Section: Pathology

Original Research Article

DELINEATING THE HISTOPATHOLOGICAL PROFILE OF UROTHELIAL LESIONS IN A TERTIARY CARE CENTRE

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ABSTRACT

Background: The aim is to evaluate the histopathological spectrum of urothelial lesions, correlate their distribution with age and sex, classify lesions into non-neoplastic and neoplastic categories, assess tumour grade and stage, and identify divergent differentiation and variant histology in urothelial carcinoma. **Materials and Methods:** A retrospective study was conducted over two years (May 2024 to April 2026) in the Department of Pathology, Government Medical College, Ramanathapuram. Twenty urinary bladder biopsy and transurethral resection of bladder tumour (TURBT) specimens were included. Clinical details and cystoscopic findings were recorded. Tissue specimens were fixed in 10% neutral buffered formalin, processed routinely, stained with haematoxylin and eosin, and evaluated microscopically according to the 2022 World Health Organization classification of urothelial tumours1. **Result:** Of the 20 cases, 14 (70%) were males and 6 (30%) were females, with a male-to-female ratio of 2.3:1. The majority of patients (70%) belonged to the 51–60-year age group. Painless hematuria was the most common presenting complaint (55%). Neoplastic lesions constituted 80% of cases, while non-neoplastic lesions accounted for 20%3. Low-grade urothelial carcinoma was the predominant neoplasm (35%), followed by high-grade urothelial carcinoma with divergent differentiation (30%), papillary urothelial neoplasm of low malignant potential (10%), and urothelial papilloma (5%). Squamous differentiation was the most frequent histological variant (66.7%) among high-grade carcinomas. Muscularis propria invasion (pT2) was identified in 83.3% of high-grade tumours. **Conclusion:** Urothelial neoplasms were the predominant bladder lesions, with low-grade urothelial carcinoma being the most frequent subtype. Histopathological evaluation remains indispensable for tumour classification, grading, staging, assessment of muscle invasion, and identification of variant histology, all of which are essential for prognostication and guiding appropriate clinical management.

INTRODUCTION

Bladder tumours are the most frequently encountered condition in urology. 98% of malignant tumours arising in the urinary bladder are of Epithelial origin, 90 % of which are usually Urothelial carcinoma. Most commonly occurs in individual in the 6th and 7th decades of life. Men are affected more than women in the ratio of 3 to 4 :1.

Urothelial carcinoma often show the ability to differentiate into multiple cell type. Both non neoplastic and neoplastic bladder lesions contribute significantly to illness and death. Early detection of these tumours along with the assessment of their invasiveness is crucial as it directly influences the patients prognosis.

Despite advances in imaging, cystoscopy with transurethral resection of bladder tumours and biopsy remains the gold standard for diagnosis. Histopathological examination is essential for confirming diagnosis, grading, staging and guiding treatment.

In this contest, the present study aims to delineate the histopathological profile of urothelial lesions in a tertiary care center based on the specimens obtained through cystoscopic biopsies and TURBT there by providing insight into their spectrum, frequency and histomorphological correlations.

MATERIALS AND METHODS

A one year study of urothelial neoplasms was conducted from may 2025 to april 2026 in the department of pathology at Government

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Ramanathapuram Medical College. Patient details, clinical history, cystoscopy findings were collected along with biopsy specimens and fixed overnight with 10% Neutral buffered formalin. Next day, routine histopathological processing was done. Hematoxylin and eosin stain was done for microscopy.

RESULTS

Demographic Characteristics: A total of 20 urinary bladder biopsy specimens were included in the present study. The study population consisted of 14 (70%) males and 6 (30%) females, with a male-to-female ratio of 2.3:1, demonstrating a clear male predominance.

