ORIGINAL RESEARCH PAPER

Pathology

CLINICOPATHOLOGICAL SPECTRUM OF LESIONS OF URINARY BLADDER AT TERTIARY CARE CENTRE

KEY WORDS: Urothelial Neoplasm, Invasive Urothelial Carcinoma, Cystoscopic Bladder Biopsy,

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ABSTRACT

Urinary bladder lesions are an important source of clinical sign and symptoms. Both neoplastic and non-neoplastic lesions are quite common. Neoplastic lesions lead to significant morbidity and mortality throughout the world. Histopathological analysis of Cystoscopic bladder biopsy and transurethral resection of the bladder tumor are the useful for diagnosis and further management of disease. The objective of the study was to study histomorphological sprectrum of urinary bladder lesions. All well preserved biopsy and specimen of urinary bladder were included in study. The specimens were grossly examined and processed as per standard protocol. Multiple sections of 3-5 micron thickness were obtained and stained with H&E, followed by examined and classified into non-neoplastic & neoplastic lesions by light microscopy. Total 60 cases were studied, out of which 47 were cystoscopic bladder biopsies and 13 were UB specimens. Neoplastic lesions were more common than non-neoplastic. Among the neoplastic lesions, urothelial carcinoma is the predominant type and was most commonly seen in age group of 51-70 years constituting 80.36%. These neoplastic lesions were more common among males with M:F ratio of 2.3:1. Invasive urothelial carcinoma was the predominant type followed by Low grade urothelial lesions. Awareness regarding the various clinical and histological features of these lesions, their neoplastic potential, risk of recurrence and possible pitfalls can help pathologists for accurate diagnosis.

INTRODUCTION

Urinary bladder cancer is one of the commonest tumors worldwide. Urinary bladder lesions are important source of clinical signs and symptoms, these are more disabling than lethal. The non- neoplastic lesions include cystitis, urachal lesions, tuberculosis and malakoplakia. Neoplastic lesions include benign and malignant, the latter being more common. Majority of urothelial malignancy are of epithelial origin and are responsible for significant morbidity and mortality. Urothelial carcinoma is the commonest type accounting for 90% of all primary tumors of the bladder.

Cancer of the bladder, also known as urological cancer or urinary bladder cancer, is the 10th most common cancer in the world, and its incidence is steadily rising worldwide. In India, it is ranked 17th in incidence and 19th in mortality, with a varying incidence across Indian population. There are marked geographical variations in incidence of bladder cancer across the globe. Similarly, there was significant variation in incidence rates of different regions in India. Highest rates are seen in Delhi in both males and females. Urinary bladder neoplasm affects men more than female, accounts for 6% of all malignancy in men and 2% of all malignancy in female. Most bladder malignancy present around age of 50 years but can rarely affect younger adults and children.

In general, the prevalence of bladder tumors in developed countries is higher compared with that in developing countries. The most common type of bladder cancer in developed countries is urothelial carcinoma, derived from the uroepithelium, which constitutes more than 90% of bladder cancer cases in USA, France or Italy. However, in other regions (e.g. Eastern and Northern Europe, Africa, Asia) the relative frequency of urothelial carcinoma of the bladder is lower. The relative frequency of histological subtype of bladder carcinoma depends on the clinical setting. About 90% of bladder carcinoma reported from the West is transitional cell type. In large series reported from Egypt, squamous cell carcinoma (SCC) accounted for 59– 73% of bilharzial bladder cases which are endemic areas for Schistosoma Haematobium. Development of urinary bladder carcinoma depends on a combination of genetic and environmental factors. Environmental factors are industrial exposure to carcinogens e.g., petrochemicals, aniline dye, arylamines; cyclophosphamide, phenacetin, cigarette smoke, long term use of analgesics, schistosoma haematobium infection etc. Genetic factors are mutation of TP53, RB, PTEN pathways. Null GSTM-1 and slow NAT-2 polymorphism are risk factors for urinary bladder malignancy.

Hematuria is most common sign and symptom for presentation of urothelial malignancy with the patient may be asymptomatic. Cystoscopy is the primary diagnostic tool and also useful for localizing tumors and biopsies. Transurethral resection of bladder tumor is a therapeutic procedure for same, also help in assessment of degree of differentiation, depth of invasion, diagnosis and prognosis.

The present study is conducted to analyse spectrum of urinary bladder lesions and histopathological features of various lesions among urinary bladder biopsies and specimens.

