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Risk Factors of Urinary Bladder Cancer in Sindh, Pakistan by Using the Logit Model

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Abstract

The main aim of this study was to investigate the risk factors of urinary bladder cancer in Sindh, a province of Pakistan, by using the Logit Model. It was a cross–sectional study which was conducted in two hospitals of Karachi from November 2009 to January 2010.The requisite information consisting of 150 subjects including 50 cases and 100 controls was obtained from urology/oncology wards of Jinnah Postgraduate Medical Centre (JPMC) and Karachi Institute of Radiotherapy and Nuclear Medicine (KIRAN). The factors were studied descriptively and analytically. Odds Ratios and 95% Confidence Intervals were obtained by using the Logistic Regression Model. Two factors including cigarette smoking and total fluid consumption were found to be significant having Odds Ratios and 95% Confidence Intervals [24.352, 9.270-63.974] and [0.260, 0.101-0.668], respectively. The cigarette smoking was found to be the major risk factor of urinary bladder cancer. On the other hand, the high amount of total fluid consumption was investigated to be a protective factor against the urinary bladder cancer.

Keywords

Logit model, Bladder cancer, Risk factors, Odds Ratio, Smoking

1. Introduction

Bladder cancer is more common in men than in women with a men women ratio of 3:1, showing sex-linked etiological reasons (Rabbani et al., 2000).

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In the United States, it is the 5th most common malignancy (Silverman et al., 1996; Ohno et al.,1985). In Belgium and Netherlands, the bladder cancer is ranked among the first five of the most common cancers in men (Steward et al., 2003; Visser et al., 2002).

Only in the United States, 51200 bladder cancer cases and more than 10600 deaths were predicted yearly (Boring et al., 1994). The frequency of bladder cancer differs very much from country to country (Schottenfeld et al., 1996). In Pakistan, the male and female ratio of bladder cancer patients was observed as 5:1 (Ahmad et al., 2011), while another study showed the male and female ratio of bladder cancer patients' as 4:1(Ahmad et al., 2010). Bladder cancer is commonly observed in the age of 70 years and above but rarely found under the age of 40 years (Visser et al., 2002). In 2009, the number of bladder cancer patients and deaths only in US were found to be 71,000 and 14,000, respectively (Jemal et al., 2009).

Cigarette smoking accounts for 50% and 31% of bladder cancers in men and women respectively (Wynder et al., 1971). Cigarette smoking is a major risk factor that causes urinary bladder cancer in about 50 to 65% male and 20 to 30% female smokers (Brennan et al., 2001; Kogevinas et al., 2000; Samanic et al., 2006). The cigarette smokers in federal area of Pakistan had 17.15 times higher risk of bladder cancer as compared to that for the non-smokers (Ahmad et al., 2011), while cigarette smokers in Khyber-Pukhtoonkhwa, a Province of Pakistan, had 19.5 times higher risk of bladder cancer as compared to that for the non-smokers (Ahmad et al., 2010). It seems that cigarettes smoked in Pakistan have severely injurious effects on health.

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).

Besides the stated risk factors, there are several other factors like family history, hair dye, personal history of cancer, amount of water daily consumed, source of drinking water, etc., that are included in this study. Keeping in view the severity of this disease, it becomes essential to utilize all possible resources in order to overcome /reduce the burden of cancer in Pakistan and all over the world.

2. Material and Method

This case-control study was conducted to assess the risk factors of urinary bladder cancer in Karachi (Provincial headquarter of Sindh, Pakistan).For this purpose, Jinnah Postgraduate Medical Centre (JPMC) and Karachi Institute of Radiotherapy and Nuclear Medicine (KIRAN) were selected. The requisite information for this study were obtained through the interview method from all the patients (cases) of urinary bladder cancer admitted in the urology/oncology wards of the stated hospitals in the month of November 2009 to January, 2010. Several questions were asked during the interview from the cases and controls like age, residential area, family history of cancer, lifestyle, diabetes, hepatitis, source of drinking water, dietary habits, cigarette smoking, etc. in order to fill the questionnaire which was developed by consulting the urologists, oncologists and statisticians, the help of the paramedics and the doctors was also taken. 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), comprising 150, were taken in the sample. The cases were diagnosed by the basic symptoms of PPP's (Profuse Periodic Painless Heamuturia) and biopsy reports while the hospital controls having the other than cancer diseases were interviewed. Cronbach's Alpha was used to measure the reliability of the questionnaire which was found to be 0.812.