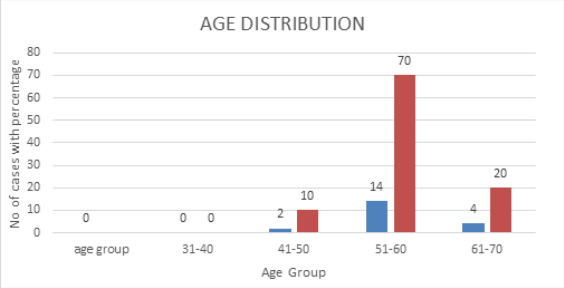
The patients ranged in age from 41 to 70 years. The majority of patients (14 cases; 70%) belonged to the 51–60 years age group, followed by 4 cases (20%) in the 61–70 years age group and 2 cases (10%) in the 41–50 years age group. No cases were encountered in patients aged 31–40 years.

Table 1: Age-wise Distribution of Patients

Age Group (Years)	Number of Cases	Percentage (%)
31–40	0	0
41–50	2	10
51–60	14	70
61–70	4	20
Total	20	100

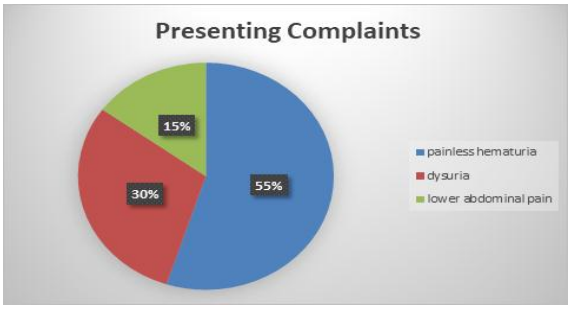
Table 2: Presenting Complaints

Presenting Complaint	Number of Cases	Percentage (%)
Painless hematuria	11	55
Dysuria	6	30
Lower abdominal pain	3	15
Total	20	100



Clinical Presentation

The most common presenting symptom was painless hematuria, observed in 11 patients (55%). Dysuria was the second most frequent complaint, occurring in 6 patients (30%), while lower abdominal pain was reported in 3 patients (15%).

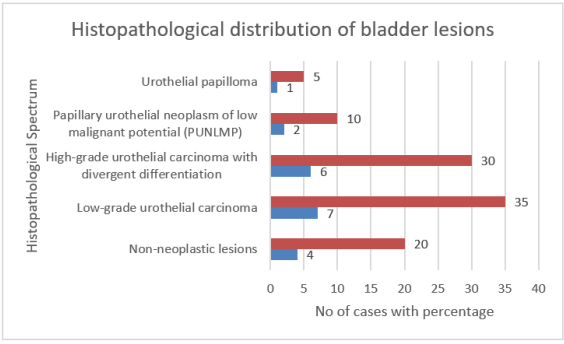


Histopathological Spectrum of Urothelial Lesions

Histopathological examination revealed 16 cases (80%) of neoplastic lesions and 4 cases (20%) of non-neoplastic lesions.

Among the neoplastic lesions, low-grade urothelial carcinoma was the most common diagnosis, accounting for 7 cases (43.75%), followed by high-grade urothelial carcinoma with divergent differentiation in 6 cases (37.5%). Papillary urothelial neoplasm of low malignant potential (PUNLMP) was identified in 2 cases (12.5%), while urothelial papilloma was diagnosed in 1 case (6.25%).

Considering the entire study population (n = 20), low-grade urothelial carcinoma constituted 35%, high-grade urothelial carcinoma with divergent differentiation 30%, PUNLMP 10%, urothelial papilloma 5%, and non-neoplastic lesions 20% of all bladder biopsies.



Histopathological Characteristics of High-grade Urothelial Carcinoma

Among the 6 cases of high-grade urothelial carcinoma, all demonstrated divergent differentiation. Squamous differentiation was the

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predominant variant, observed in 4 cases (66.7%), followed by glandular differentiation in 1 case (16.7%) and sarcomatoid differentiation in 1 case (16.7%).

