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Histopathological Spectrum of Urinary Bladder Lesions in A Tertiary Level Hospital

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HIGHLIGHTS

1. Transitional cell carcinoma most commonlesion
2. Benign lesions include cystitis and polyp
3. Male predominance noted incases
4. Peak incidence in sixth to seventh decade
5. Histopathology key for definitive diagnosis.

Key words:
Urinary bladder lesions
Urothelial carcinoma
Tumor grade
Invasion status
Lymphovascular invasion (LVI)
Histopathology
Prognosis
Transurethral resection (TURBT)

ABSTRACT

Aim: This study evaluates the histopathological spectrum of urinary bladder lesions, analyzing age and gender distribution, tumor grade, invasion status, and the correlation between tumor invasion depth and lymphovascular invasion (LVI) to assess prognostic significance. **Introduction:** Urinary bladder lesions, including both neoplastic and non-neoplastic conditions, contribute to significant morbidity, particularly in older adults. Urothelial carcinoma (UC) is the most common malignancy, with smoking and occupational exposures as major risk factors. Histopathological evaluation plays a crucial role in accurate diagnosis, tumor grading, and prognosis. Early detection and appropriate management strategies are essential for improving patient outcomes, emphasizing the importance of pathology in guiding clinical decision-making. **Materials and Methods:** A retrospective study of 60 bladder tumor cases diagnosed via TURBT and cystoscopic biopsies. Specimens were processed, stained with H&E, and classified using the WHO grading system and TNM staging. Pearson's correlation coefficient was used for statistical analysis to assess the relationship between tumor invasion depth and lymphovascular invasion (LVI), with significance set at $p < 0.05$.**Results:** Among 60 cases, 85% were male, with peak prevalence in the 61-70 age group (35%). Invasive papillary urothelial carcinoma was the most common subtype (80%). High-grade tumors predominated (73.2%), and 85.7% showed invasion. A significant correlation ($r = 0.65$, $p = 0.01$) was found between tumor invasion depth and lymphovascular invasion (LVI), indicating a higher risk of metastasis in deeply invasive tumors. **Conclusion:** Bladder cancer primarily affects elderly males, with high-grade invasive urothelial carcinoma being most common. Tumor invasion strongly correlates with lymphovascular invasion (LVI), highlighting the need for detailed histopathological evaluation. Accurate assessment improves prognosis and treatment planning, enabling early detection and targeted therapy for better patient management and outcomes.

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INTRODUCTION

Urinary bladder lesions, encompassing both neoplastic and non-neoplastic conditions, pose a significant health burden, particularly among the elderly population [1]. These lesions contribute to substantial morbidity and frequently necessitate medical intervention [2,3]. Among non-neoplastic conditions, cystitis is the most prevalent, presenting with symptoms such as dysuria, hematuria, and increased urinary frequency [4]. Conversely, urothelial carcinoma (UC) is the most common neoplastic lesion, accounting for approximately 90% of all primary bladder tumors [5]. Given the rising incidence of bladder malignancies worldwide, early detection and accurate histopathological diagnosis are essential for effective disease management.

Bladder cancer ranks as the ninth most commonly diagnosed cancer globally, with an estimated 614,000 new cases and 220,000 fatalities reported in 2022, according to GLOBOCAN 2022 data [6]. It represents 6% of cancer cases in men and 2% in women, making it the second most common malignancy of the urogenital system, following prostate cancer in males [7]. The incidence of bladder cancer is notably higher in urban regions compared to rural areas, which may be attributed to differences in environmental exposures, lifestyle factors, and healthcare access.

In India, the annual incidence of bladder cancer is estimated at 20,470 cases in men and 5,403 cases in women, with a cumulative risk of 1 in 250 for men and 1 in 1,014 for women [3,8]. This gender disparity is likely due to differences in smoking habits, occupational exposures (such as chemicals used in dye, rubber, and leather industries), and hormonal influences. Smoking is the most significant risk factor, increasing the risk of bladder cancer by two to three times compared to non-smokers. Other risk factors include chronic inflammation (e.g., recurrent urinary tract infections and schistosomiasis), exposure to arsenic in drinking water, pelvic radiation, and the long-term use of cyclophosphamide [9].

Urinary bladder lesions range from benign inflammatory conditions to highly aggressive malignant neoplasms. Non-neoplastic conditions include various forms of cystitis (infectious, eosinophilic, interstitial, and radiation-induced), tuberculosis, malakoplakia, urachal anomalies, and schistosomiasis. Among these, chronic cystitis is one of the most common symptomatic presentations, often mimicking early-stage bladder cancer [10].

