RESEARCH ARTICLE

Urinary Bladder Cancer Risk Factors: A Lebanese Case-Control Study

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Abstract

  Background: Bladder cancer is the second most incident malignancy among Lebanese men. The purpose of this study was to investigate potential risk factors associated with this observed high incidence. Methods: A case-control study (54 cases and 105 hospital-based controls) was conducted in two major hospitals in Beirut. Cases were randomly selected from patients diagnosed in the period of 2002-2008. Controls were conveniently selected from the same settings. Data were collected using interview questionnaire and blood analysis. Exposure data were collected using a structured face-to-face interview questionnaire. Blood samples were collected to determine N-acetyltransferase1 (*NAT1*) genotype by PCR-RFLP. Analyses revolved around univariate, bivariate and multivariate logistic regression, along with checks for effect modification. Results: The odds of having bladder cancer among smokers was 1.02 times significantly higher in cases vs. controls. The odds of exposure to occupational diesel or fuel combustion fumes were 4.1 times significantly higher in cases vs controls. The odds of prostate-related morbidity were 5.6 times significantly higher in cases vs controls. Cases and controls showed different clustering patterns of *NAT1* alleles. No significant differences between cases and controls were found for consumption of alcohol, coffee, tea, or artificial sweeteners. Conclusions: This is the first case-control study investigating bladder cancer risk factors in the Lebanese context. Results confirmed established risk factors in the literature, particularly smoking and occupational exposure to diesel. The herein observed associations should be used to develop appropriate prevention policies and intervention strategies, in order to control this alarming disease in Lebanon.

Keywords: Bladder cancer - risk factors - case-control study - N-acetyltransferase 1 - Lebanese

Introduction

  Urinary bladder cancer is the ninth most common cancer globally, accounting for 3.3% of all malignancies (Ferlay et al., 2010). As a general pattern, incidence is high in industrialized countries such as the United States, Canada, and the European Union, and lower in developing countries in Africa and Asia (Ploeg et al., 2009; Jemal et al., 2011). In Lebanon, however, bladder cancer incidence increased markedly in the past years (World Health Organization et al., 1999; Shamseddine et al., 2004). According to the latest Lebanese national Cancer Registry Report, bladder cancer is the second most incident cancer among Lebanese males (ASR=32 per 100,000) (MOPH et al., 2010). Various environmental and genetic factors may underlie observed geographical and ethnic differences in incidence.

  Exposure to arylamines through tobacco smoke has been well recognized as a major risk factor (Kogevinas et al., 2002). Persons who smoke are estimated to have between 4 to 6 fold greater risk for bladder cancer compared to non-smokers (Negri et al., 2001; Zeegers et al., 2004). Studies have reported a dose-response relationship between an increased number of daily smoked cigarettes and increased risk of bladder cancer (Brennan et al., 2000). Other studies investigating smoking and bladder cancer found men to have a significantly higher risk, with two thirds of the cases occurring in patients over 65 years old (Pashos et al., 2002).

  Other risk factors for bladder cancer included family cancer history (Negri et al., 2001), medical history of urinary tract diseases such as infections and stones, consumption of artificial sweeteners (Hoover et al., 1980), and frequent exposure to hair dyes (Gago-Dominguez et al., 2003). On the other hand, occupational chemical exposure is thought to be responsible for about 25% of

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bladder cancer cases (Yamaguchi et al., 1982; Schoenberg et al., 1984; Axtell et al., 1998). Subjects who worked as hairdressers for at least 10 years were found to have a 5 fold increased risk for bladder cancer (Kogevinas et al., 2003). Exposure to paint dyes, heavy metals, and polycyclic aromatic hydrocarbons (PAH) have been found to be associated with higher bladder cancer risk (Zeegers et al., 2001). Occupations involving exposure to incomplete combustion or diesel fumes such as gas workers, drivers, construction workers, glass processors, and others, were all associated with higher risk of bladder cancer (Clavel et al., 1994; Olfert et al., 2006).

