Correlation Between Tissue Changes and Clinical Outcomes in urinary Bladder Carcinoma patients in Babylon

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Abstract. **General Background:** Urinary bladder cancer is among the most prevalent malignancies worldwide, with its progression strongly influenced by clinicopathological characteristics. **Specific Background:** Despite extensive documentation of urothelial carcinoma behavior, variations in tissue morphology and their clinical correlations remain insufficiently clarified in regional populations. **Knowledge Gap:** Limited data exist regarding how histopathological patterns relate to tumor grade, stage, and patient demographics in Iraqi cohorts. **Aim:** This study examined the key pathological alterations in 50 bladder cancer patients to determine the association between tissue characteristics, tumor aggressiveness, and clinical outcomes. **Results:** High-grade tumors were predominant (80%), with most cases invading the deep muscle (78%). Men were disproportionately affected, and smoking emerged as a major risk factor. A significant correlation was observed between patient age and both tumor grade and stage, indicating that older individuals tend to present with more advanced disease. **Novelty:** The study highlights distinct high-grade T1 variants that may offer additional prognostic value, emphasizing heterogeneity within early-stage tumors. **Implications:** These findings underscore the need for improved risk-stratification strategies, earlier detection, and larger prospective studies to refine diagnostic and management protocols for bladder carcinoma..
Highlights:

1. The study shows most cases present as high-grade and advanced stage.
2. Smoking and chemical exposure appear as major contributing risks.
3. Tumor grade and invasion depth remain key indicators for diagnosis and management.

Keywords: Bladder Cancer, Papillary Carcinomas, Histopathological Features, Tumor Grade, Age

Introduction

The bladder, a vital organ in the human body, collects and excretes urine .via contractions . Congenital anomalies, systemic diseases, tumor excision, and accidental trauma are significant ailments or injuries that commonly require bladder reconstruction surgery. There are over 573,000 new cases of urinary bladder cancer, ranking it as the tenth most prevalent cancer globally and representing 3% of all cancer diagnoses[1]. Urinary bladder cancer is an age-associated ailment that occurs more frequently in males than in women, and the course of the disease is significantly greater in women. It ranks among the top twelve causes of mortality globally

Bladder cancer is primarily classified into two principal subtypes: muscle-invasive bladder cancer (MIBC) and non-muscle-invasive bladder cancer (NMIBC).

a multitude of environmental, occupational, and genetic factors are associated with the onset of bladder tumors. Urothelial carcinoma is the predominant histological variant of bladder cancer, and is, succeeded by squamous cell carcinoma[2].

The Age-Standardized Incidence Rate (ASR) is estimated at 9.6 per 100,000 for males and 2.4 per 100,000 for females, despite significant geographical variance. Tobacco consumption is the primary recognized risk factor for bladder cancer, responsible for approximately fifty percent of all cases[3]. Moreover, other recognized environmental risk factors, including carcinogens, account for approximately 20% of all cases8. Bladder cancer susceptibility is mostly determined by genetic predisposition, as well as environmental and occupational factors. A multitude of genetic alterations and polymorphisms have been identified as factors affecting an individual's susceptibility to bladder cancer[4].The Age-Standardized Incidence Rate (ASR) is calculated as 9.6 per 100,000 for males and 2.4 per 100,000 for females, albeit considerable geographical variation. Tobacco use is the principal acknowledged risk factor for bladder cancer, accounting for around fifty percent of all instances. Additionally, other acknowledged environmental risk factors, such as carcinogens, constitute around 20% of all cancer cases. The susceptibility to bladder cancer is mostly influenced by genetic predisposition, in conjunction with environmental and occupational variables[5]. Various genetic modifications and polymorphisms have been recognized as determinants of an individual's vulnerability to bladder cancer. In urothelial carcinomas (UCs), Clinic pathological variables, particularly tumor grade and stage, are recognized as significant prognostic indicators of urothelial carcinoma (UC)[6]. Moreover, recent research has provided significant insights into potential biomarkers that may predict the progression and characteristics of UC tumors.

