

RESEARCH ARTICLE

Epidemiologic and Socioeconomic Status of Bladder Cancer in Mazandaran province, Northern Iran

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Abstract

Background: Bladder cancer is one the most common malignancies of the genitourinary tract. The present study aimed to assess the epidemiology, of bladder cancer in Mazandaran, a large province in northern Iran as high-incidence cancer area, during a 2-year period. **Methods:** The data for this study were obtained from the population-based cancer registry of the Vice-Chancellor for Health Affairs of Mazandaran University of Medical Sciences and Mazandaran hospitals between March 1, 2010 and March 1, 2011. Demographic data, including sex, age, residency and symptoms were investigated through careful review of medical records. Using a questionnaire protocol, several variables were assessed for these cases such as smoking, history of opium, vegetable consumption habits, and history of other cancers. **Results:** A total of 112 cases were analyzed, 98 (87.5%) in men and 14 (12.5%) in women (mean age of 68.0±14.6 years). Urban and rural residence were 60.7% and 39.3%. Tobacco and opium use were found in 45.5% and 21.4% of patients, respectively. Approximately 60% consumed vegetables an average of fewer than one time per day. Hematuria was the first symptom in these cases which were mainly diagnosed as having bladder cancer by ultrasonography. **Conclusion:** The results showed that bladder cancer tends to be found in the elderly and the male to female ratio is high. Macroscopic hematuria is a very important symptom for indicating probably urothelial tumor that should be followed up patients with transabdominal ultrasonography as a routine modality.

Keywords: Epidemiology - bladder cancer - socioeconomic factors - northern Iran

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Introduction

Urinary bladder cancer occurs in all countries around the world, and it is the fifth most common cancer in the United States (Oberfield et al., 1996; Ben-Kasus et al., 2005; Yamada et al., 2010). Bladder cancer is the second most common malignancy of the genitourinary tract worldwide after prostate cancer. However, in Iran, it is the most common cancer of the genitourinary system and the third most common cancer in males. The incidence of bladder cancer is lower in Asia as compare to Western European and North America (Johansson and Cohen, 1997).

Globally, approximately 336,000 new cases of bladder cancer occurred in 2000, two-thirds of which were in developed countries. Bladder cancer is the fourth most common cancer in males and the ninth most common in females (Lagwinski et al., 2007; Scélo and Brennan., 2007; Yavari et al., 2009). It accounts for 7% of all new cancer cases, in men and 2% in women (Carel et al., 1999). Bladder cancer is almost three to four times more common in men than in women in most populations (Parkin et al., 2005). This reflects the more frequent exposure of men to

tobacco smoke and occupations that imply contact with certain chemicals, such as aromatic amines, which are the two major recognized risk factors for bladder cancer (Negri and Vecchia, 2001). About 65% of bladder cancer in men and 30% of female cases in some developed countries are exposed to smoking. Cigarette smoking is the most risk factor for inducing bladder cancer (Radosavljević et al., 2004; Scélo and Brennan, 2007). Several studies showed that smokers were susceptible to a 209-fold to 308-fold increase in the risk for bladder cancer (Asgari et al., 2004; Zeegers et al., 2004).

Other risk factors mainly include workers exposed to some toxic agents, less fluid intake and consumption of fruits and vegetables, urinary tract disease (Janković and Radosavljević, 2007; Anderson and Naish, 2008) and elderly persons (Lynch and Cohen, 1995). About 132,000 people each year die from bladder cancer worldwide and the mortality rate is 10 per 100,000 for males and 2.4 pre 100,000 for females. These rates nearly double for developed countries (Schottenfeld and Beebe-Dimer, 2006). Hematuria is the most common presentation of patients with bladder cancer. Other symptoms such as frequency, urgency and dysuria may be the initial

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presentation of bladder cancer. The present study aimed to assess the epidemiology and socioeconomic status of patients with bladder cancer in a 2-year period in Mazandaran province, in northern of Iran.

Materials and Methods

This cross-sectional study involved the population of Mazandaran province, the north Iran. The data for this study were obtained from the population-based cancer registry of the Vice-Chancellery for Health Affairs of Mazandaran University of Medical Sciences and Mazandaran hospitals between March 1, 2010 and March 1, 2011.

Demographic and socioeconomic data for 112 patients with bladder cancer, including sex, age, residency, economic, history of opium and smoking use, vegetable consumption, history of other cancers, diagnosis procedures and presenting symptoms were obtained from their medical records and ask questions from patients or family. The data were analyzed by SPSS software (Chicago, IL, USA, Version 16).