Among neoplastic lesions, urothelial carcinoma is the most frequently encountered malignancy, accounting for approximately 90% of all bladder tumors. This cancer type exhibits a broad spectrum of behavior, ranging from low-grade, non-invasive papillary tumors with a high recurrence rate to high-grade, muscle-invasive carcinomas (MIBC) with a poor prognosis. Approximately 20–30% of urothelial carcinomas are muscle-invasive, characterized by deep invasion into the bladder wall and a high potential for metastasis [11].

Other primary bladder tumors include squamous cell carcinoma (5%) and adenocarcinoma (2%), both of which are often associated with chronic irritation and inflammation [12]. Rare bladder neoplasms, such as small cell carcinoma and sarcomas, are highly aggressive but constitute a minor fraction of cases.

The clinical presentation of bladder lesions varies widely, with hematuria being the most common symptom in both benign and malignant conditions. Additional symptoms include dysuria, nocturia, increased urinary frequency, suprapubic pain, and urinary urgency. Due to the overlap in symptoms between benign and malignant conditions, accurate diagnosis requires a combination of clinical history, physical examination, imaging studies, cystoscopy, and histopathological analysis [13].

Histopathology plays a crucial role in evaluating tumor grade, differentiation, and depth of invasion, all of which are vital prognostic indicators. Transurethral resection of the bladder tumor (TURBT) not only provides diagnostic tissue but also serves as the initial therapeutic approach for superficial bladder tumors. However, patients with muscle-invasive bladder cancer (MIBC) often experience poor prognostic outcomes despite advancements in intravesical and systemic therapies [2].

The prognosis of bladder cancer largely depends on the histological grade, tumor differentiation, and depth of invasion. While non-invasive papillary urothelial carcinomas exhibit a relatively favorable prognosis with a high recurrence rate, muscle-invasive and high-grade tumors are associated with aggressive progression and poor survival outcomes. Treatment modalities range from intravesical therapy (e.g., Bacillus Calmette-Guérin [BCG] and chemotherapy) for non-invasive tumors to radical cystectomy and systemic chemo therapy for advanced disease [14,15].

Given the high prevalence and clinical complexity of bladder tumors, studying the histopathological spectrum of urinary bladder lesions in a tertiary-level hospital setting is crucial for improving diagnostic accuracy, treatment strategies, and patient outcomes. This study aims to

analyze the age and gender distribution, histopathological patterns, and the correlation between tumor invasion depth and lymphovascular invasion (LVI), thereby contributing to a better understanding of bladder cancer prognosis and management.

MATERIALS AND METHODS

This retrospective study was conducted in the Department of Pathology at a tertiary care hospital to evaluate the histopathological spectrum of urinary bladder lesions and their association with age, gender, tumor grade, invasion status, and lymphovascular invasion (LVI). A total of 60 cases diagnosed through transurethral resection of bladder tumors (TURBT) and cystoscopic biopsies were included, while inadequate samples, recurrent cases, and those with incomplete data were excluded. Specimens were fixed in 10% formalin, processed, embedded in paraffin, sectioned, and stained with Hematoxylin and Eosin (H&E) for histopathological evaluation. Tumors were classified according to the WHO grading system and TNM staging, with LVI and depth of invasion assessed using standard histopathological criteria. Statistical analysis was performed to determine the correlation between invasion depth and LVI using Pearson's correlation coefficient, considering a p-value < 0.05 as statistically significant. Ethical clearance was obtained, and patient confidentiality was maintained throughout the study.

RESULTS

The study included 60 cases of urinary bladder lesions. The majority of patients were male (85%), while females comprised only 15% of cases. The most commonly affected age group was 61-70 years (35%), followed by >70 years (26.67%) and 51-60 years (23.33%). Younger patients (≤40 years) accounted for only 5% of cases (Figure 1).

