Scholars Journal of Applied Medical Sciences (SJAMS)
Abbreviated Key Title: Sch. J. App. Med. Sci.
ISSN 2320-6691 (Online)
ISSN 2347-954X (Print)

A Unit of Scholars Academic and Scientific Society, India
www.saspublishers.com

Urology

Urothelial Carcinoma of Urinary Bladder: An Epidemiological Study in a Tertiary Care Centre of Eastern India

Souvik Chatterjee[1], Pramod Kumar Sharma[2*], Kanishka Samanta[3], Anshuman Aashu[4], Sudipta Kumar Singh[5], Soumendranath Mandal[6], Dilip Karmakar[7]

[1]MS General Surgery DNB General Surgery, MCh Urology Resident
[2] MS General Surgery MCh Urology, DNB Urology
[3-5] MS General Surgery MCh Urology Resident
[6] MS General Surgery MCh Urology
[7] MS General Surgery MCh Urology
Department of Urology, Calcutta National Medical College and Hospital, Kolkata, 32, Gorachand Road, Kolkata-14, West Bengal, India

Original Research Article

***Corresponding author**
Pramod Kumar Sharma

Article History
Received: 15.08.2018
Accepted: 25.08.2018
Published: 30.08.2018

DOI:
10.36347/sjams.2018.v06i08.040

Abstract: Urothelial malignancy of urinary bladder is the most common malignancy of urinary tract. It is the sixth most common malignancy in India. Few literatures are available on epidemiological data of urinary bladder cancer at eastern part of India. The aim of our study is to provide the epidemiological scenario and detecting risk factors contributing to the urothelial carcinoma of bladder in the southern part of West Bengal. It is a prospective observational study. All data regarding the urinary bladder tumors were recorded in Case Record Proforma (CRP) of Bladder Tumour Registry, department of Urology, Calcutta National Medical College, Kolkata, from June, 2015 to May, 2018. Initially total 124 patients were enrolled for the study; later only 120 patients were included as they had biopsy proven urothelial carcinoma on histopathological report of tissues obtained by transurethral resection. In our study, males were more frequently (71.6%) affected than females (28.33%) and urothelial malignancy was more prevalent in Hindus. On blood group analysis, disease was more prevalent in individuals with 'B' positive blood group. Tobacco smoking was revealed to be an important causative factor (67.5%). Low socioeconomic class (80.83%), less water intake (56.67%) were important contributory factors. Intake of alcohol and caffeine are probably confounding factors. High grade tumors with the high stage malignancy were more prevalent among aged patients. The study suggests that epidemiological survey using bladder tumor registry should be incorporated in the evaluation of bladder cancer to formulate any disease control programme.

Keywords: Urothelial Carcinoma, Bladder Cancer, Epidemiology, Risk factors.

INTRODUCTION

Urothelial carcinoma is the most common malignancy of urinary bladder. In the Western world, it is the fourth most common cancer in men and eighth most common in women [1]. Urothelial malignancy is a heterogeneous disease and its natural history is not fully understood till date. An understanding of natural history and associated risk factors is essential component for prevention of the disease. The cigarette smoking is the most important among the various known risk factors. It is responsible for almost 50% cases of bladder cancer in men and about 33% of cases in women in the USA [2]. In India, especially for the eastern India, there is increasing incidence of urinary bladder cancer, even in younger population. There are paucity of data regarding epidemiological overview of the disease and risk factors associated with urothelial malignancy [3]. There are few publications which provide the picture regarding epidemiology of urothelial cancer in northern part and western part of India, which is really lacking in eastern part of the country. The aim of our study is to provide the epidemiological scenario and detecting risk factors contributing to the urothelial carcinoma of bladder in the southern part of West Bengal. In this study, we also consider the histopathological grading of urothelial cancers of the urinary bladder according to World Health Organization (WHO) and the International Society of Urological Pathologists (ISUP) classification [4].

