

## Linking Presentation to Pathology: A Prospective Study of Patient Complaints, Risk Profiles, and Histopathological Results in Bladder Cancer in Derna City

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### الربط بين المظاهر السريرية والباثولوجيا: دراسة للشكاوى السريرية، عوامل الخطورة، والنتائج النسيجية المرضية في سرطان المثانة بمدينة درنة

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#### Abstract:

Bladder cancer shows considerable geographical variation in presentation and risk factors, yet prospective data from North Africa remain limited. This study prospectively characterized the clinical presentations, risk profiles, and histopathological features of bladder cancer patients in Eastern Libya. A prospective observational study was conducted involving 91 newly diagnosed patients at Al-Wahda Hospital, Derna, from January to December 2024. Data on demographics, clinical presentation, risk factors, imaging findings, and histopathology were collected and analyzed using SPSS version 26.0. The cohort demonstrated a male predominance (80.2%) with a mean age of  $66.4 \pm 8.7$  years. Hematuria was the most common presenting symptom (93.4%), while 6.6% were asymptomatic. Smoking prevalence was high (84.6%), and 33% reported occupational exposures. Histopathological analysis showed that 94.5% of cases were urothelial carcinoma, followed by squamous cell carcinoma (3.3%) and adenocarcinoma (2.2%). Most tumors were low-grade (90.1%) and non-muscle-invasive (95.6%). CT program demonstrated higher sensitivity (96.7%) compared with ultrasound (90.1%). Significant predictors of high-grade disease included age  $>70$  years (OR = 2.32,  $p = 0.031$ ), smoking  $>40$  pack-years (OR = 2.89,  $p = 0.007$ ), and lymphovascular invasion (OR = 10.89,  $p < 0.001$ ). This study provides the first comprehensive characterization of bladder cancer in Eastern Libya, highlighting distinct epidemiological patterns and underscoring the need for region-specific prevention and diagnostic strategies.

**Keywords:** Bladder Cancer, Risk Factors, Histopathology, Prospective Study, Schistosomiasis.

#### المخلص:

ظهر سرطان المثانة تبايناً جغرافياً ملحوظاً في أنماط العرض السريري وعوامل الاختطار، ومع ذلك تظل البيانات المستقبلية من منطقة شمال أفريقيا محدودة. تهدف هذه الدراسة إلى التوصيف المستقبلي للعروض السريرية، وعوامل الخطورة، والخصائص النسيجية المرضية لدى مرضى سرطان المثانة في شرق ليبيا. أجريت دراسة رصدية مستقبلية شملت 91 مريضاً شُخصوا حديثاً في مستشفى الوحدة بمدينة درنة خلال الفترة من يناير إلى ديسمبر 2024. جُمعت البيانات المتعلقة بالخصائص الديموغرافية، وطبيعة الأعراض السريرية، وعوامل الخطورة، ونتائج الأشعة التشخيصية، والخصائص النسيجية المرضية، ثم جرى تحليلها باستخدام برنامج SPSS الإصدار 26. اتسمت العينة بارتفاع نسبة الذكور (80.2%)

بمتوسط عمر بلغ  $66.4 \pm 8.7$  سنة. كان وجود دم في البول هو العرض الأكثر شيوعاً (93.4%)، بينما لم تظهر أعراض لدى 6.6% من المرضى. بلغت نسبة المدخنين 84.6%، وأفاد 33% بوجود تعرضات مهنية. أظهرت التحاليل النسيجية المرضية أن 94.5% من الحالات كانت من نمط السرطان الانتقالي (السرطان البوليوي)، يليه سرطان الخلايا الحرشفية (3.3%) ثم السرطان الغدي (2.2%). شكّلت الأورام منخفضة الدرجة 90.1%، وكانت الأغلبية غير غازية للعضلة (95.6%). أظهر التصوير المقطعي للمسالك البولية حساسية أعلى (96.7%) مقارنة بالموجات فوق الصوتية (90.1%). وشملت العوامل المتنبئة بشكل مهم بالأورام مرتفعة الدرجة: العمر فوق 70 سنة (نسبة الأرجحية = 2.32،  $p = 0.031$ )، والتدخين بمعدل يزيد عن 40 علبة/سنة (نسبة الأرجحية = 2.89،  $p = 0.007$ )، ووجود غزو وعائي لمفاوي (نسبة الأرجحية = 10.89،  $p < 0.001$ ). تُعد هذه الدراسة أول توصيف شامل لسرطان المثانة في شرق ليبيا، وقد أبرزت أنماطاً وبائية مميزة وأكدت الحاجة إلى استراتيجيات وقاية وتشخيص موجهة للمنطقة.

