

Occupations and the Risk of Bladder Cancer in Yazd Province: A Case-Control Study

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Abstract

Background: Bladder cancer is the most common cancer of the urinary tract, with known occupational causes. The most effective way to prevent occupational cancers of the urinary tract is to prevent exposure to known carcinogens.

Objective: To examine the relationship between occupation and the risk of bladder cancer.

Methods: This case-control study was performed on 200 patients with bladder cancer and 200 healthy individuals in Yazd. Data were collected using a researcher-made questionnaire and based on interviews with patients and controls.

Results: The mean age of cases and controls were 61.5 (SD 13.6) and 61.5 (13.3) years, respectively. Level of education, type of occupation, family history of bladder cancer in the first-degree relatives, and history of chronic and recurrent urinary tract infection, kidney and bladder stones, and using hair dye, were considered the main predictors for bladder cancer.

Conclusion: There was a significant difference between cases and controls in terms of type of occupation. The risk of bladder cancer was higher among those working in high-risk occupations—metal working, textile, driving, farming, and construction.

Keywords: Urinary bladder neoplasms; Occupations; Risk factors; Occupational exposure; Occupational diseases

Introduction

Cancer is one of the leading causes of death worldwide. With many known environmental, occupational, social, and genetic factors, cancer is multifactorial in nature. The annual deaths attributable to cancer in 2030 are estimated to be more than 13.1 million worldwide.¹ More than 90% of malignancies can be attributable to the environmental and external factors.^{2,3} More than 30% of cancer deaths attributable to risk factors such as smoking, lack

of physical activity, alcohol consumption, and urban air pollution are preventable.¹

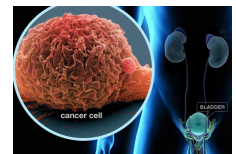
Bladder cancer is the most common urinary tract cancer in the world.⁴ It is considered the eighth cause of death due to cancers and is responsible for 3% of all tumors.⁵ Its age-standardized incidence rate is 10.1 and 2.5 per 100 000 people for men and women, respectively.⁶ Each year more than 12 million new cases of bladder cancer are diagnosed worldwide.⁷ The highest odd incidence of bladder cancer has been reported in Europe, North America, North

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Africa, and the highest rate of deaths from bladder cancer was reported in Egypt.⁸ According to the reports of WHO Centers for Disease Control and Prevention (CDC) in 2005, bladder cancer was responsible for 7.4% of cancers reported in Iran.⁹ Analysis of the data in Cancer Research Center in Iran during 2003 to 2009 showed an increasing trend of bladder cancer in the country.^{10,11}

The risk of bladder cancer is 1 in 28 for men and 1 in 87 for women.¹² The survival rate of bladder cancer in Iranian patients is less than other areas.¹³ The highest incidence of bladder cancer was observed in Yazd, Fars, Guilan, Isfahan, and Khorasan provinces.¹⁴

Compared to other malignancies, bladder cancer is strongly associated with job exposures, especially exposure to chemicals used in workplace,⁴ so that job is considered the second most important risk factor for bladder cancer after smoking.¹⁵ According to some studies, 21%–27% of all bladder cancers in men, and 11% of bladder cancers in women are caused by occupational exposures.⁴ Exposure to aromatic amines (*eg*, β -naphthyl amine, 4-amino-biphenyl, 4-chloro-ortho-toluidine, and benzidine) that can be found in chemical, paint, plastic, and rubber industries, as

well as hair dyes, fungicides, and cigarette smoke are considered the main causes of bladder cancer. Exhaust fumes of motor vehicles are often considered the most important occupational and environmental hazard for bladder cancer.¹⁶

We could not find a case-control or cohort study in Yazd, as an industrial province in Central Iran, on the risk factors of bladder cancer. So, this study was conducted to determine the relationship between job and bladder cancer in workers.

Materials and Methods

In a case-control study, Assuming type I error of 0.05, study power of 80%, and an expected OR of 2.5 (previously reported) for relevant risk factors, the minimum sample size was calculated to be 180 individuals in each group. The case group included those with biopsy-proven bladder cancer who were referred for treatment to hospitals in Yazd. Their data were gathered from Cancer Research Center during 2009–2013. The control group included healthy people who lived in the vicinity of the patients. Response rate for case and control groups was 96.7% and 93.3%, respectively.

The inclusion criteria for the case group were being residents of or living more than 15 years in Yazd and having documented bladder cancer. Controls were matched with the case group for age, sex, and place of residence.