The prior histopathological features of various bladder tissues and the associations between tumor grade and stage, along with the relationships between age and tumor histological grade and stage, constituted the basis of the present study[7].

Methodology

This study was conducted between November 2024 and April 2025 at the Hila Teaching Hospital laboratory in Babylon, Iraq. A total of 50 bladder cancer samples, were kept in standard 10% formalin. All tissues were subjected to histological investigation, treated per the standard protocol, and sectioned in paraffin. Were cut to micrometers in thickness using a semi-automatic microtome (LEICA RM 2145, Leica Instruments GmbH, and Germany). stained with Hematoxylin and Eosin, and We examined the histological slides using a fluorescence microscope (OLYMPUS) at

magnifications ranging from 40 to 400 in the hospital we worked in. Informed written consent was obtained from all patients. Patient records were thoroughly examined to collect information on age, sex, histological subtype, tumor grade, and pathological stage. depending on the two consultant pathologists. If there is any bias in the results, look into deeper bladder cancer sections .The tumor grading was determined by cellular and architectural atypical. Low-grade urothelial carcinoma exhibits minimal to moderate architectural complexity (fused, branching papillae with increased epithelial thickness) and cytological atypical (mild to moderate pleomorphism, prominent nucleoli and mitosis at various levels), whereas high-grade carcinoma demonstrates pronounced architectural complexity (complex papillae, discohesive cells) and cytological atypia (marked pleomorphism, brisk atypical mitosis). The stage was determined by the degree of tumor invasion, namely whether it was confined to the lamina propria (T1) or infiltrating the detrusor muscle (T2).

Statistical analysis

SPPS 21 was used to enter and analyze the collected data for statistical analysis. All quantitative data, including patient age, were measured using mean and standard deviation. Frequencies and percentages were employed For each qualitative variables (tumor grade, stage, and sex), To ascertain the link between tumor grade and stage, as well as between age and tumor grade and stage, the chi-square test was used, and a value of $p < 0.05$ was statistically significant.

Ethical approval

The histological sections of the patients were acquired under supervision, and the status of each patient was validated by the pathological laboratory at Hilla General Teaching Hospital. Biopsy elimination of did not adversely affect the patients. (Number of block sections .

Results

Of the 50 bladder cancer specimens, 16 (32%) were from female patients and 34 (68%) were from male patients[8]. The patients' mean age was 55.31± 12.45 years, according to Table 1. Smoking was cited as a risk factor by 60% of the patients, followed by nonsmoking at 40% and chemical exposure at 40% Table 1. As shown Table 2 of Clinic-pathological features, the most prevalent symptoms were hematuria (54%), Lower Abdominal or Back Pain (16%), and Pelvic Pain (12%). The majority of patients had tumor grade High grad (80%) but low grade (20%) followed by tumor stage T2 (78%) whileT1 (22%). Urinary Tract Infections (38%), family history (44%), and arthritis 50%.

Out of 50 carcinoma cases, 40(80%) were diagnosed as high grade papillary carcinoma (Fig 2) and 10(20%) as low grade papillary carcinoma, as shown in (fig1&3).

Of the 50 bladder cancer cases, 30 (56.5%) invaded the deep muscle and 35 (43.4%) invaded the underlying lamina propria (fig. 4, 5).

High-grade morphological tumors at advanced stages are more prevalent in elderly patients[9]. The Chi-square test was used to ascertain the correlation between patient age and tumor grade and stage, correlation was established between age of the patient's and the tumor of stage and grade ($p < 0.05$).show in Table 3.

