

Risk factors for urinary bladder cancer: a hospital-based case-control study

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The aim of this study was to determine risk factors for urinary bladder cancer at a university hospital in northern Thailand. A case-control study included 85 patients with newly diagnosed urinary bladder cancer, 170 patients without an oncological disease, and controls matched according to gender and age (± 5 years). The results showed that several factors associated significantly with urinary bladder cancer such as prolonged cigarette smoking, continual alcohol consumption and rainwater intake. In addition, some types of employment such as farming, laboring and government service also were related significantly to urinary bladder cancer. Further efforts should be made to find effective strategies for reducing or stopping cigarette smoking and alcohol consumption. Meanwhile, exploration of why rainwater intake, laboring and farming are related to urinary bladder cancer should be performed immediately. **Chiang Mai Medical Journal 2014;53(3):111-117.**

Keywords: risk factors, urinary bladder cancer, hospital-based, case-control study

Urinary bladder cancer (UBC) is the ninth most common cancer worldwide in the general population, and the thirteenth most frequent cause of cancer mortality^[1]. The incidence of UBC is about 12 million per annum, of which 5.4 and 6.7 million occur in developed and developing countries, respectively^[2, 3]. Bladder tumors occur rarely before the age of 40, but are observed most commonly in people aged 70 or more^[4].

In Thailand, UBC ranks seventh among all malignant tumors^[5] and is tenth in cancer deaths^[6]. However, the incidence of bladder cancer in Thailand is lower when compare with western countries.

UBC is attributable to the following factors; 1) demographic factors such as age^[7], gender and race^[8], 2) lifestyle factors such as cigarette smoking^[9,10] and alcohol consumption, and 3) occupational factors^[11] such as leather workers, truck drivers and aluminum production workers^[9], as well as other factors including medical history of urinary bladder infection or urinary bladder cancer^[12]. Among these factors, cigarette smoking is the major risk.

In Thailand, recent studies relating to risk factors for bladder cancer are limited, and a pilot study found that risk factors here had been altered to global changes in UBC exposure and an ever aging population. The objective of this

study was to identify risk factors of UBC in the northern Thai population. The findings obtained in a hospital-based case-control study carried out in a referral university hospital will be useful for preventive measures.

Methods

The research proposal was approved by the institutional review board of Maharaj Nakorn Chiang Mai Hospital, which is a referral hospital for the northern Thai population. A case-control study was carried out from January 1, 2009 to December 31, 2010. Inclusion was limited to patients who were at least 18 years of age, alert, oriented, able to speak Thai, and agreeable to participate by providing written informed consent.

Case-control ratio was 1:2. The cases comprised 85 consecutive patients who had primary histological confirmation of UBC and were admitted to urological surgery wards or seen at urology out-patient departments. The controls consisted of 170 consecutive patients who had no oncological disease and were admitted during the corresponding week to the cardiovascular surgery wards of the same hospital. Matching was carried out according to gender and age (± 5 years). Of patients invited to join the study, none declined participation.

A structured questionnaire was used for interviewing. It was developed from the literature that reflected the objectives of the study. There were 2 parts to the questions; 1) demographic questions such as age, gender, and education and 2) lifestyle questions including cigarette smoking, alcohol consumption and water intake. The questionnaire was approved by five local experts and the content validity index was 0.94. A pilot study for clarification of the questions was applied with 10 patients, who had similar characteristics to the study sample.

For data analysis, the baseline demographic and clinical characteristics of the patient groups were determined using descriptive statistics. The differences between the case and control group were tested by using t-tests and the chi-square test for continuous and categorical variables, respectively. The odds ratio and 95% confidence interval (CI) was calculated in order to find a possible association between UBC and each independent variable.

Results

The mean age of the study group (n=255) was 56.03 ± 14.35 years, with 41.96% of it being 60 years old or more, 51.76% being female and 79.61% single. Approximately two-thirds of the educational backgrounds in both groups were

grade 4-6 (65.88%). Half of them (50.20%) had a monthly income of less than 1,000 baht and 16.86% had no regular income. The majority of them were Buddhist (97.25%) (Table 1).

Comparisons of demographic characteristics revealed no significant differences between the case and control group, except for one exception. The proportion of patients aged 60 years or more being greater in the case group than that in the control group (68.23% vs 28.82%) was the demographic parameter that differentiated between the two groups. Apparently, the case subjects were relatively older than the controls.

