Occupational Class Groups as a Risk Factor for Genitourinary Cancer – A Matched Case-Control Study

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ABSTRACT

Cancer is a disease with huge consequences for patients and their families. It has a high mortality rate in both developed and developing countries. Eleven to 15 percent of all cancers can be attributed to occupational risk factors. The aim of this pilot study was to define the risks of specific occupational classes based on the International Standard for the Classification of Occupations 2008 (ISCO-08) in causing genitourinary (GU) cancer.

A matched case-control study was designed and 208 cancer patients were interviewed by a single physician. Controls were selected from cancer patients with different cancers. For assessment of lifestyle, the simple lifestyle indicator questionnaire was. Years of working until 5 years before the diagnosis were questioned and later categorized by the ISCO classification

In total 156 GU cases and non-genitourinary cancer patients were selected. The mean age at the time of diagnosis was 51.01 years for both groups. Except the platelet count, there was no significant difference between the groups. Some ISCO classes (1, 2, and 0) were eliminated because of low numbers. The difference between working in different classes of ISCO classification (3 through 9) was not associated with the occurrence of genitourinary cancer. No significant difference was found between the occupational classes in patients with genitourinary cancer and controls.

Keywords: Cancer; ISCO-08; Occupation; Risk factor; Genitourinary

ABBREVIATIONS LIST

GU: Genitourinary
ISCO-08: International standard classification of occupations 2008
SLIQ: Simple lifestyle indicator questionnaire
CBC: Complete blood count
RBC: Red blood cell
WBC: White blood cell count

INTRODUCTION

Cancer is a disease with great consequences for the patients and their families [1]. In 2008, 12.7 million new cancer cases and 7.6 million cancer deaths occurred worldwide. Fifty-six percent of the new cases and 63% of the deaths were in the developing countries [2]. In Iran, cancer is considered the third leading cause of death [3]. Cancer incidence depends on many factors like environmental risk factors, smoking, socio-economic status, and many other risk factors specific to the type of cancer [4-6].

Testicular cancer is an important cancer in men and its risk factors are family history of cancer and also undescended testes. Its incidence has been rising in the developed world [7]. Some studies mention the inguinal hernia as a risk factor [8]. Prostate cancer is the second most common malignant tumor in men and the sixth leading cause of cancer deaths in the world [9]. There are many risk factors for prostate cancer including family history, ethnicity, age, and environmental factors and also lifestyle factors like smoking and obesity. There are some protective factors like vegetable consumption and physical activities [10].

Job titles and job classifications have been linked to the socio-economic class of the workers [11]. There have been studies showing higher mortality rates among unskilled, semi-skilled, and skilled workers compared with managerial and professional workers [12].

There are no previous studies in Iran that define the association between standard occupational classifications and the occurrence of GU cancer. The purpose of this pilot study was to define whether specific occupational classes based on the International Standard for the Classification of

Occupations 2008 (ISCO-08) involve increasing risk for GU cancer or not.

MATERIALS AND METHODS

Study population consisted of patients with confirmed diagnosis of cancer undergoing chemotherapy or surgical interventions. These patients were hospitalized in one of the hospitals in Tehran. It was a general hospital with all the specialties and subspecialties in medicine. It was a referral hospital for cancer patients from all over the country. Only patients with pathologically defined cancer types (with documented proof) were included. The design of our study was matched case-control. Only male patients were included for an easier matching and also due to the fact that most women in Iran do not work in industrial settings. Our cases consisted of the GU cancer patients.

Only patients with prostate and testicular cancers were included as our cases. The controls were selected from other (non-genitourinary) cancer patients. The controls were matched to the cases on the grounds of the age of the person at the time of the diagnosis. Only patients that were from 40 to 70 years old at the time of the diagnosis were included. Controls were chosen from other cancer patients because this hospital was a referral center for cancers from all over the country and the source population of cases and controls would be the same. This would not have been true of other benign disorders. Cancer patients who were hospitalized for both chemotherapy and surgical interventions were included. Interviewed patients were not necessarily new cases. Because many brain tumor patients could not interview and due to the possible confounding effects of amnesia, they were excluded them from the controls. All of the cases and controls were interviewed by a single physician to reduce inter-personal variations. The duration of the study was 15 months (from June 2014 to September 2015). Exclusion criteria were the positive history of cancer in the family (not essentially the same type as the patient), work experience less than 5 years, and no occupational history beyond 5 years before the diagnosis of cancer.