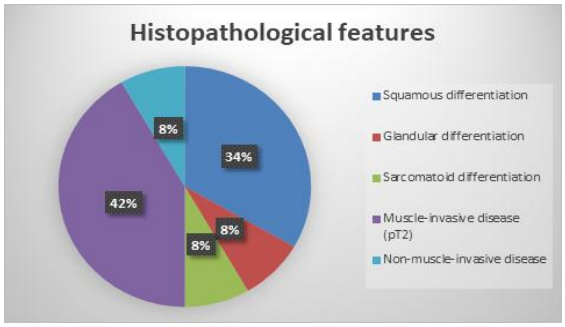
Microscopically, the tumours exhibited complex papillary architecture with marked architectural disorganization, severe nuclear pleomorphism, hyperchromatic nuclei, prominent nucleoli, increased mitotic activity including atypical mitotic figures, loss of cellular polarity, and focal tumour necrosis. The divergent components were readily identified on routine hematoxylin and eosin-stained sections. Squamous differentiation showed keratinization and intercellular bridges, glandular differentiation exhibited gland-like structures with mucin production, and sarcomatoid differentiation was characterized by spindle-shaped malignant cells with marked nuclear atypia. Muscularis propria was identified in all six specimens of high-grade urothelial carcinoma. Five cases (83.3%) demonstrated invasion into the muscularis propria (pathological stage pT2), whereas one case (16.7%) showed no evidence of muscle invasion.

Table 3: Histopathological Distribution of Bladder Lesions

Histopathological Diagnosis	Number of Cases	Percentage (%)
Non-neoplastic lesions	4	20
Low-grade urothelial carcinoma	7	35
High-grade urothelial carcinoma with divergent differentiation	6	30
Papillary urothelial neoplasm of low malignant potential (PUNLMP)	2	10
Urothelial papilloma	1	5
Total	20	100

Table 4: Histopathological Features of High-grade Urothelial Carcinoma (n = 6)

Variable	Number of Cases	Percentage (%)
Squamous differentiation	4	66.7
Glandular differentiation	1	16.7
Sarcomatoid differentiation	1	16.7
Muscle-invasive disease (pT2)	5	83.3
Non-muscle-invasive disease	1	16.7



Summary of Findings

The present study demonstrated that urothelial neoplasms constituted the majority (80%) of bladder lesions, with a distinct male predominance. The peak incidence occurred in the 51–60-year age group. Painless hematuria was the most frequent presenting complaint, followed by dysuria and lower abdominal pain.

Among the neoplastic lesions, low-grade urothelial carcinoma was the most common histological subtype. A considerable proportion of tumours (37.5% of neoplastic lesions) were high-grade urothelial carcinomas with divergent differentiation, with squamous differentiation being the predominant histological variant. Furthermore, 83.3% of high-grade tumours showed muscularis propria invasion (pT2), indicating an aggressive pathological profile. These findings underscore the importance of meticulous histopathological examination for accurate tumour grading, identification of variant histology, and assessment of muscle invasion, all of which are essential for prognostication and therapeutic decision-making.

DISCUSSION

The present study evaluated the histopathological spectrum of urothelial lesions encountered in a tertiary care centre over a two-year period. Histopathological examination remains the gold standard for the diagnosis and classification of urothelial lesions, providing essential information regarding tumour type, grade, stage, depth of invasion, and variant histology. These pathological parameters form the basis for prognostication and therapeutic decision-making and are fundamental to the management of patients with bladder neoplasms.[1-4]

In the present study, urothelial neoplasms constituted 80% of all bladder biopsies, while non-neoplastic lesions comprised 20%. This predominance of neoplastic lesions reflects the referral pattern of a tertiary care hospital and highlights the importance of biopsy in patients presenting with persistent hematuria or cystoscopically detected bladder lesions. Histopathological examination remains indispensable in differentiating reactive urothelial atypia secondary to inflammation from true neoplastic lesions, thereby preventing diagnostic errors and ensuring appropriate clinical management.