The questionnaire used in the study was designed after reviewing the literature and seeking experts' opinion. The questionnaire was then reviewed by three experts. After making the necessary changes the final questionnaire included socio-demographic profile (age, sex, religion, marital status, family size, place of residence, and blood group), socio-economic factors (education, occupation, income, home ownership, and insur-

For more information on risk factor for gastrointestinal cancer see <http://www.theijoem.com/ijoem/index.php/ijoem/article/view/851>



TAKE-HOME MESSAGE

- The most common cancer of the urinary tract is bladder cancer, the eighth cause of death.
- Compared to other malignancies, bladder cancer is strongly associated with occupational exposures, especially exposure to chemicals used in workplace.
- Environmental and external factors are the most common causes of cancer.
- Workers in some jobs including metal work, textile, driving, agriculture and livestock, and construction are at higher risk of developing bladder cancer compared to office workers.

ance coverage), lifestyle factors (cigarette, hookah or pipe smoking; drug or alcohol consumption; physical activity; and diet), family history, drug history (analgesics and cyclophosphamide), medical history (especially systemic diseases, and chronic or recurrent urinary tract infection, and kidney or bladder stones, and schistosomiasis), history of irradiation to the lower part of the body, exposure to chemicals, and use of hair dye. Participants were asked about their occupations, and their lifetime occupational history for jobs they had for at least one year.

Jobs were classified according to the exposure to known bladder carcinogens (aromatic amines, amino-biphenyl, polycyclic aromatic hydrocarbons [PAH] and azo dyes) to “high-risk” and “low-risk” jobs;¹⁷ so, textile, metal and chemical industries were considered high-risk jobs. This classification was performed by literature review and expert opinion.

The study protocol was approved by Shahid Sadoughi University Ethics Committee. To comply with the ethical principles, informed consent was obtained from each study participant.

SPSS® for Windows® ver 18 (SPSS Inc, Chicago IL, USA), was used for data analysis. Descriptive statistics, χ^2 test, and multiple logistic regression analysis were used for data analysis. Crude and adjusted odds ratio were calculated. Variables that were found significant in univariate analysis and variables with $p \leq 0.2$ that were clinically important in the induction of bladder cancer (eg, smoking, history of irradiation to the lower part of the body, bladder infection, bladder stone, family history of bladder cancer and history of analgesic use) were considered for multiple logistic regression analysis.

Results

A total of 400 people, 200 cases and 200

Table 1: Demographic characteristics in case and control groups.

Variable	Case, n (%)	Control, n (%)	OR (95% CI)
Education			
Illiterate	47 (23.5)	17 (8.5)	3.30 (1.73 to 6.27)
Primary and secondary school	86 (43)	103 (51.5)	0.99 (0.64 to 1.53)
Above diploma	67 (33.5)	80 (40)	1
Total family income (US\$)			
<300	127 (66.8)	90 (45.5)	2.32 (1.20 to 4.49)
300–450	46 (24.2)	80 (40.4)	0.94 (0.46 to 1.91)
>450	17 (8.9)	28 (14.1)	1
Family size (persons)			
≤4	42 (21)	56 (28)	1
5–6	73 (36.5)	98 (49)	0.99 (0.6 to 1.64)
≥7	85 (42.5)	46 (23)	2.46 (1.44 to 4.21)
Blood groups			
A	46 (26.7)	66 (37.9)	0.96 (0.47 to 1.97)
B	21 (12.2)	53 (30.5)	0.55 (0.25 to 1.21)
O	87 (50.6)	30 (17.2)	4.02 (1.93 to 8.39)
AB	18 (10.5)	25 (14.4)	1
Family history of bladder cancer in first relatives			
Yes	19 (9.7)	7 (3.5)	2.92 (1.2 to 7.13)
No	177 (90.3)	191 (96.5)	1

controls, was included in this study. In each group, 25 (12.5%) were females. The mean age of cases and controls was 61.5 (SD 13.6) and 61.5 (SD 13.3) years, respectively ($p=0.86$). In the case group, 4% of patients were under 30 years, 39% were 30–60 years old, and 57% were over 60 years. The ratios in the control group were 3.5%, 40.5%, and 56%, respectively. Table 1 shows other demographic characteristics of the participants.

Table 2 compares the frequency of dif-

Table 2: Frequency of different jobs in cases and controls

Job	Cases, n (%)	Controls, n (%)	Crude OR (95% CI)
Office	70 (35.0)	113 (56.5)	1
Textile	20 (10.0)	8 (4.0)	4.03 (1.68 to 9.65)
Metal	12 (6.0)	3 (1.5)	6.45 (1.76 to 23.68)
Driving	17 (8.5)	11 (5.5)	2.49 (1.1 to 5.63)
Farming	26 (13.0)	21 (10.5)	1.99 (1.04 to 3.82)
Construction	23 (11.5)	21 (10.5)	1.76 (0.91 to 3.42)
Total	168 (84.0)	177 (88.5)	—

ferent job titles between cases and controls. Frequency of job titles except for office work was different between cases and controls with the highest odds ratio observed for metal works. The frequency of bladder cancer was significantly higher in high-risk jobs (Table 3).

