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Clinicopathological Profile and Treatment Stratification in Urinary Bladder Cancer: A Retrospective Study.

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Original Research Article

ABSTRACT

Background: Urinary bladder cancer (UBC) exhibits marked heterogeneity in its clinicopathological characteristics, which directly influence treatment strategies and disease behavior. Understanding the correlation between pathological features and therapeutic approaches is crucial for optimizing patient management.

Aim: To evaluate the interplay between clinicopathological characteristics and treatment modalities in urinary bladder cancer and their implications for tumor behavior and clinical decision-making.

Method and Materials: This retrospective cohort study was conducted at the Department of Urology, Faculty of Medicine, Benghazi, in collaboration with the National Cancer Center, from January 2022 to December 2025. A total of 100 cases diagnosed via transurethral resection of bladder tumor (TURBT) and radical cystectomy were included. Non-neoplastic lesions were excluded. Data on demographics, clinical presentation, histopathology, tumor stage, grade, invasion status, and treatment were analyzed. Chi-square tests were used for associations, with $p < 0.05$ considered significant, with the calculation of odds ratios (OR) and 95% confidence intervals (CI).

Results: The data showed marked male predominance (91%; ratio 10.1:1) with a mean age of 60.2 ± 4.4 years. Most patients (90%) were aged 40–80 years. Painless hematuria (58%) and smoking (87%) were predominant. Urothelial carcinoma accounted for 92% of cases. Muscle-invasive disease was present in 62%, and 66% had high-grade tumors. A significant association was observed between tumor grade and muscle invasion ($\chi^2 = 15.60$, $p < 0.001$), with high-grade tumors being significantly more likely to present with invasive disease (OR = 5.73; 95% CI: 2.33–14.10).Treatment showed a significant association with disease category ($\chi^2 = 95.05$, $p < 0.001$).

Conclusion: UBC in this region is characterized by advanced presentation and aggressive biological behavior. The strong correlation between high grade and invasion emphasizes the urgent need for earlier detection strategies and tobacco cessation programs.

KEYWORDS: Urinary bladder cancer (UBC), clinicopathological characteristics, tumor staging, treatment strategies, clinical decision-making.

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INTRODUCTION

Urinary bladder cancer (UBC) remains a significant global health challenge due to its high incidence, recurrence rates, and variable prognosis depending on tumor stage and grade[1] . UBC is among the most common malignancies worldwide, characterized by diverse clinical behavior ranging from indolent non–muscle–invasive tumors to highly aggressive invasive disease[2] . This heterogeneity is largely attributable to underlying clinicopathological parameters, particularly tumor stage, histological grade, and invasion depth[3].

Accurate clinicopathological assessment is pivotal in shaping treatment choices, ranging from conservative management of non-muscle-invasive disease to radical interventions in muscle-invasive cases[4] . Emerging insights have revealed molecular signatures and immune microenvironment features that govern treatment efficacy and long-term outcomes [5]

Notwithstanding these advances, integrating comprehensive pathological features with real-world treatment approaches remains fundamental for disease stratification and selection of therapeutic strategies[6] . Nevertheless, increasing evidence demonstrates that staging alone may not fully capture tumor biology. Histopathological parameters, including tumor grade and invasion status, provide additional insights into tumor aggressiveness and potential progression[7] .

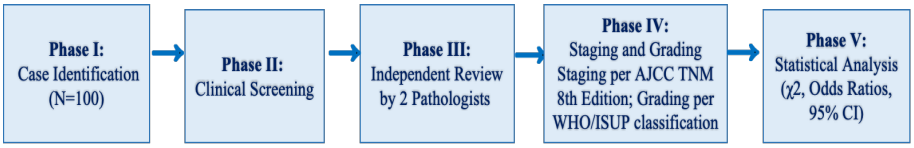
The management of UBC is guided chiefly by disease stage, with therapeutic options ranging from transurethral resection to radical cystectomy and systemic therapies[8] . However, variations in treatment patterns are regularly noted, reflecting disparities in histopathological findings and clinical practice[9] . Although the recognized importance of clinicopathological factors and their integrated role in shaping treatment strategies remain insufficiently explored, particularly in practical clinical settings[10] . Therefore, this study aims to determine how clinicopathological features of urinary bladder cancer influence tumor behavior and guide pathology-driven treatment decisions.

Material Methods

Study Design and Population

This retrospective cohort study was conducted at the Department of Urology, Faculty of Medicine, Benghazi, in collaboration with the National Cancer Center, from January 2022 to December 2025. The study included 100 consecutive cases of primary urinary bladder cancer diagnosed via transurethral resection of bladder tumor (TURBT) and radical cystectomy. Patients with non-neoplastic lesions, such as acute or chronic cystitis, were excluded.