A male predominance (70%) with a male-to-female ratio of 2.3:1 was observed, and the majority of

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patients belonged to the 51–60-year age group. These findings are comparable with previous Indian and international studies, which consistently report bladder cancer as a disease predominantly affecting middle-aged and elderly men. This demographic distribution has been attributed to greater exposure to carcinogens such as tobacco smoke, occupational aromatic amines, petroleum products, and environmental pollutants, together with hormonal and genetic influences.[2,3]

Painless hematuria was the most frequent presenting complaint (55%), followed by dysuria and lower abdominal pain. These findings are consistent with the established clinical presentation of urothelial carcinoma. However, clinical features alone cannot reliably distinguish benign from malignant lesions, emphasizing the indispensable role of histopathological examination in establishing a definitive diagnosis.[7]

According to the 2022 World Health Organization (WHO) Classification of Urinary and Male Genital Tumours, papillary urothelial lesions are classified into urothelial papilloma, papillary urothelial neoplasm of low malignant potential (PUNLMP), low-grade papillary urothelial carcinoma, and high-grade papillary urothelial carcinoma6. This classification provides a standardized framework that correlates histological morphology with biological behaviour and clinical outcome. The distribution of lesions observed in the present study aligns well with this classification system.[1]

Low-grade urothelial carcinoma was the most common neoplastic lesion in the present series. Histologically, these tumours demonstrated slender papillary fronds with delicate fibrovascular cores lined by urothelium showing mild architectural disorganization, relatively uniform nuclei, mild hyperchromasia, preserved cellular polarity, and infrequent mitotic figures confined mainly to the basal layers. These microscopic features correspond to the WHO/ISUP criteria for low-grade papillary urothelial carcinoma and explain their relatively favourable prognosis despite their well-recognized tendency for recurrence.[8-10]

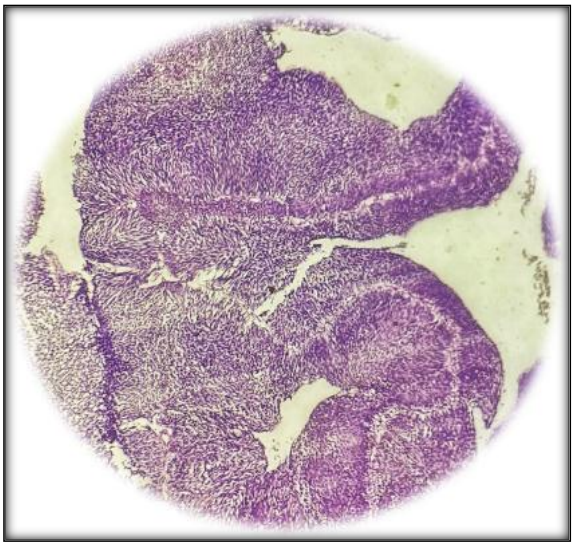

Figure 1 Low grade urothelial carcinoma. H&E 100X magnification

Papillary urothelial neoplasm of low malignant potential (PUNLMP) accounted for 10% of all cases. Histologically, these lesions exhibited papillary architecture with increased urothelial thickness but minimal cytological atypia, preserved polarity, and rare mitotic activity. Although recurrence may occur, progression to invasive disease is uncommon. Accurate distinction between PUNLMP and low-grade urothelial carcinoma is therefore clinically important because of differences in surveillance protocols and long-term prognosis.

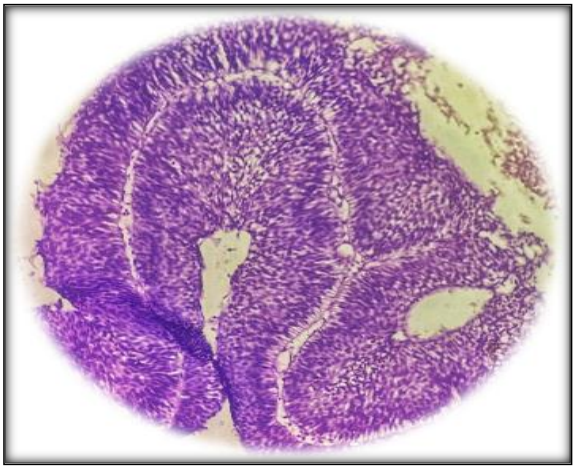

Figure 2: PUNLUMP. Papillary urothelial neoplasm of low malignant potential. H&E 400XMagnification

Urothelial papilloma was identified in one case. Microscopically, it displayed delicate papillary fronds lined by urothelium of normal thickness with preserved maturation, orderly cell arrangement, and absence of cytological atypia or increased mitotic activity5. Recognition of this benign lesion is important because of its excellent prognosis and low recurrence rate.

