

Histopathological spectrum of urinary bladder cancer — experience from a tertiary care hospital

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ABSTRACT

Background: Urinary bladder cancer is a disease of elderly and ranks 9th most common malignancy around the globe and 4th commonest in the men. In Pakistan it is the commonest urological malignancy and 4th commonest in men. Type of the tumor, grade and stage are important prognostic factors. The purpose of the study is to evaluate demography, types of the tumors along with grading and staging in patients presenting at a tertiary care teaching hospital.

Patients and Methods: This was a descriptive cross-sectional study done at the Department of Pathology, King Edward Medical University, Lahore in collaboration with Urology Department of Mayo Hospital Lahore from January 2010 till December 2017. Total of 377 cases with diagnosis of urinary bladder cancer were studied. Demographic details, diagnosis, tumour grade and stage were evaluated. SPSS version 20 was used for data analysis. Descriptive analysis and results were tabulated as frequencies and percentages. The results were then compared with local and international studies.

Results: Out of 377 cases of urinary bladder cancer, 319 were male and 59 were female (male to female ratio of 5.4:1) with mean age of 58.9±12.9 years. Transitional cell carcinoma comprised 92.3% of bladder cancer followed by squamous cell carcinoma (4%) and adenocarcinoma (2.4%). Majority of cancers were high grade (61%). Results of Stage PTa, PT1 and PT2 were 160 (42.4%), 56 (14.8%) and 161 (42.7%) respectively. High grade was associated with higher stage at diagnosis. Total of 41 (25.6%), 36 (64.3%) and 153 (95%) cases of high grade tumors were seen out of 160, 56 and 161 cases against PTa, PT1 and PT2 stages.

Conclusion: Transitional cell carcinoma was the commonest malignant tumor among urinary bladder cancers followed by squamous cell carcinoma and adenocarcinoma. High grade cancer was the most common finding and was associated with advance stage of disease.

Keywords:

Urinary bladder cancer, Histology, Grade, Stage

INTRODUCTION

Urinary bladder cancer (BC) is mainly a disease of elderly with high morbidity and mortality. It is ranked the 9th most common malignant tumor worldwide, 4th in men and 8th in women.¹ In Pakistan it is most common urological malignancy and also 4th commonest cancer in men.² Reported rate from South East Asia is 2.1/100000, whereas higher rate of up to 8.9/100000 have been reported in local studies from Pakistan.^{3,4} The cancer is more common in males and smoking and industrial carcinogens are most commonly implicated etiological factors.³⁻⁸ Transitional cell carcinoma (TCC) is the commonest BC followed by squamous cell

carcinoma (SCC).^{1,3,8,9} However SCC is a significant deviation in Middle East and African countries with relatively high prevalence and incidence due to higher prevalence and association with Schistosomiasis in these regions.⁶ Grade and stage are the main prognostic factors of BC.^{9,10} Some authors used three tiers grading system as grade I, II and III while others limited only to low and high grade.^{4,10}

This study evaluates the histopathological spectrum of BC including demography, frequency of various types and prognostic factors like cancer grade and stage at presentation. Considering the high prevalence of BC in Pakistan, the study will help the clinicians to update and rationalize their treatment plans more effectively.

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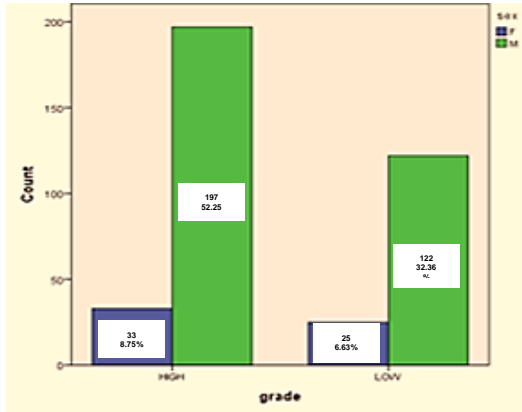