MATERIALS AND METHODS

The present Observational cross-sectional study was conducted in the Department of Pathology at Tertiary health care centre in South Gujarat. The cases included were those urinary bladder biopsy and specimens received at the histopathology section, Department of Pathology during period of January 2016 to June 2021. Brief clinical data were retrieved from the request form sent by clinician which included the age, gender, clinical finding, routine investigations, radiological investigation and clinical diagnosis.

Inclusion criteria:

- All bladder biopsy received in Histopathology section, Pathology department
- All urinary bladder specimen received in Histopathology section, Pathology department

Exclusion criteria: Autolysed specimen and poorly preserved biopsy.

The biopsies and specimens were received in glass or plastic container containing 10% neutral buffered formalin. Specimens were fixed in 10% formalin and processed according to standard procedures. The tissues were processed, embedded in paraffin wax and 1 section was cut which was stained with Hematoxylin and Eosin for morphological assessment.

All tissue sections were examined under light microscope. Reporting of Urinary bladder lesion was done according to CAP protocol, WHO classification of tumour of the urothelial tract and TNM classification of carcinomas of the urinary bladder.

The clinical and histological data so obtained were analyzed and compared with other similar studies.

RESULTS

A total of 60 urinary bladder cases were studied which included both bladder biopsy and UB specimens. There were 4 cases of non-neoplastic lesions (6.67%) and 56 cases of neoplastic lesions (93.33%) among all urinary bladder lesions. Out of 60 patients, 42 were males (70%) and 18 were females (30%) with a male to female (M:F) ratio of 2.33:1. Among non-neoplastic lesions, one case of cystitis cystic with cystitis glandularis along with two case of dysplastic urothelium were reported (Table 2). Among the neoplastic lesions, there was clustering of cases in the age group of 51 to 70 years together constituting 53.58% with nil cases observed in younger age group and there was male predominance constituting of 69.64% of all cases with a M:F ratio of 2.29:1 (Table 1). Out of all neoplastic lesions of various histomorphological categories, invasive urothelial carcinoma (IUC) was more common which included 22 cases. Among all urothelial neoplasm (N=52) superficially invasive bladder cancer (invasion up to lamina propria) seen in 28 cases and muscle invasive bladder cancer (invasion into muscularis propria) seen in 13 cases(Table-3). There was histological differentiation seen among IUC which included 2 cases of squamous variant. Apart from IUC, various other lesions were studied which included 3 cases of (5%) Papilloma, 3 cases (5%) of papillary urothelial neoplasm of low malignant potential, 11 cases (18.33%) of low grade papillary urothelial carcinoma, 10 cases (16.67%) of high grade papillary urothelial carcinoma, 2 cases (3.33%) of squamous cell carcinoma and 1 case (1.67%)each of Poorly differentiated carcinoma and PNET (Table-2).

Table-1: Age and gender wise distribution of cases urinary bladder lesions (n=60)

Age (In Years)	Male		Female		Total Number of cases	
	No.	%	No.	%	No.	%
<30	00	00%	00	00%	00	00%
31-40	01	1.67%	05	8.33%	06	10%
41-50	11	18.33%	01	1.67%	12	20%
51-60	13	21.67%	05	8.33%	18	30%
61-70	10	16.67%	03	05%	13	21.67%
71-80	07	11.66%	04	6.67%	11	18.33%
>81	00	00%	00	00%	00	00%
Total	42	70%	18	30%	60	100%

Table-2: Distribution of cases according to histopathological diagnosis (n=60)

Morphology	Male		Female		Total	
	No.	%	No.	%	No.	%
Non- neoplastic						
Normal	1	1.67 %	0	00 %	1	1.67 %
Dysplasia	1	1.67 %	1	1.67 %	2	3.34 %
Cystitis cystic and cystitis glandualris	1	1.67 %	0	00 %	1	1.67 %
Neoplastic						
Papilloma	1	1.67 %	2	3.33 %	3	5 %
Inverted urothelial Papilloma	1	1.67 %	0	00 %	1	1.67 %
PUNLMP	1	1.67 %	2	3.33 %	3	05 %
Low grade papillary urothelial carcinoma	8	13.33 %	3	05 %	11	18.33 %
High grade papillary urothelial carcinoma	6	10 %	4	6.67 %	10	16.67 %
Invasive urothelial carcinoma	17	28.33 %	5	8.33 %	22	36.66 %
Urothelial carcinoma with squamous differentiation	1	1.67 %	1	1.67 %	2	3.33 %
Squamous cell carcinoma	2	3.33 %	0	00 %	2	3.33 %
Poorly differentiated carcinoma	1	1.67 %	0	00 %	1	1.67 %
PNET/ Ewing's sarcoma	1	1.67 %	0	00 %	1	1.66 %
Total	42	70%	18	30%	60	100 %

