



Urinary Bladder Carcinoma: A Clinicopathological Study

Pathology

Mansi Sharma Senior Resident, Department of Pathology, GMC Jammu,

K. C. Goswami Professor, Department of Pathology, ASCOMS Jammu

Sunil Gupta Professor and Head, Department of Urology and Surgery, GMC Jammu

ABSTRACT

Introduction: Urinary bladder cancer represents a global health problem. The objective of this study was to analyse the clinicopathological features of histologically confirmed urinary bladder carcinoma cases at a tertiary care hospital of Jammu.

Material and Methods: A total of 85 urinary bladder carcinoma specimens received in the department of Pathology, GMC Jammu over a period of 3 years w.e.f. 1st Nov. 2008 to 31st Oct. 2011 were taken up for the study.

Results : The relative frequency of urinary bladder carcinoma among all the malignant tumours was 12.61%. TURBT specimens constituted 87% and cystectomy specimens constituted 13%. The mean age was 59.15 ± 1.65 years with Male: Female ratio 7.5:1. 88% patients were smokers. Most common presenting symptom was hematuria. 83.01% of the growths were on lateral wall and posterior wall and 89.41% growths were grossly polypoidal/ papillary. Most common histological type of urinary bladder carcinoma found was urothelial carcinoma (97.65%) of which 19.27% showed divergent differentiation. Among TURBT urothelial carcinoma cases, 48.61% were high grade but among cystectomy specimen, majority were high grade (81.81%). Muscularis propria was present in 56.76% of TURBT specimens only, out of which 19.05% had pTa, 30.95% pT1 and 50% cases \geq pT2 stage. Out of 11 cystectomy specimens, pTa, pT1, pT2, pT3 and pT4 stages were seen in 0, 3, 5, 3 and 0 cases respectively. Most (82.35%) of the low grade urothelial carcinomas were of pTa and pT1 stage, where as most (72.72%) of the high grade carcinomas were of \geq pT2 stage.

Conclusion : Urinary bladder carcinoma is a common malignancy in patients attending our institution and is diagnosed at a relatively late stage when compared to the west. However, the situation can be improved by adopting proper education and screening programmes to increase awareness among people.

KEYWORDS:

TURBT, Urinary bladder, High grade papillary urothelial carcinoma, PUNLMP.

INTRODUCTION

Urinary bladder cancer represents a global health problem.¹ It accounts for about two-thirds of all urinary cancers and is the ninth most common cancer worldwide, although the rates in different parts of the world vary. It is almost 3-4 times more common in men than in women in most populations.² Bladder cancer incidence and mortality rise sharply with age and about two-thirds of cases occur among persons 65 years and older.³

Risk factors for bladder cancer are smoking, chronic cystitis, pelvic irradiation, cyclophosphamide, genetic predisposition, some occupations, aniline dyes, schistosomal infection and urachal remnants.^{4,7} Most arise from the lateral wall or posterior wall (base) of the urinary bladder.⁸ Pattern of growth of urothelial tumours can be exophytic or endophytic or a combination of both and when exophytic, can be papillary or solid/nodular.⁹

Gross and microscopic painless hematuria is the most common form of presentation followed by symptoms related to associated urinary tract infection (frequency, urgency, dysuria). When ureteral orifice is involved, pyelonephritis/hydronephrosis may follow leading to flank/abdominal pain.¹⁰

Urothelial tumours represent 90% of all bladder tumours and encompass a spectrum from benign papillomas to highly aggressive anaplastic cancers.⁸ Several grading classification systems of urothelial tumours have been proposed over the years. All these have been superseded by the World Health Organization/International Society of Urological Pathology classification.¹¹ Urothelial cancer, mostly found in its pure form, however is known to show divergent differentiation.¹² Squamous cell carcinoma comprises about 5% of all the malignant bladder tumours and adenocarcinoma of the bladder is rare.¹⁰

The most commonly used staging system is the staging proposed by American Joint Committee on Cancer. Non-invasive papillary urothelial carcinoma is designated as pT_{is}; while stages pT₁, pT₂, pT₃ and pT₄ refer to invasion into the lamina propria, muscularis propria, perivesical tissue and adjacent organs respectively. Non-invasive flat urothelial carcinoma i.e. carcinoma-in-situ is stage Tis.¹³

Cystoscopy is the gold standard for the detection of bladder cancer.

