

RESEARCH COMMUNICATION

A Case-Control Study on the Etiology of Urinary Bladder Cancer in Istanbul, Turkey

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Abstract

Background: Urinary bladder cancer is the third leading cancer in male in Turkey. The incidence rates of bladder cancer are 13.0 and 2.1/ 100,000 for males and females, respectively, in Turkey. Smoking and occupation are the main causes of urinary bladder cancer. Our goal was to investigate the etiologic factors of urinary bladder cancer in our region to improve our preventive services. **Methods:** We conducted a hospital-based case-control study of patients with bladder cancer and of controls drawn randomly from the acute non-urinary patients of three hospitals in Istanbul. Controls were matched for age, sex, and residence. **Results:** We interviewed 290 cases and 580 controls. Smoking and occupation were found to be related factors in urinary bladder cancer. **Conclusion:** Preventive measures should be planned regarding smoking and occupational factors for urinary bladder cancer in Turkey.

Key Words: Urinary bladder cancer - etiology - occupation - tobacco - risk

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Introduction

Urinary bladder cancer (UBC) occurs in all countries around the world, and it is the fifth most common cancer in the United States (Silverman, 1996; Ohno et al., 1985) and is a common cause of mortality (Ferlay et al., 2001; Yamamoto, 2001; Zeb et al., 2006). UBC is the third leading cancer in males in Turkey, with incidence rates of 13.0 and 2.1/ 100,000 for males and females, respectively (Ferlay et al., 2001; Fidaner et al., 2001).

The risk factors associated with UBC are tobacco use, occupational exposure to some chemical carcinogens and *Schistosoma haematobium*, coffee drinking, use of artificial sweeteners, analgesics abuse, and urine stasis and human papilloma virus (Silverman 2001; Ohno et al., 1985; Fidaner et al., 2001; Wivanitkit V, 2005). Important chemical carcinogens are 2- naphthylamine, benzidine and 4-aminobiphenyl (Fukushima et al., 2000). Workers in the dyestuff industry, rubber and leather industries show a high risk of bladder cancer. Occupations in which workers are suspected of having an elevated UBC risk include painter, driver of trucks and other vehicles, aluminum worker, machinist, chemical worker, printer, metal- worker, hair dresser, and textile worker (Silverman, 1996). Genetic differences in the metabolism of these chemicals have been suggested to modify individual susceptibility to

environmentally induced bladder cancer (Mittal et al., 2005). In a study conducted in Istanbul, a significant difference was reported between the cases and controls on the use of artificial fertilizers and insecticides in the farmers. People who were exposed to unspecified chemical substances were reported to be more prone to develop UBC, and both personal habits and exogenous carcinogens were reported to play a role in the etiology of bladder tumors in the same study (Akdas et al., 1990). In a study in the Aegean region of Turkey (Gumus et al., 1999), UBC was reported to be related closely to tobacco consumption and occupation.

Istanbul is the largest city of Turkey with a population of 13,000,000 and almost 1/5 of the total, acting as the center of Turkish industry in receiving immigrants from other cities (Turkstat, 2006). In the light of the studies suggesting risk factors are preventable, we undertook a case-control study of UBC in Istanbul. Our goals were to investigate the etiologic factors of UBC in Istanbul to improve our preventive services.

Materials and Methods

Between January 1st 1997 and December 31st 1999, we conducted a hospital-based case-control study of patients with UBC and of controls drawn randomly from the acute non-urinary patients of the outpatient clinics of the same

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hospitals in Istanbul. The hospitals were; Istanbul University Institute of Oncology, Taksim Education and Research Hospital, and Beykoz State Hospital, which were selected because they are three different types of hospitals located in three different regions of Istanbul. We interviewed 290 cases and 580 controls.

Case identification: We identified the UBC cases that have applied to the outpatient or inpatient clinics of Istanbul University Institute of Oncology, Taksim Education and Research Hospital, or Beykoz State Hospital. To be eligible for the present study, a patient had to have received an initial histological diagnosis of a primary neoplasm of the urinary bladder. In addition, patients had to be 20 years of age or older at the time of diagnosis. Patients aged 95 years or older or patients with dementia and having no relative familiar with their habits were ineligible for interview.

Control selection: We selected controls by random-sampling procedures from the patients of the different outpatient clinics of the same hospitals who applied for acute problems (i.e., upper respiratory tract infections, minor extremity traumas) other than urinary causes in the same day. The sampling was designed to select twice as many controls as patients by frequency matching procedures. Controls were matched for age, sex, and residence. Controls aged 95 years or older or the ones with dementia were ineligible.

Data collection: Epidemiological information was collected by direct interviews conducted by the researchers. After the informed consent of the subjects were taken, we conducted face-to-face interviews with all of the eligible cases; however, if a case was too ill, or could not be contacted, we tried to talk with a relative who was familiar with the case's habitual and occupational background in a small group. Interviews were conducted in the inpatient or outpatient clinic rooms in the hospitals.

Epidemiological data surveyed by the interviews were: demographic data, detailed smoking habits, occupational history, coffee consumption, use of artificial sweeteners, and pathologic diagnosis. Each case's occupational history was collected for each job held for 5 years or longer since the age 16 in the order from the last job to the first one along with exposure durations. Simple chi-square test was used in the analysis of the occupation.

Results

During the study period, 301 eligible patients (35-95 years), and 600 controls were identified. Among the 301 identified patients, 290 (96.3%) were interviewed, and among the 600 controls 580 (96.7%) were interviewed successfully.

Of the patients, 39 (13.4%) were female, 251 (86.6%) were male, 78 (13.4%) of the controls were female, and 502 (86.6%) were male. The primary histologic type (99.3%) was transitional cell carcinoma.