Figure 1: Distribution of grade against sex. M=Male, F=Female

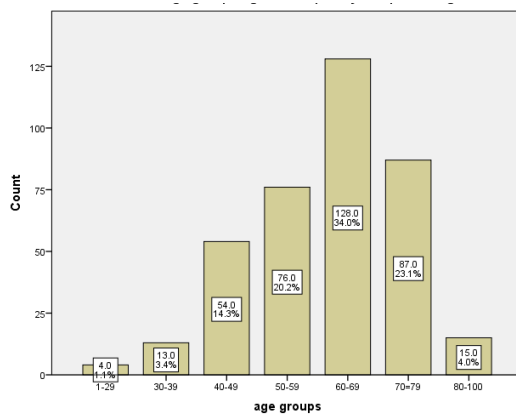


Figure 2: Distribution of study population into different age groups

PATIENTS AND METHODS

This was a descriptive cross-sectional study conducted at the Department of Pathology of King Edward Medical University, Lahore from January 2010 till December 2017 in collaboration with Department of Urology at Mayo Hospital, Lahore after ethical approval of the Institutional Review Board of King

Edward Medical University Lahore. Total of 377 patients of urinary bladder cancer were evaluated; including 39 simple cystoscopic and 338 biopsies obtained through transurethral resection of bladder tumors (TURBT). The urothelial tumors were classified and graded according to World Health Organization/International Society of Urological Pathology (WHO/ISUP).¹¹ Primary tumor (PT) staging was assessed through American Joint Commission on Cancer/Union for the International Cancer Control (AJCC/UICC) system.¹² Accordingly, pTa and pT1 tumours were graded into LG (low grade) and HG (high grade) and all detrusor muscle-invasive urothelial carcinomas were considered to be HG tumours. pTa tumours do not invade the lamina propria (no lymphovascular invasion and distant metastasis). However, pT1 tumours do grow under the basement membrane into the lamina propria with lymphovascular invasion. Similarly, PTa, PT1 and PT2 means tumors confined above the basement membrane, invasive into the lamina propria and muscularis propria respectively. Records of the patients were evaluated and information about age, sex, diagnosis, grade and stage were analyzed. SPSS version 20 was used for descriptive analysis and the results were tabulated as frequencies, percentages and ratios.

RESULTS

A total of 377 cases of bladder cancer were studied. Tumor type comprised 92.3% cases of TCC followed by 4% of SCC and 2.4% of AC. Non-transitional cell carcinoma (nonTCC) histology comprised of only 7.7%. High grade versus low grade cancer comparison revealed 61% high grade against 39% low grade cancers. Male to female ratio was 5.4:1. Mean age was 58.9±12.9 years (range 2 to 90 years) and 61% cancers were found above the age of 59 years whereas 34% cancers were found between 60-69 years (Table 1). Figure 1 and 2 depict the age and gender distribution and grade of cancer. Table 2 reflects the gender-wise

Table 1. Age and gender distribution of urothelial cancer (N=377)

Age group (years)	Sex		Total	Percentage
	Female	Male		
1-29	1	3	4	1.1
30-39	1	12	13	3.4
40-49	13	41	54	14.3
50-59	10	66	76	20.1
60-69	25	103	128	34
70-79	7	80	87	23.1
80-100	1	14	15	4
Total	58	319	377	100

Table 2. Histopathological cancer type with percentage, grade and sex distribution

Diagnosis	Percent	Sex Distribution				Total
		Female		Male		
		Low Grade	High Grade	Low Grade	High Grade	
TCC	92.3%	25	30	122	171	348
SCC	4.0%	0	2	0	13	15
AC	2.4%	0	0	0	9	9
RBT	0.5%	0	0	0	2	2
AC/METS	0.3%	0	1	0	0	1
SARCOMA	0.3%	0	0	0	1	1
CARCINOSARCOMA	0.3%	0	0	0	1	1
TOTAL	100%	25	33	122	197	377

TCC=Transitional cell carcinoma, SCC=Squamous cell carcinoma, AC=Adenocarcinoma, METS= Metastatic, RBT = Round blue cell tumor