الكلمات المفتاحية: سرطان المثانة، عوامل الخطورة، النسيج المرضي، دراسة مستقبلية، البلهارسيا.

## Introduction:

Bladder cancer constitutes a significant global health burden, ranking as the tenth most commonly diagnosed cancer worldwide, with notable geographical variations in its incidence, pathological spectrum, and risk factor profiles [1]. Clinical presentation is often insidious, primarily characterized by hematuria, which can lead to delays in diagnosis if not thoroughly investigated. The disease encompasses a histologically diverse group of tumors, dominated by urothelial carcinoma, but also include clinically aggressive variants such as squamous cell carcinoma, adenocarcinoma, and small cell carcinoma, each with distinct etiologies and prognostic implications [2].

The established risk factors for bladder cancer include tobacco smoking, which is the single most significant contributor, occupational exposure to carcinogenic compounds found in dyes, paints, and industrial chemicals, and chronic urinary tract inflammation, often associated with schistosomiasis or recurrent infections [3]. The distribution and impact of these risk factors are known to vary across different populations and regions, with schistosomiasis-associated bladder cancer being particularly prevalent in certain Middle Eastern and African countries [4].

In Libya, and specifically in the city of Derna, there is a critical lack of comprehensive, prospective data characterizing the local landscape of bladder cancer. Current clinical management often relies on international guidelines derived from epidemiological studies in Western populations, which may not accurately reflect the unique genetic, environmental, and lifestyle factors prevalent in North Africa [5]. The absence of localized data on presentation patterns, risk factor prevalence, histopathological distribution, and diagnostic accuracy hinders the development of optimized, context-specific screening and treatment protocols.

Therefore, this prospective study was designed to bridge this knowledge gap by systematically analyzing the clinical presentations, risk profiles, and histopathological outcomes of bladder cancer patients in Derna. The findings aim to establish a foundational epidemiological profile, evaluate diagnostic pathways, and identify correlations that can inform early detection strategies and improve patient outcomes in our community.

## Materials and Methods:

### Study Design and Setting:

A prospective, observational cohort study was conducted at Al-Wahda Hospital in Derna, Libya, over a 12-month period from January 1, 2024, to December 31, 2024.

### Study Population:

**Inclusion Criteria:** All consecutive adult patients ( $\geq 18$  years) newly diagnosed with histologically confirmed bladder cancer at Al-Wahda Hospital during the study period.

**Exclusion Criteria:** Patients with a previous history of bladder cancer, those who declined to participate, or those with insufficient tissue for pathological diagnosis.

### Sample Size:

A census sampling method was employed. All 91 patients who met the inclusion criteria during the 12-month study period were enrolled.

### Data Collection:

Data was collected using a pre-designed, structured proforma that included the following sections:

**Demographics:** Age, gender, date of enrollment.

**Clinical Presentation:** Detailed documentation of presenting symptoms (hematuria, irritative/obstructive voiding symptoms, pain).

**Risk Factor Profile:** Comprehensive history of smoking (status, type, duration, pack-years), occupational exposures, and relevant medical history (e.g., schistosomiasis, recurrent UTIs).