Table 4 compares the frequency of some non-occupational risk factors between the two groups. The frequency of positive non-occupational risk factors was significantly higher among the cases, with the highest odds ratio observed for irradiation to the lower part of the body. Table 5 shows the effects of occupational and non-occupational risk factors on the frequency of bladder cancer using logistic regression model.

Discussion

In this study, we examined the relationship between the occupations and bladder cancer. The results of the current study showed that workers in some jobs including metal work, textile, driving, agriculture and livestock, and construction were more

likely to develop bladder cancer than office workers. After classification of jobs into two categories of high-risk and low-risk, the results of univariate analysis showed that there were significant differences between groups—high-risk occupations increased the chance of developing bladder cancer. Study of Aminian, *et al*, after job classification into two groups of low-risk and high-risk categories showed that the risk of developing this disease in high-risk occupations (textile, weaving, spinning, wood working, plastic processing, petrochemical, driving, welding, construction and repair of footwear, and production of bags and seat covers) was significantly higher than the control group,⁴ which is consistent with the results of the current study.

In a case-control study of 22 jobs studied, housekeeping, agriculture, construction, metal working (such as welding, and cutting), and driving, were identified as high-risk occupations for bladder cancer;¹⁸ most of the high-risk jobs were similar to the jobs assessed in the current study. Another similar study showed that odds ratios for cooks, drivers, painters, textile workers, and metal workers were high.¹⁹

In the present study, an increased risk of bladder cancer was observed among those with metal work including welding, cutting and making doors and windows

Table 3: Frequency of workers in high-risk and low-risk jobs in cases and controls

Job category	Cases, n (%)	Controls, n (%)	OR (95% CI)
High-risk	71 (35.5)	29 (14.5)	3.24 (1.99 to 5.29)
Low-risk	129 (64.5)	171 (85.5)	1

compared to the control group, which was consistent with results of similar studies conducted in North of England, Pakistan, and Columbia.¹⁹⁻²¹ This increased frequency of bladder cancer is probably due to exposure to the fumes of some heavy metals or metal working fluids;²⁰ although identifying the exact cause is difficult due to different composition of the fumes and working fluids. The results of the current study showed an increased risk of bladder cancer among textile workers, which was consistent with the results obtained by Riza Ahmad, *et al*, and Aminian, *et al*,^{4,19} although another study could not find a relationship between working in textile industry and bladder cancer except for workers who were exposed to chemicals and synthetic fibers.²² According to the results, it seems that, exposure to some chemicals, especially those in dyes (*eg*, aromatic amines) in textile industry increases the risk of bladder cancer.

In the current study, risk of bladder cancer in drivers was higher as well, which was in agreement with the results of some other studies.^{15,23,24} These individuals are potentially exposed to exhaust smoke or some petroleum derivatives, and aromatic compounds, which may be considered carcinogen.¹⁵ Some drivers, especially bus or truck drivers, may also work as a mechanic or repairman, which is another explanation for increased risk of bladder cancer in this occupation.²⁰

Results of the present study also showed an increased risk of bladder cancer among agricultural and livestock workers compared to office workers, inconsistent with results of some previous studies.²⁵⁻²⁸ Nonetheless, some other studies found similar results in agricultural workers.^{15,29,30} The relationship could probably be due to long-term exposure to some pesticides or fertilizers,¹⁵ and the difference is possibly due to different pesticides used in different parts of the world and also different work