Transitional cell carcinoma (TCC) for cases (n=85) was the most common histological type (90.60%), with almost two-thirds of the cases (63.53%) being in stage 0-I, while the remain-

Table 1. Demographic characteristics

Parameter	Case N(%) n=85	Controls N(%) n=170	Total N(%) n=255
Age			
<50	7 (8.24)	81 (47.65)	88 (34.51)
50-59	20 (23.53)	40 (23.53)	60 (23.53)
≥ 60	58 (68.23)	49 (28.82)	107 (41.96)
Gender			
Male	47 (55.29)	76 (44.71)	123 (48.24)
Female	38 (44.71)	94 (55.29)	132 (51.76)
Marital status			
Married	3 (3.50)	19 (11.20)	22 (8.63)
Single	61 (71.80)	142 (83.50)	203 (79.61)
Widowed/ separated	21 (24.70)	9 (5.30)	30 (11.76)
Education			
\geq Grade 9	29 (34.12)	43 (25.30)	72 (28.24)
<Grade 4-6	51 (60.00)	117 (68.82)	168 (65.88)
no formal education	5 (5.88)	10 (5.88)	15 (5.88)
Income (Baht/month)			
>3,000	21 (24.71)	17 (10.00)	38 (14.90)
1,000-3,000	8 (9.41)	38 (22.35)	46 (18.04)
<1,000	15 (17.64)	113 (66.47)	128 (50.20)
No income	41 (48.24)	2 (1.18)	43 (16.86)
Religion			
Buddhist	80 (94.10)	168 (98.80)	248 (97.25)
Other	5 (5.90)	2 (1.2)	7 (2.75)

ing proportion was in stage II. One hundred and nineteen (70%) of 170 subjects in the control group had valvular heart disease, 18.24% had vascular disorder, 10% had septal defect and 1.76% had pericarditis.

With regard to cigarette smoking (Table 2), ex- and current smokers showed no statistically significant differences in smoking habits regarding the amount they smoked (number of rolls/day), type of cigarettes and period of time since quitting. However, those who had smoked for 20 years or longer were associated significantly with a six fold UBC risk, and an odds ratio of 6.23 (95% confidence interval [CI]: 2.69-14.74).

The risk of UBC from habitual alcohol consumption (Table 3) was associated significantly with duration of drinking. People who had been drinking for 25 years or longer had 6 times the risk of contracting UBC when compared with those who had drank for less than 25 years (OR = 6.48, 95% CI=2.29-11.38).

Total fluid intake was associated with water consumption that decreases the risk of UBC (Table 4). However, a significant inverse associa-

tion was observed for water intake (for <4 vs. \geq 4 cups/day, OR=0.27; 95% CI, 0.09-0.78). In addition, types of water was related to the development of UBC, particularly among subjects who relied on drinking rainwater (OR=3.97, 95% CI= 1.09-14.46), and their risk was almost 4 fold.

Regarding occupational history (Table 5), significant associations were found for those who had worked as a farmer (OR=6.87, 95% CI=3.39-13.91), laborer (OR=15.54, 95% CI= 5.73-42.18), or government officer (OR=27.33, 95% CI=7.26-106.01).

Discussion

This study was similar to most previous ones, whereby subjects who had smoked for 25 years or longer had a higher risk (more than six times) of contracting UBC than those who had smoked for a shorter time. Previously, a greater risk of bladder cancer was observed with increased duration of smoking in various populations^[13], whereas a shorter duration was better in terms of reducing bladder cancer risk. Therefore, identifying strategies to reduce and stop smoking is

Table 2. Cigarette smoking

Variable	Cases N (%)	Controls N (%)	OR	(95% CI)
Smoking status	n=85	n=170		
Never smoked	38 (44.71)	97 (57.06)	1	
Ex-smoker	38 (44.71)	70 (41.18)	0.13	(0.03-0.51)
Current smoker	9 (10.58)	3 (1.76)	0.18	(0.05-0.71)
Number of cigarettes/day	n=47	n=73		
<15	35 (74.47)	62 (84.93)	1	
\geq 15	12 (25.53)	11 (15.07)	1.68	(0.67-4.23)
Type of cigarettes***				
Butt cigarette (cigarette with filter)	23 (48.94)	49 (67.12)	3.47	(1.04-11.50)
Cheroot cigarette (cigarette without filter)	29 (61.70)	31 (42.47)	1.30	(0.40-4.21)
Duration since quitting (Years)	n=38	n=70		
<4	11 (28.95)	25 (35.71)	1	
\geq 4	27 (71.05)	45 (64.29)	1.46	(0.62-3.44)
Duration of smoking (Years)	n=47	n=73		
<20	16 (34.04)	59 (80.82)	1	
\geq 20	31 (65.96)	14 (19.18)	6.23**	(2.69-14.74)