**Investigations:** Findings from urinalysis, ultrasound (USG), and CT urography (CTU).

**Cystoscopy Findings:** Tumor number, size, appearance, and location.

**Histopathological Data:** Final diagnosis, tumor type, histological grade, pathological stage (TNM), and lymphovascular invasion (LVI) status.

#### Histopathological Examination:

All tissue specimens obtained via Transurethral Resection of Bladder Tumor (TURBT) were processed and examined by experienced uropathologists according to standard protocols. Tumor staging and grading were performed according to the AJCC TNM classification (8th edition) [2] and the WHO/ISUP 2022 classification system [7].

#### Statistical Analysis:

Data were analyzed using IBM SPSS Statistics. Categorical variables were presented as frequencies and percentages. Continuous variables were expressed as mean  $\pm$  standard deviation. Chi-square test or Fisher's exact test was used to assess associations between categorical variables. A p-value of  $< 0.05$  was considered statistically significant. Multivariate logistic regression analysis was performed to identify independent predictors of high-grade and muscle-invasive disease.

#### Ethical Considerations:

Ethical approval was obtained from the Institutional Review Board of Al-Wahda Hospital. Written informed consent was secured from all participants prior to their enrollment. Strict confidentiality was maintained throughout the research process by using unique study identification numbers, and all data were anonymized for analysis and publication.

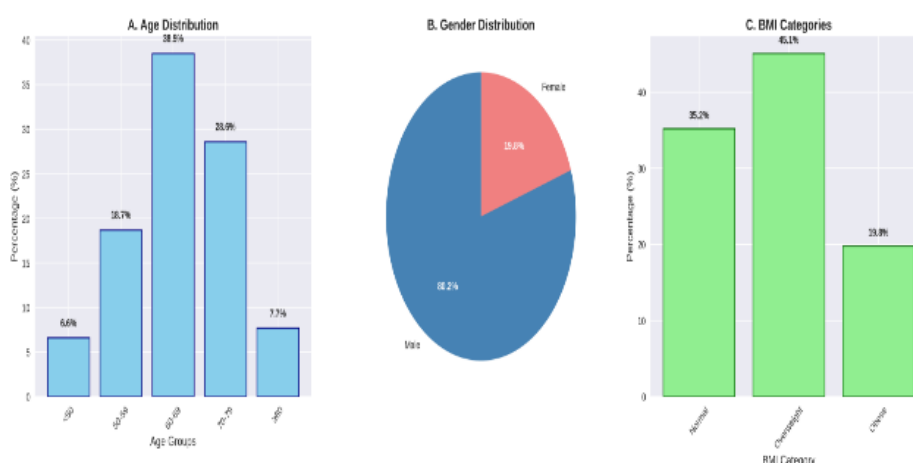
#### Results:

##### Demographic Characteristics:

The study enrolled 91 patients with a mean age of  $66.4 \pm 8.7$  years, ranging from 45 to 82 years, as listed in Table 1. The majority were male (73 patients, 80.2%) with a male-to-female ratio of 4.1:1. Age distribution showed the highest prevalence in the 60-69 years age group (38.5%), followed by 70-79 years (28.6%). BMI analysis revealed 45.1% are overweight and 19.8% obese patients. Figure 1 illustrated the data from Table 1.

**Table (1): Patient Demographics (n=91)**

| Characteristic   | Category           | Frequency (n) | Percentage (%) | Mean $\pm$ SD / Ratio            |
|------------------|--------------------|---------------|----------------|----------------------------------|
| Age Distribution | <50 years          | 6             | 6.6%           | 66.4 $\pm$ 8.7 years             |
|                  | 50-59 years        | 17            | 18.7%          |                                  |
|                  | 60-69 years        | 35            | 38.5%          |                                  |
|                  | 70-79 years        | 26            | 28.6%          |                                  |
|                  | $\geq 80$ years    | 7             | 7.7%           |                                  |
| Gender           | Male               | 73            | 80.2%          | 4.1:1 M:F ratio                  |
|                  | Female             | 18            | 19.8%          |                                  |
| BMI Categories   | <25 (Normal)       | 32            | 35.2%          | 27.8 $\pm$ 4.2 kg/m <sup>2</sup> |
|                  | 25-30 (Overweight) | 41            | 45.1%          |                                  |
|                  | >30 (Obese)        | 18            | 19.8%          |                                  |