The interview: All the interviews were performed by one physician to reduce interpersonal differences. The interview was performed during the patients' stay in the hospital. Those patients who did not give us informed consent after the explanation about the purpose of the study were not interviewed. The role of the companions of the patients was only auxiliary and data were only entered the patient's approval. The interview consisted of a comprehensive assessment of the occupational (vocational) history, simple lifestyle indicator questionnaire (SLIQ) for assessment of the lifestyle and some other questions (e.g. marital status, the level of education, and shift work). All the patients who fulfilled the inclusion criteria were interviewed and questions about the occupational history from childhood up until five years before the diagnosis of their cancer and also the duration of each occupation was asked. Even the occupations performed in childhood or part-time occupations and seasonal occupations were asked to detail. If a patient had worked in several different occupations, each job would have been written separately while indicating its duration. These 5 years were considered because of the latency for development of overt cancer and the span of time from the onset of the disease and its diagnosis. Demographic data included age, marital status, cigarette smoking, history of shift work and living in rural or urban areas for most of the life since birth. Information about family history of cancer and lifestyle was also asked. The SLIQ questionnaire inquiries about the diet (use of vegetables, fruits, and whole grain), exercise (light, moderate, and vigorous physical activities), alcohol consumption, smoking, and perceived stress level [13]. It scores the variables from 0 to 2. For diet, higher scores mean more frequent consumption of fruits and vegetables and for physical activity, higher scores mean more vigorous activities with higher frequency. For alcohol, smoking, and life stress, higher scores means lesser consumption of alcohol, negative history of smoking and lower stress respectively (scoring high in all these variables means healthier lifestyle). Its validity and reliability have been investigated in previous studies [14]. Because every patient who is hospitalized in this hospital should have a complete blood count (CBC), the red blood cell (RBC) counts were included, hemoglobin levels, and platelet counts for each patient. Because of the possibility of the transfusion during the hospitalization, the admission CBCs which were taken before any intervention was performed were included. White blood cell count (WBC) was excluded due to many confoundings.

Occupations asked during the interview were categorized into 10 different job classes based on the ISCO-08 [15]. This classification or its older versions was used in many investigational studies about cancer [16, 17]. In this classification, job activities are grouped in terms of specific tasks and duties for that job. Skill specialization and skill level is the two dimensions that this classification is based on. The former is a criterion of competence and professionalism and the latter is about the complexity of the job. Different ISCO groups have different job characteristics [18]. The major groups consist of 1) Managers, 2) Professionals, 3) Technicians and associate professionals, 4) Clerical support workers,

5) Service and sales workers, 6) Skilled agricultural, forestry and fishery workers, 7) Craft and related trades workers, 8) Plant and machine operators, and assemblers, 9) Elementary occupations, 0) Armed forces [15]. The number of working years in any category was noted. The person who performed the coding was blinded to the type of cancer. Only the one digit major occupational groups were chosen for having enough power. If a person had worked in more than one occupational category, the number of years in each category was noted accordingly. This means that the number of years of working and not the workers themselves were used for risk assessment. The number of years was averaged for each category for cases and controls. The average years of working in each category were compared between the cases and the controls.

Each GU cancer case was matched with one patient with another type of cancer on grounds of the age of the person at the time of diagnosis (within one year). There was no need for matching for the interviewer (only one interviewer was involved in the whole study), the hospital of admission, and sex due to the design of the study.

Occupational classes (as exposures) were averaged between the two groups and t-test was used to define the difference in the means between the GI cancer group (cases) and other cancers group (controls). Working in an occupational class was also analyzed as ever and never workers (those who have worked in that class and those who had never worked in that class). The data were analyzed using SPSS ver. 16 and the level of significance were $P<0.05$ and all tests were two-tailed.