At the genetic level, in addition to cancer genes and genomic instability, polymorphism of drug-metabolizing enzymes has been reported to influence toxic outcomes of environmental carcinogens, hence, potentially modifying individual cancer risk (Hein et al., 2000). Of particular importance are the N-Acetyltransferase (*NAT*) enzymes, known to mediate metabolism of bladder carcinogens, mainly aromatic amines and heterocyclic amines. We have reported *NAT1* to have an unusual allelic frequency distribution in a Lebanese community residing in Michigan in an earlier study (Dhaini et al., 2000).

Our current case-control study particularly seeks to investigate the potential association of environmental risk factors and bladder cancer among Lebanese men residing in Lebanon.

Materials and Methods

Study design and population

A case-control study was conducted in two major medical centers in the Capital Beirut: St. Georges Hospital and Bahman Hospital. 54 cases and 106 hospital controls were randomly selected for this study. A total of 284 bladder cancer patients were identified from medical records of both hospitals between 2002 and 2008. Contact information was obtained from hospitals' archives. Excluded patients were females, men under age of 50, deceased patients before the beginning of the study, patients with missing contact information, in addition to patients who refused to participate. The remaining patients were included in the study as detailed in Figure 1.

The sample size for this study was guided by power analysis that revolved around the following: power of 80%; Type 1 error of 5%; and estimated OR of 3; and the proportion of exposure of suspected *NAT1* alleles among the cases (21.4% based on data observed in an earlier study) (Butcher et al., 1998; Hughes et al., 1998; Dhaini

et al., 2000). A ratio of 1:2 of cases to controls was made use of.

Inclusion and exclusion criteria

Recruited cases were Lebanese males above the age of 50 with histologically confirmed bladder cancer diagnosed at Saint Georges Hospital University Medical Center and Bahman Hospital between 2002 and 2008. Cases were randomly selected as per year of reporting starting with the most recent year of diagnosis. Controls were conveniently selected from the same settings. These were subjects attending to both settings either for a social visit or a routine check-up. They were Lebanese males, 50 years or older, with no present or previous history of cancer, or any other systemic illness or chronic disease.

The study excluded women, non-Lebanese, and all subjects that are less than 50 years of age for both cases and control groups. In addition, all first degree relatives were excluded from both cases and control groups. In the control group, all subjects with history of bladder cancer or any other type of cancer or systemic illness or chronic disease were excluded.

IRB and consent

University of Balamand and Hospitals IRB approvals were obtained prior to conducting the study. All cases and controls were asked to provide consent prior to questionnaire administration and blood withdrawal. The consent, which provides a detailed explanation of the study aims, was read to the patient in their native language. Risks and benefits of the study were also clearly explained during consent. The consent ensured confidentiality and privacy of the patient, as well as his ability to withdraw at any time from the study.

Questionnaire

Data collection involved combining a structured face-to-face interview questionnaires and genetic analysis of collected blood samples. Interviews were conducted by trained graduate students, with previous experience. It was not possible to mask the interviewers on the subject's status (i.e. whether cases or controls). The questionnaire covered the following sections: Socio-economic Characteristics, Lifestyle Factors, Medical History, Family Cancer History, and Chemical Exposure. All questions targeted the period prior to diagnosis. Socio-economic Characteristics collected information on age, years of education, current residence, and salary. Lifestyle Factors obtained information on cigarette smoking habits (assessed based on years of smoking and time of first cigarette after sleep); water pipe smoking; as well as passive exposure to smoking at home or at the workplace; alcohol consumption (assessed by times per day multiplied by years and multiplied by addiction); fruits and vegetables consumption, assessed by days multiplied by daily portion (defined as the number of individual fruit or vegetable units consumed per day); coffee consumption (assessed by times per day multiplied by years); tea and soft drinks consumption (assessed by years multiplied by number of cups per day). Other lifestyle factors included: artificial sweetener consumption, use of butter, margarine,