MATERIALS AND METHODS

Our study is a prospective observational study, which was conducted from June, 2015 to May, 2018. We have included total 124 newly diagnosed bladder

tumor patients, who had attended in the department of Urology, Calcutta National Medical College and Hospital, Kolkata. When bladder tumor was identified on cystoscopy, the location, number, and nature of the disease were recorded in a Case Record Proforma (CRP) of Bladder Tumour Registry, department of Urology. For confirmation of diagnosis, transurethral resection of the bladder tumor (TURBT) or biopsy was performed using monopolar current. The deep biopsy was taken separately from tumor bed to include the detrusor muscle. Report of histopathological examination (HPE) of tissue obtained by TURBT is essential for detection of tumor stage and grade of urothelial malignancy. Only 120 patients were found to have transitional cell carcinoma (TCC) on HPE.

STATISTICAL ANALYSIS

Data obtained by CRP in our study were analyzed using 'Medcalc' software (version 16.8). Categorical data were analysed by chi-square test and 'p' values <0.05 were considered to be statistically significant.

RESULTS

The table 1 shows distribution of age among the study population. Most of our patients are between the age group of 50 – 70 years, whereas median age is 62 years. The table 2 depicts epidemiological profile and distribution of risk factors among the study population. It shows that preponderance urinary bladder urothelial malignancy among male patients (71.67%), and patients of low socioeconomic class (80.83%). Most of the affected individuals belong to Hindu community (60.83%). On blood group analysis, it has been found that patients having the blood group of 'B' positive are more frequently (35.83%) affected, which is closely followed by patients with blood group of 'O' positive (32.5%).

Table-1: Division of the patients according to the age

Age division (Years)	No. of patients (Total patients = 120)	Percentage of the total patients
30 – 39	7	5.83%
40 – 49	15	12.5%
50 – 59	37	30.83%
60 – 69	46	38.33%
70 – 79	13	10.83%
80 – 90	2	1.67%

Urothelial malignancy is more prevalent among the patients taking non-vegetarian diet (85.83%). Tobacco smoking (67.5%) is strongly related with bladder cancer whereas there is no such relation is detected with tobacco chewing (31.67%). Although alcohol intake (60.83%) and caffeine intake (90%) are found to be prevalent among cancer patients, they are probably confounding factor. Less amount of water (less than or equal to 1.5 litters per day) intake (56.67%) is a significant contributory factor. Subjects of our study population belong to diverse occupations. Most of the male patients are farmer (31.67%) and labour (25%). Only 4.17% of the patients are working in dye and rubber industry. Among 34 female patients, 31 subjects are housewife. Only 7.5% of the patients are taking analgesic medications for long duration for arthritic joint pains. Few patients are found to have relevant history of radiation exposure (3.33%) and family history of malignancy (4.17%).

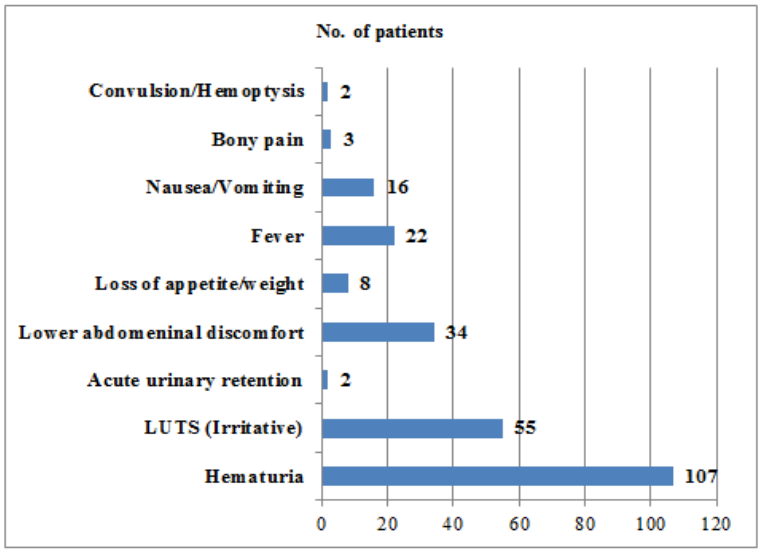

Fig-1: Presenting symptoms

Table-2: Epidemiological characteristics of patients and distribution of risk factors