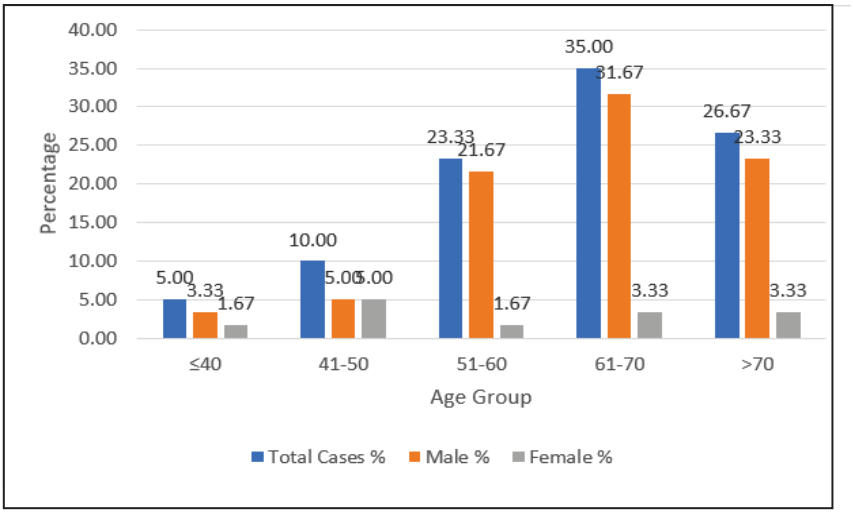


Figure 1: Age group and Gender distribution among the study patients

Histological examination revealed that 80% of cases were invasive papillary urothelial carcinoma, making it the most common diagnosis. Non-invasive papillary urothelial carcinoma accounted for 16.67%, while papillary urothelial neoplasm of low malignant potential (PUNLMP) represented only 3.33% (Figure 2).

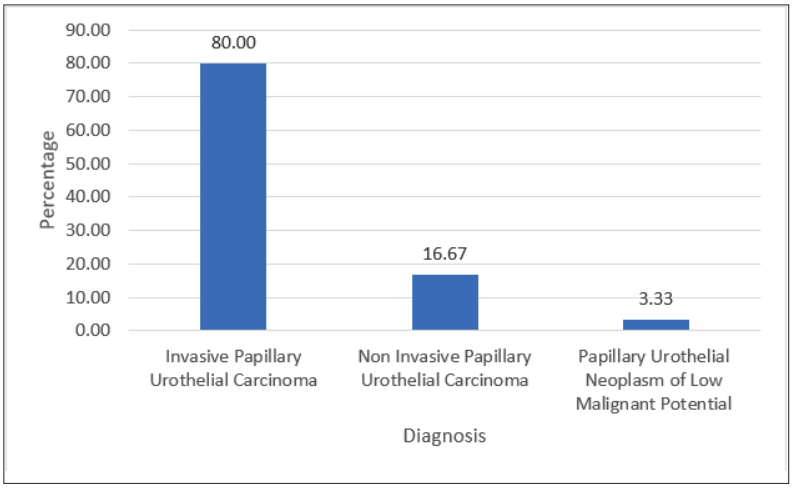


Figure 2: Histological Diagnosis Distribution in Urological Specimens

The analysis of tumor grade distribution (Figure 3) shows that high-grade tumors are more prevalent, with 41 cases (73.2%), compared to 15 cases (26.8%) of low-grade tumors.

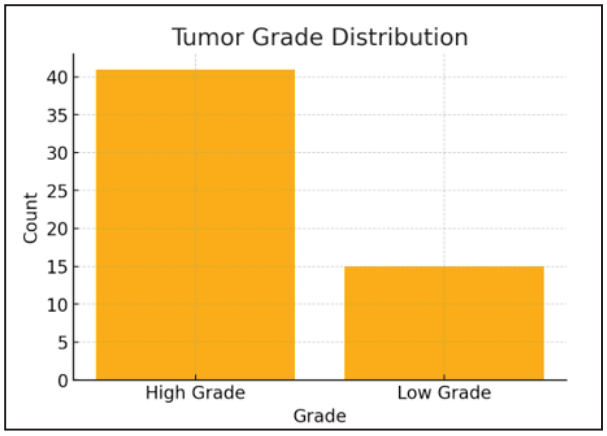


Figure 3: Tumor Grade Distribution

Figure 4 illustrates the invasion status distribution, where tumor invasion is present in 42 cases (85.7%), while it is absent in 7 cases (14.3%).