Results

Data from a total of 112 patients were analyzed in this study (Table 1). The male/female ratio was 7:1. Among the various age groups (Table 1), the largest proportion of patients (57 cases, 58.89%) was more than 70 years

Table 1. Distribution of 112 Cases of Bladder Cancer in Mazandaran Province, North of Iran

Characteristic	Frequency	(%)
Age	≤40	5
	41-50	5
	51-60	24
	61-70	21
	71-80	38
	≥81	19
Mean age (years)	68.01±14.6	
Sex	Male	98 (87.5%)
	Female	14 (12.5%)
Place of living	Urban (city)	68 (60.7%)
	Rural (Village)	44 (39.3%)
Education	Illiterate	49 (43.8%)
	Primary and preparatory school	54 (48.2%)
	University or higher	7 (6.25%)
	Unknown	2 (1.78%)
Status of marriage	Single	4 (3.6%)
	Married	107 (95.53%)
	Unknown	1 (0.89%)
Economic	Good	1 (0.4%)
	Fair	65 (58.03%)
	Weak	43 (38.39%)
	Unknown	3 (2.67%)
Occupation	Unemployed	3 (2.7%)
	Member of staff	23 (20.5%)
	Housewife	11 (9.8%)
	Workman	9 (8%)
	Business	24 (21.4%)
	Farmer	34 (30.4%)
	Unknown	8 (7.1%)

old. Sixty-eight cases (60.7%) were from the cities of Mazandaran province. Only seven cases (6.25%) have a university grade education. The incidence of bladder cancer was more among married patients with 95.53%. Most of the cases (58.03%) have a fair economy. Forty-Fifty-two cases (46.42%) have smoked cigarette. Most of the patients (76%) have consumed the vegetables along main food less than one time per day (Table 2). Only twenty-five cases have a history of cancer in their family, more than half cases have a history of genitourinary surgery before diagnosis of bladder cancer. Thirty cases (19.64%) had a history of consume of opium addicts (Table 2). Hematuria was mainly a first sign related to

Table 2. Living Habits Among Bladder Cancer Patients in Mazandaran Province

Characteristic	Frequency	(%)
Smoking	No smoking	56 (50.00)
	Smoking	52 (46.42)
	Unknown	4 (3.57)
Sport (hour per day)	No	77 (68.80)
	<1 h	12 (10.70)
	>1 h	15 (13.40)
	Unknown	8 (7.10)
History of opium	Yes	22 (19.64)
	No	87 (77.67)
	Unknown	3 (2.67)
Vegetable consumption per day	0	40 (35.71)
	1	46 (41.07)
	2	9 (8.00)
	3	11 (9.82)
	>3	1 (0.90)
	Unknown	5 (4.46)
Weight of patient	High	29 (22.90)
	Middle	57 (51.40)
	Thin	18 (17.90)
	Unknown	8 (7.10)

Table 3. History of Diseases Among Bladder Cancer Patients in Mazandaran Province

Characteristic	Frequency	(%)
History of cancer in family	Yes	25 (22.32)
	No	82 (73.21)
	Unknown	4 (3.57)
History of genitourinary surgery	Yes	57 (50.90)
	No	47 (42.00)
	Unknown	8 (7.10)

Table 4. Symptoms and Metastasis Related to Bladder Cancer Patients

Characteristic	Frequency	(%)
First symptoms	Urinary tract infection	2 (1.80)
	Hematuria	55 (49.10)
	Difficulty urinating	7 (6.20)
	Frequent urination	4 (3.60)
	Dysuria	14 (12.50)
	Asymptomatic	14 (12.60)
	Unknown	16 (14.30)
Metastasis	Non	78 (69.64)
	Liver	8 (7.14)
	Lung	4 (3.57)
	Prostate	8 (7.14)
	Bone	1 (0.90)
	Unknown	13 (11.60)

Table 5. Clinical and Para-Clinical and Microscopic Methods for Diagnosis of Bladder cancer

Method		Frequency	(%)
Clinical and para-clinical	Clinical	6	(5.4)
	X-ray	8	(7.1)
	Sonography	83	(74.1)
	CTscan	5	4.5)
	MRI	1	(0.9)
	Unknown	9	(8.0)
Microscopic	Main pathology	79	(70.5)
	Metastatic	1	(0.9)
	Cytology	4	(3.6)
	Hematology	2	(1.8)
	Unknown	26	(23.2)

bladder cancer in these cases (Table 4). Seventy-three cases (69.64%) have not shown any metastasis due to bladder cancer. However, prostate and liver were main metastasis organ caused by this cancer. Sonography was first and main para-clinical procedure for diagnosis of bladder cancer in these patients. However, forty-four cases applied more than one procedure for diagnosis. Most of the bladder cancer was verified with respect to pathology of sample of cancerous tissue (Table 5).