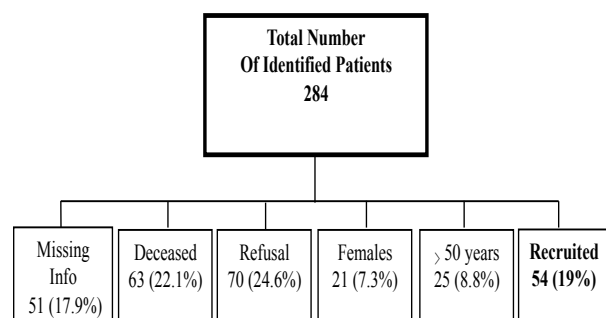**Figure 1. Chart Detailing Recruitment of Cases**

Total Number Of Identified Patients 284

Missing Info 51 (17.9%)	Deceased 63 (22.1%)	Refusal 70 (24.6%)	Females 21 (7.3%)	⟩ 50 years 25 (8.8%)	**Recruited 54 (19%)**

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olive oil, and vegetable oil in cooking, source of drinking water at home and at work, and occupational exposures to combustion fumes.

The Medical History section assessed the presence of the following chronic diseases: arthritis, asthma, congestive heart failure, coronary heart disease, heart attack, angina pectoris, hypertension, thyroid disorder, chronic bronchitis, liver conditions (such as hepatitis, cirrhosis), prostate-related morbidity (determined qualitatively by yes/no question based on a physician's indication), diabetes, Alzheimer's, osteoporosis, eczema or any skin allergy, urinary tract infections, and cystitis. The Family History Section assessed the presence of cancer in the immediate family. These chronic diseases were assessed qualitatively by a yes/no question.

Chemical exposures were assessed through the use of hair dyes and potential exposures to occupational diesel or fuel combustion fumes (assessed qualitatively by a yes/ no question).

Genotyping

DNA was extracted from obtained blood samples using a ready-to-use extraction kit (Qiagen) according to manufacturer's instructions. *NAT1* genotypes were determined using PCR-RFLP as described previously (Deitz et al., 1997) and according to consensus nomenclature (Hein et al., 2000).

Statistical analysis

After collection, data were coded, entered and analyzed using the Statistical Package for Social Sciences (version 16; SPSS, Chicago, IL). Univariate analysis consisted of frequency and percentage distributions for different categorical variables in the study. Means, SDs, and ranges were computed for different continuous variables, with checking for normality and outliers. Bivariate analysis mainly used Chi2 and Fisher's exact test to test the association between the main outcome variable (urinary bladder) and the various exposure and confounding variables. The purpose of this analysis was to examine crude associations and to check for potential confounders and effect modifiers. Multivariate analysis involved a backward logistic regression model, where different exposure and confounding variables that yielded significant results during bivariate analysis, were included in the model. Odds ratios, p-values, and confidence intervals were computed at a type I error alpha value of 5%. The final model incorporated the exposure and confounding variables that displayed the most significant odds ratios.

Results

Socio-demographic characteristics

There were no significant differences between cases and controls in terms of age and education (Table 1). The average age in cases was 67.1 (+8.1) years compared to 65.6 (+11.3) years in controls. Most subjects had completed junior-high school (around 8 years of education). The average monthly income in both groups was around US $1,800. The majority of cases and controls

resided in the capital Beirut (33.3% vs. 79%), and Mount Lebanon (46.5% vs. 15%).

