

## Non-occupational risk factors of urinary bladder cancer in Faisalabad and Lahore, Pakistan

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### Abstract

**Objective:** To investigate the non-occupational risk factors of the urinary bladder cancer in Faisalabad, Pakistan.

**Method:** Several risk factors related to urinary bladder cancer - smoking, gender, residential area, fluid consumption, family history of cancer, use of tea and coffee - were examined. For the retrospective study, 149 subjects, 20 women and 129 men, were interviewed. Descriptive and inferential statistics were used to explain the risk factors of the disease. Odds ratios (OR) and 95% Confidence Intervals (CIs) of odds ratios were computed using the logistic regression model.

**Results:** The significant odds ratios for moderate lifestyle, education, smoking and fluid consumption were: (OR: 0.103, 95% CI: 0.037-0.290), (OR: 0.193, 95% CI: 0.058-0.638), (OR: 13.129, 95% CI: 4.215-40.9) and (OR: 0.116, 95% CI: 0.040-0.333), respectively.

**Conclusions:** The study suggests that smoking increases the chances of an individual getting the disease. Protective agents include a moderate lifestyle, awareness and the use of 10 or more glasses of water per day.

**Keywords:** Bladder cancer, Controls, Odds ratio, Retrospective, Risk factors (JPMA 62: 236; 2012).

### Introduction

Bladder cancer is the ninth most common malignant disease in the world.<sup>1</sup> In the USA, it is the fourth most common malignancy in men and the 8th in women.<sup>2</sup> In Pakistan, urinary bladder cancer is one of the top ten malignancies in men and the most common urological malignancy in both sexes.<sup>3</sup> The overall new bladder cancer cases and deaths were found to be 330,000 and 130,000, respectively, across the world in 2005.<sup>4</sup>

In the United States, the fresh number of such cases and deaths in 2005 were over 63,000 and 13,000, respectively.<sup>4</sup> In 2009, the number of these cases and deaths were observed to be 71,000 and 14,000, respectively, in the US.<sup>5</sup> The stated figures of bladder cancer deaths in 2005, 2009 and 2010 were 13,000, 14,000 and 14,680, respectively, which shows an increasing trend in the US. The incidence rate of bladder cancer in the developed countries has increased, and found to be higher in men as compared to women during the previous decades.<sup>6,7</sup> But from 1987 to 2005, a downward trend in the incidents of bladder cancer cases was observed in the US.<sup>8</sup>

The precise number of bladder cancer cases and deaths annually are not available at the national level in Pakistan. But like the other developing countries, Pakistan is also facing the double burden of the diseases with the

significant incidents of cancer and an increasing trend in risk factors' profile.<sup>1,9</sup> Shoukat Khanam Cancer Hospital (private) situated in Lahore has tried to complete the cancer registry, but has remained limited to that hospital. Another registry was also developed in Karachi, Pakistan, by Bhurgri et al,<sup>9</sup> but that was also limited to the hospitals of the city.

Tobacco smoking is considered to be the main risk factor for urinary bladder cancer and about 50% of the cases have had a history of smoking.<sup>10</sup> Approximately four times higher risk of bladder cancer was observed in the cigarette smokers as compared to the non-smokers.<sup>11-13</sup> A significantly increased risk of about 2 times was found in those who were smoking for a period of less than 10 years as compared to the non-smokers with odds ratio being 1.9 and 95% CI: 1.1 -3.1. The corresponding values for those smoking for a period of over 40 years were 4.1, and 3.0-5.5, respectively.<sup>14</sup> The risk of bladder cancer also reduces in ex-smokers as compared to the smokers.<sup>15</sup> The odds ratios and 95% CI in current smokers and ex-smokers were [7.4; 5.3-10.4] and [3.8; 2.8-5.3] as compared to the non-smokers.<sup>16</sup>

A poor association was observed between the urinary bladder cancer and daily fluid consumption in males.<sup>17</sup> On the other hand, there was a significant decrease in the odds ratio 0.34 [95% CI: 0.11-0.99] for the females who consume more than two liters of fluid per day.<sup>17</sup>

Consequently, it becomes necessary to take steps for

controlling such a fatal, life threatening and aggressive disease. The statisticians, oncologists and medical researchers should try to put their combined efforts for the detection and analysis of the causes of cancer and utilise the results for bringing the numbers down.

This study was conducted to investigate the risk factors of urinary bladder cancer in Lahore and Faisalabad by using the descriptive and analytical approaches in order to understand and create awareness about the severity of the risk factors of the disease in Pakistan.

## Patients and Methods

The hospital-based retrospective case-control study was conducted in three hospitals — two in Lahore and one in Faisalabad. The selected hospitals were: Services Hospital, Lahore; Mayo Hospital, Lahore; and Allied Hospital, Faisalabad.