Table 4: Risk factors of bladder cancer

Variable	Cases, n (%)	Controls, n (%)	Crude OR (95% CI)
Chronic or recurrent urinary tract infections			
No	118 (59.0)	179 (89.5)	1
Yes	82 (41.0)	21 (10.5)	5.92 (3.47 to 10.09)
History of chronic or recurrent urinary tract infection			
≤1 yrs	27 (32.9)	17 (81.0)	1
2–3 yrs	39 (47.6)	3 (14.3)	8.18 (2.18 to 30.69)
≥4 yrs	16 (19.5)	1 (4.8)	10.07 (1.22 to 83.04)
Analgesic use			
No	152 (76)	175 (87.5)	1
Yes	48 (24.0)	25 (12.5)	2.21 (1.30 to 3.75)
History of analgesic use			
≤1 yr	11 (22.9)	15 (60.0)	1
2–3 yrs	11 (22.9)	7 (28.0)	2.14 (0.62 to 7.30)
≥4 yrs	26 (54.2)	3 (12.0)	11.81 (2.83 to 49.18)
Irradiation to pelvis			
No	123 (61.5)	146 (73.0)	1
Yes	77 (38.5)	54 (27.0)	1.69 (1.10 to 2.58)
History of irradiation to pelvis			
1 time	11 (14.3)	31 (57.4)	1
2 times	31 (40.3)	15 (27.8)	5.82 (2.31 to 14.66)
3 times	17 (22.1)	4 (7.4)	11.97 (3.3 to 43.43)
≥4 times	18 (23.4)	4 (7.4)	12.68 (3.51 to 45.76)
Kidney and bladder stones			
Yes	134 (67.0)	175 (87.5)	1
No	66 (33.0)	25 (12.5)	3.44 (2.06 to 5.75)
History of kidney and bladder stones			
≤1 yr	26 (39.4)	21(84.0)	1
≥2 yrs	40 (60.6)	4 (16.0)	8.07 (2.48 to 26.22)
History of diabetes			
No	148 (74.0)	172 (86.0)	1
Yes	52 (26.0)	28 (14.0)	2.15 (1.29 to 3.59)

Continued

Table 4: Risk factors of bladder cancer

Variable	Cases, n (%)	Controls, n (%)	Crude OR (95% CI)
History of other kidney diseases			
No	120 (60.0)	162 (81.0)	1
Yes	80 (40.0)	38 (19.0)	2.84 (1.8 to 4.46)
History of hypertension			
No	47 (23.5)	171 (85.5)	1
Yes	153 (76.5)	29 (14.5)	1.81 (1.08 to 3.02)
History of smoking			
No	74 (37.0)	129 (64.5)	1
Yes	98 (49.0)	54 (27.0)	3.16 (2.04 to 4.9)
Ex-smoker	28 (14.0)	17 (8.5)	2.87 (1.47 to 5.59)

processes and protective measures. The results about the carcinogenicity of pesticides or fertilizers are still controversial.²⁰

In the current study, a significant relationship was observed between construction jobs and increased risk of bladder cancer, consistent with the study of Khoubi, *et al.*¹⁵ This relationship may be attributed to exposure to petroleum derivatives in some tasks in construction industry;¹⁵ however, most studies failed to show this relationship.^{31,32}

In the current study, other possible non-occupational risk factors of the bladder cancer were also evaluated. In agreement with the results of some other studies, this study showed a relationship between blood group 'O' and risk of bladder cancer.^{9,18} In the present study, a history of bladder cancer in first-degree relatives in the case group is more than the control group and it remained in the model in the presence of other variables, which was consistent with the results of some other studies.^{33,34} Increased risk of bladder cancer in people with a positive family history can be justified by genetic commonalities in family

Table 5: Effects of occupational and non-occupational risk factors using logistic regression model

Variables	Adj OR (95% CI)
Job classification	
High-risk	6.34 (2.64 to 15.24)
Low-risk	1
Family history of bladder cancer	6.91 (1.55 to 30.89)
Recurrent chronic urinary tract infections (per year)	
No	1
≤1	2.33 (0.86 to 6.33)
2–3	31.51 (6.59 to 150.62)
≥4	13.32 (1.37 to 128.83)
Kidney and bladder stones	
No	1
≤1	1.38 (0.48 to 3.99)
≥2	16.15 (4.03 to 64.8)
Hair dye use	
≤1	1
>1	3.05 (1.15 to 8.04)
Education	
Illiterate	3.11 (1.1 to 8.8)
Primary and secondary	0.62 (0.29 to 1.32)
Above diploma	1

members.

In the present study, in the univariate analysis, history of chronic and recurrent urinary tract infections, kidney and bladder stones, and smoking had a significant relationship with the risk of bladder cancer and remained in the model with the presence of other variables, especially job, which was in agreement with the results reported by Vermeulen, *et al*, study.³⁵

Our study had some strength and weakness. The study was performed in an in-

dustrial province with various industries and various risk factors of bladder cancer (occupational and non-occupational) were assessed. The first limitation was the likelihood of recall bias, which is the inherent weakness of all case-control studies. In this study, we assessed job title as the risk factor of bladder cancer and it was not possible to evaluate specific tasks and occupational exposures in detail, so we did not have enough information about the exact occupational exposures.

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Conflicts of Interest: None declared.

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