Study Implementation Flowchart



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Pathological Assessment

Histopathological slides were independently reviewed by two experienced pathologistsDiscrepancies regarding tumor grade or staging were resolved through consensus review to ensure diagnostic reliability .Tumor staging was performed according to the AJCC TNM Classification8 ,th Edition .Grading followed the WHO/ISUP classification system, categorizing tumors into low-grade (LG)and high-grade (HG).

Statistical Analysis

Data were analyzed using descriptive statistics for demographics and clinical featuresBivariate associations between categorical variables) e.g ,.grade vs. Invasion status (were assessed using the chi-square (X^2) test ,with a significance threshold :a value of P 0.05>was taken as significant and P 0.01> as highly significant ,whereas P 0.05< was taken as non-significant.

To quantify the strength of the association between tumor grade and invasion, odds ratios (ORs) were calculated using standard formulae, with 95% confidence intervals (CIs) reported. A univariate chi-square test was employed rather than multivariate logistic regression due to the sample size (N = 100). Logistic regression models generally require a sufficient number of events per variable (EPV), typically at least 10:1, to ensure model stability and avoid overfitting. Given the cohort size and the distribution of variables, the use of a multivariate model would have risked generating unstable coefficients and potentially inflated effect estimates.

3. Result

A total of 100 cases diagnosed with urinary bladder cancer were included in this study. There was a marked male predominance (91% males vs 9% females), yielding a male-to-female ratio of 10.1:1 (Table 1).

Table (1): Clinicodemographic Characteristics and Risk Factors in UBC Patients (N=100)

Variable	Frequency (%)
Age group	
≤20 Y	1(1%)
20–40 Y	6 (6%)
40–60 Y	52 (52%)
60–80 Y	38 (38%)
≥80 Y	3 (3%)
Sex	91(91%)
Male	9 (9%)
Female	M: F = 10.1:1
Clinical presentation	
Painless hematuria	58 (58%)
Hematuria with burning micturition	9 (9%)
Hematuria with urinary retention	22 (22%)
Urinary retention	4 (4%)
Burning micturition	6 (6%)
Loin pain	1 (1%)
Associated risk factor	
Smoking history	
Yes	87%
No	13%
Total	**100 (100%)**

The age range of the patients was 18-80 years. The mean age at diagnosis was 60.2 ± 4.4 years, with most patients (90%) falling within the 40–80 years age group. Only 6% (6 of 100) of the patients presented with bladder cancer at a younger age than 40 years, while only 1 patient presented at less than 20 years of age. Painless hematuria alone was the most common clinical presentation in (58%) of cases, followed by hematuria associated with urinary retention (22%) and burning micturition (9%). Smoking was identified as the predominant risk factor, present in 87% of the cohort.

In Table 2, histopathological analysis demonstrated that urothelial carcinoma (transitional cell carcinoma) (TCC) was the dominant histopathological subtype (92%), whereas squamous cell carcinoma (SCC) constituted only 8%. Regarding tumor staging, (22%) cases were urothelial confined carcinoma (PTa), (16%) lamina propria invasive carcinoma (PT1), and (62%) muscle-invasive carcinoma (PT2). Among the studied cases, high-grade urinary bladder carcinoma was found to be the most common, with (66%), and low-grade carcinoma com-

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prised (34%).

This highlights the aggressive biological behavior of bladder tumors in this cohort. Consistently, muscle-invasive bladder cancer (MIBC) was observed in 62% of patients, compared to 38% with non-muscle-invasive bladder cancer (NMIBC).

Table (2): Clinicopathological Characteristics of UBC Patients in Our Study.

Variable	N (%)
Tumor histology	
TCC	92 (92%)
SCC	8 (8%)
Pathologic Stage	
(PTa) non-invasive	22 (22%)
(PT1)Lamina propria invasion	16 (16%)
(PT2) Muscle invasive	62 (62%)
Grade	
Low (LG)	34 (%)
High (HG)	66 (66%)
Muscle invasion	
Non-Muscle invasion (NMIBC) =PTa,PT1	38 (38%)
Muscle invasion (MIBC)=PT2-PT4	62 (62%)
Total	**100%**

Regarding the association between Grade and Muscle Invasion ;A highly significant association was found between histological grade and the presence of muscle invasion (χ^2=15.60, df=1, p<0.001). High-grade tumors were significantly more likely to present with muscle-invasive disease (OR=5.73;95% CI: 2.33−14.1 as shown in Table.(3).

Table (3): Association of Tumor Grade and Muscle Invasion Status in Bladder Cancer

Grade	MIBC	NMIBC	Total
High grade	50	16	66
Low grade	12	22	34
Total	**62**	**38**	**100**

Chi-square test showed a highly significant association between tumor grade and muscle invasion status ($\chi^2 = 15.60$, df = 1, $p < 0.001$).