The sample of the patients was taken by visiting the selected hospitals in June and July, 2009. All the attendants and cancer patients of urinary bladder admitted in the urology wards were interviewed. These cases were diagnosed by basic symptom of PPPs (Profuse Periodic Painless Haematuria) and biopsy report. A self-designed questionnaire was used to collect the requisite information from the individuals about the characteristics like age, income, marital status, residential area, lifestyle, profession, education, family history of cancer, smoking habits, use of tea and coffee, use of alcohol, fluid consumption, eating habits (like fast food, fried food, fruits, etc.). All this 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 the treatment of urinary bladder cancer were included in the study. The cases (patients) and controls (healthy persons) were taken. The attendants of the patients (healthy persons) having age 40 years or more with the same sex were taken as controls. These were better controls than the hospital controls because they had come from the same environment and the same area as the patient had. In case where such controls were not available, hospital controls having a disease other than cancer were included. There were 92% controls from the attendants, while 8% were hospital controls. The total selected sample was comprised 149 subjects consisting of 50 cases and 99 controls.

The response variable was binary, and all the other explanatory variables were nominal ordinal and quantitative type. The reliability of the questionnaire was assessed by using Cronbach's Alpha which was 0.7. Some descriptive measures were used to explain the variables under study and the logistic regression model was used for the inferential purpose. Chi-square, Phi-statistic and Kendall's Tau b were used to measure the association between the individual

factors and the disease. The Phi-statistics is used when both the variables are nominal, while the Kendall's Tau b is used when at least one of both variables is ordinal. A variable is considered as significant if p-value is less than 0.05.

Lifestyle of the subjects was the ordinal variable in which three categories, sedentary, moderate and active lifestyle, were taken and assigned codes as 0, 1 and 2 respectively. A sedentary lifestyle is a lifestyle having no leisure-time or physical activity (exercises, sports, physically active hobbies). A moderate lifestyle is the one in which up to 30 minutes are consumed for leisure-time with physical activity, and the active lifestyle has more than 30 minutes for leisure-time or physical activity. According to the 1998 Population Census, a literate person has been defined as "One who can read the newspaper and write a simple letter in any language."

## Results

The study consisted of 50 (33.6%) cases and 99 (66.4%) controls comprising the 149 total subjects from the three selected hospitals. The study had 20 (13.4%) females and 129 (86.6%) males in which 73 (49%) belonged to the industrial and 76 (51%) to non-industrial areas. Of the total, 133 (89.3%) were married, and 64 (43%) respondents were literate. Of all the subjects, 34 (22.8%) reported cancer history in their families. The smokers in the cases and the controls were 32(64%) and 34 (34.3%) respectively. The minimum age among the diseased persons was 35 years. The monthly income was taken in rupees and the socioeconomic status was derived from the monthly income using three categories: low (<Rs.10,000), medium (Rs. > 10,001 and < Rs.30,000), and high ( $\geq$  Rs.30,000). Of the subjects, 105(70.5%) belonged to the low category, while 44 (29.5%) to the medium. There was no one in the high socioeconomic status of the study.

Six factors, including lifestyle, education, smoking, fried items, fruits and fluid consumption, were significantly associated with urinary bladder cancer both by Chi-square and Phi-statistic (Table-1). The fluid taken is a highly significant factor having the maximum value  $p = 0.0001$ . The study had no one using coffee or alcohol. Thus, the six factors were found to be significant of which four, including lifestyle, education, fluid taken and use of fruits, were negatively associated. It means that as the level of these factors increases, the chance of getting the disease decreases. Hence, these four factors are protective against the diseases. On the other hand, two factors, smoking and high use of fried items, were positively associated with the disease which indicates that as the level of these factors increases, the chance of getting the disease also increases.

The accuracy of the diagnostic tests is estimated by

**Table-1: Association of different factors with bladder cancer.**

S No.	Variables	Chi-Square	Phi-Statistic	p-value	Tau_b	p-value
1	Gender	1.904	0.113	0.168	-	-
2	Area industrial	0.031	0.014	0.861	-	-
3	Marital status	0.043	0.017	0.836	-	-
4	Socioeconomic Status	3.284	-	0.070	-0.148	0.054
5	Education	6.867	-0.215	0.009	-	-
6	Family history	2.203	0.122	0.138	-	-
7	Cigarette smoking	11.842	0.282	0.001	-	-
8	Tea	1.704	0.071	0.192	-	-
9	Coffee	-	-	-	-	-
10	Alcohol	-	-	-	-	-
11	Life style	34.017	-	0.0001	-0.478	0.0001
12	Fried items	3.972	-	0.046	0.200	0.050
13	Fats items	0.986	-	0.321	0.081	0.313
14	Fast-food	0.759	-	0.384	0.071	0.355
15	Fruits	8.863	-	0.003	-0.244	0.004
16	Fluid taken	59.993	-	0.0001	-0.635	0.0001

\* The bold factor showing the significant association.

\* One glass of fluid contains 250 ML fluid.

