

A STUDY ON IDENTIFICATION OF BLADDER CANCER CASES ACCORDING TO OCCUPATIONS AND JOB DESCRIPTIONS IN İZMİR

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Bladder cancer is a disease, the incidence of which is increasing day by day and which results in illness and death, but which is preventable. Studies on cancer have shown that, except mesothelioma, bladder cancer is the type of cancer probably most closely related to occupation. When we compare our results with the ten most common types of cancer for men all over the world, it can be seen that bladder cancer has relatively higher incidences in İzmir.

Firstly, causal issues have to be clearly defined so as to decrease occupational bladder cancer cases. In order to establish the causal connection between cancer and occupation, "exposure history" of employees participating in the study is required. Exposure history is derived from data on "type of factors, duration and intensity of exposure to these factors" encountered due to participant's occupation.¹ In defining the casual factors, it is important to gather complete and accurate information regarding the occupations of participants.

A disease is occupational only if a causal connection between cancer and the occupation is established. In our country, a diagnosis of occupational disease is only considered for employees in the status of "worker". It has been planned to regulate occupational health services to embrace all employees with the "Draft Law on Occupational Health and Safety". Labor Law no 4857 defines a worker as "a real person working on the basis of an employment contract" (article 2)² Regulation on Social Insurance and Health Procedures indicates the necessary steps to be followed when there is the possibility of an occupational disease. The list annexed to this Regulation classifies diagnosis of occupational bladder cancer in Group A, titled "Occupational Diseases Caused by Chemicals". Determining that an individual has worked with a liability of 10 years in the manufacture of A-24 aromatic amines and hydrazines, and halogen, phenol and nitro or sulpho derivatives thereof and in chemical,

pharmaceutical, rubber and explosive industries which use thereof as intermediary products; in manufacture of leather shoes, hair medicament, in hairdressing as hair dyes, and in photography as developer fluids; in timber impermealization, in treatment of coal bitumen, and in heating air gas requires that an occupational bladder cancer diagnosis is given.³ In assessment of whether or not a bladder cancer case applying to the Occupational Diseases Hospital is occupational, as in other occupational diseases, if there is an exposure to active materials specified in the List due to reasons other than type of work or engagement period, then diagnosis can be determined by means of literature knowledge and consulting to universities. On the other hand, if the case is not diagnosed as an occupational disease by Occupational Diseases Hospital and the affected person still claims otherwise, he/she holds the right of appealing to Social Security Higher Council of Health for reassessment.

There is no diagnosis of “occupational bladder cancer” in our country according to the records of Ankara Occupational Diseases Hospital, Social Security Higher Council of Health and Social Security Organization Short Term Security Branch Service. Ankara Occupational Diseases Hospital assessed a bladder cancer application in 2005, however this case was concluded with “the decision of occupational health suspicion”.⁴

Diagnosis and notification of occupational diseases and occupational cancers is insufficient in Turkey just as in many developing countries. However, Turkey is one of the many countries which have signed International Labor Organization’s (UÇÖ) agreement regarding notification of occupational diseases.⁵ UÇÖ anticipates occurrence of 4-12 /year new occupational disease cases per thousand workers. Number of anticipated occupational diseases for 2005 is at least 27,674 according to the 2005 data of SSK Annual Abstract of Statistics. The number of anticipated occupational cancer cases can be calculated as at least 6600 on the basis of the relatively conservative estimations of Doll and Peto.⁶ In 2005, only 519 occupational diseases were diagnosed in Turkey, and there are no occupational cancers among them. Basic principles regarding notification of occupational cancer were determined by the Regulation which was published in Official Gazette dated 26/12/2003 and numbered 25328. “Occupational diseases resulting from exposure to carcinogenic or mutagen materials shall be notified to the Ministry of Labor and Social Security”.⁷

BLADDER CANCER

Bladder is an internally empty organ which stores urine: Urine is produced by the kidney and carried into the bladder by ureters, it is kept

until it reaches a certain volume, and stored by the bladder until it is expelled by urethra voluntarily. The bladder which meets waste various chemicals simultaneously is exposed to these materials during storage of urine until it is expelled voluntarily. In the multi-layered bladder wall, cancer starts in the membrane where it first contacts these materials, and spreads towards the bladder wall.