Risk-adapted therapeutic strategies in patients with urothelial bladder cancer (UBC) demonstrated clear stratification based on histopathological classification and disease severity level. Patients with low-risk NMIBC (PTa, low grade) were predominantly managed with TURBT followed by intravesical chemotherapy (18/22, 81.8%), reflecting standard conservative management for low-risk disease, with minimal use of BCG (18.2%) and no use of trimodal therapy. In contrast, high-risk NMIBC (PT1, high grade) required more intensive management, including TURBT combined with Bacillus Calmette–Guérin (BCG) therapy (12/16, 75%), with consideration of early radical cystectomy for BCG-unresponsive disease. A small proportion received chemotherapy (18.8%) or trimodal therapy (6.2%), likely reflecting individualized clinical decisions or disease progression risk .Therapeutic approaches were appropriately escalated according to disease category ($\chi^2 = 15.60$, df = 1, $p < 0.001$). For patients with MIBC (PT2–PT4), the majority were treated with trimodal therapy (50/62, 80.6%), incorporating radical cystectomy, neoadjuvant chemotherapy, and radiotherapy. Notably, none of the MIBC patients received TURBT with chemotherapy alone, highlighting the appropriate escalation of treatment intensity. A minority received BCG (19.4%), which may reflect selected cases with mixed features or transitional management, as shown in Tables (4).

Table (4): Risk-Adapted Treatment Stratification and Clinicopathological Correlation

Grade / Invasion group	Risk Stratification	TURBT + chemotherapy	TURBT + BCG	Trimodal therapy	Total
NMIBC	Low-risk (PTa, LG)	18	4	0	22
NMIBC	High-risk (PT1, HG)	3	12	1	16
MIBC	(PT2–PT4)	0	12	50	62
Total		**21**	**28**	**51**	**100**

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TURBT: Transurethral Resection of Bladder Tumor .BCG :Bacillus Calmette-Guérin) Intravesical Immunotherapy .(Trimodal therapy = (radical cystectomy with neoadjuvant chemotherapy + radiotherapy).

Chi-square test showed A significant relationship was observed between disease category and treatment approach.

($\chi^2 = 95.05$, df = 4, $p < 0.001$).

DISCUSSION

The clinicopathological profile observed in this Benghazi cohort reveals an aggressive disease behavior characterized by advanced presentation at diagnosis. The male-to-female ratio of approximately 10:1 demonstrates a profound male predominance. This disparity markedly exceeds the global average, where bladder cancer prevalence is typically three to four times higher in males than in females [11,12] It also surpasses the 7:1 ratio reported in recent epidemiological data from Tripoli, indicating regional variations within Libya itself [11,13]. This stark gender imbalance is heavily influenced by local sociocultural habits, specifically the 87% smoking rate recorded among males in this cohort compared with the near-zero tobacco use reported among local females [14].

Age remains a critical demographic determinant; 87% of all bladder cancer cases in this study occurred between the ages of 40 and 80. This concentrated age distribution mirrors established global patterns demonstrating a rising incidence of urothelial malignancies with advancing age, a phenomenon driven by decades of cumulative exposure to environmental carcinogens and tobacco smoke [11,12]. This distinct age clustering underscores the clinical necessity of establishing targeted secondary screening and diagnostic pathways for individuals presenting with lower urinary tract symptoms aged 40 and older [6,12].

Painless gross hematuria emerged as the primary clinical presentation within this cohort. This clinical pattern is highly consistent with international literature confirming that patients presenting with gross hematuria have a significantly higher risk of advanced stage disease at initial resection than those presenting with microscopic hematuria or storage symptoms [13]. While painless hematuria represents the classic diagnostic hallmark of urothelial malignancy, its absence cannot definitively rule out underlying disease [1,13] Prompt diagnostic evaluation of any presentation of hematuria remains the single most critical factor in mitigating diagnostic delay and improving long-term oncological outcomes [6,10].

Tobacco use represents the primary preventable risk factor driving both the incidence and mortality of bladder carcinoma in this population. Large-scale pooled analyses indicate that current smokers experience a 3-fold higher risk of developing bladder cancer than never-smokers, with a clear dose-dependent relationship between smoking intensity and poor long-term prognosis [14] The heavy tobacco burden identified in this cohort directly correlates with the aggressive disease characteristics observed at the time of surgical resection.