distribution of different cancer types along with grades. Among the 348 cases of TCC, 293 (84.2%) were noticed in males and a similar trend of male dominance was maintained in nonTCC histological diagnoses. Out of 348 cases of TCC, 201 (57.7%) were high grade while 147 (42.2%) tumors were low grade, including 2 cases of papillary urothelial neoplasm of low grade malignant potential (PUNLMP). All non TCC cancers were of high grade and thus total 230 (61%) cancers were of high grade (Table 2). Stage analysis highlighted some peculiar outcomes. Significant number of primary tumor (PT) of TCC had not invaded lamina propria and accordingly PTa constituted 160 cases (42.4%) out of total 377. Cases of (PT1) were 54 (14.3%) however stage PT2 which is more important prognostically comprised 134 cases (35.5%). All nonTCC diagnoses 27 (7.16%) were of aggressive stage PT2 except two cases (0.5%) of AC. Combining TCC and nonTCC histological diagnoses, number of cases in stages PTa, PT1, PT2 became 160 (42.4%), 56 (14.8%) and 161 (42.7%) respectively in favor of PT2. Table 3 summarizes the stage-wise frequency of different cancer types in 377 reports. At stage PTa, only 41 (10.87%) cases were of high grade nature against 119 (31.56%) cases of low grade malignancy. As the grade advances, increasing trends of high grade tumors at stage PT1 and PT2 was observed. This was well reflected by the results where 36 (9.5%) and 153 (40.6%) high grade tumors out of 56 and 161 cases respectively against PT1 and PT2 stages were found.

DISCUSSION

Bladder cancer is more prevalent in Pakistan as compared to the neighboring countries. It is primarily a disease of older and male patients.¹ In Pakistan it is the 8th commonest malignant tumor. It is gaining importance due to increasing incidence in South East Asia attributed to increasing trends of smoking in developing countries.^{1,13} In a study from Agha Khan University it is ranked at 10th commonest (3.2%) solid

malignancy.¹⁴ In another local study BC was commonest malignancy of urinary tract and constituted 5.6% of all reported cancers in Pakistan.¹⁵ Male to female ratio in this study is comparable as quoted in local and international studies.^{1,11-18} Generally, TCC is ranked highest worldwide in different studies however SCC is more common in some African and Middle East countries.^{1,13,14} Grade and stage carry the pivotal role in terms of prognosis.¹ In the current study predominant age group was of 60-69 years (34%) and 61.1% cases were above the 59 years of age and 81.2% above age 50 years. Mean age in this study was 58.9 years. In a local study 60% cases were seen between age group of 50-59 years and 86.3% cases above 50 years.⁸ Yet another local study noticed similar results with 89.1% cases of BC above age of 50 years.⁴ These figures are well supported by various national and international reports. A relatively younger mean age (58.9 years) is observed in this study compared to international reports which is similar to other local reports from this part of the world.^{9,14-17} This observation invites further research to find out the etiology leading to UB cancer in early age in this region. Gender based evaluation of BC came out with variable results in different local and international studies. Results of this study depicted male predominance with male to female ratio at 5.4:1. This is similar to various local and international studies.^{1,4,9,18-21} This can be attributed to different environmental and genetic variations. Break up of 377 cases of BC revealed 92.3% tumors of TCC followed by 4% of SCC and 2.4% of AC. Remainder constituted only minor fraction. In total, variant histological diagnosis comprised of 7.7%. These results were in agreement with Mubarak and coworkers who reported 93.3% TCC, 2.6% AC and 2% SCC.¹⁰ These were also well supported by a local study with results of TCC, SCC and AC as 90.5%, 6.3% and 3.2%.⁸ One study from Shaukat Khanum Hospital described the results of TCC, SCC and AC as 86%,3.8% and 2.6%

Table 3. Tumor diagnosis with stage

Diagnosis	Stage			Total
	PTa	PT1	PT2	
TCC	160	54	134	348
SCC	0	0	15	15
AC	0	2	7	9
RBT	0	0	2	2
AC/METS	0	0	1	1
Carcinosarcoma	0	0	1	1
Sarcoma	0	0	1	1
Total	160	56	161	377

TCC=Transitional cell carcinoma, SCC=Squamous cell carcinoma, AC=Adenocarcinoma, METS=Metastatic, RBT=Round blue cell tumor

respectively, which are in little variation with this study.¹ Almost similar trends of TCC with 91.7% were reported from United Kingdom while AC and SCC were at 1.7% and 1.6% in order.⁹ Figures from Ramezani and colleagues from Iran were in lines with final histopathological conclusion found in this study.¹⁶ There have been variations from African countries where SCC was relatively predominant with 8.6% and 18%.^{7,21} Nigerian study reported one of the highest numbers of SCC (44.6%). Obviously, this was due to high prevalence of Shistosomiasis in this part of the world.^{6,20}