Remarks: **significant $p < 0.01$; ***Subject could choose more than one item

Table 3. Alcohol consumption

Variable	Cases N (%)	Controls N (%)	OR	(95% CI)
Alcohol use status	n=85	n=170		
Never	38 (44.71)	97 (57.06)	1	
Ex-drinker	34 (40.00)	65 (38.24)	0.24	(0.09-0.63)
Currently drink	13 (15.29)	8 (4.71)	0.32	(0.12-0.85)
Duration of drinking (years)	n=47	n=73		
<25	23 (48.94)	65(89.04)	1	
≥25	24 (51.06)	8 (10.96)	6.48*	(2.29-11.38)
Duration since quitting (years)	n=34	n=65		
<4	10 (29.41)	23 (35.38)	1	
≥4	24 (70.59)	42 (64.62)	1.31	(0.54-3.22)
Type of alcohol consumed***				
Beer	29 (61.70)	47 (64.38)	0.67	(0.32-1.41)
Liquor	40 (85.11)	55 (75.34)	1.79	(0.89-3.59)
Wine	9 (19.15)	5 (6.85)	2.14	(0.55-8.41)
Fermented herbal alcohol	12 (25.53)	11 (15.07)	1.58	(0.59-4.19)

Remarks: *significant $p < 0.05$; ***Subject could choose more than one item

Table 4. Water consumption

Variable	Cases N (%)	Controls N (%)	OR	(95% CI)
Water source***				
Public water source	31 (36.47)	55 (32.35)	1.37	(0.74-2.52)
Artesian well water	9 (10.59)	19 (11.18)	1.06	(0.47-2.49)
Domestic well water	33 (38.82)	45 (26.47)	1.63	(0.86-3.08)
Bottled water	45 (52.94)	121 (71.18)	0.62	(0.34-1.14)
Rain	8 (9.41)	4 (2.35)	3.97*	(1.09-14.46)
Total water intake/day(cup)	n=85	n=170		
<4	10 (11.76)	6 (3.53)	1	
≥4	75 (88.24)	164 (96.47)	0.27*	(0.09-0.78)

Remarks: *significant $p < 0.05$; *** subject could choose more than one source

warranted, while progressive movement to alert the public of the risks of smoking must be continued.

This study found that prolonged alcohol consumption associated significantly with UBC. When compared to other studies, previous findings were not consistent. For example, Pelucchi and Vecchia (2009)^[14] provided evidence of no association between alcohol drinking and UBC risk. Meanwhile, a study in China found that the consumption of Chinese herbal products

was associated with an increased risk of UBC^[15], while on the other hand, the consumption of wine associated with reduced risk of bladder cancer^[16]. For both habits (smoking and alcohol consumption), an explanation of the risk observed in this study might be attributed to residual confounding by smoking.

The inverse association for water intake and UBC risk in this study is consistent with findings from a previous case-control research conducted in Spain^[17]. Michaud and colleagues (2007)^[17]

Table 5. Occupation

Type	Cases N (%) n=85	Controls N (%) n=170	OR	(95% CI)
No job	20 (23.53)	128 (75.29)	1	
Farmer	29 (34.12)	27 (15.88)	6.87**	(3.39-13.91)
Laborer	17 (20.00)	7 (4.12)	15.54**	(5.73-42.18)
Merchant	6 (7.06)	5 (2.94)	7.68	(2.14-27.54)
Government Officer	13 (15.29)	3 (1.76)	27.33**	(7.26-106.01)

Remarks: **significant $p < 0.01$

found a 53% lower risk of bladder cancer in individuals who consumed at least 1,400 mL of water per day, when compared with those who consumed less than 400 mL/day.