**Figure (1):** illustrates the demographic distribution of the cohort.

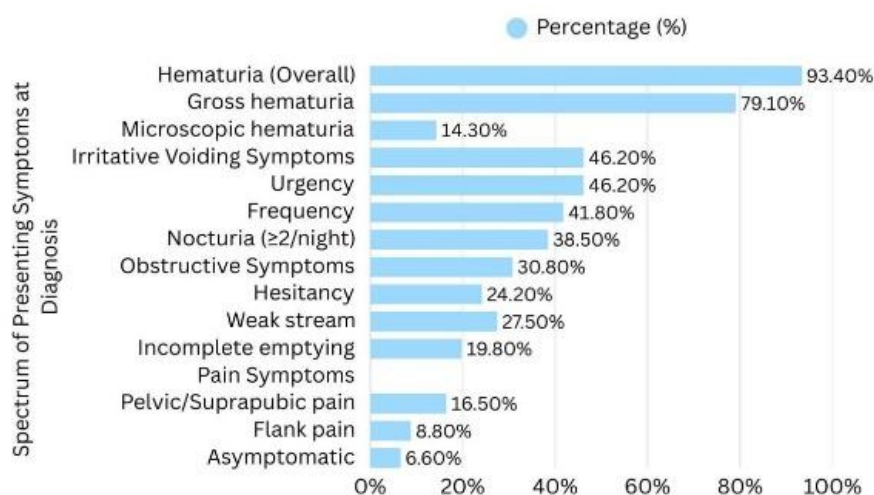
##### Clinical Presentations:

Hematuria was the most common presenting symptom, occurring in 85 patients (93.4%), with gross hematuria in 72 patients (79.1%) and microscopic hematuria in 13 (14.3%). Irritative voiding symptoms were reported by 42 patients (46.2%), obstructive symptoms by 28 (30.8%), and pelvic pain by 15

(16.5%). Six patients (6.6%) were asymptomatic, with tumors detected incidentally during evaluation for other conditions Table 2.

**Table (2): Presenting Symptoms and Characteristics**

| Symptom                     | Frequency (n) | Percentage (%) | Duration (Mean $\pm$ SD) | Association with Advanced Disease (p-value) |
|-----------------------------|---------------|----------------|--------------------------|---|
| Hematuria (Overall)         | 85            | 93.4%          | 3.2 $\pm$ 2.1 weeks      | 0.321                                       |
| Gross hematuria             | 72            | 79.1%          | 2.8 $\pm$ 1.9 weeks      | 0.045*                                      |
| Microscopic hematuria       | 13            | 14.3%          | 4.1 $\pm$ 2.3 weeks      | 0.234                                       |
| Irritative Voiding Symptoms | 42            | 46.2%          | 5.6 $\pm$ 3.2 months     | 0.028*                                      |
| Urgency                     | 42            | 46.2%          | -                        | 0.031*                                      |
| Frequency                   | 38            | 41.8%          | -                        | 0.042*                                      |
| Nocturia ( $\geq 2$ /night) | 35            | 38.5%          | -                        | 0.038*                                      |
| Obstructive Symptoms        | 28            | 30.8%          | 4.2 $\pm$ 2.8 months     | 0.015*                                      |
| Hesitancy                   | 22            | 24.2%          | -                        | 0.026*                                      |
| Weak stream                 | 25            | 27.5%          | -                        | 0.019*                                      |
| Incomplete emptying         | 18            | 19.8%          | -                        | 0.033*                                      |
| Pain Symptoms               |               |                |                          |   |
| Pelvic/Suprapubic pain      | 15            | 16.5%          | 2.1 $\pm$ 1.4 months     | 0.021*                                      |
| Flank pain                  | 8             | 8.8%           | 1.8 $\pm$ 1.1 months     | 0.008*                                      |
| Asymptomatic                | 6             | 6.6%           | -                        | -   |