Occupational bladder cancer and bladder cancers due to other reasons are not different from each other pathologically and clinically.⁸ Table 1, prepared by International Agency for Research on Cancer (IARC), indicates agents which probably result in bladder cancer, and conditions of exposure to these agents.

Table 1. Potential risk factors of bladder cancer

Source: IARC Descriptive Epidemiology Study Group

Material / Condition	Type of exposure		
	Occupational	Medical	Social
Alkylating agents : Cyclophosphamide		+	
Aromatic amines: 4-Aminodiphenyl Benzidine 2- Naphthylamine	+ + +		
Chlornaphazine		+	
Ionized radiation	+	+	
Chimney sweeping Usage of aluminum products Distillation of coal bitumen Cooked products Painting Asphalting and roof isolation Rubber industry Hair dyeing	+ + + + + + + +		
Schistosoma haematobium			+
Cigarette Smoke Passive smoking			+ +

BLADDER CANCERS IN THE WORLD

Quantities and types of agents which cause cancer may vary from one region of the world to another, and hence the common type of cancer can differ in each particular region. Whereas bladder cancer is the fifth most common cancer in developed countries, it is not so in developing countries.⁹ In Table 2, the most common ten types of cancer in the world according to GLOBOCAN publications, which has been developed by IARC and used widely all over the world, and which anticipates incidence, mortality and prevalence of cancer for 175 countries is given.

Bladder cancer is the seventh most common type of cancer for men all over the world.

Table 2. Ten most common types of cancer for men in the world and their incidences

Rank	Type of Cancer	All ages	YSH (World)
1	Lung	30.9	35.5
2	Prostate	21.7	25.3
3	Stomach	19.3	220
4	Colon and intestine	17.6	20.1
5	Liver	14.1	15.7
6	Esophagus	10.1	11.5
7	Bladder	8.8	10.1
8	Oral cavity	5.6	6.3
9	Non-Hodgkin lymphoma	5.6	6.1
10	Leukemia	5.5	5.9

*YSH= Age standardised rate

Source: GLOBOCAN 2002, access date: 19 January 2007, 15:08

BLADDER CANCERS IN TURKEY

Contrary to the world ranking, bladder cancer is the third most common type of cancer for men in Turkey according to estimations of GLOBOCAN and it is the second most common type of cancer for men in İzmir according to data of KİDEM. It is possible to observe bladder cancer among boys younger than 15 in countries such as Bahrain, Iraq and Turkey.

Table 3. Incidences of cancer among men in Turkey

Order	Age	0-14	15-44	45-54	55-64	65+	All Age	YSH* (World)
1	Lung	20	1046	2084	4337	5375	12862	47,7
2	Stomach	6	360	461	1000	1493	3320	12,2
3	Bladder	8	180	336	792	1636	2952	11,0
4	Colon and rectum	12	437	387	669	1040	2545	9,1
5	Larynx	3	255	461	758	729	2206	8.0
6	Prostate	0	28	96	506	1469	2099	8.0
7	Leukemia	299	500	199	309	440	1747	5.8
8	Brain, nerve system	124	425	210	301	294	1354	4.5
9	Non-Hodgkin lymphoma	167	318	175	192	302	1154	3.8
10	Oral cavity	7	132	120	250	378	887	3.2

*YSH= Age standardized rate

Source: GLOBOCAN 2002 - 19 January 07 15:04

İzmir Cancer Registry (KİDEM) has published two incidences specific for the İzmir Province since it was established in 1992; the first

one is the 1993-1998 incidence, and the second one is the 1996-2000 incidence. When the latter incidences are taken into consideration, types of cancer diagnosed in İzmir between 1996 and 2000 differ from men to women just as in other parts of the world. Whereas bladder cancer is the second most common type of cancer for men; it is not one of the five most common types of cancer for women¹⁰.