The independent variables used in this study were nominal, ordinal and quantitative type but the response variable was binary. In order to modelling the response variable, the Binary Logistic Regression Model was run and the Regression coefficients, Odds Ratios, p-values and 95% Confidence Intervals for Odds Ratios were calculated. p-value was compared with the predefined values alpha (5%) for the significance of the variables. If the p-value was less than 0.05 then factor was taken as significant otherwise insignificant. The discussions of the significant results about the risk factors were made on the basis of Odds Ratios and its 95% Confidence Intervals. Adequacy of the model was observed by using the Omnibus Test. For the purpose of statistical analysis, SPSS (Version-16) was used.

It is well known that Probit Regression, based on the Probability Integral transformation, has a major drawback is that it lacks natural interpretation of Regression parameters. On the other hand, Discriminant Analysis computationally much simpler than the Probit Model but assumes that all the predictor variables are normally distributed and jointly assume a Multivariate Normal Distribution.

The Logistic Regression Model makes no assumption about the variable distribution. An added advantage of the Logit Model is its ability to provide valid estimates, regardless of study design (Harrell, 2001).

Let 'y' is binary random variable and $p = P(y = 1)$. Let $x_1, x_2, ..., x_n$ be a set of predictor variables, then the Logistic Regression of y on $x_1, x_2, ..., x_n$ estimates the parameters $\beta_1, \beta_2, ..., \beta_n$ using the Maximum Likelihood method of the following equation:

$$\log it(p) = \log\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + ... + \beta_n x_n$$

which can be written as:

$$\frac{\exp(\beta_0 + \beta_1 x_1 + \beta_2 x_2 + ... + \beta_n x_n)}{1 + \exp(\beta_0 + \beta_1 x_1 + \beta_2 x_2 + ... + \beta_n x_n)}.$$

(Agresti, 2002)

Goodness of Fit of the model can be observed by using the Cox and Snell R^2 and Nagelkerke R^2. Both the measures Cox and Snell R^2 and Nagelkerke R^2 are the same having range from 0 to 1 and similar to R^2 in interpretation. Nagelkerke model can attain its maximum value 1 but the Cox and Snell's R^2_{cs}can never attain its maximum value 1. These R^2 used to measure the strength of association between the dependent variables and the predictors. (Hosmer and Lemeshow, 1989)

3. Results

This study was based on the 30 females and 120 males comprising 150 subjects in which 50 were cases and 100 controls. Male and female ratio in patients was found to be 4:1; the disease is four times higher in men than in women. From Table 1, it was observed that the counts (percentages) of rural and urban patients were 10 (20%) and 40 (80%), respectively. Similarly, the counts (percentages) of rural and urban controls were 19 (19%) and 81 (81%), respectively. The counts (percentages) of literate and illiterate patients were 26 (52.0 %) and 24 (48.0%), respectively. Similarly, counts (percentages) of literate and illiterate controls were 42 (42 %) and 58 (58%), respectively.

In order to study the social status, income (in rupees) of the individuals was considered and converted into three categories such as low (Income < 10,000),

medium (10,001< Income < 20,000) and high (Income ≥ 20,000). The counts (percentages) of all subjects having low, medium and high social status were 79 (52.7%), 56 (37.3%) and 15 (10%), respectively. The counts (percentages) of patients having low, medium and high social status were 27(54%), 18 (36%) and 5 (10%), respectively. Similarly, the counts (percentages) of the controls having low, medium and high social status were 52(52%), 38 (38%) and 10 (10%), respectively. The percentage of the cases in the category of low status was a little higher than in controls.

Lifestyle was assessed through the exercise which was taken in three categories sedentary, normal and active. Third and second categories of lifestyle were not reported in the sample. Hence, all the subjects were included in this sample had sedentary lifestyle. Having no variation in lifestyle with reference to exercise, none of the analysis was done to study the effect of lifestyle.