Radiographic imaging is a significant part of bladder cancer staging.¹⁴ Exfoliative (urine) cytology is of little practical value in the initial evaluation of most bladder tumours because of its accessibility to formal biopsy.¹⁰ The transurethral resection of bladder tumour (TURBT) is diagnostic, prognostic and often therapeutic.¹⁵ The treatment of bladder cancer depends on grade and stage of tumour.¹⁶

OBJECTIVE

To our knowledge, there is no histopathological study of bladder cancer from Jammu region to compare with other regions. The objective of this study was to analyse the clinicopathological features of histologically confirmed urinary bladder carcinoma cases at a tertiary care hospital of Jammu.

MATERIAL AND METHODS

The study was conducted in the Postgraduate Department of Pathology; Government Medical College, Jammu and consisted of two year retrospective study and one year prospective study. Retrospective study comprised of all urinary bladder carcinoma cases histologically confirmed over a period of two years w.e.f. November 1, 2008 to October 31, 2010. Histopathology requisition forms containing clinical information, along with all the paraffin blocks and stained slides were retrieved and reviewed. Prospective study comprised of urinary bladder carcinoma specimens that were presented in the Department over a period of one year w.e.f. November 1, 2010 to October 31, 2011. In each case, introductory data and clinical information regarding age, sex, type of specimen, clinical symptoms along with USG/cystoscopic findings got from the patient and his/her medical records was noted in a prestructured proforma.

A detailed histopathological examination of the H&E stained sections was carried out under light microscope including histological typing, grading of urothelial tumours and pathological staging. Grading of urothelial tumours was done according to WHO/ISUP classification I1 and pathological staging was done according to system proposed by AJCC13. The data collected was tabulated, analysed and compared to other similar studies.

RESULTS

A total of 85 urinary bladder carcinoma cases were studied. The relative frequency of urinary bladder carcinoma among all the malignant tumours was 12.61%. TURBT specimens constituted 87%

and cystectomy specimens constituted 13%. The mean age ± standard error was 59.15 ± 1.65 years with age ranging from 18-90 years. Maximum cases (57.65%) of urinary bladder carcinoma were in 6th and 7th decade. Male: Female ratio was 7.5: 1.

88% patients were smokers. The incidence of smoking was much higher among males compared to females (94.7% vs. 40%). Most common presenting symptom was hematuria (88.23%) followed by anaemia, irritative urinary symptoms, wasting, abdominal/flank pain, pelvic mass and urinary retention. Average duration of hematuria was 5.83 months. Maximum number (83.01%) of the urinary bladder growths were on lateral wall and posterior wall. 22.35% urinary bladder growths were multicentric, 89.41% growths were grossly polypoidal/ papillary and 10.59% were diffusely infiltrating or solid (nodular). Maximum number (69.37%) of urinary bladder growths were 1-5 cm in size.

Most common histological type of urinary bladder carcinoma found was urothelial carcinoma (97.65%)(Fig.1), 95.18% of which were papillary. 80.72% of urothelial carcinomas were pure and 19.27% showed divergent differentiation; half of which had squamous differentiation (Fig.2). (Table I) Among TURBT urothelial carcinoma cases, half were high grade but among cystectomy specimen, majority were high grade. (TableII)

Table I Histological spectrum of urinary bladder carcinoma. n=85

HISTOLOGICAL TYPE	VARIANT	NO. OF CASES	PERCENTAGE %
Urothelial carcinoma		83	97.65
	Pure Urothelial Carcinoma	67	78.82 (80.72)a
	Urothelial Carcinoma with divergent differentiation	16	18.82 (19.27)a
	• Squamous differentiation	8	9.41
	• Clear cell differentiation		
	• Sarcomatoid differentiation	1	1.17
	• Nested pattern		
	• Multiple variant histologies	1	1.17
		1	1.17
		5	5.88
Adenocarcinoma		1	1.17
Carcinosarcoma		1	1.17
Others		0	0
Total		85	100

a=percentage out of total urothelial carcinoma cases

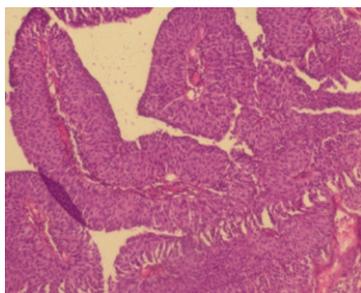


Fig. 1 Low grade papillary urothelial carcinoma. (H & E, 200X)

