

## Occupation, smoking, opium, and bladder cancer: A case-control study

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## Abstract

**Purpose:** The aim of this study was to investigate occupational risk factors associated with bladder cancer. **Materials and Methods:** In this case-control study, control group included patients who referred to a specialized clinic in the same city and hospitals where patients had been registered. Data were entered into SPSS software. Odds ratios (OR) were calculated for occupational variables and other characteristics. Then, using logistic regression, the association between cancer and drugs was studied while smoking was controlled. **Results:** Cigarette smoking, even after quitting, was also associated with bladder cancer (OR = 2.549). Considering the classification of occupations, the OR of working in metal industry in patients was 10.629. Multivariate analysis showed that use of the drug by itself can be a risk factor for bladder cancer. Drug abuse together with the control of smoking increased the risk of bladder cancer by 4.959. **Conclusion:** According to the findings of this study, contact with metal industries such as welding, and working with tin was found as a risk factor for bladder cancer. In addition, cigarette smoking and opium abuse individually were associated with bladder cancer.

**Key words:** Bladder cancer, cigarette, drugs, occupational factors, risk factors

## Introduction

Nowadays, about 10% of deaths worldwide are due to cancers and it is estimated that the incidence of cancer worldwide would undergo an increasing trend.<sup>[1-3]</sup> Bladder cancer is a common cancer in the world.<sup>[3,4]</sup> Of cancers known and under investigation in the country, bladder cancer is ranked fifth,<sup>[5,6]</sup> however, in Kurdistan province it is ranked third in men and fourth in both sexes.<sup>[7,8]</sup> Overall, bladder cancer is the twelfth major cause of years of life lost due to premature death or disability per every 1000 people in Iran.<sup>[8]</sup>

This disease is more prevalent in industrial environments. Nowadays, it has been indicated that smoking and some occupational factors are the most important causes of bladder cancer; recognizing these factors will help to increase the possibility of intervention and risk reduction. Occupational and other risk factors may vary in different regions and it is necessary to check the occupational factors associated with various cancers in every area.<sup>[9]</sup> In a study in Isfahan it was revealed that drivers of heavy vehicles, farmers, metal industry workers, housewives, and construction workers are among high risk groups.<sup>[10]</sup> In Samanic *et al.*'s study, the odds ratio (OR) was calculated 5.6 for those with jobs related to publication, 1.6 for those involved in transportation, 3.9 for those involved in electrical jobs, and 2.1 for those working in manufacturing jobs.<sup>[11]</sup> Several studies have provided different results and there is a need for further investigation.<sup>[11,12]</sup>

Moreover, in some studies, the use of opium has been proposed as a risk factor for some cancers.<sup>[13-15]</sup> Using opium is very high in Iran and it is estimated that there are about two million opium users in the country.<sup>[16,17]</sup> As a result, the study of the relationship between substance abuse and bladder cancer may be effective in identifying risk factors; however, limited studies have been carried out in this area. Accordingly, the aim of this study was to evaluate risk factors for bladder cancer in the past 3 years in Kurdistan.

## Materials and Methods

## Design

This case-control study was approved by Ethic Committee of Kurdistan University of Medical Sciences. Case group included

all patients with bladder cancer who had been diagnosed histologically according to the International Classification of Diseases-10 by pathology laboratories and recorded in the cancer registry system<sup>[18]</sup> in Kurdistan province (west of Iran) during the past 3 years. Exclusion criteria were death and suffering from other cancers. An exclusion criterion for control group was cancer.

## Sampling method

The names and address of patients were extracted via cancer registration software. Control group were chosen from patients who referred to a specialized clinic in the same city and hospitals where patients had been registered. During the visit to the clinic in the same city and hospitals, the people who were waiting in the waiting room for appointments by specialist were asked for permission to participate in the study and then the study objectives were explained to them. To select the control group, frequency matching was carried out in terms of age ( $\pm 5$  years), sex, and place of residency.

## Tools

After taking permission and explaining the objectives of the study, a questionnaire was completed for every patient. Demographic characteristics and history of smoking and drug abuse were asked. Using the questionnaire, the employment status of the individual and the type of job activities over the last 20 years were asked. Interviews were conducted by trained personnels. Occupational classification was based on Standard Classification of Occupations (ISCO 08),<sup>[19]</sup> and during conducting the interviews their most focused jobs were considered as individuals' main occupation.