Smoking habit was found to be a significant risk factor ($p=0.0001$) and the results are summarized in Table 1. Of

Table 1. Smoking Habits and Urinary Bladder Cancer Risk of the Patients

Sex	Subjects		Smokers		Nonsmokers		OR	95% Confidence Interval
	n	%	n	%	n	%		
Males								
Patients	251	(100)	206	(82.1)	45	(17.9)	1.15	1.14-3.04
Controls	502	(100)	360	(71.7)	142	(28.3)		
Females								
Patients	39	(100)	21	(53.8)	18	(46.2)	2.80	0.98-7.72
Controls	78	(100)	15	(19.2)	63	(80.8)		

the total, 227 patients and 375 controls were ex smokers or had smoked at some time, and 141 (62.1%) of the patients and 91 (24.3%) of the controls have been smoking more than 20 cigarettes/day and 20 years or over. Intensive passive smoking was evaluated in the occupation list (Table 2).

Regarding occupational history, we evaluated the high occupational cancer risk jobs in male cases. We did not observe any industrial or high-risk occupations in either the female patient or the control groups. All of the female subjects were housewives, working or retired officers or teachers. Of the total, 152 (60.6%) of the male patients and 160 (31.9%) of the male controls have been working or retired from a high-risk job. This difference was statistically significant ($p=0.01$). Farmers were included in the high-risk occupation list because of their exposure history to biphenyl and unknown chemicals and insecticides. Cafe owners were included to the list because of exposure to passive tobacco smoke. High-risk occupations within the male cases and controls are presented in Table 2.

Coffee consumption habits were similar in patient and control groups. 261 (90.0%) of the patients and 504 (86.9%) of the controls consumed one cup of coffee on average each day. There was no significant difference regarding coffee consumption between patients and controls ($p=0.06$).

Forty-four (15.2%) patients and 79 (13.6%) control subjects used artificial sweeteners for diabetes mellitus, these data suggesting no significant difference between the two groups.

Table 2. High-risk Occupations of the Male Patients and Controls

Occupation	Patients		Controls	
	Frequency	%	Frequency	%
No high-risk	99	39.4	342	68.1
Textile	23	9.2	19	3.8
Petroleum	18	7.2	16	3.2
Driver-transport	19	7.6	31	6.2
Aluminum	12	4.8	19	3.8
Cafe owner	9	3.6	4	0.8
Rubber	7	2.8	3	0.6
Painting	6	2.4	5	0.9
Leather	5	1.9	4	0.8
Asbest worker	2	0.8	3	0.6
Farmer	51	20.3	56	11.2
Total	251	100.0	502	100.0

Discussion

In our study, male/female ratio was 6.4/1, and the most common histologic type was transitional cell carcinoma (Puente et al., 2003).

Our results showed smoking causes higher risk in developing UBC, which is consistent with many studies in the literature (Silverman, 1996; Katoh et al., 1999; Moore and Tsuda, 2002), and it was more effective on women than men. Most of our smoking patients were smokers over 20 package-year. Like another study, an association with higher rates can be shown among those who started to smoke before 18 years of age and those who smoked more than 30 cigarettes per day (Sadetzki et al., 2000). We found smoking to be the predominant risk factor for UBC, which is like a study in the literature that confirmed smoking to be the predominant risk factor in women (Peluchi et al., 2002).

We found the role of industrial occupation in our study was an important factor for men. Similar to our results, excess risk among men had been observed for industries including plumbing, air conditioning, rubber and plastic products, motor vehicle parts and supplies and occupations including supervisors for transportation and material moving, material-moving-equipment operators, automobile mechanics painters and metal- and plastic-working machine operators (Zheng et al., 2002). We observed all of these occupations, except plumbing and air conditioning, in our subjects as a risk factor. Painting was reported to be a risk factor, and our group of painter patients was almost seven times larger than the control subjects group (Brown et al., 2002). The same study suggests that significant excess risk among women was observed for secondary school teachers and record clerks. Housekeepers, butlers, and workers in laundering and dry cleaning facilities were also at increased risk (Zheng et al., 2002). Almost half of our female subjects in both the case and control groups were retired teachers. However, in our study we could not find an occupational risk in women similar to another study reporting no excess risk for cancer among women (Rafnsson, 2001).

We observed exposure to asbestos, petrochemicals, benzene, dyes, polycyclic aromatic hydrocarbons, plating work and chrome as reported chemicals and industries in which occupational cancer will be important (Soo-Hun, 1997). Another study confirmed the role of industrial occupation and exposure to three or more metals as risk factors (Katoh et al., 1999). Similar to this study, we observed metal exposure to be a common factor in our patients.

Biphenyl has been widely used as a dye, a synthetic resin, a constituent of agricultural chemicals, and a post-harvest fungicide agent. Its carcinogenic role in UBC was supported with animal studies (Umeda et al., 2002). We observed similarities between our biphenyl exposure history in our painter and farmer groups and a previous study conducted in Istanbul in 1990 (Akdas et al., 1990). People who were exposed to unspecified chemical substances were reported to be more prone to develop UBC, and both personal habits and exogenous carcinogens were reported to play a role in

the etiology of bladder tumors in the same study (Akdas et al., 1990). In another study in Turkey, UBC was found to be related to tobacco consumption and occupation in 1999 (Gumus et al., 1999).

We found the same factors to be playing a role in UBC almost ten years after a study suggested that smoking and occupational exposures in Turkey are the risk factors. Our results may suggest that we need to translate our large body of data for modifiable risk factors into practical intervention strategies (Tajima and Moore, 2001) and preventive measures should be planned regarding smoking and occupational factors for UBC in Turkey.

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