Interestingly, consistent rainwater drinking was related to UBC risk. This information was new and will need to be explored further in order to answer whether carcinogenic contamination was from air pollutant, the process of obtaining rainwater, or the reservoir. The information acquired might prove useful for preventive measures.

This study found that those employed as a government officer had the highest risk of UBC (OR=27.33), which may be due to several reasons. Firstly, the study hospital is a referral center and known as one of the best hospitals in northern Thailand. Secondly, the hospital used is popular among most government officers because it is a government establishment that provides them with almost full medical coverage.

The second and third-highest risks were among laborers and farmers. Laborers are usually hired to work in rice fields, farms, gardens and golf courses. Laborers and agricultural workers are exposed to carcinogens through several routes. In addition to direct contact with carcinogen from fertilizers, pesticides and herbicides, water is a major factor, especially rainwater. Rainfall containing smoke, dust, chemical fumes, and germs flows through the soil into rivers and streams, while picking up fertilizers, pesticides and herbicides. All this can account for carcinogen in the working environment, which

differs from previous western studies^[18], where the highest risks of UBC were seen in waiters, bartenders and occupations related to medicine and health.

Finally, this study has a limitation regarding selection of the control group. Selection of cardiovascular patients might not be suitable for comparison with the case group, because their underlying disease is an important factor that prevents them from activities such as farming and laboring, as well as prolonged smoking or alcohol drinking. Appropriate controls should be planned for future study.

Conclusion

In conclusion, this hospital-based case-control study confirmed the well-known risk factors of UBC, especially prolonged cigarette smoking and continual alcohol consumption. However, some factors such as rainwater intake and occupations like government officer, laborer and farmer also were related to UBC. Therefore, preventive measures against urinary bladder cancer should be planned regarding smoking, alcohol consumption and rainwater intake as well as occupational factors. Lastly, this topic may need further investigation for preventing bladder cancer in agricultural workers in Thailand.

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References

1. **Ferlay J, Shin HR, Bray F, et al.** GLOBOCAN 2008: Cancer incidence and mortality worldwide: IARC Cancer Base No.10 version 1.2. Lyon, France: IARC Press [serial online]. 2010. Available from URL: <http://globocan.iarc.fr> Accessed Dec 16, 2010
2. **Ferlay J, Bray F, Pisani P, Parkin DM.** GLOBOCAN 2002: Cancer incidence, mortality and prevalence worldwide. International Agency for Research on Cancer [IARC] Cancer Base No. 5. version 2.0. Lyon, France: IARC Press [serial online]. 2004. Available from URL: <http://globocan.iarc.fr> Accessed Dec 16, 2010
3. **Garcia M, Jemal A, Ward EM, et al.** Global cancer facts and figs 2007. Atlanta: American Cancer Society 2007.
4. **Visser O, Coeberg J, van Dijck J, Siesling S.** Incidence of cancer in the Netherlands 1998. Utrecht: Association of comprehensive cancer centres; 2002.
5. **National Cancer Institute [NCI], Ministry of Public Health.** Cancer statistic. Bangkok: Ministry of Public Health 2008. (Thai)
6. **Health and Safety Executive [HSE].** The burden of occupational cancer in Great Britain : Technical annex 5: Bladder cancer [serial online]. 2007. Available from URL:<http://www.hse.gov.uk/research/rrhtm/rr595.htm>. Accessed Mar 9, 2008.
7. **American Cancer Society.** Cancer Facts and Figures 2007. Atlanta: American Cancer Society [serial online]. 2007. Available from URL: <http://www.cancer.org/downloads/STT/CAFF2007PWSecured.pdf>. Accessed Mar 9, 2008.
8. **Parkin DM.** The global burden of urinary bladder cancer. *Scand J Urol Nephrol Suppl* [serial online]. 2008; 218:12–20. Available from URL: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2694323/>. doi:10.1080/03008880802285032. Accessed Mar 13, 2008.
9. **Yu MC, Skipper PL, Tannenbaum SR, Chan KK, Ross RK.** Arylamine exposures and bladder cancer risk. *Mutat Res* 2002;506-507:21-8.
10. **Zeeegers MP, Tan FE, Dorant E, van den Brandt PA.** The impact of characteristics of cigarette smoking on urinary tract cancer risk: a meta-analysis of epidemiologic studies. *Cancer* 2000;89:630–39.
11. **Pukkala E, Martinsen JI, Lyng E, et al.** Occupation and cancer—follow-up of 15 million people in five Nordic countries. *Acta Oncologica* 2009;48:646-790.
12. **National Cancer Institute [NCI].** What you need to know about bladder cancer [serial online]. 2002. Available from URL: <http://www.cancer.gov/cancertopics/wyntk/bladder>. Accessed Mar 13, 2008.
13. **Brennan P, Bogillot O, Cordier S, et al.** Cigarette smoking and bladder cancer in men: A pooled analysis of 11 case-control studies. *IJC* 2000;86:289-94.
14. **Pelucchi C, Vecchia C.** Alcohol, coffee, and bladder cancer risk: a review of epidemiological studies. *Eur J Cancer Prev* 2009;8:62-8.
15. **Lai MN, Wang SM, Chen PC, Chen YY, Wang JD.** Population-Based Case–Control Study of Chinese Herbal Products Containing Aristolochic Acid and Urinary Tract Cancer Risk. *J Natl Cancer Inst* 2010;102:179-86.
16. **Mao Q, Lin Y, Zheng X, Qin J, Yang K, Xie L.** A meta-analysis of alcohol intake and risk of bladder cancer. *Cancer Causes Control* 2010;21:1843-50.
17. **Michaud DS, Kogevinas M, Cantor KP, et al.** Total fluid and water consumption and the joint effect of exposure to disinfection by-products on risk of bladder cancer. *Environ Health Perspect* 2007;115:1569–72.
18. **Cassidy A, Wang W, Wu X, Lin J.** Risk of urinary bladder cancer: a case-control analysis of industry and occupation. *BMC Cancer* 2009;15:443.