## Data analysis

Data were entered into SPSS 16 software (SPSS, Chicago, IL). Using *t*-test and Mann-Whitney U-test, univariate analysis was conducted to compare the quantitative values in the two groups, and Chi-square and Fisher tests were used to compare the qualitative values in the two groups. Then, OR for occupational variables and exposure (with or without a history) and also the confidence intervals were calculated. Finally, using logistic

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regression, the association between cancer and drugs was studied while smoking was controlled.

## Results

In this study, 152 patients with bladder cancer were examined from whom 124 patients (81.6%) were male and 28 (18.4%) were female. In the case group, 93 patients (61.2%) were urban and 59 persons (38.8%) were rural. The mean age of participants was 63.6 ( $\pm 15.3$ ) years in the group of patients with bladder cancer and 61.8 ( $\pm 14.1$ ) years in the control group ( $P = 0.288$ ). In univariate analysis, there was no statistically significant difference between the two groups in terms of the incidence of high blood pressure, kidney stones, undergoing radiography, literacy levels, and body mass index [Table 1].

Smoking history was significantly higher in the case group than the control group. Moreover, the history of drug abuse was significantly different between cases and controls (OR = 8.824). The OR for being affected by bladder cancer in active smokers (OR = 6.697) was higher than that of ex-smokers (OR = 2.549). All cases of drug addicts were abusing opium through smoking. Multivariate analysis showed that the use of drug by itself could be a risk factor for bladder cancer. Adjusted OR for smoking and

opium were 4.29 (2.614–7.038) and 4.96 (1.073–22.924), respectively.

Considering the classification of occupations, the OR for patients working in metal industry was 10.629. However, none of the other occupations had a significant relationship with the bladder cancer [Table 2].

## Discussion

Working with metal industries such as welding, and working with tin was found as a risk factor for bladder cancer. In addition, cigarette smoking and opium abuse individually were associated with bladder cancer. Other occupations were not associated with bladder cancer.

Until now, many studies have been conducted on the occupational risk factors associated with bladder cancer and in most of these studies there has been little findings to show a significant association between occupation and bladder cancer; in fact, the results of the studies has been different. Most studies just have found a weak level of association.<sup>[11,12]</sup> These differences are due to the fact that various jobs in different parts of the world may have different levels of exposure and they have not necessarily the same level of contact.

**Table 1: Univariate analysis to compare the characteristics of cases and controls**

Variable	Control (%)	Case (%)	OR	95% CI for OR		P
				Lower	Upper	
Sex						
Male	124 (81.6)	124 (81.6)	1	0.56	1.786	1
Female	28 (18.4)	28 (18.4)				
Residency						
Urban	93 (61.2)	93 (61.2)	1	0.63	1.586	1
Rural	59 (38.8)	59 (38.8)				
Smoking history	41 (27)	97 (63.8)	4.775	2.932	7.775	<0.001
Smoking status						
Nonsmoker	111 (73)	55 (36.2)	-	-	-	-
Ex-smoker	19 (12.5)	24 (15.8)	2.549	1.287	5.048	0.007
Current smoker	22 (14.5)	73 (48)	6.697	3.765	11.912	<0.001
Drug abuse	2 (1.3)	16 (10.5)	8.824	1.992	39.08	0.001
Hypertension	37 (24.3)	34 (22.4)	0.896	0.526	1.524	0.684
Nephrolhytiasis	26 (17.1)	33 (21.7)	1.344	0.759	2.381	0.310
Radiography	84 (55.3)	94 (61.8)	1.312	0.830	2.073	0.244
Education						
Illiterate	84 (55.3)	80 (52.6)	-	-	-	-
Primary	45 (29.6)	49 (32.2)	1.143	0.688	1.899	0.605
High school or higher	23 (15.1)	23 (15.1)	1.050	0.546	2.019	0.884
BMI >25	67 (44.1)	64 (45.1)	1.041	0.657	1.649	0.86

BMI=Body mass index, OR=Odds ratio, CI=Confidence interval

**Table 2: Univariate analysis to compare the occupations of the two groups of cases and controls**

Job relation	ISCO 08 code	Control (%)	Case (%)	OR	95% CI for OR		P
					Lower	Upper	
Driver	8321, 8322, 8331, 8332	13 (8.6)	21 (13.8)	1.714	0.824	3.563	0.145
Loom	7318, 7322, 7318, 7532	0	4 (2.7)	5.134	0.593	44.47	0.214
Carpenter	7115, 7317, 7319, 7521, 7523, 8172	0	2 (1.3)	3.039	0.312	29.551	0.622
Cleaner	9111, 9112, 9129	30 (19.9)	22 (14.8)	0.688	0.376	1.258	0.286
Painter	2651, 7131, 7132	3 (2)	4 (2.7)	1.342	0.295	6.101	0.99
Metal	7211, 7213, 7214, 7224, 8122	0	9 (6)	10.629	1.343	84.093	0.01
Construction worker	8114, 9313	25 (16.4)	21 (13.8)	0.814	0.434	1.528	0.521
Farmer	6310, 6320, 6330, 9211, 9212, 9213, 9214	59 (39.1)	52 (34.9)	0.819	0.513	1.308	0.402
Governmental employee	3341, 4414, 4110, 4416	18 (11.9)	20 (13.4)	1.128	0.571	2.228	0.729