A significant finding of the present study was the relatively high proportion of high-grade urothelial carcinoma with divergent differentiation (37.5% of

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neoplastic lesions). Histologically, these tumours exhibited marked architectural complexity with fused papillae, complete loss of polarity, severe nuclear pleomorphism, coarse chromatin, prominent nucleoli, frequent atypical mitotic figures, apoptotic bodies, and extensive tumour necrosis. Such morphological features are well-recognized indicators of aggressive biological behaviour and correlate strongly with increased risk of progression and metastasis.

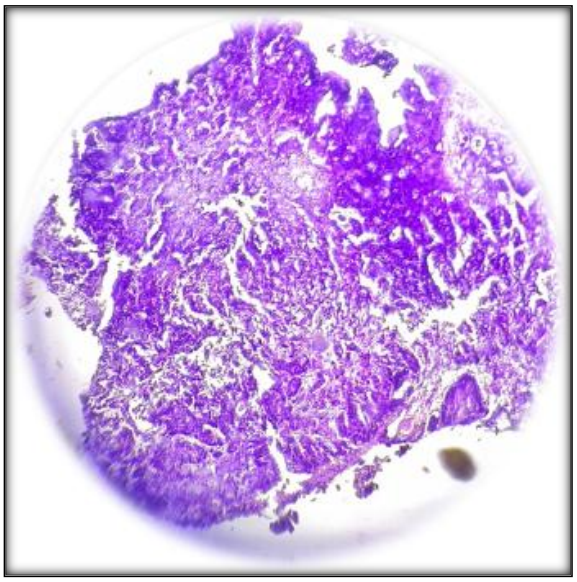

Figure 3: High grade urothelial carcinoma.H&E 100X magnification

Variant histology has emerged as an important prognostic parameter in contemporary bladder pathology. All high-grade tumours in the present study demonstrated divergent differentiation. Squamous differentiation was the predominant variant, followed by glandular and sarcomatoid differentiation. Squamous differentiation was characterised by keratin pearl formation, dyskeratosis, eosinophilic cytoplasm, and intercellular bridges. It is the most common divergent differentiation encountered in urothelial carcinoma and has been associated with chronic irritation, advanced pathological stage, and reduced response to intravesical therapy.

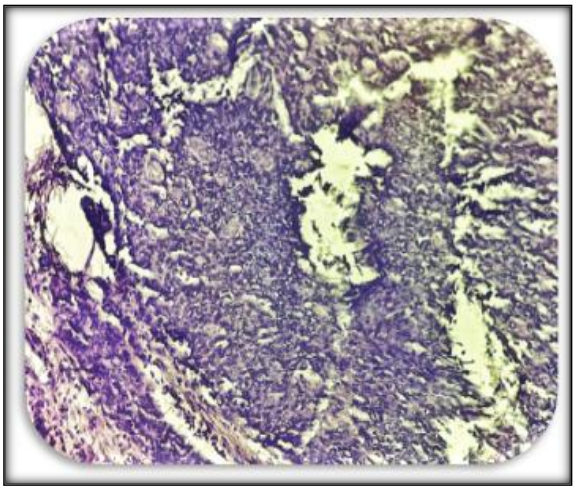

Figure 4: High grade urothelial carcinoma with squamoid differentiation. H&E 400X magnification

The tumour with glandular differentiation demonstrated true gland formation with mucin-containing lumina. This variant requires careful distinction from primary adenocarcinoma of the urinary bladder and metastatic colorectal adenocarcinoma through clinicopathological correlation and, where necessary, immunohistochemistry. Sarcomatoid differentiation, observed in one case, consisted of highly pleomorphic spindle-shaped malignant cells with marked nuclear atypia and brisk mitotic activity. This rare variant is associated with epithelial-mesenchymal transition and carries an extremely poor prognosis because of its highly aggressive clinical course.