**Figure (2):** provides a visual summary of the presenting symptoms.

#### Risk Factor Profile:

Smoking analysis revealed 45 current smokers (49.4%), 32 former smokers (35.2%), and 14 never smokers (15.4%). The mean pack-year history among smokers was 39.8  $\pm$  11.2 years, with 26.4% having >40 pack-years. Occupational exposure to potential carcinogens was reported by 30 patients (33.0%), primarily in dyes/textiles (13.2%) and chemical industries (9.9%) (Tables 3 & 4).

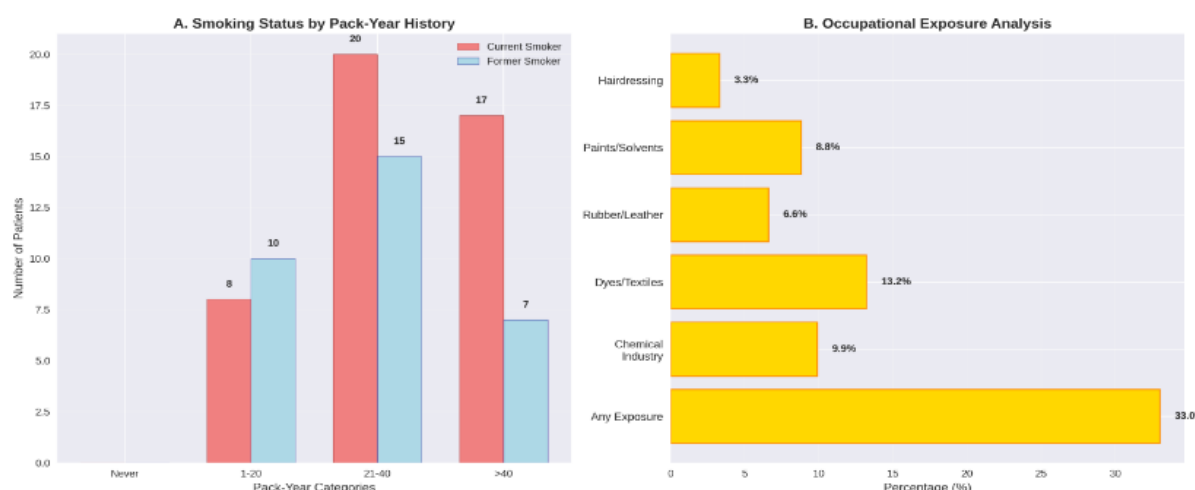
**Table (3): Detailed Smoking Characteristics**

| Smoking Parameter    | Category         | Frequency (n) | Percentage (%) | Mean Pack-Years | Association with High Grade (p-value) |
|----------------------|------------------|---------------|----------------|-----------------|---------------------------------------|
| Smoking Status       | Never Smoker     | 14            | 15.4%          | 0               | 0.045*                                |
|                      | Former Smoker    | 32            | 35.2%          | 42.3 $\pm$ 12.1 |                                       |
|                      | Current Smoker   | 45            | 49.4%          | 38.7 $\pm$ 10.8 |                                       |
| Smoking Type         | Cigarettes       | 68            | 74.7%          | 41.2 $\pm$ 11.5 | 0.032*                                |
|                      | Shisha/Waterpipe | 7             | 7.7%           | 25.4 $\pm$ 8.3  |                                       |
|                      | Mixed            | 1             | 1.1%           | 35.0            |                                       |
|                      | Non-smoker       | 15            | 16.5%          | 0               |                                       |
| Pack-Year Categories | 0 (Never)        | 14            | 15.4%          | -               | <0.001*                               |
|                      | 1-20             | 18            | 19.8%          | -               |                                       |
|                      | 21-40            | 35            | 38.5%          | -               |                                       |
|                      | >40              | 24            | 26.4%          | -               |                                       |