PREVENTABLE RISK FACTORS FOR BLADDER CANCER

SMOKING

The main impact of smoking is on the lung cancer incidence; the risk for a regularly smoking late middle-aged person is ten times more than a person who has never smoked during his/her lifetime. But smoking has also a major effect on mouth, pharynx, larynx, esophagus, bladder and probably on pancreas and perhaps on kidney incidences. The difference in incidences between a smoker and a non-smoker is less significant in bladder, pancreas and kidney cancers than lung and upper digestive system. The influence of smoking on the bladder and kidney is hardly surprising, since the cigarette smoke comprises a number of mutagens and other chemicals and some of these chemicals are absorbed by lungs and spread to further organs through blood; especially urine of smokers include waste products of these materials intensively¹. Cigarette smoke cannot directly affect the bladder just as known polycyclic aromatic hydrocarbons (PAH) which may be carcinogenic; it is initially absorbed by blood and then carried to the bladder, afterwards bladder cells try to resist the carcinogenic influences of these compositions⁶.

In the West, cigarette smoke is the sole and most significant reason of bladder cancer cases and it is predicted as constituting 40-70% of all cases. The risk of bladder cancer is three times higher for smokers than it is for non-smokers⁶.

OCCUPATION

The working atmosphere is very important for cancer researchers in terms of scientific, social and public health results. According to Bofetta, 23 % of European Union labor force is exposed to one or more IARC Group 1 or IARC Group 2B agents¹¹ in working places. In the United States of America (USA), Infante anticipates that there are 20 million employees with occupational cancers; and 12.864,000 of them have IARC Group 1, and 7,321,000 of them have Group 2A carcinogens⁶. In a public-based case-control study which was performed in 10 regions of the USA within the context of national bladder cancer study, it was stated

that 21 – 25 % of bladder cancers diagnosed for white men can be assumed to be occupational. Silverman anticipated that the most common occupational cancer is probably bladder cancer if we do not take mesothelioma into account; and 25 % of male cases as well as 11 % of female cases result from occupational exposures.¹²

In a study, occupation was listed as the second most significant risk factor after smoking. It was anticipated that almost 20 % of all bladder cancers arise from exposure to occupational factors.¹³

Working by using coal bitumen, especially with polycyclic aromatic hydrocarbons (PAH), working with cooking products and also melting aluminum, isolating roofs, working in foundry and chimney sweeping are determined as risk factors for bladder cancer. Exposure to aromatic amines during production of pigment and tyre (benzidine, 4-aminobiphenyl, b-naphthylamine, 4-chloro-o-toluidine) are self-evidently specific agents related to bladder cancer. Increases in risk are widely observed for painters, machine operators, aluminum or other metal workers, leather workers and shoemakers, hair dyers and shipment employees^{14 15}.

In a study combining 11 case-controls, which are conducted in six countries in the Western Europe and which comprise 3346 cases and 6840 controls for men aged between 30-79, the lifetime occupation and smoking history of the patients were taken. The attributed risk was assessed on the basis of the fact that whether or not the patient has ever worked during any part of his/her whole life time in an occupation previously defined as hazardous. Table 4 summarizes occupations which are hazardous regarding bladder cancer and Table 5 summarizes sectors which are hazardous regarding bladder cancer.

Table 4. Occupations considered hazardous regarding bladder cancer for Western European Men

Occupation	Number of exposure cases	Number of exposure controls	OR*	95GA %
Mould-shaping machine operator	7	5	5.21	1.48 -19.31
Wiring	7	4	3.99	1.10 -14.51
Gardening	6	13	3.57	1.24 -10.29
Flexor-operator metal worker	8	9	3.35	1.19 -9.44
General metal worker	14	15	2.27	1.03 -5.00
Metal treatment supervisor	15	21	2.11	1.04 -4.32
Miner	135	222	1.30	1.02 -1.64
Shipment equipment operator	444	869	1.17	1.02 -1.34
Metal worker-machine operators	518	1086	1.16	1.02 -1.32

*OR's are corrected for age, smoking and working areas.

Table 5. Sectors considered hazardous regarding bladder cancer for Western European Men

Occupation		Number of exposure cases	Number of exposure controls	OR*	95GA %
Salt mine	9	6	4,41		1.43 -13.6
Production of carpet and rug	12	6	4.07		1.44 -11.5
Production of paint and varnishers	22	15	2.94		1.48 -5.84
Production of plastic products	35	31	1.79		1.06 -3.00
Production of chemical raw materials	64	57	1.58		1.07 -2.33
Education Services	93	75	1.47		1.06 -2.05

*OR's are corrected for age, smoking and working areas.