Discussion

This study analyzed the epidemiological features of 112 patients with bladder cancer during a 2-year period in Mazandaran province, in the north of Iran. Bladder cancer is the fourth most common malignancy among men in the Western world, following prostate, lung, and colon cancers (Kirkali et al., 2005). Murta-Nascimento reported that bladder cancer was the seventh most common cancer worldwide in men (10.1 new cases per 100,000 person-years) and the 17th in women (2.5 per 100,000 person-years) (Murta-Nascimento et al., 2007). In Iran, it is 5th in men (Cancer Occurrence in Iran in, 2002; an International Perspective, 2005). These differences in incidence rates between genders have been attributed in part to differences in smoking habits (Murta-Nascimento et al., 2007). In our study, mean age of this case was 68.01±14.6 years old. Some researcher reported that a mean age of 65.1, 61.9 and 55.5 years old from the south of Iran, the capital of Iran and Pakistan, respectively (Badar et al., 2009; Yavari et al., 2009; Salehi et al., 2011). The proportion of these patients with older than 71 years old was same in the previous study (Salehi et al., 2011) and higher than other studies reported from other studies reported from Iran (Ahmad et al., 2003; Farahmand et al., 2009; Yavari et al., 2009). Male to female ratio generally in the incidence of bladder cancer is between 3 and 4; however, this ratio is varied in different part of the world. It has been reported as 1.1:1.0 in East Africa, 2.1:1.0 in South Africa, 5:1 in Northern Africa and 5.1:1.0 in several areas of southern Europe (Scélo and Brennan, 2007; Yavari et al., 2009), and 4.8:1 in the south of Iran (Salehi et al., 2011). It was interested that in this study, we were found this ratio is 7:1 that is higher than more middle range ratio from other studies. However, it was about same to other report from Iran (Yavari et al., 2009). The excess of bladder cancer in

men versus women is not fully explained by differences in smoking habits, opium and occupation (the 3 most well-known risk factors for bladder cancer) (Kirkali et al., 2005; Samanic et al., 2006). Usually, the smoking habit is most popular in male than women in Iran; this risk factor may be affected on higher ratio male to women in our cases. Due to low prevalence of smoking, tobacco was not a relevant risk factor in women (Bedwani et al., 1997). In our sample, 46.42% had a positive history of tobacco use. In addition, 21.4% of the patients we analyzed were opium users. Cigarette smoking is one of the most common risk factors for bladder cancer. Since cigarette smoking increased bladder cancer risk 2-4 fold, and 30-50% of all bladder cancers are caused by cigarette smoking (Bedwani et al., 1997; Kirkali et al., 2005) Some studies in Iran have found that opium consumption can increase the risk of bladder cancer (Behmard et al., 1981; Asgari et al., 2004; Hosseini et al., 2010). In this study, more than 70% cases have not vegetable's consumption habits more than one time per day. Moreover, it has been demonstrated that vegetables with antioxidant properties have possessed protective effects (La Vecchia and Negri, 1996). A meta-analysis reported an increased risk associated with diets with low fruit content (Steinmaus et al., 2000) In a population-based case-control study was shown that vegetable consumptions in the control group were significantly more than in patients with bladder cancer (Shakhssalim et al., 2010). Twenty-two percent of our cases had a history of cancer in their family. In a cohort study of Scandinavian countries, it was estimated that 31% of the risk of bladder cancer might be explained by heritable factors, although the estimation was not statistically significant (Aben et al., 2002). It seems that a slightly increased risk of bladder cancer is associated with individuals with a family history of cancer (Murta-Nascimento et al., 2007). Most of the patients with bladder cancer had hematuria as a first sign for future follow up. It is important for awareness for any hematuria in patients referred to urologist. It is widely accepted that macroscopic hematuria is indicative of an urothelial tumor, until proven otherwise. Researchers observed a 65% higher likelihood that men would be referred to an urologist than women by their primary provider for new onset or recurrent hematuria (Johnson et al., 2008; Fajkovic et al., 2011). A delay in urologic referral for hematuria could result in a delay in diagnosis of potentially life threatening bladder cancer and upstaging (Nielsen et al., 2007; Gore et al., 2009). Approximately 47% of patients demonstrated distant metastasis, which prostate and liver are more common than other organs.