In order to study the daily fluid consumption, the amount of water was considered in terms of no. of glasses (about 2500 ml/per glass) of water. The percentages of the cases daily consuming the less than 10 glasses and 10 or more glasses of total fluid were 64% and 36%, respectively. Similarly, the percentages of the controls daily consuming the less than 10 glasses and 10 or more glasses of total fluid were 25% and 75%, respectively. The much higher percentage of cases was using the less than 10 glasses of water as compared to that for the controls.

The percentages of all subjects consuming tap water and government provided water were 26% and 74%, respectively. The percentages of patients consuming tap water and government provided water were 28% and 72%, respectively. Similarly, the percentages of controls using tap water and government provided water were 25% and 75%, respectively. These percentages showed that the similar situation in cases and controls with reference to use the tap water and government provided water.

The percentages of the cases and controls using fruits 2 or less than 2 days per week were 86% and 84%, respectively. Similarly, the percentages of the cases and controls using fruits 3 or 4 days per week were 14% and 16%, respectively. The much higher percentage of controls was not using the fruits 3 or 4 days per week as compared to the cases.

The Omnibus Test was used to assess the overall significance of the model which provided χ^2 =75.085 which was significant at p-value =0.000 indicating that at least one of the factors is significantly affecting the response variable. In order to

observe the Goodness of Fit, the values of Cox and Snell R^2 and Nagelkerke R^2 are 0.394 and 0.547, respectively.

From Table 2, it was observed that the overall percentages of correctly classified and misclassified of subjects were 85.3% and 14.7%, respectively. While out of total controls 91.0% are correctly predicted as controls and 9% were misclassified as patients. Similarly, out of total cases 74.0% were correctly predicted as cases and 26% were misclassified as controls.

Table 3 indicates that the two factors including cigarette smoking and fluid consumption were found to be significantly associated with the risk of bladder cancer in Sindh (a Province of Pakistan). The Logit Model is given below:

$Z = -1.121+3.193\ X\ -1.346\ Y$

where X= cigarette smoking: 1 for smokers and 0= otherwise; Similarly, Y= Total fluid consumption: 1 for using more than 10 glasses of total fluid and 0 otherwise.

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 its 95% Confidence Intervals are valid for inferences.

4. Discussion

4.1 Cigarette Smoking: This study stated that out of 50 cases of urinary bladder cancer, 37 (74%) were observed to be smokers while 13 (26%) were non-smokers. A study conducted in the hospitals of Islamabad, federal city of Pakistan explained that 72% cases were found to be smokers (Ahmad et al., 2011). According to the studies (Brennan et al., 2001; Kogevinas et al., 2000; Samanic et al., 2006), cigarette smoking is a major risk factor that causes to develop the urinary bladder cancer about 50% to 65% in males and 20% to 30% in females.

From table 3, it was observed that the Odds Ratio and 95% Confidence Interval for the Odds Ratios in cigarette smokers were found to be 24.352 and (9.27, 63.974), respectively. According to these results, cigarette smokers in Sindh, a province of Pakistan have 24.35 times higher risk of bladder cancer as compared to that for the non-smokers. Hence, the cigarette smoking is directly (positively) associated with urinary bladder cancer. It means that as the smoking increases, the risk of urinary bladder cancer also increases.

A similar study conducted in the hospitals of Islamabad, federal city of Pakistan explained that the cigarette smokers had 17.15 times higher risk of bladder cancer as compared to the non-smokers (Ahmad et al., 2011). A study conducted in Spain, found that smokers have 7.4 times higher risk of bladder cancer in males and 5.1 times in females as compared to the nonsmokers (Samanic et al., 2006). Similarly, cigarette smokers in Khyber-Pukhtoonkhwa, another province of Pakistan, had 19.5 times higher risk of bladder cancer as compared to the non-smokers (Ahmad et al., 2010).

As the results of this study are supported by the studies (Ahmad et al., 2011; Ahmad et al., 2010; Brennan et al., 2001; Kogevinas et al., 2000; Samanic et al., 2006), therefore, it is established that the cigarette smoking is a major risk factor of bladder cancer in Pakistan and other areas of the world and have severely bad effects (by causing cancer) on the health of mankind.