Metal workers, machine operators, handling equipment operators and miners are considered within the category of hazardous works in European Union. The fact that even the highest risks in this study are so minor shows that exposure to aromatic amines and other carcinogenic substances diminishes even in occupations specifically hazardous regarding bladder cancer.

In Iowa, in a study that covers 1452 bladder cancer case incidents and 2434 controls for both men and women, for each job conducted for 5 or more years after 16 years of age, data has been collected by means of interviews. In men, OR=2.2 (95 % GA=1.0-5.0) for sanitary installers and heating and air conditioning workers, OR=3.1 (%95 GA=1.2-8.5) for tire and plastic production, OR=4.5 (95 % GA=1.2-16.5) for production of motor vehicle parts, and OR=1.9 (95 % GA=1.0-3.6) for shipment and freight transportation, OR=1.6 (95 % GA=1.0-2.6) for automobile repairing, OR=2.7 (95 % GA=1.0-7.7) for painters, OR=2.0 (95 % GA=1.1-3.4) for metal and plastic machine operators.¹⁶

In a study based on hospitals and comprising 194 cases and the same number of controls in Turkey, we see that there is a statistically significant increase in the risk (p=0.01) for farmers and (p=0.001) for people who are exposed to chemicals.¹⁷

In a study conducted in Northern Italy, Turin, where many car workers are living, comprising interviews with 512 cases and 596 controls, it is determined that the risk of bladder cancer increases for pigment producers RR=8.8 (GA=2.7-28.6), and tire producers RR=2.5 (GA=1.0-6.0).¹⁸

As a result of a community based case-control study relying on data collected from 10 regions of the USA during a national bladder cancer study; 2,100 cases and 3,874 control cases were interviewed: the risk of bladder cancer increases for painters RR=1.5 (GA=1.2-2.0), truck drivers

RR=1.3 (GA=1.1-1.4), and people working in drilling and pressing RR=1.4 (95% GA=0.9-2.1). Long term employment in these occupations almost doubles the RR.¹⁹ Various publications mention increase in the risk of bladder cancer for miners.^{20 21} Just as in truck driving, underground works cause exposure to diesel exhaust due to common usage of diesel devices. Diesel exhaust is within IARC's Group 2A which includes materials probably carcinogenic to humans.^{22 23}

If we consider the hospital based study which was carried out in Brescia in Northern Italy in 1992-1993 and which comprised 355 bladder cancer cases and 579 controls; increase in the risk of bladder cancer was determined for men who were employed as workers in construction and building industries (OR=2.1; 95 % GA=1.1-3.9) as well as men who were working in entertainment and culture services (OR=5.0; 95 % GA=1.3-18.9). Passive smoking is considered as a factor in entertainment and culture services.²⁴

Increase in risks is reported in laundry employees in some studies.²⁰
²⁵ Carbon tetrachloride with chlorine and aliphatic hydrocarbons including perchloroethylene are assumed as causal factors; IARC accepts carbon tetrachloride as carcinogenic as an item of Group 2A (high possibility) and perchloroethylene as carcinogenic an item of Group 2B (possibility).^{26 27 28}

Various publications point out to the increase in the risk of bladder cancer for machine operators.^{20 29 30 31} Metal grinding and cutting may include PAH when mineral oils are used, and aromatic amines when synthetic cutting oils are used. According to IARC, mineral oils are covered by Group 1 which includes materials carcinogenic to humans.²⁸

In recent years, increases in the risk of bladder cancer have been observed for hair dyers and hair dressers.^{22 26 32} Recently, IARC classified hair drying and hair dressing as in Group A according to its carcinogenicity to humans. In these occupations, materials which are considered as carcinogenic factors are coal bitumen, oil products and also hair dye.³³

OTHERS

Schistosoma haematobium is the basic reason for high incidence of bladder cancer especially in the Middle East and in some regions of Africa; 75 % of the incidences are of squamous-cell carcinoma histological type. Cyclophosphamide, which is a cytostatic used for medical purposes, and radiotherapy used for treatment of uterine cancer can cause bladder cancer.

PURPOSE AND METHOD OF STUDY

First of the two purposes of the study is to provide the sector definition of bladder cancer cases comprising men who are above 15 years old, who have social security and who are diagnosed in İzmir province between 1993-1998. The second purpose of the study is to determine the influence of the identified sectors on bladder cancer.