Patient characteristics and risk factors				No. of patients (Total patients = 120)	Percentage of patients
Sex distribution	Male			86	71.67%
	Female			34	28.33%
Religion	Hindu			73	60.83%
	Muslim			47	39.17%
Occupations	Farmer			38	31.67%
	Labour			30	25%
	Dye and rubber industry worker			5	4.17%
	Driver			4	3.33%
	Housewife			31	25.33%
	Others			12	10%
Socioeconomic class	Low			97	80.83%
	Medium			21	17.5%
	High			2	1.67%
Blood groups	A	Positive		16	13.33
		Negative		4	3.33%
	B	Positive		43	35.83%
		Negative		14	11.67%
	O	Positive		39	32.5%
		Negative		1	0.83%
	AB	Positive		2	1.67%
		Negative		1	0.83%
Food habit	Vegetarian			17	14.17%
	Non-vegetarian			103	85.83%
Daily water intake	≤1.5 lit			68	56.67%
	>1.5 lit			52	43.33%
Caffeine intake	Yes			108	90%
	No			12	10%
Smoking habit	Yes			81	67.5%
	No			39	32.5%
Tobacco chewing	Yes			38	31.67%
	No			82	68.33%
Alcohol intake	Yes			73	60.83%
	No			47	39.17%
Long term analgesic use	Yes			9	7.5%
	No			111	92.5%
History of radiation exposure	Yes			4	3.33%
	No			116	96.67%
Family history of malignancy	Yes	Breast CA		1	4.17%
		GU malignancy		2	
		GI malignancy		2	
	No			115	95.83%

Most of our patients (107 patients among 120 subjects) presented with painless hematuria. Irritative lower urinary tract symptoms were present among 45.83% of patients. Lower abdominal discomfort is another frequent mode of presentation. (Figure 1)

Table 3 shows that single lesion was more prevalent (53.33%) among the subjects and most of the lesions were located at lateral wall (75%) and posterior wall and trigone (20%) of urinary bladder. HPE revealed that 79.17% of our patients were having non-muscle invasive bladder cancer (NMIBC) and low grade urothelial carcinoma was more prevalent (47.5%). High grade malignancy was found in 41.67% of the patients. Carcinoma in-situ was present in 21.67% of patients.

Table-3: Tumor characteristics

Tumor characteristics		No. of patients (Total patients = 120)	Percentage of patients
No. of lesions	Single	64	53.33%
	Multiple	56	46.67%
Tumor location	Posterior & trigone	24	20%
	Anterior	3	2.5%
	Lateral (right/left)	90	75%
	Dome	3	2.5%
Staging of tumors	NMIBC	95	79.17%
	MIBC	25	20.83%
Grading of tumors	PUNLMP	13	10.83%
	Low grade	57	47.5%
	High grade	50	41.67%
Other Cystoscopic characteristics	Visualization of ureteric orifices	88	73.33%
	Involvement of UB neck	22	18.33%
	Presence of CIS	26	21.67%

On analysis of the grade and stage of the cancer according to age and sex distribution, we have found a significant relationship between age of the patient with the grade and stage of the tumor. High grade tumors with the high stage malignancy were more prevalent among aged patients (Table 4). There was no correlation between genders of the patients with the histopathological characteristics of tumour.

Table-4: Impact of age and gender on tumor grade and stage

Tumor		Age			Gender		
		<60 yrs	≥60 yrs	p Value	Male	Female	p Value
Grade	PUNLMP	8	5	0.00001	7	6	0.214
	Low	41	16		40	17	
	High	10	40		39	11	
Stage	NMIBC	52	43	0.0173	65	30	0.124
	MIBC	7	18		21	4	
Smoking	Yes	38	43	0.477	80	1	0.0001
	No	21	18		6	33	
Tobacco chewing	Yes	23	15	0.09	37	1	0.0001
	No	36	46		49	33	

Smoking and tobacco chewing is statistically more prevalent among male patients, though no such relation with increment of age.

DISCUSSION

Urinary bladder cancer is sixth most common malignancy in India [5]. Urothelial carcinoma of bladder is common in 6th decade of life [6]. In our study, maximum numbers of patients are between 50 – 70 years. High grade tumors and muscle invasive bladder carcinoma (MIBC) are more common in elder age group individuals. Young individuals generally suffer from low-grade and low-stage tumors than their elderly counterparts and their tumors take more indolent course [7]. Urothelial carcinoma is biologically distinct from that of the elderly individuals. The genetic alteration seen among older patients are generally rare in young patients [8].