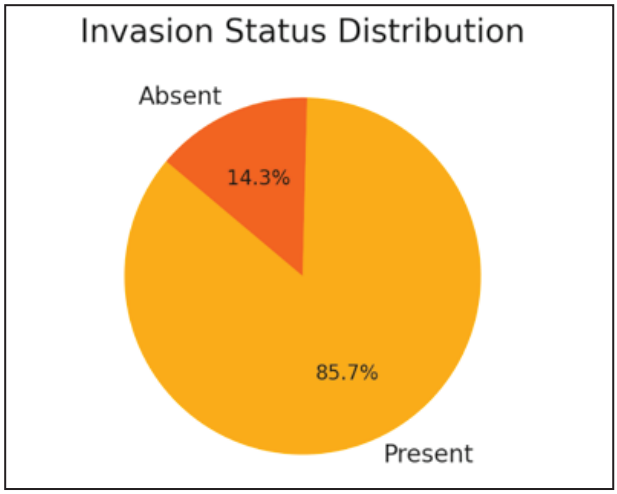


Figure 4: Invasion Status Distribution

Figure 5 further breaks down invasion status by tumor grade, indicating that the majority of both high-grade and low-grade tumors exhibit invasion. Among high-grade tumors, 36 cases (87.8%) show invasion, while 5 cases (12.2%) are non-invasive. In low-grade tumors, 6 cases (40%) exhibit invasion, whereas 9 cases (60%) do not. These results suggest a possible correlation between higher tumor grade and an increased likelihood of invasion.

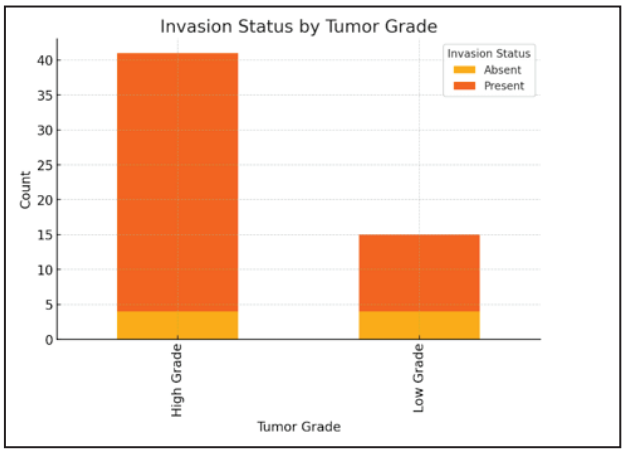


Figure 5: Invasion Status By Tumor Grade

A significant positive correlation (r = 0.65, p = 0.01) was observed between tumor invasion depth and lymphovascular invasion (LVI). This suggests that tumors invading deeper layers of the bladder wall are more likely to exhibit LVI, which may contribute to tumor progression and metastasis.

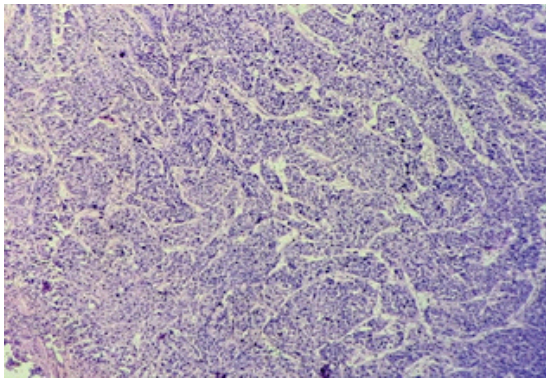
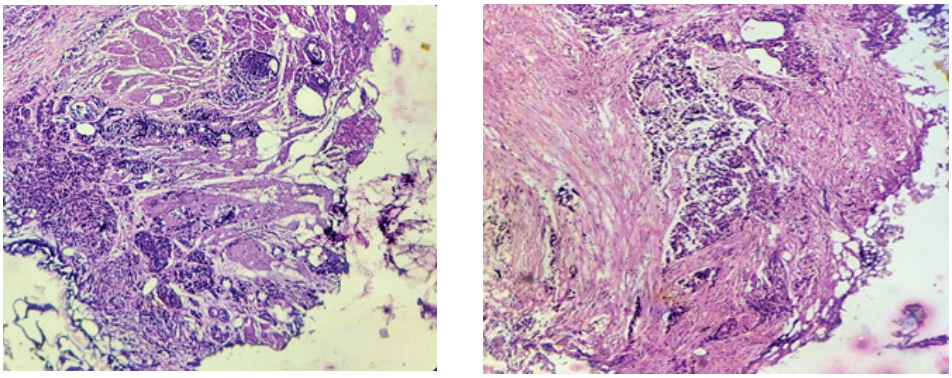