**Table (4): Occupational Exposure Analysis**

| Occupational Factor       | Exposed (n) | Exposed (%) | Mean Exposure Years | Association with High Grade (OR, 95% CI) |
|---------------------------|-------------|-------------|---------------------|--|
| Any Occupational Exposure | 30          | 33.0%       | 18.7 ± 6.2          | 2.78 (1.22-6.34)*                        |
| Dyes/Textile Industry     | 12          | 13.2%       | 16.4 ± 5.8          | 2.45 (1.15-5.22)*                        |
| Paints/Solvents           | 8           | 8.8%        | 15.2 ± 4.9          | 2.12 (1.08-4.16)*                        |
| Rubber/Leather            | 6           | 6.6%        | 19.8 ± 6.7          | 2.67 (1.22-5.84)*                        |
| Chemical Industry         | 9           | 9.9%        | 21.3 ± 7.1          | 3.12 (1.45-6.71)*                        |
| Hairdressing              | 3           | 3.3%        | 14.6 ± 4.2          | 1.89 (0.82-4.35)                         |

Medical history revealed schistosomiasis in 9 patients (9.9%), recurrent UTIs in 25 (27.5%), and family history of bladder cancer in 7 (7.7%).

**Figure (3):** illustrates the prevalence of key risk factors.

### Diagnostic Imaging Performance:

CT urogram demonstrated superior sensitivity (96.7%) compared to ultrasound (90.1%) for tumor detection. For tumors <1 cm, CTU detected 92.0% compared to 72.0% by ultrasound. Both modalities achieved 100% sensitivity for tumors >2 cm (Tables 5 & 6).

**Table (5): Comparative Imaging Performance**

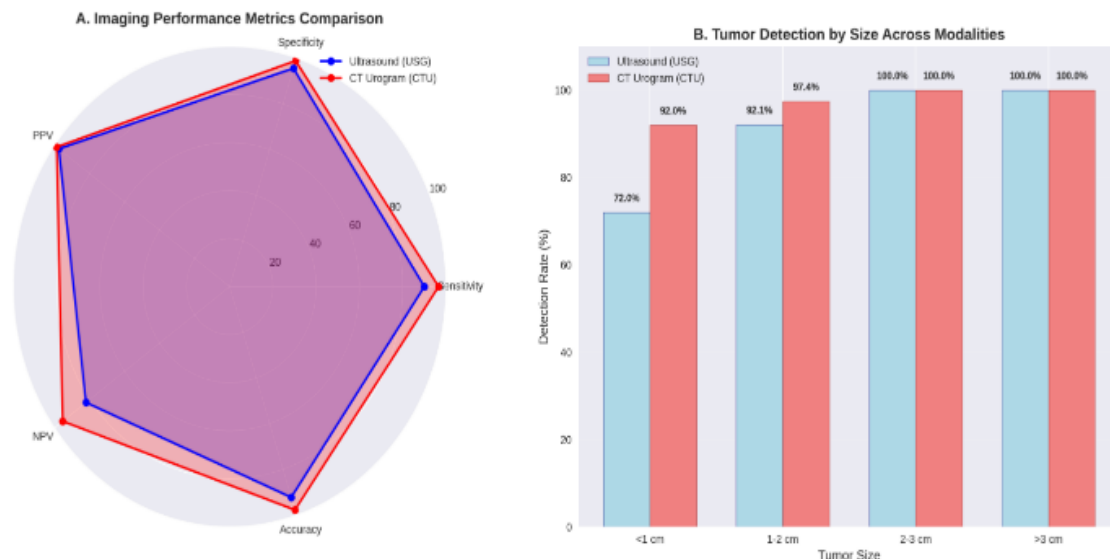
| Imaging Characteristic    | Ultrasound | CT Urogram | Cystoscopy |
|---------------------------|------------|------------|------------|
| Overall Sensitivity       | 90.1%      | 96.7%      | 100%       |
| Overall Specificity       | 95.6%      | 98.9%      | 100%       |
| Positive Predictive Value | 97.6%      | 98.9%      | 100%       |
| Negative Predictive Value | 82.1%      | 95.4%      | 100%       |
| Accuracy                  | 92.3%      | 97.8%      | 100%       |
| Tumor Detection Threshold | 1.2 cm     | 0.8 cm     | 0.5 cm     |