Table-3: Distribution of cases according to Invasion in urothelial Neoplasm (N=52)

Invasion	Present		Absent		Inconclusive	
	No. of cases	%	No. of cases	%	No. of cases	%
Lamina propria	28	53.85%	20	36.47%	4	7.69%
Detrusor muscle	13	25%	6	11.54%	33	63.46 %

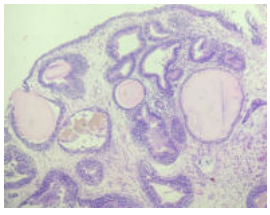

Figure-1: Cystitis cystica. Superficial nests of urothelial mucosa with cystic change in the background of chronic inflammation (H&E, 10X)

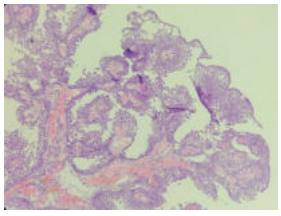

Figure-2: Urothelial papilloma. Discrete papillary structure with central fibrovascular cores, Branching papillae without fusion (H&E, 10X)

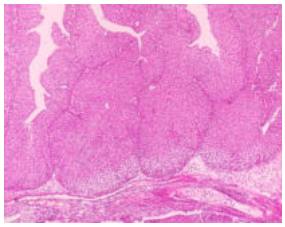

Figure-3: Papillary urothelial neoplasm of low malignant potential (H&E, 10X)

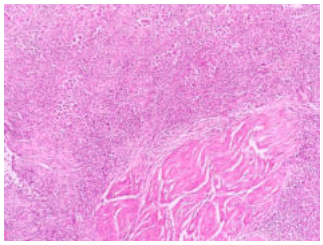

Figure-4: Invasive urothelial carcinoma invading detrusor muscle fibers (H&E, 10X)

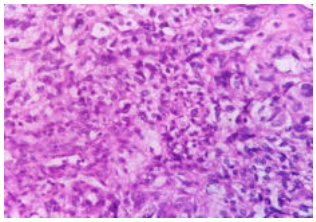

Figure-5: Invasive urothelial carcinoma. Nuclear pleomorphism, hyperchromasia, high N: C ratio with frequent mitotic figures (H&E, 40X)

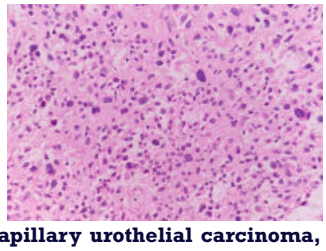

Figure-6: Papillary urothelial carcinoma, High Grade. Nucleomegaly, irregular clumped chromatin, prominent nucleoli and brisk mitosis also show atypical mitosis (H&E, 40X)

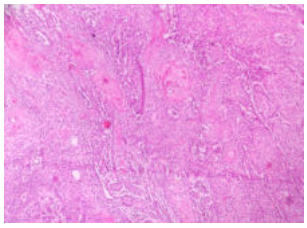

Figure-7: Squamous cell carcinoma of urinary bladder. Infiltrating nests, lobules and sheets of malignant squamous epithelial cells (H&E, 10X)

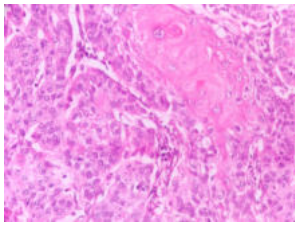

Figure-8: Squamous cell carcinoma of urinary bladder (H&E, 40X)

DISCUSSION

In the present study non neoplastic lesions were 6.67% and neoplastic lesions were 93.33%. These findings were in concordance with studies done by Vaibhav K et al and Aparna c et al– which also show predominance of neoplastic lesions in their respective study.

Table-4: Comparison of incidence of neoplastic and non neoplastic lesions with other studies

Study Name	Total	Non neoplastic (%)	Neoplastic (%)
Vaibhav K et al(2015)(3)	100	4 (4%)	96 (96%)
Aparna c et al (2016)(8)	38	12(31.5%)	26 (68.4%)
Present study	60	4 (6.67%)	56 (93.33%)

The most common affected age group by urinary bladder lesions were 51 to 60 years. These findings were in concordance with studies done by Mahesh k et al (51-60)(9) and Aparna C et al (41-60)(8).