Lifestyle factors

Compared to controls, cases were significantly more likely to be severe smokers (mean 77.2±37.9 vs. 44.9±47.3 years-cigarettes), to eat fruits (mean 27.7±25.9 vs. 10.2±10.9 days-portion), to eat vegetables (mean 15.9±16.8 vs. 7.6±7.2 days-portion), and slightly more likely to drink tea (not significant- mean 10.9±16.9 vs. 9.8±25.4 years-cups/day) (Table 2). On the other hand, cases were less likely to drink coffee (although not significant-mean 125.8±169.9 vs. 154.5±142.8). Cases and controls were almost equal in exposure to passive smoking at home and use of regular artificial sweeteners. In addition, cases were more likely to report use of olive oil during cooking (87%) compared to controls (68%). Cases were significantly more likely to report exposure to occupational diesel or fuel combustion fumes (50%) compared to controls (33%). Cases were significantly less likely to report waiting for long hours to use the restroom at work (13.2%) compared to controls (40.2%). Cases were significantly more likely to report use of bottled water at home (63% vs. 25.5%) and at work (60% vs. 25%) compared to controls.

Family cancer history and NAT1 genotypes

Cases were significantly more likely to report the presence of cancer in the immediate family than controls (33.3% vs. 7.6%) (Table 3). Cancer cases were more likely to be clustered between brother and father compared to other members in the immediate family. In addition, cases and control showed different clustering patterns of *NAT1* alleles. *NAT1*14A* allele showed higher clustering in cases versus controls (53.7% vs. 11.3%), statistically significant. A detailed description of results and analysis on *NAT1* findings is published elsewhere (Yassine et al., 2012).

Medical history

Compared to controls, cases were significantly more

Table 1. Socio-Demographic Background of Cases and Controls (n=160)

Variables	Bladder Cancer Cases	Control	P value
Age Mean (SD)	67.1 (8.1)	65.6 (11.3)	0.39
Years of Education Mean (SD)	8.2±6.7	7.88±5.3	0.69
Salary (US$) Mean (SD)	1721 (2435)	1885 (2230)	0.003
	N (%)	N (%)	
Salary (US $)		(P-value=0.003)	
Less than 500$	11 (27.5)	36 (52.9)	
Between 500$ and 1000$	16 (40)	27 (39.7)	
Between 1000$ and 5000$	12 (30)	5 (7.4)	
More than 5000$	1 (2.5)	0 (0)	
Current Residence		(P-Value=0.00)	
Beirut	18 (33.3)	79 (79)	
Mount Lebanon	25 (46.3)	15 (15)	
North	2 (3.7)	4 (4)	
South	4 (7.4)	2 (2)	
Bekaa	5 (9.3)	0 (0)	

Table 2. Bivariate Analysis of Life-style Risk Factors among Cases and Controls (n=160)

Variables	Bladder Cancer		P value
	Cases Mean (SD)	Controls Mean (SD)	
Smoking severity index (Years smoking * Frequency)	77.2±37.9	44.90±47.3	0.003
Fruit consumption index (Days * portion)	27.7±25.9	10.29±10.9	0.00
Vegetables consumption index (Days * portion)	15.94±16.82	07.63±07.27	0.00
Coffee consumption index times/day * years	125.8±169.9	154.5±142.8	0.37
Tea consumption index Years * cups/day	10.9±16.9	9.8±25.4	0.068