Figure 6 : Invasive Urothelial Carcinoma (100X)



A **B**

Figure 7 (A and B) : Muscle Invasion by Invasive Cancer (100X)

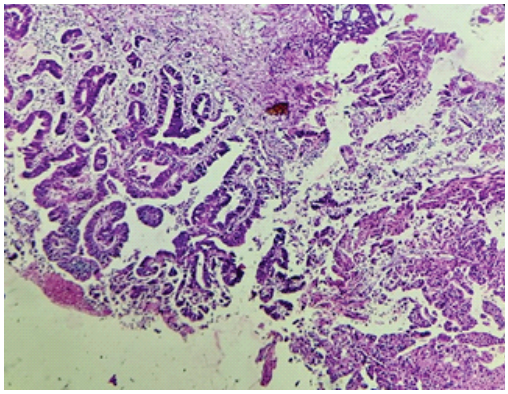


Figure 8 : Invasive Urothelial Carcinoma with Glandular Differentiation (100X)

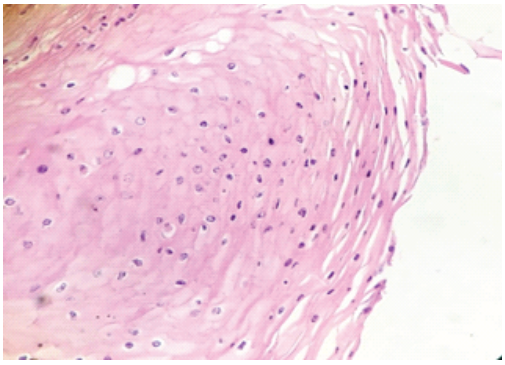


Figure 9 : Squamous Differentiation in a case of Invasive Urothelial Carcinoma (400X)

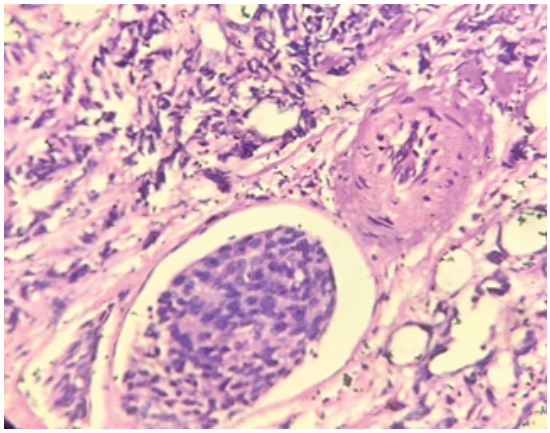


Figure 10 : Vascular Invasion by Invasive Urothelial Carcinoma (100X)

DISCUSSION

The present study provides valuable insights into the histopathological spectrum of urinary bladder lesions, with a focus on gender distribution, age-related prevalence, histological subtypes, tumor grade, invasion status, and the correlation between tumor invasion depth and lymphovascular invasion (LVI).

The study observed a strong male predominance (85%), with only 15% of cases occurring in females. This aligns with findings from studies by Roshed et al. and Lashiram et al., which also reported a higher incidence of bladder lesions in men [16,17]. The increased male susceptibility to bladder cancer may be attributed to occupational exposures, smoking, and prolonged industrial exposure to carcinogens such as aromatic amines and acrylamide. Cigarette smoking, in particular, is a well-established risk factor for bladder cancer due to the accumulation of carcinogenic metabolites in urine.

Age-wise, the majority of cases were in the 61-70 years group (35%), followed by >70 years (26.67%) and 51-60 years (23.33%). This is consistent with studies by Paudel et al., which also found that bladder cancer predominantly affects the elderly [7]. The increased incidence in older individuals may be linked to cumulative exposure to carcinogens, aging-related immune dysfunction, and underlying comorbidities that predispose to malignancy. The low occurrence (5%) of bladder lesions in patients ≤40 years suggests that bladder cancer is uncommon in younger populations, though rare cases may be associated with genetic predispositions or specific environmental factors.

Histopathological analysis revealed that invasive papillary urothelial carcinoma was the most prevalent diagnosis, accounting for 80% of cases. Non-invasive papillary urothelial carcinoma comprised 16.67%, while papillary urothelial neoplasm of low malignant potential (PUNLMP) was relatively rare (3.33%). These findings highlight the aggressive nature of most bladder

cancers in our study population. Similar results were reported by Kriti Piya et al., who also identified invasive high-grade urothelial carcinoma as the most common bladder tumor [18]. However, studies by Thapa et al. and Mainali et al. showed a predominance of low-grade urothelial neoplasms, accounting for approximately 50% of cases, which contrasts with our findings [19,20]. These variations may be attributed to differences in population demographics, risk factor exposure, and diagnostic criteria used across studies.