Table-5: Comparison of commonest age group involved with other studies

Study Name	Age (Years)
Mahesh k et al (2018) (9)	51-60
Aparna C et al (2016)(8)	41-60
Present study	51-60

Male to female ratio was 2.33:1 which was similar to above other studies by Aparna C et al (2.8:1)(8) and Preeti N et al (3.63:1)(10) highlights the association of bladder neoplasm and increased male susceptibility. However there is wide range of M: F ratio observed between various studies ranging from least being observed is 2.29:1 in study by Shah PY et al(11) to highest observed in study by Aparna C et al(8) having M:F ratio of 5:1. Smoking had a predominant role in development of bladder cancer in males along with other factors like occupational carcinogens. This increased incidence of among females can be explained by use of smokeless tobacco in the forms like gutka, paan, khaini or surti. These contain many procarcinogenic agents like tobacco, betel nuts, saccharin, sugar coated fennels and heavy metals like silver. (12)

Table-6: Comparison of Male: Female Ratio for lesions of urinary bladder with various Studies

Study	M: F
Aparna C et al (2016)(8)	2.8:1
Preeti N et al (2020)(10)	3.63:1
Present study	2.33:1

Hematuria was the most common clinical symptom (76.67%) which was correlated with study of Bhavna G et al(1) and umesh J et al(13) who find that 75% and 87.9% of urinary bladder patients were presented with hematuria.

Table-7: Comparison of clinical presentation with various studies

Study	Hematuria
Bhavna G et al (2016)(1)	75%
Umesh J et al (2020)(13)	87.9%
Present study	76.67%

Neoplastic lesions were most common (n=56; 93.33%), among which urothelial carcinomas accounted 80.36% (n=45) of all neoplasm while the squamous cell carcinoma and other variants were 3.57% (n=2) respectively. Study results were correlated with study of Mahesh K et al(9) and Preeti N et al(10) who find 81.81% and 89% cases of urothelial carcinoma in their respective studies.

Table-8: Comparison of Histomorphological diagnosis of urinary bladder neoplasm with various studies

Study	Urothelial carcinoma	Squamous cell carcinoma	Adeno-carcinoma	Other variants
Mahesh K et al (2012)(9)	81.81%	6%	6%	-
Preeti N et al (2020)(10)	89%	5.4%	-	5.4%
Present study	80.36%	3.57%	-	3.57%

Among the neoplastic lesions which were studied, 42.31%cases of Invasive urothelial carcinoma, 21.15% cases of Low grade papillary urothelial carcinoma, 19.23% cases of High grade papillary urothelial carcinoma and 5.77% cases of PUNLMP and papilloma each, correlated with study of Susmita S et al(12) and Bhavna G et al(1) who find 60.71% and 53.12% cases of invasive urothelial carcinoma in their respective studies.

Out of 52 cases of urothelial Neoplasm, 53.85% cases were lamina propria invasive and 25% cases were muscularis propria (Detrusor muscle) invasive. This results shows correlation for lamina propria invasion of urothelial neoplasm with study of Aparna C et al (50%) (8) and Rajesh L et al (46.15%%)(14).

Table-9: Comparison of Invasion in urothelial neoplasm

Study	Lamina propria invasion	Muscularis propria invasion
Aparna C et al (2016)(8)	50%	62.5%
Rajesh L et al (2012)(14)	46.15%	30.77%
Present Study (n=52)	53.85%	25%

In the present study, out of 52 cases of urothelial carcinoma 33 cases (63.46%) were shows superficial biopsy with absence of detrusor muscle (muscularis propria) due to very superficial biopsy. In the present study, Muscularis propria invasion among urothelial neoplasm were 25% which was 27.02% and 3% in study of Preeti N et al(10) and Binita G et al(15) respectively.

CONCLUSION

Cystoscopic biopsies play an important role in early diagnosis of bladder tumours. It is important to recognize the variants that are associated with different outcomes and invasion of muscularis mucosa and muscularis propria (Detrusor muscle) has to be differentiated carefully as the prognostic and therapeutic aspects are entirely different in both of them. In case of dilemma immunohistochemistry is most helpful. Awareness is very much needed in the public about hematuria because they neglect it causing advanced stage of bladder neoplasm at the time of presentation. Recent advances have been developed in cystoscopy with new imaging modalities such as narrow band imaging and blue light cystoscopy. Urine markers are also investigated for diagnosis and prognosis of urological conditions. Despite of all such recent advances being carried out for detection of urothelial lesions, histopathology still remains the gold standard for diagnosis.

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