It is a case-control study and comprises 316 insured cases and 319 controls within the provincial boundaries of İzmir.

DATA SOURCES OF THE STUDY

Data sources used within the context of the study are as follows:

1. Cancer Registry, İzmir
2. Social Insurance Institution (**SSK**)
 - a. SSK Registration in Internet : [http:// www.ssk.gov.tr/wps/portal](http://www.ssk.gov.tr/wps/portal)
 - b. SSK Pensioners Department, Ankara
 - c. SSK Data Processing Department, Ankara
 - d. SSK Etlik Archive, Ankara
 - e. SSK İzmir District Directorate
 - f. SSK Manisa Directorate
 - g. Aydın, Denizli, Afyon, ... SSK Directorates of 42 provinces
3. Tepecik SSK Tumor Registration Unit, İzmir
4. Bozyaka SSK Tumor Registration Unit, İzmir
5. Buca SSK Tumor Registration Unit, İzmir
6. Tepecik SSK Urology Service, İzmir

Department of Cancer Control contributed to the study within the context of receiving required permits.

METHOD OF DATA COLLECTION IN THE STUDY

Information of exposure was derived from "Number of Days of Premium Paid (PÖGS)" in SSK records. Cases and controls were selected from people who were working or had worked as insurance-covered employees. In the first phase of data processing; the work places to which PÖGS of presently active employees belonged according to their Employment Recording, and to which PÖGS of pensioners belonged according to pensioner files as well as total premium payment days of them were recorded. In the second phase, data was collected regarding the sectors of the recorded work places.

Sectors and business types were classified so as to perform analyses. For this purpose, "Premium Tariff on Occupational Accidents and Diseases" of the General Directorate of SSK and also "Classification of

Sectors according to Statistics of Occupational Life" of the General Directorate of Labor were used. ORs, 95 % GA's and p values were estimated in accordance with classification of sectors, employment or non-employment of people, and their employment periods.

FINDINGS

In men, 1746 bladder cancer cases which were diagnosed between 1993 and 1998 are taken from the KIDEM database so as to specify groups of cases. After reviewing 1746 cases, it was determined that there were 367 cases who worked as insurance-covered employees; data regarding business types and sectors of 316 of them were obtained; no information could be found regarding business places of the remaining 51 cases; it was considered that these cases either had changed their social security organizations or they did not have social security at the moment. A control group was established from people whose ages and employment periods were similar, and who had an allocation and social security numbers; in this respect 319 people were selected according to SSK records.

15 of 316 cases were active employees, and 301 of them were pensioners; 6 cases passed away during occupational life; 158 cases passed away during retirement. On the other hand, 9 of 319 controls were active employees, and 310 of them were pensioners; 3 controls passed away during occupational life; 84 cases passed away during retirement.

Table 4 indicates connection between bladder cancer and sectors. ORs were higher than "1" in agriculture, livestock, forestry sectors; tobacco, textile, arboriculture sectors; press sector, metal sector; shipping, energy, overland and railway transportation sectors; however these were not significant statistically. On the other hand, it was determined that the increase in bladder cancer risk was statistically significant in petroleum, chemistry, tire and leather sectors.

Table 6. Relation between working and bladder cancer for each sector

Sector no	Title of Sector	Case number	Control number	OR	OR*	95 % GA*	P value*
1	Agriculture, Forestry, and Livestock	18	13	1.42	1.39	0.66 -2.91	0.39
2	Mining	13	19	0.67	0.69	0.33 -1.41	0.30
3	Petroleum, Chemistry and Tire	39	17	2.49	2.58	1.42 -4.67	0.002
4	Food Industry	75	82	0.90	0.92	0.64 -1.32	0.65
5	Tobacco	50	50	1.007	1.03	0.67 -1.59	0.89
6	Textile	82	74	1.15	1.21	0.85 -1.74	0.32
7	Leather	11	3	3.79	3.81	1.05-13.77	0.04
8	Arboriculture	20	18	1.13	1.03	0.52 -2.01	0.93
9	Press	6	4	1.52	1.28	0.34 -4.82	0.71
10	Cement, Soil and Glass	27	30	0.90	0.83	0.47 -1.45	0.52
11	Metal	73	58	1.35	1.32	0.88 -1.96	0.18
12	Ship	6	3	2.03	2.04	0.50 -8.26	0.31
13	Construction	143	148	0.95	0.97	0.71 -1.33	0.86
14	Energy	66	60	1.13	1.13	0.76 -1.67	0.56
15	Trade, Office, Education	105	109	0.95	0.92	0.66 -1.29	0.64
16	Overland Transportation	54	49	1.13	1.08	0.70 -1.67	0.70
17	Railway Transportation	6	4	1.52	1.60	0.45 -5.76	0.47
18	Ocean Transportation	8	9	0.89	0.93	0.35 -2.44	0.88
19	Accommodation and Entertainment Places	39	42	0.92	0.94	0.58 -1.50	0.79
20	General Affairs	20	21	0.96	0.92	0.48 -1.76	0.81