OR=Odds ratio, CI=Confidence interval

In Reulen *et al.*'s study<sup>[12]</sup> bladder cancer had a statistical significant associating with the occupation of mine workers, bus drivers, mechanics, beauticians, and leather related occupations, however, the levels of the associations were low. In Cassidy *et al.*'s study<sup>[9]</sup> working as servant, working in bars, and careers related to medicine and agriculture had a significant relationship with the occurrence of bladder cancer. In a study conducted in Egypt, agricultural jobs were identified as a job which was extremely associated with the high risk for bladder cancer.<sup>[20]</sup> Some studies have shown that working in agricultural jobs for more than 25 years increased the risk of bladder cancer.<sup>[21]</sup> Farmers and ranchers may have contact with chemicals that are carcinogenic. However, in recent years such types of exposure have had a decrease.<sup>[9]</sup> In Dryson *et al.*'s study<sup>[22]</sup> knitters and beauticians had a greater chance of developing bladder cancer, however, other jobs were not associated with bladder cancer.

Some studies also observed a relationship between bladder cancer and occupations related to metals (metal cutters, mechanics, and metal polishers),<sup>[23-25]</sup> though there are some other studies which did not have such a finding.<sup>[22]</sup> These people working in these jobs can have contact with aromatic amines which are used in cooling and lubricating oils. In some studies, working in electrical and electronics industry has been reported to be associated with an increased risk of bladder cancer.<sup>[9,26]</sup> Those working in these positions may experience other types of exposure which have not been studied yet.

Zeegers *et al.*'s study<sup>[27]</sup> showed that people who had contact with colors and painting, those who used aromatic amines, and individuals exposed to the vapors of diesel machines had an increased risk for bladder cancer. However, the associations were weak in their study. Some of the jobs in which individuals drink less liquid or have less time to urine may be associated with bladder cancer.<sup>[28]</sup>

People who use hair color can also be at risk.<sup>[29]</sup> Unfortunately, this issue was not investigated in our study. However, some other studies did not find a significant association between hair color use and bladder cancer<sup>[29-31]</sup> and this issue is still controversial.

In Baris *et al.*'s study,<sup>[32]</sup> people with a history of smoking were 3 times more at risk of bladder cancer and people who were smoking at that time were 5.2 times more at risk of bladder cancer. Their study, as in our study, showed a dose-dependent effect of smoking. Risks of smoking have been also shown in other studies.<sup>[33]</sup> Smoking is a risk factor for a variety of different cancers.

The evaluation of the effect of opium abuse in bladder cancer is a new issue that has recently been investigated on a few limited studies. According to the results of our study, opium abuse, could have a significant association with bladder cancer. In Ketabchi *et al.*'s study<sup>[14]</sup> it was found that the use of opium in patients with bladder cancer was higher than in the controls. Shakhssalim *et al.*'s study<sup>[34]</sup> also showed that opium abuse was a risk factor. Another study in Iran showed a link between the use of opium and bladder cancer and according to the results opium was associated with the incidence of invasive bladder cancer.<sup>[35]</sup> In our study, using regression analysis, the effect of smoking as a confounding factor was controlled and it was showed that opium abuse even without smoking may also be

associated with bladder cancer. The opium effect mechanism could be similar to that of smoking, and the presence of impurities which may be carcinogenic could also be involved in this mechanism. Hydroxyphenanthrenes which is found in opium can also be a possible carcinogen and may lead to cancer development.<sup>[35]</sup>

Given the occupational mixes in Iran, the career mixtures may complicate the assessment of the risk factors associated with the each job. One of the limitations of this study was that it was not possible to assess occupational conduct blood or urine tests to demonstrate occupational exposure. Our study had other limitations as well. The control group was selected from a hospital which increases the possibility of Berkson's bias, because most jobs are risk factors for certain diseases that may increase the referral of patients to hospital. However, even in case of the incidence of such a bias, the results of this study may have underestimated the association between opium, smoking, and bladder cancer, and the association might even be stronger than the findings of the study.

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### Conflicts of interest

There are no conflicts of interest.

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