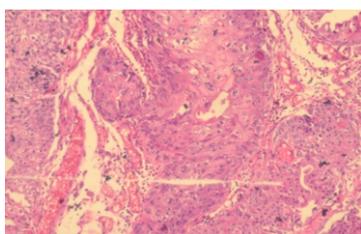


Fig. 2 High grade papillary urothelial carcinoma (small arrows) with focal squamous differentiation (big arrow). (H & E, 200X)

Table II Histological Grading of Urothelial carcinoma cases (WHO/ISUP)

SPECIMEN	PAPILLOMA	PUNLMP	LOW GRADE	HIGH GRADE
TURBT (72)	0 (0%)	1 (1.38%)	35 (48.61%)	36 (50%)
Cystectomy (11)	0 (0%)	0 (0%)	2 (18.81%)	9(81.81%)

Muscularis propria was present in 56.76% (42/74) of TURBT specimens only. Out of these 42 cases, 19.05% had pTa stage, 30.95% had pT1 stage and 50% cases had ≥pT2 stage. Among non muscle invasive tumours, 61.9% invaded lamina propria. Muscularis propria was absent in 43.24% (32/74) of TURBT specimens. Out of these 32 cases, 34.37% were of pTa stage and 65.62% were of ≥pT1 stage. Out of 11 cystectomy specimens, majority (81.81%) had high grade urothelial carcinoma and only 2 cases (18.18%) were of low grade urothelial carcinoma. pTa, pT1, pT2, pT3 and pT4 stages were seen in 0, 3, 5, 3 and 0 cases respectively. 6 cystectomy specimens included lymph nodes, of which 4 cases showed metastatic deposits of urinary bladder carcinoma. None of the cases showed distant metastasis.

Most (82.35%) of the low grade urothelial carcinomas were of pTa and pT1 stage, where as most (72.72%) of the high grade carcinomas were of ≥pT2 stage. None of the high grade urothelial carcinoma had pTa stage. Majority (84.21%) of muscle invasive tumours were high grade, while majority (71.42%) of non-muscle invasive tumours were low grade and PUNLMP. (Table III)

Table III Relation between grading and staging among urothelial carcinoma cases in TURBT specimens with muscularis propria

STAGE GRADE	pTa	pT1	pT2
PUNLMP	1	0	0
LOW GRADE CARCINOMA	7	7	3
HIGH GRADE CARCINOMA	0	6	16

Cohen's Kappa = 0.3284 (0.0735- 0.5833)

DISCUSSION

Urinary bladder carcinoma represents a global health problem. In the USA, bladder cancer is the 4th most common cancer in men and 12th in women.¹ Bladder cancer is the 9th most common cancer accounting for 3.9% of all cancer cases in India.¹⁷ In our study, the relative frequency of urinary bladder carcinoma among all the malignancies is 12.61% which is higher than reported in other studies (2.8 to 11.7)¹⁷⁻²².

In our study, the mean age was found to be 59.15 ± 1.65 years with more than half cases in 6th and 7th decade which is very close to other studies (60.2-60.6)²³⁻²⁵. However male: female ratio in our study was 7.5: 1 which though very close to Indian studies (7.26: 1 to 8.6: 1)^{23,25} but much higher than non-Indian studies (2.46: 1 to 3.9: 1)^{26,27}. This high male: female ratio may be related to a lower number of Indian women who smoke and who work outside home, especially in industries and get exposed to industrial carcinogens like aniline dyes. 25.88% of our patients were smokers. This is slightly higher than other studies (65- 77%)^{25,28,29} and may be due to higher male: female ratio in our study. Hematuria was the most common complaint like other studies^{25,26,30}.

The most common sites of urinary bladder growths were lateral wall and posterior wall in ours as well as previous studies^{18,28}.

In our study, the most common histological type of bladder cancer was urothelial carcinoma (97.65%) followed by adenocarcinoma (1.17%) and carcinosarcoma (1.17%) which is in concordance with most other studies except for the study from Nigeria by Mandong BM et al²⁶ in which squamous cell carcinoma accounted for a large proportion (42.3%). This is because schistosomal infection is not endemic in our country unlike African ones e.g. Nigeria. (Table V) 19.27% of urothelial carcinomas showed divergent differentiation in this study which was in between the percentages seen by Bills A et al (7.27%)³² and Wasco MJ et al (25%)³³. Differences seen may be due to different sampling techniques.