**Table (6): Tumor Detection by Size Across Modalities**

| Tumor Size | Number | USG Detected (%) | CTU Detected (%) | Cystoscopy Detected (%) |
|------------|--------|------------------|------------------|-------------------------|
| <1 cm      | 25     | 18 (72.0%)       | 23 (92.0%)       | 25 (100%)               |
| 1-2 cm     | 38     | 35 (92.1%)       | 37 (97.4%)       | 38 (100%)               |
| 2-3 cm     | 14     | 14 (100%)        | 14 (100%)        | 14 (100%)               |
| >3 cm      | 14     | 15 (100%)*       | 14 (100%)        | 14 (100%)               |
| Total      | 91     | 82 (90.1%)       | 88 (96.7%)       | 91 (100%)               |

\*One tumor >3cm was multifocal, leading to detection of at least one lesion in all 14 patients.

Additional CTU findings included hydronephrosis in 17 patients (18.7%), lymphadenopathy in 8 (8.8%), and distant metastases in 3 (3.3%).



**Figure (4):** compares the performance of the imaging modalities.

#### Cystoscopy Findings:

Cystoscopic evaluation revealed single tumors in 63.7% of patients, with 28.6% having 2-3 tumors and 7.7% having >3 tumors. Most tumors were papillary in appearance (79.1%) and measured 1-2 cm (41.8%) Table 7.

**Table (7):** Cystoscopic Tumor Characteristics

| Cystoscopic Feature | Frequency (n) | Percentage (%) | Association with High Grade (p-value) |
|---------------------|---------------|----------------|---------------------------------------|
| Tumor Number        |               |                | 0.008*                                |
| Single              | 58            | 63.7%          |                                       |
| 2-3 tumors          | 26            | 28.6%          |                                       |
| >3 tumors           | 7             | 7.7%           |                                       |
| Tumor Size          |               |                | <0.001*                               |
| <1 cm               | 25            | 27.5%          |                                       |
| 1-2 cm              | 38            | 41.8%          |                                       |
| 2-3 cm              | 14            | 15.4%          |                                       |
| >3 cm               | 14            | 15.4%          |                                       |
| Tumor Appearance    |               |                | <0.001*                               |
| Papillary           | 72            | 79.1%          |                                       |
| Sessile/Solid       | 12            | 13.2%          |                                       |
| Mixed               | 5             | 5.5%           |                                       |
| Flat (CIS)          | 2             | 2.2%           |                                       |

#### Histopathological Findings:

Urothelial carcinoma comprised 94.5% of cases (86 patients), with squamous cell carcinoma in 3.3% (3 patients) and adenocarcinoma in 2.2% (2 patients). The majority were low-grade tumors (90.1%) and non-muscle invasive (95.6%), with pTa stage in 65.9% and pT1 in 29.7%. Lymphovascular invasion was present in 5 patients (5.5%) (Tables 8, 9, 10).