A critical, defining feature of this Benghazi cohort is that 62% of patients presented with muscle-invasive bladder cancer (MIBC; stages ≥pT2) at initial diagnosis. This distribution represents a striking reversal of the epidemiological patterns typically documented in Western populations, where non-muscle-invasive bladder cancer (NMIBC) accounts for approximately 75% of new cases [15]. This profound discrepancy points to a significant diagnostic gap within the local healthcare infrastructure. Patients frequently overlook or misinterpret intermittent, painless hematuria, delaying clinical consultation until the tumor has breached the muscularis propria [1,7,13]. Furthermore, our findings show a powerful statistical association between high tumor grade and muscle invasion (OR=5.73, p<0.001), demonstrating that high-grade tumors in this region are nearly six times more likely to be deeply invasive at presentation than low-grade lesions. Compared to historical data from Benghazi collected between 1983 and 2009, which reported a poorly differentiated/high-grade rate of only 16.6%, the 66% high-grade rate identified in the current cohort indicates

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either an alarming evolutionary shift toward more aggressive biology or a substantial improvement in modern histopathological diagnostic precision [1,3,7]. Because traditional tumor staging and grading systems can sometimes exhibit limited prognostic sensitivity—particularly in predicting individual progression rates for high-risk pT1 disease or muscle-invasive tumors there is an increasing clinical reliance on advanced risk-stratification models [2,16,17]. Modern frameworks incorporate detailed morphological and microenvironmental criteria, including tumor budding, specific growth patterns, and tumor-infiltrating immune cells, to better capture aggressive tumor biology [2,5,17]. For NMIBC, standard risk models integrate tumor stage, grade, size, multiplicity, and the concurrent presence of carcinoma in situ (CIS) to tailor therapeutic intensity appropriately [15].

The therapeutic choices documented in this study demonstrate close adherence to a risk-adapted strategy, in which treatment intensity scales directly with the biological aggressiveness of the tumor. A highly significant association was observed between tumor stage, grade, and the selected treatment modality (χ 295.05= , P0.001>). Patients presenting with low-risk NMIBC (pTa, low-grade) were managed primarily via transurethral resection of bladder tumor (TURBT) combined with immediate intravesical chemotherapy; an approach robustly supported by evidence demonstrating a substantial reduction in short-term recurrence rates [18,19].

For patients diagnosed with high-risk NMIBC (pT1, high-grade), treatment was appropriately escalated to TURBT followed by induction and maintenance intravesical Bacillus Calmette-Guérin (BCG) immunotherapy [15,20,21]. Radical cystectomy was selectively reserved as an upfront strategy for very high-risk disease or as a salvage intervention for BCG-unresponsive cases, balancing long-term oncological control with patient quality of life [22,23]. Furthermore, emerging data indicate that alternative intravesical combinations, such as sequential gemcitabine and docetaxel, offer an effective secondary therapeutic avenue for patients facing BCG shortages or treatment failure [24]. For the majority of patients presenting with MIBC (pT2–pT4), treatment shifted toward a multimodal approach. This strategy centered on radical cystectomy, neoadjuvant platinum-based combination chemotherapy, and targeted radiotherapy, aligning with modern global standards designed to optimize overall survival while attempting bladder preservation where clinically feasible [4,8,25].

LIMITATIONS

This study has several limitations that must be considered when interpreting the data. First, its retrospective nature introduces potential documentation bias, particularly regarding the quantification of secondary risk factors, occupational exposures, and precise smoking histories (such as pack-years). Second, as a single-center study conducted within a major tertiary hospital in Benghazi, the findings may not fully capture the complete epidemiological, socioeconomic, or geographic diversity of the broader Libyan population. Third, the sample size (N=100) restricted our ability to execute stable multivariate logistic regression analyses to simultaneously control for age, gender, and smoking intensity as independent predictors of stage progression. Finally, the absence of advanced molecular subtyping and long-term survival data limits our capacity to evaluate the ultimate, multi-year survival efficacy of the risk-adapted treatment strategies deployed in this cohort.

CONCLUSION AND RECOMMENDATIONS

Urinary bladder cancer in eastern Libya presents predominantly as an aggressive, high-grade, and muscle-invasive malignancy at the time of initial diagnosis. It primarily affects middle-aged and older males with a heavy history of tobacco use. The strong statistical correlation between high tumor grade and deep muscle invasion demands a shift from reactive management to proactive, early diagnostic interventions.

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RECOMMENDATIONS

Public Health Initiatives: Establish and fund aggressive, targeted tobacco cessation programs as a form of primary oncological prevention, focusing heavily on high-risk male demographics.

Early Detection & Education: Launch widespread public health campaigns and primary care educational seminars focusing on the critical clinical significance of painless gross hematuria. This is essential to encourage early presentation, reduce diagnostic delays, and capture urothelial tumors at the highly treatable, non-muscle-invasive stage.

Pathological Standardization: Implement standardized synoptic pathology reporting protocols across all regional diagnostic centers in eastern Libya, strictly adhering to the updated AJCC Cancer Staging manual and WHO grading criteria to optimize risk stratification.

Expanded Research: Fund prospective, multi-center registry studies across Libya that incorporate survival tracking and molecular biomarker analysis to address the diagnostic gaps identified in this cohort.

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Conflicts of interest

There are no conflicts of interest.

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