Table1 : Characteristic in patients of Bladder carcinoma

Age (years), mean ± SD	55.31± 12.45
Gender,	N (%)
-Male	34(68%)
Female	16(32%)
Smoking history	, n (%)
-Smoker	30(60%)
-Nonsmoker	20(40%)
Exposure to chemicals	20(40%)
Urinary Tract Infections	19(38%)
Family history	22 (44%)

Table 2: Clinical-pathological features

Pain in the lower abdomen or back	8(16%)
Pelvic pain	6(12%)
Hematuria	27(54%)
Tumor stage	
T1	11(22%)
T2	39(78%)
Tumor Grad	
High grad	40(80%)
Low grad	10(20%)

Table3: Correlation of patient's age with tumor grade and stage

(n=50)

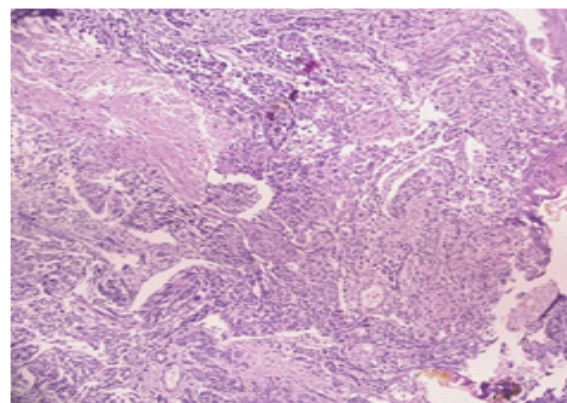| Age	Tumor grade low grad	High grad	Tumor stage T1	T2	P value
30-40	2 (4%)	1 (2%)	2 (4%)	1 (2%)	
41-50	3 (6%)	8 (16%)	3 (6%)	5 (10%)	P < 0.05
51-60	4 (8%)	19 (38%)	5 (10%)	18 (36%)	
61-70	1 (2%)	12 (24%)	1 (2%)	15(30%)	
Total	10(20%)	40(80%)	11(22%)	39(78%)	
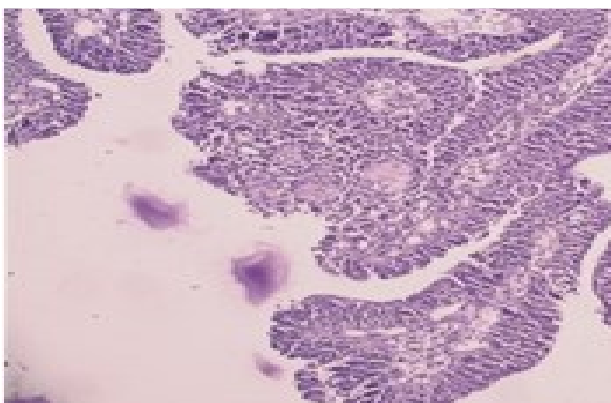
Figs 1: low grad carcinoma

Fig2: High grade papillary carcinoma
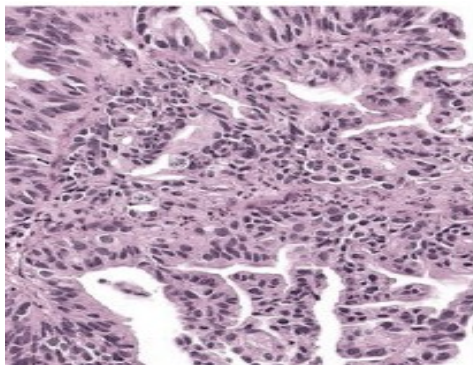
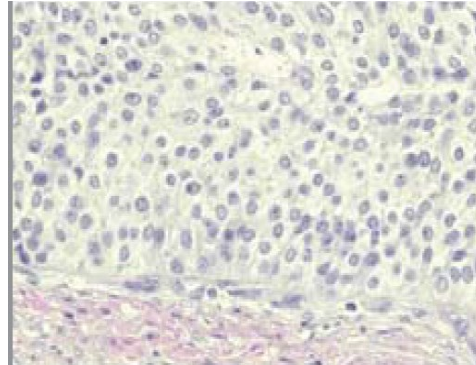**Fig 3:** papillary carcinomas