RESULTS

In total 208 cancer patients were interviewed (95 GU cancer patients and 113 non-genitourinary cancer patients). Nine GU cancer patients had positive family history of cancer in their first-degree relatives and were excluded from the study. Five patients were grouped into the ISCO classes of 1, 2 and 0 and were also excluded. Three patients had jobs that were not classifiable by ISCO classification and were also excluded. At last 78 patients with GU cancer were included in our study. The above-mentioned exclusion criteria were applied to the controls and after that 102 non-genitourinary cancer patients remained. From these patients, 78 matched controls were selected.

In table 1, the demographic data of these 156 patients can be seen. Only the platelet counts were different between the groups. The mean age of cases and controls was 50.01±5.7. The T-test was used to define the significance of the differences between quantitative variables and the chi-square test was used for the qualitative variables.

Table 1. Demographic data in the cases and controls.

Variables			Genitourinary cancer (cases)	Other cancers (controls)	P-value
Quantitative variables	Shiftwork (years)		11.4±5.6	8.0±6.3	0.23
	Smoking (Pack years)		9.6±4.8	8.4±4.7	0.45
	Red Blood Cell count ($x10^6/mm^3$)		3.76±0.5	3.77±0.4	0.902
	Hemoglobin (g/dL)		12.3±1.3	12.5±1.2	0.435
	Platelet count ($x10^3/mm^3$)		441±139	328±144	0.001
	BMI		26.9±3.2	26.3±2.8	0.252
Qualitative variables	Marital status	Married	66	71	0.328
		Single or divorced	12	7	
	Living place	Urban area	51	43	0.252
		Rural area	27	35	
	Smoking history	Positive	15	19	0.561
		Negative	63	59	
	Shiftwork	Positive	10	9	0.999
		Negative	68	69	
	Level of education	Under 6 years	19	21	0.316
		6-12 years	37	28	
		More than 12 years	22	29	
	Stress level score	0	8	6	0.999
		1	31	35	
		2	39	37	
	Activity level	Light	11	11	0.259
		Moderate	36	26	
		Vigorous	31	41	
	Diet score	0	17	15	0.618
		1	46	46	
		2	15	17	

In table 2, the comparison between the average years of working in different occupational classes between cases and controls can be seen. Independent sample t-test was performed for assessment of the significance of the differences in means.

Table 2. Quantitative assessment of working history in different ISCO groups (cases and controls)

ISCO groups	Mean years of work history for Genitourinary cancer patients	Mean years of work history for other cancer patients	p-value (two-tailed)
ISCO group 3	1.65	1.43	0.81
ISCO group 4	1.50	2.94	0.19
ISCO group 5	2.48	3.69	0.32
ISCO group 6	5.43	3.83	0.27
ISCO group 7	4.57	3.83	0.61
ISCO group 8	3.65	3.07	0.65
ISCO group 9	3.56	3.83	0.83

* Calculated using t-test

In table 3 the odds ratios of ever working in an ISCO group versus never working in that group is presented. It means that all of the patients that have ever worked in an ISCO group and those who had not worked in that group were considered between GU cancer and non-genitourinary cancer groups and a 2x2 cross-tab was drawn and Chi-square test was used to determine the level of significance and odds ratios were calculated.

Table 3. Odd's ratios and significance level of the ever worked category in each ISCO group (between cases and controls)

ISCO groups	P-value *	Odd's ratio	CI for Odd's ratio
ISCO group 3	0.754	1.21	0.35-4.16
ISCO group 4	0.174	2.14	0.69-6.60
ISCO group 5	0.259	1.67	0.67-4.14
ISCO group 6	0.438	0.73	0.34-1.58
ISCO group 7	0.416	0.71	0.32-1.60
ISCO group 8	0.837	1.08	0.48-2.44
ISCO group 9	0.832	0.91	0.39-2.09

* Calculated using chi square test, two sided

DISCUSSION

In our study, there was no difference between the cases and controls on the grounds of epidemiologic, lifestyle, and occupational risk factors. This study shows that there is no association between working in different ISCO classes of occupations and the occurrence of genitourinary cancers.