Sonography is the main procedure for diagnosis of these cases. Actually, ultrasonography is more available than CT-scan and MRI in Mazandaran hospitals. Transabdominal ultrasonography is the preferred imaging machine for assessment of bladder cancer, including noninvasive, easily repeatable and reproducible, relatively inexpensive, readily available, can be performed on an outpatient basis, not necessary any advanced trained personnel (Malone, 1989; Yip et al., 1998). Dibb established that transabdominal ultrasonography is a useful diagnostic modality for screening and detecting bladder tumors in patients with painless gross hematuria

(Dibb et al., 2001).

In conclusion, comparisons with previous studies showed that bladder cancer tends to elderly and male to female ratio is high. Low vegetable's consumption habit is more risk of bladder cancer. Macroscopic hematuria is a very important symptom for indicating probably urothelial tumor that should be follow up patients with a common modularity as transabdominal ultrasonography.

References

- Aben KK, Witjes JA, Schoenberg MP, et al (2002). Familial aggregation of urothelial cell carcinoma. *Int J Cancer*, **98**, 274-8.
- Ahmad E, Ghasemkhani O, Dastoori P (2003). Recurrence rate and prognostic factors of superficial bladder cancer in shiraz shahid faghihi hospital during the years 1998-2001. *J Zanjan Univ Med Sci*, **11**, 7-1. (Persian)
- Anderson B, Naish W (2008). Bladder cancer and smoking. Part 1: addressing the associated risk factors. *Br J Nurs*, **17**, 1182-6.
- Asgari MA, Kaviani A, Gachkar L, Hosseini Nasab SR (2004). Is bladder cancer more common among opium addicts? *Urol J*, **1**, 253-5.
- Badar F, Sattar A, Meerza F, Irfan N, Siddiqui N (2009). Carcinoma of the urinary bladder in a tertiary care setting in a developing country. *Asian Pac J Cancer Prev*, **10**, 449-52.
- Bedwani R, el-Khwsy F, Renganathan E, et al (1997). Epidemiology of bladder cancer in Alexandria, Egypt: tobacco smoking. *Int J Cancer*, **73**, 64-7.
- Behmard S, Sadeghi A, Mohareri MR, Kadivar R (1981). Positive association of opium addiction and cancer of the bladder. Results of urine cytology in 3,500 opium addicts. *Acta Cytol*, **25**, 142-6.
- Ben-Kasus T, Ben-Zvi Z, Marquez VE, Kelley JA, Agbaria R (2005). Metabolic activation of zebularine, a novel DNA methylation inhibitor, in human bladder carcinoma cells. *Biochem Pharmacol*, **70**, 121-33.
- Carel R, Levitas-Langman A, Kordysh E, Goldsmith J, Friger M (1999). Case-referent study on occupational risk factors for bladder cancer in southern Israel. *Int Arch Occup Environ Hlth*, **72**, 304-8.
- Dibb MJ, Noble DJ, Peh WC, et al (2001). Ultrasonographic analysis of bladder tumors. *Clin Imaging*, **25**, 416-20.
- Fajkovic H, Halpern JA, Cha EK, et al (2011). Impact of gender on bladder cancer incidence, staging, and prognosis. *World J Urol*, **29**, 457-63.
- Farahmand M, Khademolhosseini F, Medhati M, et al (2009). Trend of bladder cancer in fars province, Southern Iran, 2002-2006. *Iran Red Cres Med J*, **11**, 470-2.
- Gore JL, Lai J, Setodji CM, Litwin MS, Saigal CS (2009). Mortality increases when radical cystectomy is delayed more than 12 weeks: results from a surveillance, epidemiology, and end results-medicare nalysis. *Cancer*, **115**, 988-96.
- Hosseini SY, Safarinejad MR, Amini E, Hooshyar H (2010). Opium consumption and risk of bladder cancer: A case-control analysis. *Urol Oncol*, **28**, 610-6.
- Janković S, Radosavljević V (2007). Risk factors for bladder cancer. *Tumori*, **93**, 4-12.