Table IV Comparison of histological spectrum of urinary bladder carcinoma in various studies

Study	Urothelial Carcinoma	Squamous cell Carcinoma	Adenocarcinoma	Others
Mandong BM et al (2000) ²⁶	50.5%	43.3%	3%	3%
Matalka I et al (2008) ²⁴	95.7%	1.7%	2.6%	0%
Badar F et al (2009) ³¹	86%	4%	3%	7%
Gupta P et al (2009) ²⁵	97.71%	1.04%	1.25%	0%
Nakao M et al (2009) ²⁷	97.45%	1.82%	0.73%	0%
Our study	97.65%	0%	1.17%	1.17%

High grade urothelial carcinoma predominated in both TURBT (50%) and cystectomy (81.81%) specimens in our study which is comparable to studies by Gupta P et al²⁵ and Mamoon N et al³⁴ but in some studies^{24,35} low grade carcinoma predominated. Cheng L et al (87.61%)²⁸ found a very high proportion of high grade ca even in TURBT specimens. Muscle invasive disease ($\geq pT2$) had more proportion (55.55%) of cases in our study than previous ones (20- 33%)^{24,30,35,36}. So in our study patients presented at late stages which may be due to lack of awareness among patients. This is also supported by longer average duration of hematuria (5.3 months) before patients present to clinician in our study.

Most of the previous studies^{24, 25, 28, 37} found a correlation between advancing tumour grade and muscle invasion like us. We found that most (82.35%) of the low grade urothelial carcinomas were of pTa and pT1 stage, whereas most (72.72%) of the high grade carcinomas were of $\geq pT2$ stage and none of the high grade urothelial carcinoma had pTa stage. But this association was not statistically significant (Kappa statistics) due to small sample size in our study.

Conclusion Urinary bladder carcinoma is a common malignancy in patients attending our institution and is diagnosed at a relatively late stage when compared to the west. However, the situation can be improved by adopting proper education and screening programmes to increase awareness among people. Our study forms the basis for further evaluation of bladder cancer in Jammu region. There is need for prospective studies with higher number of patients in future for better understanding of the clinicopathological features of bladder cancer in Jammu.

References

- American Cancer Society: Cancer Facts and Figures, 2007.
- Parkin DM, Bray FI, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin* 2005; 55: 74-108.
- World Cancer Report, WHO, 2003.
- American Cancer Society: Detailed Guide: Bladder Cancer, 2009.
- Rehn L. Blasengeschwulste bei fuschin-arbeitern. *Arch. Klin. Chir* 1895 50: 588-600.
- Ferguson AR. Associated bilharziasis and primary malignant disease of the urinary bladder with observation series of forty cases. *J Path Bacteriol* 1911; 16:76-94.
- Nocks BN, Heney NM, Daly JJ. Primary adenocarcinoma of urinary bladder. *Urology* 1983; 21: 26-29.
- Kumar V, Abbas AK, Fausto N (eds), Epstein JI. The lower urinary tract and male genital system. In: Robbins and Cotran Pathologic Basis of Disease, 7th ed. Saunders 2004: 1028-1033.
- Murphy WM, Deana DG. The nested variant of transitional cell carcinoma. A neoplasm resembling proliferation of Brunn's nests. *Mod Pathol*. 1992; 5: 240-243.
- Rosai J. Urinary tract. In: Rosai and Ackerman's Surgical Pathology, 9th ed. Vol 1. Elsevier 2004: 1327-1340. ISBN: 978-81-8147-440-7.
- 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: 1435-48.
- Chalasanani V, Chin JL, Izawa JI. Histologic variants of urothelial bladder cancer and nonurothelial histology in bladder cancer. *Can Urol Assoc J*. 2009; 3(6 Suppl 4): S193-S198.
- American Joint Committee on Cancer. AJCC cancer staging manual. Philadelphia: Lippincott-Raven, 1997: 241-3.
- Jacobs LB, Lee CT, Montie JE. Bladder Cancer in 2010: How Far have We Come? *CA Cancer J Clin* 2010; 60: 244-272.
- Miladi M, Peyromaure M, Zerbib M, Saighi D, Debre B. The value of a second transurethral resection in evaluating patients with bladder tumours. *Eur Urol* 2003; 43: 241-245.
- Raghavan D, Shipley WU, Garnick MB, Russell PJ, Richie JP. Biology and management of bladder cancer. *N Engl J Med*. 1990; 322: 1129-1138.
- Kurkure AP. Cancer incidence and patterns in urban Maharashtra. Consolidated report of the population based cancer registries, Year 2001.
- Sharma S, Nagar R, Singh K, Gupta S, Gupta CL. Transurethral resection in superficial urinary bladder carcinoma. *JK Science* 2000; 2(1): 33-36.
- Roohullah, Nusrat J, Hamdani SR, Burdy GM, Khurshid A. Cancer urinary bladder--5