There were 348 cases of TCC in current study. High grade TCC, 201 (53.3%) outnumbered the low grade which were 147 (39%). In this study all the nonTCC histology were also of high grade nature and thus after sum up, 230 (61%) diagnoses were of high grade type. These outcomes of grading were well supported by Ahmad and group who reported 61.3% of high grade papillary tumors as compared to low grade (38.7%). Non-papillary nonTCC diagnoses was 8.9%. After sum up burden of low grade tumors was 35.3% while high grade tumors were 64.7%.⁴ Variable results were depicted from local authors where the results were described as grade 1, 2 and 3 with 8.4%, 26.3%, 65.3% and 13.5%, 61%, 25.4% correspondingly.^{8,10} In a study from Iran, low (G1), moderate (G2) and high grades (G3) were 39.7%, 28.4% and 31.2%.⁵ A United Kingdom based study gave the results as 31.1%, 39% and 28.5% against these grades.⁹ These local and international descriptions highlighted the differences which are possibly linked to the environmental and genetic variations.

In BC, stage remained the most significant prognostic factor. In this study no case of PTis was found. Noninvasive (PTa) BC of TCC type were 160 and the invasive were 54 and 134 corresponding to PT1 and PT2. All the nonTCC cases were seen at high stage i.e. at PT2 except two cases of AC. Number of cases

against PTa, PT1, PT2 were 160 (42.4%), 56 (14.8%) and 161 (42.7%) respectively. In one study from neighboring country, similar figures regarding PTa (42.2%) but marked degree of variations were noted against PT1 (33.3%) and PT2 (24.4%).¹⁹ In Pakistan, a researcher noticed PTa and PT1 both with 63.3% and PT2 (23.3%).² Special concern is for PT2 where some local authors came out with results of 35.3%, 38% and 24.2% respectively.^{4,8,10} In the Western world from UK and Spain, results against PTa, PT1 and PT2 were 47.7%, 26.7%, 16.6% and 29%, 45.9%, 15.9% correspondingly. Differences are quite marked against PT2 stage.^{9, 19} This could be due to early diagnosis, geographical and environmental differences. A step ladder pattern was noticed in this study when the grades were stratified against stage. More number of low grade tumors (119/160) were seen at stage PTa against high grade tumors (153/161) which were seen at muscle invasive stage of PT2. At PT1 still high grade tumors dominated (36/56). One of the small scale (n=30) local study also validated similar results where 9 cases at stage PTa were restricted to grade 1 and 2 whereas 5 cases were noticed at grade 2 and 3 against PT1; again at PT2 equal number of cases i.e. 2 were seen against grade 2 and 3. Rest of his cases were stratified at advanced stages.² In a large scale study from United Kingdom at stage Ta, grade 1 (21.2%) and 2 (23.4%) dominated over grade 3 (3.4%). At T1 and T2, grade 1 tumors comprised of minor fraction against grade 2 and 3.⁹ These results are strongly supporting results of this study.

CONCLUSION

TCC was the commonest tumor of urinary bladder followed by SCC and adenocarcinoma. High grade tumors were more common as compared to low grade tumors. High grade cancers were seen with advance stage at diagnosis. Relatively earlier age at presentation of BC in this region needs further research.