	Cases N (%)	Controls N (%)	P value
Passive Smoking (no. of individuals who smoke inside the house)			0.287
None	28(51.9)	65(61.3)	
One	18(33.3)	33(31.1)	
Two or more	08(14.8)	08(07.5)	
Passive Smoking (no. of individuals who smoke at work)			0.00
None	11 (26.6)	16(21.1)	
One	03 (7.1)	15 (19.7)	
Two or more	28 (66.3)	45 (59.2)	
Artificial Sweetener Intake			0.074
Never	40 (74.1)	71 (78.0)	
Rarely	03 (05.6)	07 (07.7)	
Frequently	01 (01.9)	07 (07.7)	
Always	10 (18.5)	05 (05.5)	
Olive oil used in cooking			0.016
Never	2 (3.7)	1 (1)	
Rarely	0 (0)	4 (3.8)	
Frequently	5 (9.3)	28 (26.7)	
Always	47 (87)	72 (68.6)	
Exposure to Occupational Diesel and Fuel combustion			0.037
Yes	27 (50)	35 (33)	
No	27 (50)	71 (67)	
Waiting for long hours to use toilet at work			0.001
Yes	07 (13.2)	37 (40.2)	
No	46 (86.8)	55 (59.8)	
Source of drinking water at home			0.00
Public irrigation	07 (13.0)	75 (70.8)	
Well water	03 (05.6)	00 (00.0)	
Spring water or river	02 (03.7)	01 (00.9)	
Alcitern or improvised road	04 (07.4)	00 (00.0)	
Mineral Water	34 (63.0)	27 (25.5)	
Own filter	04 (07.4)	03 (02.8)	
Source of water at work			0.00
Public irrigation	11 (22)	74 (74)	
Well water	03 (06)	00 (00)	
Alcitern or improvised road	02 (04)	00 (00)	
Mineral Water	30 (60)	25 (25)	
Own filter	03 (06)	01 (01)	
Other sources	01 (02)	00 (00)	

Table 3. Bivariate Analysis of Familial Cancer History and *NAT1* Genotypes among Cases and Controls (n=160)

	Cases N (%)	Controls N (%)	P value
Familial History of Cancer			0.00
Yes	18 (33.3)	8(07.6)	
No	36 (66.7)	97(92.4)	
Family members			
Father (Yes)	6 (11.1)	2 (1.9)	0.012
Mother (Yes)	3 (05.6)	3 (2.9)	0.40
Sister (Yes)	4 (07.4)	1 (1)	0.027
Brother (Yes)	8 (14.8)	1 (1)	0.00
Grandfather-father side (Yes)	0	0	0.16
Grandfather-mother side (Yes)	0	0	
Grandmother-father side (Yes)	0	0	
Grandmother-mother side (Yes)	1 (1.9)	0	
Other relatives (Yes)	0	1 (1)	0.48
NAT1 Allele Clustering			
*NAT1*15	26 (48.1)	43 (40.6)	0.36
*NAT1*14A	29 (53.7)	12 (11.3)	0.00
*NAT1*14B	7 (13)	05 (04.7)	0.06
*NAT1*10	11 (20.4)	54 (50.9)	0.00
*NAT1*3	7 (13)	14 (13.2)	0.96
*NAT1*4 (wild-type)	14 (25.9)	49 (46.2)	0.013

Table 4. Bivariate Analysis of Pre-existing medical conditions (as indicated by a Physician) among Cases and Controls (n=160)

	Cases N (%)	Controls N (%)	P value
Arthritis	11 (20.4)	9 (08.6)	0.034
CHD	1 (01.9)	19 (18.3)	0.03
Heart Attack	17 (31.5)	5 (04.8)	0.00
Angina Pectoris	16 (29.6)	7 (06.7)	0.00
Prostate Morbidity	28 (51.9)	23 (21.9)	0.00
Skin problems	12 (22.2)	8 (07.6)	0.009
Urinary Tract Infections	2 (03.7)	23 (21.9)	0.003

Histological Type and Grade	Bladder Cancer Cases N (%)
Papillary Transitional Cell Carcinoma	45 (84.9)
Transitional Cell Carcinoma (NOS)	05 (09.4)
Adenocarcinoma (NOS)	01 (01.9)
Unspecified Bladder Cancer	02 (03.8)
Low Grade	26 (51.0)
High Grade	25 (49.0)

likely to report the following conditions: arthritis (20.4% vs. 8.5%), heart attacks (31.5% vs. 4.8%), angina pectoris (29.6% vs. 6.7%), prostate-related morbidity (51.9% vs. 21.9%), and skin problems (22.2% vs. 7.6%). Cases, however, were significantly less likely to report CHD (1.9% vs. 18.3%) and urinary tract infections (3.7% vs. 21.9%) compared to controls (Table 4). Most of the cases were diagnosed with papillary transitional cell carcinoma (84.9%). Fifty-one percent had a low cancer grade vs. 49% with a high grade.