4.2 Total Fluid Consumption: In this study, the daily fluid consumption was found to be inversely (negatively) significant with the urinary bladder cancer having Odds Ratio and 95% Confidence Interval of Odds Ratio 0.260 and (0.101, 0.668), respectively. It means that a person who consumes 10 or more glasses of water per day has 0.260 times risk of getting disease (i.e., 74% protection against the disease) as compared to the person who intakes the less than 10 glasses of total fluid daily. According to this study, higher consumption of total fluid provides the protection against the disease. This study has showed that the percentages of the patients and controls daily consuming less than 10 glasses of total fluid were 64% and 25%, respectively. The percentage of patients was very high as compared to controls who were taking the total fluid less than 10 glasses of water. Less intake of total fluid reduces the frequency of urination and hence increases the concentration and stay time of chemicals in the bladder.

A similar study conducted in the hospitals of Khyber-Pukhtoonkhwa, a province of Pakistan in which the total fluid consumption was found to be negatively significant with the urinary bladder cancer having Odds Ratio and 95% Confidence Interval for odd ratios 0.025 and (0.005, 0.115), respectively. This result showed the 97.5% protection against the urinary bladder cancer to those subjects who were consuming 10 or more glasses of total fluid as compared to those who were consuming less than 10 glasses of total fluid daily (Ahmad et al., 2010). According to another study, high fluid consumption is associated with a decreased risk of bladder cancer in men, and lesser intake of daily fluids proportionally increases the risk of bladder cancer (Claus et al., 1996).

As the results of this study are supported by the studies (Ahmad et al., 2010; Claus et al., 1996), therefore, it is stated that the high consumption of total fluid is a protection against the urinary bladder cancer.

5. Conclusion and Summary

In order to assess the risk factors of urinary bladder cancer in Sindh (a province of Pakistan), Jinnah Postgraduate Medical Centre (JPMC) and Karachi Institute of Radiotherapy and Nuclear Medicine (KIRAN) was selected to conduct the study. Fifty cases and 100 controls were interviewed from both of the hospitals. Two factors cigarette smoking and the total fluid consumption were observed to be significant. Cigarette smoking was positively associated while the consumption of more than 10 glasses of total fluid per day was investigated to be inversely associated with urinary bladder cancer.

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Table 1: Classification of cases/ controls with different risk factors

Factors	**Categories**	**Bladder Cancer**		
		No	**Yes**	**Total**
Gender	Female	20	10	30
	Male	80	40	120
Industrial Area	Non-industrial	96	47	143
	Industrial	4	3	7
Residential Area	Urban	81	40	121
	Rural	19	10	29
Marital Status	Unmarried	0	0	0
	Married	100	50	150
Education	Illiterate	58	24	82
	Literate	42	26	68
Family history of cancer	No	100	50	150
	Yes	0	0	0
Lifestyle	Sedentary	100	50	150
	Normal	0	0	0

Factors	Categories	Bladder Cancer		
		No	Yes	Total
	< Rs. 10000	52	27	79
	Rs.10000-20000	38	18	56
	≥ Rs.20000	10	5	15
Chemical Exposure	No	83	38	121
	Yes	17	12	29
Use of tea	No	4	1	5
	Yes	96	49	145
Hair dye	No	99	46	145
	Yes	1	4	5
Fluid taken (Glasses)	< 10 glasses	25	32	57
	≥ 10 glasses	75	18	93
Source of Drinking Water	Tap	25	14	39
	Govt. Provided	75	36	111
	Low	85	37	122
Fried items	Normal	15	13	28
	Low	99	49	148
Fats items	Normal	1	1	2
	Low	84	43	127
Fruits	Normal	16	7	23
Cigarette Smoking	No	91	13	104
	Yes	9	37	46
Pan chewing	No	100	50	150
	Yes	0	0	0

Table 2: Correct classification and misclassification of subjects

Observed		Predicted		
		BC		Percentage Correct
		No	Yes	
BC	No	91	9	91.0
	Yes	13	37	74.0
Overall Percentage				85.3

Table 3: Model coefficients with Odds Ratios and 95 % CI's for Odds Ratio

Factors	B	S.E.(β)	Wald	Sig.	exp(β)	95% CI	
						Lower	Upper
Cigarette Smoking	3.193	0.493	41.973	0.000	24.361	9.270	63.974
Fluid Consumption	-1.346	0.481	7.843	0.005	0.260	.101	.668
Constant	-1.121	0.388	8.327	0.004	0.326		

Note: Significance of the variables has been discussed on the basis of p-value (sig.) and the existence of p-value is on the basis of Wald test.

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