ปัจจัยเสี่ยงต่อการเกิดมะเร็งกระเพาะปัสสาวะ: การศึกษาย้อนหลังในโรงพยาบาลในกลุ่มศึกษาและกลุ่มควบคุม

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คณะพยาบาลศาสตร์ มหาวิทยาลัยเชียงใหม่

การวิจัยครั้งนี้ เพื่อศึกษาปัจจัยเสี่ยงต่อการเกิดมะเร็งกระเพาะปัสสาวะโดยทำการศึกษาย้อนหลังในกลุ่มศึกษาและกลุ่มควบคุมในโรงพยาบาลมหาวิทยาลัยในภาคเหนือของประเทศไทย โดยกลุ่มศึกษา คือ ผู้ป่วยที่ได้รับการวินิจฉัยเป็นมะเร็งกระเพาะปัสสาวะจำนวน ราย สำหรับกลุ่มควบคุม คือ ผู้ป่วยที่ไม่มีประวัติการเจ็บป่วยด้วยโรคมะเร็งจำนวน 170 ราย ที่มีคุณสมบัติคล้ายคลึงกับกลุ่มศึกษา คือเป็นเพศเดียวกัน และอายุไม่แตกต่างกันเกิน 5 ปี ผลการวิจัยพบว่า มีหลายปัจจัยที่มีความสัมพันธ์กับการเกิดมะเร็งกระเพาะปัสสาวะ เช่น การสูบบุหรี่เป็นเวลานาน การดื่มเครื่องดื่มที่มีแอลกอฮอล์เป็นเวลานาน และการดื่มน้ำฝน นอกจากนี้การประกอบอาชีพบางอย่าง เช่น เกษตรกร รับจ้าง และข้าราชการ มีความสัมพันธ์กับการเกิดมะเร็งกระเพาะปัสสาวะเช่นเดียวกัน ดังนั้นควรมีการศึกษาต่อไปถึงกลยุทธ์ในการลดหรืองดสูบบุหรี่และดื่มสุรา ในขณะที่เดียวกันควรมีการศึกษาว่าทำไมการดื่มน้ำฝน การประกอบอาชีพรับจ้างและเกษตรกรรม ถึงมีความสัมพันธ์กับการเกิดมะเร็งกระเพาะปัสสาวะ **เชียงใหม่เวชสาร 2557;53(3):111-117.**

คำสำคัญ: การศึกษาในกลุ่มศึกษาและกลุ่มควบคุม การศึกษาในโรงพยาบาล ปัจจัยเสี่ยง มะเร็งกระเพาะปัสสาวะ