Mungan *et al*. [9] found urinary bladder cancer is 3 to 4 times more prevalent in male patients than in females. In present study, we also finds that incidence of carcinoma is almost 3 times more prevalent in men. The increased frequency of bladder cancer among male individuals is explained by tobacco smoking and more exposure to environmental toxin in men than women. Different studies [10-12] suggest that parity has got a protective role in urothelial carcinoma as it is more predominate in nulliparous women. In present study, we did not find such relationship. In animal experimental studies, androgenic hormone treated rats developed more bladder malignancies than estrogenic hormone treated animals [13]. It is concluded from those studies that androgenic hormones may have an important role in oncogenesis [14]. In present study, most of the study subjects belong to Hindu community. This finding is not at par with other studies as they did not find any religious variation in development of the disease. It is evident that biological variations among different races have an important role in modification of various phases of carcinogenesis. African Americans have only half the risk of development of urothelial malignancies than white Americans [15].

Tobacco smoking is well established risk factor for development of urothelial tumor. There are evidences in literatures that populations with high smoking rates may have low bladder cancer rates [16]. This discrepancies may explained by two forms of N-acetyltransferase- 2. The slow acetylators are more likely to develop bladder cancer than rapid acetylators [17]. There is strong relationship between bladder cancer with amount and duration of smoking [2]. In present study, smoking and tobacco chewing are more prevalent among men. Although alcohol intake (60.83%) and caffeine intake (90%) are found to be prevalent among cancer patients, they are probably confounding factor.

Although familial bladder cancer is a rare entity [18], Goldgar *et al*. [19] has showed clustering of urothelial cancer in families with development of malignancies among young individuals. In our study, only 5 of our patients had family history of malignancies. We had searched for the relationship between blood group and urothelial malignancy. The present study shows that TCC is more prevalent in blood group of 'B Positive' and 'O Positive'. The causal relationship remains inconclusive.

The occupational exposures may account for almost 20% of all bladder cancer. Exposure to naphthylamine and benzidine among dye and rubber industry workers is unequivocally associated with carcinogenesis of bladder cancer [20]. The workers of these industries should therefore be monitored at regular interval [3]. In present study, only 4.17% of individuals were related to dye and rubber industry. Most of the patients in present study were working as farmer and labour, so any firm occupational relationship could not be established with TCC.

In our study, non-vegetarian diet (85.83%) and lesser water intake (56.67%) are more frequently seen to be associated with affected individuals. Lack of affordability of balanced diet containing anti-oxidants like fruits and vegetables in lower socio-economic status is a major contributing factor of development of urothelial malignancy in that social stratum. High Arsenic level in water is found in the regions from where most of the study individuals belong. This may be considered as one of the risk factors for development of urothelial malignancy.

In present study, almost 90% of the patient presented with hematuria, which is at par with the data provided by Gupta *et al*. [21] Irritative LUTS is more frequently seen as presenting symptom among our study population than that of the literatures.

CONCLUSION

Urothelial carcinoma generally present with painless hematuria and irritative LUTS. Male individuals are 3-4 times more frequently affected than their female counter part. Elderly patients present with higher grade and higher stage disease than younger patients. The natural history of urothelial malignancy is not yet fully understood. The present study indicates the need of detailed epidemiological survey for understanding the disease biology. Larger prospective multicentric studies are required to design a well organised disease control programme.