- Johansson SL, Cohen SM (1997). Epidemiology and etiology of bladder cancer. *Semin Surg Oncol*, **13**, 291-8.
- Johnson EK, Daignault S, Zhang Y, Lee CT (2008). Patterns of hematuria referral to urologists: does a gender disparity exist? *Urology*, **72**, 498-502.
- Kirkali Z, Chan T, Manoharan M, et al (2005). Bladder cancer: epidemiology, staging and grading, and diagnosis. *Urology*, **66**, 4-34.
- La Vecchia C, Negri E (1996). Nutrition and bladder cancer. *Cancer Causes Control*, **7**, 95-100.
- Lagwinski N, Thomas A, Stephenson AJ, et al (2007). Squamous cell carcinoma of the bladder: a clinicopathologic analysis of 45 cases. *Am J Surg Pathol*, **31**, 1777-87.
- Lynch CF, Cohen MB (1995). Urinary system. *Cancer*, **75**, 316-29.
- Malone PR (1989). Transabdominal ultrasound surveillance for bladder cancer. *Urol Clin North Am*, **16**, 823-7.
- Murta-Nascimento C, Schmitz-Dräger BJ, Zeegers MP, et al (2007). Epidemiology of urinary bladder cancer: from tumor development to patient's death. *World J Urol*, **25**, 285-95.
- Negri E, La Vecchia C (2001). Epidemiology and prevention of bladder cancer. *Eur J Cancer Prev*, **10**, 7-14.
- Nielsen ME, Palapattu GS, Karakiewicz PI, et al (2007). A delay in radical cystectomy of >3 months is not associated with a worse clinical outcome. *BJU Int*, **100**, 15-20.
- Oberfield RA, Zinman LN, Leibenhaut M, Girshovich L, Silverman ML (1996). Management of invasive squamous cell carcinoma of the bulbomembranous male urethra with co-ordinated chemo-radiotherapy and genital preservation. *Br J Urol*, **78**, 573-8.
- Parkin DM, Bray F, Ferlay J, Pisani P (2005). Global cancer statistics, 2002. *CA Cancer J Clin*, **55**, 74-108.
- Radosavljević V, Janković S, Marinković J, Dokić M (2004). Non-occupational risk factors for bladder cancer: a case-control study. *Tumori*, **90**, 175-80.
- Salehi A, Khezri AA, Malekmakan L, Aminsharifi A (2011). Epidemiologic status of bladder cancer in Shiraz, southern Iran. *Asian Pac J Cancer Prev*, **12**, 1323-7.
- Samanic C, Kogevinas M, Dosemeci M, et al (2006). Smoking and bladder cancer in Spain: effects of tobacco type, timing, environmental tobacco smoke, and gender. *Cancer Epidemiol Biomarkers Prev*, **15**, 1348-54.
- Scélo G, Brennan P (2007). The epidemiology of bladder and kidney cancer. *Nat Clin Pract Urol*, **4**, 205-217.
- Schottenfeld D, Beebe-Dimmer J (2006). Alleviating the burden of cancer: a perspective on advances, challenges, and future directions. *Cancer Epidemiol Biomarkers Prev*, **15**, 2049-55.
- Shakhssalim N, Hosseini SY, Basiri A, et al (2010). Prominent bladder cancer risk factors in Iran. *Asian Pac J Cancer Prev*, **11**, 601-6.
- Steinmaus CM, Nuñez S, Smith AH (2000). Diet and bladder cancer: a meta-analysis of six dietary variables. *Am J Epidemiol*, **151**, 693-702.
- Yamada T, Tsuchiya K, Kato S, et al (2010). A pretreatment nomogram predicting recurrence- and progression-free survival for nonmuscle invasive bladder cancer in Japanese patients. *Int J Clin Oncol*, **15**, 271-9.
- Yavari P, Sadrolhefazi B, Mohagheghi MA, Mehrazin R (2009). A descriptive retrospective study of bladder cancer at a hospital in Iran (1973-2003). *Asian Pac J Cancer Prev*, **10**, 681-4.
- Yip SK, Peh WC, Tam PC, Li JH, Lam CH (1998). Day case hematuria diagnostic service: use of ultrasonography and flexible cystoscopy. *Urology*, **52**, 762-6.
- Zeegers MP, Kellen E, Buntinx F, van den Brandt PA (2004). The association between smoking, beverage consumption, diet and bladder cancer: a systematic literature review. *World J Urol*, **21**, 392-401.