- year experience at Cinar, Quetta. *J Ayub Med Coll Abbottabad* 2001; 13(2): 14-6.
- Ochicha O, Alhassan S, Mohammed AZ, Edino ST, Nwokedi EE. Bladder cancer in Kano-a histopathological review. *West Afr J Med*. 2003 Sep; 22(3): 202-4.
- Gouda I, Mokhtar N, Bilal D, El-Bolkainy T, El-Bolkainy MN. Bilharziasis and bladder cancer: A time trend analysis of 9843 patients. *Journal of the Egyptian Nat. Cancer Inst., Vol 19, No. 2, June: 2007, 158-162.*
- Pushkar DY, Govorov AV, Matveev VB. The epidemiology of bladder cancer in Russia. *Scand J Urol Nephrol Suppl*. 2008; 218: 21-24.
- Langer B. An epidemiological study of malignancies in Jammu province: A thesis submitted to the Jammu University, 2005.
- Matalka I, Bani-Hani K, Shotar A, Bani Hani O, Bani-Hani I. Transitional cell carcinoma of the urinary bladder: a clinicopathological study. *Singapore Med J* 2008; 49(10): 790-4.
- 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(2): 207-10.
- Mandong BM, Iya D, Obekpa PO and Orkar KS. Urological tumours in Jos University Teaching Hospital, Jos, Nigeria (A hospital based histopathological study). *The Nigerian Journal of Surgical Research* 2000; 2(3-4): 108-113.
- Nakao M, Nakagawa S, Toyoda K, Nukui M, Takada H, Ebisui K, Watanabe H. [Clinico-statistical study on bladder tumor] *Nippon Hinyokika Gakkai Zasshi* 1989; 80(7): 1037-44.
- Cheng L, Neumann RM, Nehra A, Spotts BE, Weaver AL, Bostwick DG. Cancer heterogeneity and its biologic implications in the grading of urothelial carcinoma. *Cancer* 2000; 88: 1663-70.
- Rafique M, Javed AA. Clinico-pathological features of bladder carcinoma: experience from a tertiary care hospital of Pakistan. *Int Urol Nephrol*. 2006; 38: 247-250.
- Al-Bazzaz PH. Stage of urinary bladder cancer at first presentation. *Saudi J Kidney Dis Transplant*. 2009; 20(4): 628-31.
- Badar F, Sattar A, Meerza F, Irfan N, Siddiqui N. Carcinoma of the urinary bladder in a tertiary care setting in a developing country. *Asian Pac J Cancer Prev*. 2009; 10(3): 449-52.
- Bills A, Schenka AA, Ramos CC, Cameiro LT, Araujo V. Squamous and/or glandular differentiation in urothelial carcinoma: prevalence and significance in transurethral resections of the bladder. *Int Urol Nephrol*. 2001; 33(4): 631-3.
- Wasco MJ, Daignault S, Zhang Y, Kunju LP, Kinman M, Braun T, Lee CT, Shah RB. Urothelial carcinoma with divergent histologic differentiation (mixed histologic features) predicts the presence of locally advanced bladder cancer when detected at transurethral resection. *Urology* 2007; 70(1): 69-74.
- Mamoon N, Iqbal MA, Jamal S, Luqman M. Urothelial neoplasia of urinary bladder-comparison of interobserver variability for WHO classification 1972 with WHO/ISUP Consensus Classification 1998. *J Ayub Med Coll Abbottabad* 2006; 18(2).
- Wen YC, Kuo JY, Chen KK, Lin ATL, Chang YH, Hsu YS, Chang LS. Urothelial carcinoma of urinary bladder in young adults - Clinical experience at Taipei Veterans General Hospital. *J Chin Med Assoc*. 2005 June; 68(6): 272-75.
- Sciarrà A, Matteis AD, Mariotti G, Voria G, Lucera R and Disilverio F. Histopathological aspects of transitional cell carcinoma of the bladder: analysis of 20 years experience. *International journal of urology* 2004; 11(7): 467-475.
- Ahmed Z, Muzaffer S, Khan M, Kayani N, Pervez S, Husseini A S and Hasan SH. Transitional cell carcinomas of the urinary bladder. A histopathological study. *J Pak Med Assoc*. Sep 2002; 52(9): 396-8.