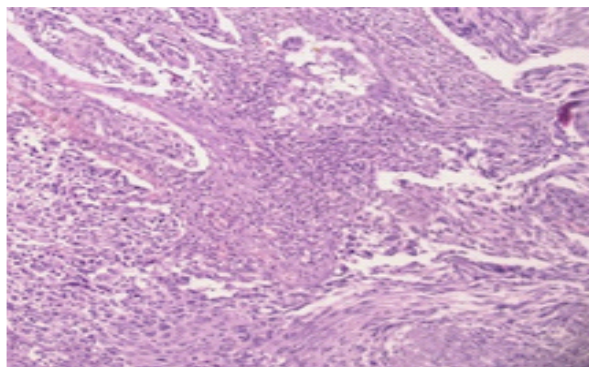**Fig4:** High grade tumor invading underlying lamina

Fig5: High grade tumor invading the muscle

Discussion

Bladder carcinoma displays morphological heterogeneity too wing intra-tumoral heterogeneity, ultimately resulting in the presence of many bladder cancer variants (variant histology)[10].

The mean age of the patients was 55.31±12.45, indicating that the bulk of the study group was old[11]. In this study, males (34; 68%) with a mean age of 59 years had a higher incidence of bladder cancer than females (16; 32%). Research by Al-Thuwaini MM et al. and Kim TJ et al. indicated that bladder cancer is 3–4 times more prevalent in older men than in women, with the etiology of this disparity in men still unidentified[12]. , The male predominance in our study illustrates the lifestyle disparities between men and women in our country, as males are more prone to smoking, acquiring schistosomal infections, and encountering occupational dangers that may lead to bladder cancer[13]. The established link between tobacco exposure and carcinogenesis is reinforced by the correlation between smoking history and bladder cancer risk[14].

 These results are comparable to those of the current investigation. Similar to the findings of our study, other studies haves demonstrated a correlation between high Grade morphology and tumor Stage as well as between patient Age and Tumor Grade and Stage[15].

The current study additionally examined the correlation between depth of invasion and tumor grade[16]. Low-grade tumors exhibited lamina propria invasion in 9 (60%) cases and deep muscle involvement in only 6 (40%) cases[17]. Only nine (29%) of the tumors with grade morphology were restricted to the lamina propria (T1), while 22 (70%) invaded the deep muscle (T2). Detrusor muscle invasion was seen in 16% of patients with low grade bladder carcinoma and 76.92% of cases with high grade tumors, according to a study by Shrestha EP and Akhtar ZM et al., which is in good agreement with our study[18].

Currently, micropapillary or, infrequently, nested variations have been the focus of the majority of articles on T1 bladder carcinoma with variant histology[19]. A depiction of other polymorphisms found in HGT1 carcinomas with varying susceptibilities to survival and recurrence were also included in our analysis[20]. We were able to determine the low- and high-risk classifications linked to various variations using this method[21]. This encompasses both nested and micropapillary lesions, reportedly associated with aggressive behavior

Various studies have demonstrated a correlation between high-grade morphology and tumor stage, as well as a relationship between patient age and tumor grade and stage, which aligns with our findings[22]. The findings of a local study by Samoa RP et al, which examined the correlation between bladder cancer, age, and sex, contradicted our study results.

Conclusion

The findings of this study indicate that men are more predisposed to develop bladder cancer than women. Our study identified several high-grade T1 bladder carcinomas where specific variants offer additional predictive insights in this heterogeneous tumor, underscoring the importance of early diagnosis based on the clinico-pathological characteristics of bladder carcinoma. Consequently, additional research utilizing a larger sample size and a- prospective longitudinal study design is necessary. Early detection not only improves patient prognosis but also aids clinicians in selecting appropriate therapeutic strategies, thereby reducing the risk of recurrence and disease progression. Furthermore, understanding the distribution of tumor variants may assist in refining risk-stratification models and guiding individualized patient management.

Despite the strength of our findings, this study is limited by its sample size and retrospective design. Therefore, future research with a larger cohort, preferably through prospective longitudinal studies, is essential to validate these results, clarify the prognostic significance of the identified variants, and enhance current diagnostic and management protocols for bladder carcinoma.

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