REFERENCES

1. 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.
2. Hussain K, Khan MA, Amin I, Butt MK. Carcinoma of urinary bladder; Extent of carcinoma of urinary bladder on first presentation and its impact on management. *Professional Med J*. 2017; 24(11): 1691-6.
3. Sasikumar S, Wijayarathna KSN, Karunaratne KAMS, Gobi U, Pathmeswaran A, Abeygunasekera AM. Pathological characteristics of primary bladder carcinoma treated at a Tertiary Care Hospital and changing demographics of bladder cancer in Sri Lanka. *Advances in Urology*. 2016. <http://dx.doi.org/10.1155/2016/5751647>.
4. Ahmed R, Hashmi SN, Din HU, Muhammad I. Clinicopathological spectrum of urothelial carcinoma of the urinary bladder—a study of 541 cases at AFIP Pakistan. *Pak Armed Forces Med J*. 2015; 65(4): 544-7.
5. Salehi A, Khezri AA, Malekmakan L, Aminsharifi A. Epidemiologic status of bladder cancer in Shiraz, southern Iran. *Asian Pac J Cancer Prev*. 2011; 12(5): 1323-7.
6. Sule AA, Ochicha O, Ibrahim Y, Adam S, Abubakar A, Haruna MS. Update on bladder cancer in Kano, Northern Nigeria. *Niger J Basic Clin Sci*. 2017;14(1):26-9.
7. Ngowi BN, Nyongole OV, Mbwambo JS, Mteta AK. Clinicopathological characteristics of urinary bladder cancer as seen at Kilimanjaro Christian Medical Centre, Moshi-Tanzania. *East Cent Afr J Surg*. 2015; 20(3): 36-45.
8. Altaf J, Mahesar MA, Jatoi T. Clinicopathological features of bladder tumors in a single institution in Hyderabad, Sindh, Pakistan. *Int J clinical & case studies*. 2017; 1(1): 22-9.
9. Boustead GB, Fowler S, Swamy R, Kocklebergh R, Hounscome L. Stage, grade and pathological characteristics of bladder cancer in the UK: British Association of Urological Surgeons (BAUS) urological tumour registry. *BJU Int*. 2014; 113(6): 924-30.
10. Mubarak M, Kazi JI, Hashmi A, Hussain M, Naqvi SA, Rizvi SAH. Urinary Bladder Tumors in Southern Pakistan: A Histopathological Perspective. *Middle East J Cancer*. 2014; 5(3): 167-73.
11. Comperat EM, Burger M, Gontero P, Mostafid AH, Palou J, Roupret M. Grading of Urothelial Carcinoma and The New “World Health Organisation Classification of Tumours of the Urinary System and Male Genital Organs 2016”. *Eur Urol Focus* (2018), <https://doi.org/10.1016/j.euf.2018.01.003>.
12. Paner GP, Stadler WM, Hansel DE, Montironi R, Lin DW, Amin MB. Updates in the Eighth Edition of the Tumour-Node-Metastasis Staging Classification for Urologic Cancer. *Eur Urol*. 2018; 73(4): 560-9.
13. Naeem A, Naseem N, Anwar S, Butt S, Nagi AH. Clinicopathological pattern, classification and staging of urinary bladder carcinomas—a five years experience at a tertiary care hospital in central punjab. *J Ayub Med Coll Abbottabad*. 2015; 27(1): 131-4.
14. Ahmad Z, Idrees R, Fatima S, Uddin N, Ahmed A, Minhas K, et al. Commonest cancers in Pakistan—findings and histopathological perspective from a premier surgical pathology center in Pakistan. *Asian Pac J Cancer Prev*. 2016; 17(3): 1061-75.
15. Farhan M, Nazim SM, Ahmed J, Ather MH. Frequency and predictors of recurrence of bladder tumour on first check cystoscopy—a tertiary care hospital experience. *J Pak Med Assoc*. 2016; 66(Suppl 3)(10): S125-30.
16. Ramezani M, Naderi N, Almasi A, Sadeghi M. Epidemiological and Clinicopathological Features of Bladder Cancer: A Report from Kermanshah Province, Iran. *IJBC*. 2016; 8(2): 43-6.
17. El-Siddig AA, Albasri AM, Hussainy AS, Alhujaily AS. Urinary bladder cancer in adults: a histopathological experience from Madinah, Saudi Arabia. *J Pak Med Assoc* 2017; 67(1): 83-6.
18. Bonfill X, Martinez-Zapata MJ, Vernooij RW, Sánchez MJ, Suárez-Varela MM, De la Cruz J, et al. Clinical interval and diagnostic characteristics in a cohort of bladder cancer patients in Spain: a multicenter observational study. *BMC Res Notes*. 2017; 10(1): 708.
19. Niraj T, Agbo CA, Agrawal CS. Transurethral resection of bladder tumour (TURBT): Experience of a Tertiary Centre. *Jos Journal of Medicine*. 2017; 11(1): 17-9.
20. Paul ENJ, Beyeme S, Herve M, Celestin F, Yoan L, Bruno DD, et al. Urinary bladder cancer in Cameroon: histo-epidemiological aspects of 81 cases. *JMR*. 2016;2(5):145-8.
21. Thapa R, Lakhey M, Bhatta AD. Spectrum of histomorphological diagnosis in cystoscopic bladder biopsies. *J Pathol Nepal*. 2017; 7(1): 1062-5.