Multivariate analysis

The multivariate analysis is illustrated in Table 5.

The best-fit model was constructed at p-values of 0.1 or lower. Smoking, Prostate-related morbidity, exposure to occupational diesel and fuel combustion, and *NAT1*14A allele were found to be independently significant risk factors for bladder cancer. The odds of smoking addiction were 1.02 times higher in cases than controls, statistically significant. The odds of occupational diesel and fuel combustion were 4.1 times higher in cases than controls. The odds of prostate- related morbidity were 5.6 times higher in cases than controls. The odds of *NAT1*14A allele were 7 times higher in cases compared to controls, statistically significant. There was an independent gradient increase in the odds with salary (but not significant) when comparing cases to controls. The odds of having an income higher than 1000 US$/month were 8.1 times higher in cases compared to controls, while the odds of an income

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Table 5. Multivariate Logistic Regression Analysis Testing for Independent Effects**

Variable		Adjusted OR (CI)
Income (Reference<500$/month)	500-1000	2.7 (0.05-12.5)
	>1000	8.08 (1.03-63.5)
Smoking Severity (Years x Frequency)		1.02* (1.01-1.04)
Exposure to Occupational Diesel and Fuel combustion (Reference No)		
		4.1* (1.01-16.8)
Prostate-Related Morbidity (Reference: None)		5.6* (1.07-29.5)
NAT1 Allele (Reference: None)	NAT1*14A	6.9* (01.2-38.5)
	NAT1*10	1.3 (00.2-07.8)
	NagelKerke R^2	0.56

*Significant at or less than 0.05. **This is the best fit model based on the following crude model: income, family history, passive smoking at the work place, occupational exposure to combustion fumes, previous history of prostate cancer, and history of urinary tract infections

ranging between 500-1000 US$/month were 2.7 times higher in cases than controls.

Discussion

The current incidence of bladder cancer in Lebanon is one of the highest in the world (Ferlay et al., 2010; Shamseddine et al., 2010; Jemal et al., 2011). The present report is the first case-control study on bladder cancer in the country. Our results demonstrate a number of risk factors among Lebanese men. Smoking severity, prostate-related morbidity, exposure to occupational diesel or fuel combustion fumes and *NAT1* genotype are presented as independent predisposing risk factors for bladder cancer. No significant differences between the cases and controls were found for consumption of alcohol, coffee, tea, or artificial sweeteners.

The observed association between tobacco smoking and bladder cancer risk is not particularly new. In the Lebanese context, however, this finding is particularly important, given the alarming smoking epidemic, mainly water-pipe smoking, that is invading the country since the early 1990s (Saade et al., 2008; Nakkash et al., 2011). Our results show statistically significant differences in smoking severity in cases compared to controls, which is consistent with previous findings (Samanic et al., 2006; Wilhelm-Benartzi et al., 2011). Our results on occupational exposure to diesel fumes are also in agreement with the reported literature (Iyer et al., 1990). Our findings of no association between bladder cancer and consumption of artificial sweeteners or coffee are also consistent with the literature (Renwick et al., 1993; Wakai et al., 2004). In opposite, our data analysis for consumption of fruits and vegetables are conflicting with previous reports. Cases were more likely to report consumption of vegetables and fruits than controls (La Vecchia et al., 1996). This might be explained by a reporting bias. It is likely that cases have enhanced their nutritional habits following diagnosis, which could explain our observed findings.

Our findings on prostate-related morbidity may be clinically significant. Potentially, partial blockage of bladder outflow due to prostate-related disorders may increase contact time of chemicals with mucosal cell lining, thereby increasing the odds of malignant transformation.