Interestingly, papilloma and other benign neoplastic lesions were not observed in our cohort, a finding that contrasts with other studies documenting these lesions, though at lower frequencies. This variation could be attributed to the nature of the study population or the inclusion criteria.

In terms of tumor grade, our study found that highgrade urothelial carcinoma (HGUC) (73.2%) was significantly more common than low-grade urothelial carcinoma (LGUC) (26.8%), which highlights the predominance of aggressive bladder cancers. This is important because high-grade tumors are more likely to progress, invade deeper layers of the bladder wall, and metastasize. These findings align with previous studies, including those by Roshed et al. and Lashiram et al., which reported that high-grade urothelial carcinomas exhibit a much higher frequency of muscle invasion compared to low-grade tumors [16,17]. For instance, a retrospective study in 2016 showed that 85% of high-grade urothelial carcinomas showed muscle invasion, while only 12.5% of low-grade urothelial carcinomas showed muscle invasion [15]. In our study, 87.8% of high-grade urothelial carcinoma cases exhibited invasion, with the majority showing

muscle invasion, underscoring the aggressive behavior of high-grade tumors. In contrast, none of the low-grade urothelial carcinoma cases in our study were muscle-invasive, which is consistent with findings from other studies [3,5].

Regarding invasion status, 85.7% of tumors were invasive, while 14.3% were non-invasive. Further analysis revealed a clear association between tumor grade and invasion, with 87.8% of high-grade tumors exhibiting invasion compared to only 40% of low-grade tumors. These findings support the well-established concept that high-grade bladder cancers have a greater propensity for invasion and poor clinical outcomes.

A statistically significant positive correlation ($r = 0.65$, $p = 0.01$) was observed between tumor invasion depth and LVI. This suggests that as tumors invade deeper into the bladder wall, the likelihood of LVI increases. The presence of LVI is a crucial prognostic factor, as it indicates a higher risk of tumor dissemination through blood and lymphatic vessels, leading to metastasis. This finding underscores the importance of assessing LVI in bladder cancer cases to guide treatment decisions and predict patient outcomes.

Histomorphology remains the most powerful tool in predicting the risk of recurrence, disease progression, and therapeutic response in bladder cancer. While the diagnosis of most bladder lesions is straightforward, occasional cases present diagnostic challenges. Pathologists play a vital role not only in establishing the diagnosis but also in providing critical information regarding tumor grade, invasion depth, and LVI, all of which significantly impact treatment decisions.

Histopathology is particularly crucial in differentiating benign from malignant urothelial lesions. Each histological variant has unique characteristics that influence its metastatic potential and responsiveness to treatment, such as chemotherapy or radiation therapy. Therefore, accurate histopathological evaluation is essential for proper disease management.

Our study findings are largely in agreement with previous research, particularly regarding male predominance, the prevalence of high-grade invasive urothelial carcinoma, and the strong correlation between tumor invasion and LVI. However, variations in the frequency of low-grade vs. high-grade tumors across studies suggest that geographical, genetic, and environmental factors may influence bladder cancer characteristics in different populations.

Additionally, non-neoplastic lesions were uncommon in our study, with cystitis cystica being the most frequently encountered entity. This finding is in line with Shah et al., who reported various forms of cystitis as the predominant non-neoplastic bladder lesions [21]. The low incidence of benign lesions, such as urothelial papilloma and adenocarcinoma, further emphasizes the predominance of malignant urothelial tumors in our patient cohort.

CONCLUSION

This study highlights the predominance of high-grade invasive urothelial carcinoma in elderly males, emphasizing the strong correlation between tumor invasion depth and lymphovascular invasion (LVI). The findings reinforce the importance of early detection and comprehensive histopathological evaluation in guiding prognosis and treatment. The association of high-grade tumors with increased invasiveness underscores the need for aggressive management in such cases. LVI serves as a critical prognostic marker, indicating a higher risk of metastasis. Accurate tumor grading and invasion assessment remain essential for optimizing patient outcomes. Further research with larger cohorts and molecular studies may enhance therapeutic strategies and survival rates.

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