REFERENCES

1. Parkin DM, Whelan SL, Ferlay J, Teppo L, Thomas DB, editors. Cancer Incidence in Five Continents. Vol. VIII. Lyon, France: IARC Publications No. 155; 2002.
2. Kirkali Z, Chan T, Manoharan M, Algaba F, Busch C, Cheng L, Kiemeney L, Kriegmair M, Montironi R, Murphy WM, Sesterhenn IA. Bladder cancer: epidemiology, staging and grading, and diagnosis. Urology. 2005 Dec 1;66(6):4-34.
3. Biswas RR, Mangal S, Guha D, Basu K, Karmakar D. An epidemiological study of cases of urothelial carcinoma of urinary bladder in a tertiary care centre. J Krishna Institute of Med Sci. 2013;2(1):82-.
4. Epstein JI, Amin MB, Reuter VR, Mostofi FK. The World Health Organization/International Society of Urological Pathology consensus classification of urothelial (transitional cell) neoplasms of the urinary bladder. Bladder Consensus Conference Committee. Am J Surg Pathol 1998; 22 (12):1435.48.
5. Ray D, Mondal R, Acharya S, De S, Mondal S. A retrospective study of bladder cancer and the impact of age, sex and smoking habits related clinicopathological correlations in tribal population of Bankura, WB, India. IOSR J Dent Med Sci. 2013;10(4):29-32.
6. Kamangar F, Dores GM, Anderson WF. Patterns of cancer incidence, mortality, and prevalence across five continents: defining priorities to reduce cancer disparities in different geographic regions of the world. Journal of clinical oncology. 2006 May 10;24(14):2137-50.
7. Linn JF, Sesterhenn I, Mostofi FK, Schoenberg M. The molecular characteristics of bladder cancer in young patients. The Journal of urology. 1998 May 1;159(5):1493-6.
8. Wild PJ, Giedl J, Stoehr R, Junker K, Boehm S, van Oers JM, Zwarthoff EC, Blaszyk H, Fine SW, Humphrey PA, Dehner LP. Genomic aberrations are rare in urothelial neoplasms of patients 19 years or younger. The Journal of Pathology: A Journal of the Pathological Society of Great Britain and Ireland. 2007 Jan;211(1):18-25.
9. Mungan NA, Aben KK, Schoenberg MP, Visser O, Coebergh JW, Witjes JA, Kiemeney LA. Gender differences in stage-adjusted bladder cancer survival. Urology. 2000 Jun 1;55(6):876-80.

10. Cantor KP, Lynch CF, Johnson D. Bladder cancer, parity, and age at first birth. Cancer Causes & Control. 1992 Jan 1;3(1):57-62.
11. Green A, Beral V, and Moser K. Mortality in women in relation to their childbearing history. BMJ 1988; 297(6645): 391-5.
12. Plesko I, Dimitrova E, Somogyi J, Preston-Martin S, Day NE, Tzonou A. Parity and cancer risk in Slovakia. International journal of cancer. 1985 Nov 15;36(5):529-33.
13. Reid LM, Leav I, Kwan PW, Russell P, Merk FB. Characterization of a human, sex steroid-responsive transitional cell carcinoma maintained as a tumor line (R198) in athymic nude mice. Cancer Res 1984; 44(10):4560-73.
14. Yeole BB, Jussawalla DJ. Descriptive epidemiological assessment of urinary bladder and kidney cancers in Greater Bombay. Indian J Med Res. 1997;106:517–23.
15. Ries LAG, Eisner MP, Kosary CL, eds. SEER Cancer Statistics Review. 1975-
2002. Bethesda, Md: National Cancer Institute, 2005. Last accessed June 1, 2012.
http://www.seer.cancer.gov/csr/1975_2002
16. Schairer C, Hartge P, Hoover RN, Silverman DT. Racial differences in bladder cancer risk a case-control study. Am J Epidemiol. 1988; 128 (5): 1027.37.
17. Marcus PM, Hayes RB, Vineis P, Garcia-Closas M, Caporaso NE, Autrup H, Branch RA, Brockmöller J, Ishizaki T, Karakaya AE, Ladero JM. Cigarette smoking, N-acetyltransferase 2 acetylation status, and bladder cancer risk: a case-series meta-analysis of a gene-environment interaction. Cancer Epidemiology and Prevention Biomarkers. 2000 May 1;9(5):461-7.
18. Kiemeney LA, Schoenberg M. Familial transitional cell carcinoma. The Journal of urology. 1996 Sep 1;156(3):867-72.
156 (3): 867.72.
19. Goldgar DE, Easton DF, Cannon-Albright LA, Skolnick MH. Systematic population-based assessment of cancer risk in first-degree relatives of cancer probands. JNCI: Journal of the National Cancer Institute. 1994 Nov 2;86(21):1600-8.
20. Markowitz SB and Levin K. Continued epidemic of bladder cancer in workers exposed to ortho-toluidine in a chemical factory. J Occup Environ Med 2004; 46 (2): 154-160.
21. Gupta P, Jain M, Kapoor R, Muruganandham K, Srivastava A, Mandhani A. Impact of age and gender on the clinicopathological characteristics of bladder cancer. Indian J Urol. 2009;25:207–10.