Furthermore, the observed associations with smoking and exposures to occupational diesel or fuel combustion could be linked with exposures to arylamine derivatives, which have been reportedly implicated with a higher bladder cancer risk (Vineis et al., 2001; Band et al., 2005; Kellen et al., 2007).

In the context of genetic risk factors, two important findings were observed. First, family cancer history is confirmed as a risk factor for bladder cancer in Lebanon. Second, cases and controls showed distinct clustering patterns of *NAT1* alleles. Knowing the high frequency of *NAT1*14A* in Lebanese based on a previous study we conducted in a Lebanese community residing in Detroit, Michigan, our study suggests *NAT1*14A* as a possible biomarker (Dhaini et al., 2000). Our study did not investigate schistosomiasis as a potential risk factor since this infection is very rare in Lebanon, and may be more relevant in countries like Egypt (Mostafa et al., 1999). Schistosomiasis is known to be associated with squamous cell carcinoma (SCC) (Zheng et al., 2012). The majority of our cases had papillary transitional cell carcinoma and absence of SCC.

This study has few limitations. One limitation relates to the study's external validity, given the fact that a hospital-based sample might overshadow the ability to generalize to the overall population. Besides, cases' recruitment in the current sample, represented 23% of the cases identified during 2002- 2008 as shown in Figure 1. However, to minimize this selection bias, two major medical centers in two different locations were chosen during recruitment and data collection. Even though cases were more likely to reside in Mount Lebanon whereas more controls resided in Beirut, Mount-Lebanon area is adjacent to Beirut and is as urbanized and represents a natural expansion of the population growth from Beirut. Hence, as far as place of residence, it could be considered that the cases and controls originated from the same pool. Another limitation is the sample size. Although, our sample size was guided by power analysis, it would have been more optimal to include a larger number of cases (double or triple than the minimum sample size calculated). This was not possible due to the high proportion of refusals, deceased, and subjects with no contact information (added together, they make 65% of the total number of identified patients). This limited sample size also explains the observed conservative values of ORs in our study findings, when compared to those published in the literature. Moreover, in a retrospective study, the possibility of recall bias cannot be excluded. We tried to overcome such limitation by initiating cases' recruitment starting with those most recently diagnosed. Controls were also randomly selected based on the premise that came from the population of cases. Another potential limitation of this study is the possibility of other environmental factors and genetic polymorphisms not investigated by the current study, which may modify bladder cancer risk. Further studies should be conducted in the future to address this point.

At the same time, this study also has several strengths. First, the quality of the measures used is high, given the combined data collection of indirect exposure data with genetic analysis. Second, no major challenges existed for adjusting for missing and non-response

data. Third, several statistical models were constructed before determining the adopted best-fit model; and most importantly, all considered models demonstrated similar patterns of the documented observed findings. This reflects a high internal validity of the reported results.

In conclusion, this report highlights smoking, occupational exposure to diesel or combustion fumes, prostate-related morbidity, and N-Acetylation genotype as important risk factors for bladder cancer in Lebanese men. Results presented in the current study emphasize the importance of investigating the etiology of the disease in the context of the communities where it arises. Identified risk factors, particularly smoking, are important in the Lebanese context, given the double burden of the two highest reported cancer incidences: lung and bladder. Our results also highlight the need for both expanding research targeting bladder cancer in the country, and developing constructive preventive strategies to control incidence levels. In fact, our study is the first case-control study in the country that reports on the values of the above-noted established bladder cancer risk factors in the literature, when it comes to the Lebanese context. Although, results confirm established risk factors in the literature, particularly tobacco smoking and occupational exposure to aromatic amines (Jankovic et al., 2007; Kellen et al., 2007), yet, the herein values of the observed ORs are instrumental, when recommending prevention strategies as well as interventions measures to reduce the burden of bladder cancer in the country. We recommend building upon these observations by carrying out larger multi-center studies and incorporating a larger sample size.

Acknowledgements

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