It has been shown that the occupational class has an effect on the prevalence of testicular cancer [19]. In a case-control study on 323 patients with testicular cancer, salesmen (RR = 1.5), managers (relative risk = 1.5), electricians, and sailors/fishermen (RR = 3.1) (RR = 2.8) had higher risk for testicular cancer [20]. In another study on 271 men, there was no association between testicular cancer and the occupational class [21]. There are also conflicting data about the association between occupational class and prostate cancer. In a study on 250 patients with prostate cancer, there was no association between the two [10]. In another study, it was shown that the level of activity of a job can influence the prevalence of the prostate cancer [22]. In a cohort study in Denmark, there was also no association between social class and the prevalence of prostate and testicular cancer but there was an association between these cancers and higher levels of education [23].

In our study, there was no significant difference between cases and controls in terms of the lifestyle and other demographic risk factors. One significant difference in terms of lab data was lower platelet count in controls which can be due to the cases of leukemia/lymphoma which usually have lower platelet count.

There are limitations to our study. This study was only performed on male subjects and females were not included. The exposure levels were not directly assessed and only the occupational title was used. The number of hours working in a day and the level of exposure to other probable carcinogens was not assessed. It is known that many carcinogens are environmental and are not related to the occupation of the person and there may be synergistic effects between occupational and non-occupational factors, but this effect was reduced by matching the cases and controls. Because only the occupations were studied and exposure was not assessed for the workers, it is not possible to discuss the association of GU cancer with specific exposures like diesel exhaust, asbestos, etc. Considering that the data pertinent to occupational classes are easily available, using these classes can be important when no exposure data are available. In this study, there was no difference between the diets, physical activities, and level of perceived stress among cases and controls. Because drinking alcohol is punishable by law in Iran and people usually deny its use, this variable was excluded (only 3 persons mentioned its use). The same was true about the use of illicit drugs (narcotics, cannabis, etc.) and they were also excluded from the study. Occupational subcategories were not included in our study because dividing the categories would have caused reduced power as it was the case in previous studies with an even larger number of cases and controls [24]. Recall bias is an inseparable part of case-control studies. By using cancer patients as controls, the differences in recall biases that would have happened with non-malignant controls were reduced. Socio-economic levels were not directly assessed and some of the associations can be

attributable to this variable but our classification is somehow inclusive of this variable to some degrees and assessing this variable would have resulted in over matching. Sometimes when socio-economic data are not available, occupational classes can be used as surrogates.

The strengths of our study are as follows. Using cancer patients as controls (as opposed to hospital controls) is beneficial because it reduces interview bias and recall bias and also the source populations are similar because both are referred from all over the country to the same hospital. Our data gathering was conducted by direct interview with the cancer patient. Using one interviewer and asking the same questions in similar environments and almost the same duration for the interviews helped reduce many possible biases (e.g. inherent biases pertinent to the use of questionnaires etc.). The process of gathering data and analysis was performed by a team of physicians specialized in occupational medicine. Racial differences were not of concern in our study because there is only one dominant race in Iran (all white) and none of the patients were from different races. The case-control design of the study is most appropriate for evaluating relatively rare diseases like cancer and is commonly used in the field of occupational medicine. Occupational classes are a mixture of different exposures. No one in any particular occupation is solely exposed to a single carcinogen. There are great correlations between exposures [25]. Using occupational class as a risk factor helps us to include all of these exposures as a single risk factor. Using ISCO classification which divides the occupations into 10 major categories and then divides them into minor subcategories helps us in future research and assessment of more specific occupations included in high-risk major categories. Using a quantitative measure of occupations (years of work) and comparing them between cases and controls reduces the effects of a possible bias of not differentiating between 1 year of work or 30 years of work history in an occupational class. This study was not previously performed in any country in the Middle East.

CONCLUSION

No statistically significant difference was found between the occupational classes in patients with genitourinary cancer and controls. This means that in this study the risk of GU cancer for the patients was not associated with their occupational class.

ETHICAL ISSUES

This study was approved by the ethics committee of Iran University of medical sciences. Informed consent was acquired before inclusion of patients in the study. All the interviewed patients knew the purpose of the study and they agreed to share their lab data. If a patient refused to cooperate during the interview, he was excluded from the study without any consequences for him.

AUTHORS' CONFLICT OF INTEREST

Authors declare no conflict of interest.

AUTHORS CONTRIBUTION

All the authors contributed equally in the conception, performance, analysis and writing the article.

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