One of the most critical pathological parameters evaluated in the present study was muscularis propria invasion. Adequate sampling of detrusor muscle in transurethral resection specimens is considered an essential quality indicator in bladder pathology10. In the present series, muscularis propria was identified in all high-grade tumours, permitting reliable pathological staging. Five of six cases demonstrated muscle invasion (pT2). This observation underscores the aggressive nature of high-grade urothelial carcinoma and emphasizes the importance of complete tumour resection with adequate sampling of muscularis propria. Failure to include detrusor muscle in biopsy specimens may result in pathological understaging, inappropriate conservative treatment.

Histopathological evaluation plays a pivotal role in predicting the biological behaviour and prognosis of urothelial lesions8. Tumour grade and pathological stage are the two most important prognostic determinants in urothelial carcinoma. Low-grade papillary urothelial carcinomas generally have a favourable prognosis, with a low risk of progression to muscle-invasive disease; however, they are associated with a relatively high rate of local recurrence, necessitating long-term cystoscopic surveillance. In contrast, high-grade urothelial carcinomas exhibit aggressive biological behaviour,

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characterised by increased cellular atypia, high mitotic activity, architectural disorganisation, and a greater propensity for lamina propria and muscularis propria invasion, lymph node metastasis, and disease progression. The presence of muscularis propria invasion (pT2) is associated with significantly reduced disease-specific survival and often necessitates radical cystectomy with or without systemic therapy. Furthermore, the identification of divergent differentiation, particularly squamous, glandular, or sarcomatoid variants, has important prognostic implications, as these tumours are frequently associated with advanced pathological stage, treatment resistance, and poorer clinical outcomes. Therefore, a comprehensive histopathological assessment that includes tumour classification, grade, stage, depth of invasion, and recognition of variant histology is essential for accurate risk stratification, prognostic assessment, and individualized patient management.

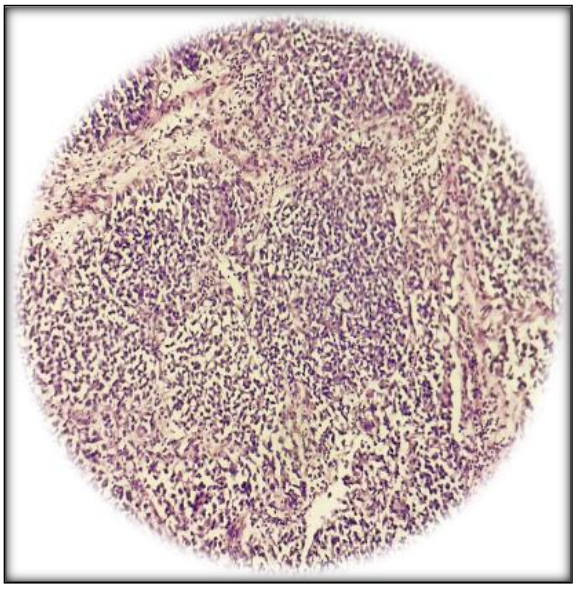

Figure 5: High grade urothelial carcinoma with muscle invasion (pT2). H&E 400X magnification

The present study reinforces the pivotal role of meticulous histopathological examination in the evaluation of urothelial lesions. Accurate classification according to the WHO 2022 criteria, appropriate tumour grading, identification of muscularis propria invasion, and careful recognition of divergent differentiation are essential for accurate diagnosis, prognostication, and selection of optimal therapeutic strategies. Comprehensive pathology reporting incorporating these parameters remains fundamental to improving the clinical management and outcomes of patients with urothelial carcinoma.

CONCLUSION

Accurate histopathological characterization of urothelial lesions is indispensable for distinguishing benign from malignant pathology and identifying aggressive tumour features. Meticulous evaluation of tumour grade, stage, muscle invasion, and divergent differentiation provides critical prognostic information and facilitates evidence-based clinical decision-making.

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