*OR was arranged for each sector according to age.

In the light of the analyzed results regarding employment in a specific sector for more than 10 years (no / yes); employment in gasoline, tyre and chemistry sectors for five years or a longer period increased the risk of bladder cancer significantly. The tobacco and alcohol sectors, the textile sector, leather sector and land transportation sector increased the risk of bladder cancer, however, insignificantly.

RESULTS

This research is a case-control study which defines the occupational risks of bladder cancer cases obtained from a public-based cancer registration center according to social security records.

Working in the petroleum, chemistry and tire sectors, as well as in the leather sector, causes significant increase in bladder cancer

statistically. Working in the petroleum, chemistry and tire sector for a five-year or longer period causes significant increase in bladder cancer statistically. Working in this sector has a direct dose-response relation with bladder cancer. Occupations such as mining, painting, motor vehicle production, agriculture which are considered as having a high degree of relevance, have been found as irrelevant within the context of this study.

POWER AND LIMITS OF THE RESEARCH

The most powerful aspect of our study is that it is the first case-control study which defines the connection between bladder cancer and occupational risks on the basis of employees that have social security in İzmir and in Turkey. In Turkey, cases have been obtained from the public-based cancer registration center for the first time, and controls have been selected from records of the Social Security Organization. Furthermore, exposure information has also been obtained from social security records.

The basic limit of this study is that smoking information could not be obtained. During the planning of the study, both study groups were selected from the same population so as to diminish the distorting influence of cigarette as far as possible; both the defined group and the selected control group are from among employees having social security. When both groups are composed of the same social class, then the influence of distorting elements will be minimized.¹

In this study, it is observed that working in the petroleum, tire, chemistry sector, as well as in the leather sector, causes increase in the risk of bladder cancer; ORs are higher than 1.5. In analyzes, if ORs are higher than 1.5, increase in the risk is so high that it cannot be explained by smoking.¹

Another major limit of the present study is that the premium payment dates from which exposure information is obtained may be incomplete. This may result in our access in incomplete information regarding the employment periods of the sample employees in their actual sectors. But, even if it had been possible to interview with samples face to face, they would not have been remembering their complete employment periods in specific sectors could have also caused incomplete information. A further major limit is that the records of the Social Security Organization do not comprise occupation of employees in relevant sectors. Moreover, since people working in agriculture sector are unregistered in our country just as in other developing countries, it is not possible to indicate the risks for farmers in this study.

RECOMMENDATIONS

Cancer is an illness which has a long induction and latent period. That is why it is impossible to observe existence of the sources of

exposure at the time when the case is specified. The sources of data required for establishing a causal relationship between cancer and occupational exposure are very limited in our country.

A surveillance system can be established between social security records and health records for cancers. An environment in which occupational data and health data can be jointly used can be created by establishing an organic connection between the Ministry of Labor and Social Security and the Ministry of Health on the basis of specific types of cancers which are considered as occupationally relevant.

Employees of specific sectors can be recorded in a different system; cancer cases can be stored in a separate system after making certain arrangements in SSK computer records. Such a system can be also used for other illnesses which may be occupational.

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This work has been composed from my Doctorate Thesis of Dokuz Eylül University Health Sciences Institute Public Health Department Occupational Health Program regarding "Occupational and Professional Identification of Bladder Cancer Cases for Diagnosed Men Above 15 Years Old in Smyrna Province Between 1993 and 1998".

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