**Table-2: Specificity and Sensitivity for assessing model accuracy.**

Observed		Predicted BC		Conditional Probabilities
		No	Yes	
BC	No	92	7	0.93 (Specificity)
	Yes	19	31	0.62 (Sensitivity)
Total		111	38	

BC: Bladder cancer.

using the sensitivity and specificity (Table-2), which are both conditional probabilities. Sensitivity =  $P[\text{test shows that the subject has disease, given that the subject has disease}] = 31/149 / 50/149 = 0.62$  and Specificity =  $P[\text{test shows that the subject does not have disease, given that the subject is free from disease}] = 92/149 / 99/149 = 0.92$ . Both the probabilities are high, so the performance of the test is reliable.

The study also observed the significant risk factors and their predictive strengths. Four factors, lifestyle, education, smoking and fluid taken (number of glasses taken per day), were found to be significant (Table-3). The logit model is given below:

$$Z = 1.109 - 2.27 * (\text{Life style}) - 1.646 * (\text{Literate}) + 2.575 * (\text{Cigarette Smoking}) - 2.155 * (\text{Fluid taken}).$$

Where Z is a logit that is  $Z = \ln [\pi(x) / 1 - \pi(x)]$ , this

**Table-3: Model coefficients with odds ratios and 95% CIs for odds ratio.**

	$\beta$	SE( $\beta$ )	Wald	df	Sig.	Exp( $\beta$ )	95% CI	
							Lower	Upper
Lifestyle	-2.270	0.527	18.567	1	0.0001	0.103	0.037	0.290
Education	-1.646	0.610	7.274	1	0.0070	0.193	0.058	0.638
Cig. smoking	2.575	0.580	19.726	1	0.0001	13.129	4.215	40.900
Fluid taken	-2.155	0.538	16.063	1	0.0001	0.116	0.040	0.333
Constant	1.109	0.474	5.477	1	0.0190	3.031		

transformation can be used to transform the S-shaped curve into the linear form and  $Z = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \dots + \beta_k X_k$ .

Further more,  $\pi(x) = e^z / 1 + e^z$ , which generates the probabilities for different risk factors.

## Discussions

The study found, lifestyle to be negatively associated with urinary bladder cancer, indicating that the better the lifestyle, the lesser the chances of getting the disease. The odds ratio for the moderate lifestyle was 0.103 which indicated that a person with such a lifestyle had 0.33 time chances of getting the disease (i.e., 89.7% protection against the disease) as compared to the person living a sedentary lifestyle. In our knowledge, no previous study is available in literature that may explain the association between physical exercise (lifestyle is a factor representing different levels of exercise) and bladder cancer. Further research is needed to observe the effect of exercise and confirm this association.

Education creates awareness about health-related matters. The study considered education in two categories, illiterate and literate. The odds ratio and the 95% CI of odds ratio were 0.193 and [0.058-0.638], respectively. It means that the literate subjects have 0.193 times risk of bladder cancer as compared to the illiterate subjects. On the other hand, the

literate subjects have 80.7% protection against the disease as compared to the illiterate persons. A case-control study by Radosavljevic et al stated that higher educational level and more frequency of urination were investigated as the protective factors against the urinary bladder cancer.<sup>18</sup> Further research is required to observe and determine this association.

In our study, the OR and 95% CI for the smokers were 13.129 and [4.215-40.9], respectively. It shows that the smokers in Punjab have 13 times higher risk of bladder cancer as compared to the non-smokers. A study in Spain found that the OR and 95% CI for current smokers in men were 7.4 and [5.3-10.4], respectively.<sup>16</sup> From several studies, about four times more risk was observed in the smokers as compared to the non-smokers.<sup>11-13</sup> Similarly, a pooled analysis of 11 case-control studies conducted in Europe estimated that about 66% of bladder cancer cases in men and 30% in women were attributable to smoking.<sup>19</sup> A study was conducted by pooling primary data from 14 case-control studies of bladder cancer from Europe and North America and found that the OR for current smokers compared to non-smokers was 3.9 for males and 3.6 for females.<sup>20</sup>

In this context, the fluid consumption is observed to be negatively associated with OR 0.116 and 95% CI [0.040-0.333]. It means that a person who consumes 10 or more glasses (10 glasses means 2500 ML) of water per day has 0.116 times chance of getting the disease (i.e., 88.4% protection) as compared to the person who consumes less than ten glasses of water per day. Hence, consumption of more water is a protective agent against the disease. Excess water in the bladder reduces the concentration and stay time of chemicals by frequent urination. The result of fluid taken in the study is supported by the finding of the study by Hermann et al<sup>17</sup> which observed a significant decrease in the OR 0.34 and 95% CI [0.11-0.99] for females who consumed more than two liters of fluid per day.

### Conclusion

The study aimed at locating risk factors of urinary bladder cancer in Lahore and Faisalabad. The 149 subjects, including cases and controls, were taken from three public-sector hospitals. The analysis was based on descriptive and inferential measures. Six variables were found to be significant. Four of them, lifestyle, education, smoking and fluid consumption, are very important in order to control or reduce the urinary bladder cancer in Lahore and Faisalabad.

Although the sample size was small in the study, but the results are consistent with previous studies elsewhere. No contradictions/inconsistencies were observed in the results. However, further research can enhance the authenticity of the

results by taking a large sample size from hospitals across Punjab, Pakistan.

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