	Yes	
Bladder	No	91	9	91.0
Cancer	Yes	14	36	72.0
Overall Percentage				84.7

Table 3 indicates that the three factors including cigarette smoking, source of drinking water and fried items were found to be significantly associated with the risk of bladder cancer. The logit model is given below:

$$Z = -1.750 + 2.842 * (\text{Cigarette Smoking}) - 1.650 * (\text{Source of drinking water}) + 2.502 * (\text{Fried items})$$

It is evident from the omnibus test, percentages of the correct classification, Cox and Snell R^2 and Nagelkerke R^2 that the fitted model is adequate and the odds ratios and 95% confidence intervals for the odds ratios are valid for inferences.

Table 3. Model coefficients with odds ratios and 95% CI's for odds ratio

Factors	Model coefficients (β)	Std. Error of β	Wald	Significant	Exp(β) (odds ratios)	95% Confidence Intervals of odds ratios	
						Lower	Upper
Cigarette Smoking	2.842	0.516	30.378	0.000	17.158	6.244	47.147
Drinking Govt. Provided	-1.650	0.584	7.983	0.005	0.192	0.061	0.603
Fried items	2.502	0.669	13.995	0.000	12.206	3.291	45.275
Constant	-1.750	0.340	26.475	0.000	0.174		

4. DISCUSSION

It was observed from the data that cigarette smoking was the major risk factor of the urinary bladder cancer as compared to the other risk factors. Out of 50 patients of bladder cancer, 36 (72%) were found to be smokers. According to the studies of (Silverman, et al., 1996; Brennan, et al., 2001; Kogevinas and Trichopoulos, 2000), cigarette smoking was a major risk factor that causes to develop the urinary bladder cancer about 50% to 65% in males and 20% to 30% in females. Another study (Wynder and Goldsmith, 1971) stated that cigarette smoking accounted for 50% and 31% of bladder cancers in men and women, respectively. In this study, the odds ratio and 95% confidence interval for the odds ratio in cigarette smokers were 17.158 and (6.244, 47.147), respectively. This result showed that the cigarette smokers in federal area had 17.15 times higher risk of bladder cancer as compared to the non smokers. The studies (Burch, et al., 1989; Clavel, et al., 1989; Morrison, 1984) investigated about 4times higher risk of bladder cancer in the cigarette smokers as compared to the non-smokers. Similarly, a study conducted in Spain, investigated the 7.4 times and 5.1 times higher risk of bladder cancer in males and females, respectively as compared to the nonsmokers (Samanic, et al., 2006). Another study conducted in the four western provinces of Canada observed an increasing risk of bladder cancer in cigarette smokers with an odds ratio 3.32 and 95% confidence interval (2.28-4.82) which indicated that the cigarette smokers had more than 3 times higher risk of bladder cancer as compared to the nonsmokers (Ugnat, et al., 2004). Many earlier studies (Silverman, et al., 1996; Brennan, et al., 2001; Kogevinas and Trichopoulos, 2000; Wynder and Goldsmith, 1971; Burch, et al., 1989; Clavel, et al., 1989; Morrison, 1984; Samanic, et al., 2006; Ugnat, et al., 2004) support the results of this study and hence it could be confirmed that cigarette smoking is the major risk factor of bladder cancer in Islamabad (Pakistan) and other parts of the world.

Generally four sources of drinking water including tap, canal, government provided and mineral water are being used in Pakistan. These four categories were considered in this sample but none of the respondent reported about the use of canal water and mineral water. Hence, only two categories including tap water and government provided water for drinking were reported by the respondents. Government provided water is generally considered better due to the filtration as compared to the tap water which may be contaminated due to

the chemicals and other reasons. In the sample of federal area, the percentages of the cases and controls consuming tap water were 74% and 56%, respectively. Similarly, 26% of the cases and 44% of the controls in the sample were consuming the government provided water. High percentage of cases was consuming the tap water as compared to the controls. The consumption of government provided water was found to be negatively significant with the odds ratio and 95% confidence interval 0.192 and (0.061-0.603), respectively as compared to the tap water. It means that the subjects using government provided water has 81% protection against the urinary bladder cancer as compared to the subjects using the tap water. A study conducted by pooling the data of 6 case-control studies including 2 studies from the US and one from each Finland, Canada, Italy and France investigated the higher risk of bladder cancer in the users of tap water and suggested that the tap water may contain high carcinogenic chemicals (Villanueva, et al., 2006). In this context, government provided water is better than the tap water because government provides water to the public for drinking purpose keeping in view the hygienic conditions.

The use of fried items was found to be significant with odds ratio and 95% confidence interval of odds ratio 12.206 and (3.291, 45.275), respectively. A subject who was using fried items more than 2 days per week have 12.206 times higher risk of bladder cancer as compared to those who consume the fried items 2 or less than two days per week. In this sample, 42% of the patients and 4% of the controls were using the fried items more than two days per week. The percentage of the patients using the fried items more than 2 days per week was much higher as compared to the controls. A retrospective study conducted in the 7 provinces of Canada to investigate the dietary and occupational risk factors of the urinary bladder cancer found significantly higher risk of bladder cancer among males who were taking the higher amount of fried food (Reimar, et al., 2004). Keeping in view the results of the both stated studies, it is concluded that the excessive use of fried food is a problematic for urinary bladder.

5. CONCLUSION

Three factors cigarette smoking, source of drinking water and fried items were found to be significant risk factors for causing urinary bladder cancer. Cigarette smoking and high use of fried items increase the risk of bladder cancer but the government provided water for drinking reduces the risk of bladder cancer as compared to the tap water. The cigarette smokers had 17 times higher risk of urinary bladder cancer as compared to the non smokers while the high user of fried items had 12 times higher risk of bladder cancer as compared to the low users. In the similar way, the subjects using government provided water for drinking had 81% protection against the urinary bladder cancer as compared to the subjects using the tap water.

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