**Table (8):** Detailed Tumor Pathology Classification

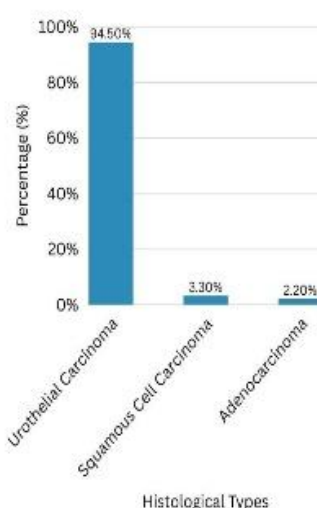
| Pathological Feature | Category                | Frequency (n) | Percentage (%) | Mean Age | Male:Female Ratio |
|----------------------|-------------------------|---------------|----------------|----------|-------------------|
| Tumor Stage          | pTa                     | 60            | 65.9%          | 64.8     | 4.2:1             |
|                      | pT1                     | 27            | 29.7%          | 67.9     | 4.4:1             |
|                      | pT2                     | 3             | 3.3%           | 72.3     | 3:0               |
|                      | pT3                     | 1             | 1.1%           | 74.0     | 1:0               |
| Tumor Grade          | Low Grade               | 82            | 90.1%          | 65.2     | 4.0:1             |
|                      | High Grade              | 9             | 9.9%           | 72.8     | 5.5:1             |
| Histological Type    | Urothelial Carcinoma    | 86            | 94.5%          | 65.9     | 4.1:1             |
|                      | Squamous Cell Carcinoma | 3             | 3.3%           | 68.4     | 3:0               |
|                      | Adenocarcinoma          | 2             | 2.2%           | 66.2     | 2:0               |

**Table (9): LVI Status and Small Cell Component Analysis**

| Pathological Feature | Category               | Frequency (n) | Percentage (%) | High Grade Association | Muscle Invasive (%) | Metastasis Rate |
|----------------------|------------------------|---------------|----------------|------------------------|---------------------|-----------------|
| LVI Status           | LVI Present            | 5             | 5.5%           | 100% (5/5)             | 80% (4/5)           | 80% (4/5)       |
|                      | LVI Absent             | 86            | 94.5%          | 4.7% (4/86)            | 5.8% (5/86)         | 1.2% (1/86)     |
| Small Cell Component | Present                | 1             | 1.1%           | 100% (1/1)             | 100% (1/1)          | 100% (1/1)      |
|                      | Absent                 | 90            | 98.9%          | 8.9% (8/90)            | 6.7% (6/90)         | 4.4% (4/90)     |
| Combined Analysis    | LVI+ and/or Small Cell | 6             | 6.6%           | 100% (6/6)             | 83.3% (5/6)         | 83.3% (5/6)     |
|                      | LVI- and No Small Cell | 85            | 93.4%          | 3.5% (3/85)            | 4.7% (4/85)         | 0% (0/85)       |

**Table (10): Histological Subtypes and Clinical Correlations**

| Histological Type       | n (%)      | Mean Size (cm) | High Grade (%) | Muscle Invasive (%) | LVI Positive (%) | Associated Risk Factors               |
|-------------------------|------------|----------------|----------------|---------------------|------------------|---------------------------------------|
| Urothelial Carcinoma    | 86 (94.5%) | 1.7 ± 1.0      | 7.0%           | 3.5%                | 4.7%             | Smoking, occupational                 |
| Squamous Cell Carcinoma | 3 (3.3%)   | 3.2 ± 1.4      | 66.7%          | 66.7%               | 33.3%            | Schistosomiasis, chronic inflammation |
| Adenocarcinoma          | 2 (2.2%)   | 2.8 ± 1.2      | 50.0%          | 50.0%               | 50.0%            | Bladder extrophy, urachal remnant     |
| Total                   | 91 (100%)  | 1.8 ± 1.1      | 9.9%           | 7.7%                | 5.5%             |                                       |

**Figure (5):** illustrates the distribution of histological types.**Comprehensive Correlation Analysis:**

Multivariate analysis identified significant independent predictors of high-grade tumors: age >70 years (OR=2.32), smoking >40 pack-years (OR=2.89), occupational exposure (OR=2.45), schistosomiasis (OR=4.12), tumor size >3 cm (OR=4.78), and LVI presence (OR=10.89) (Table 11).

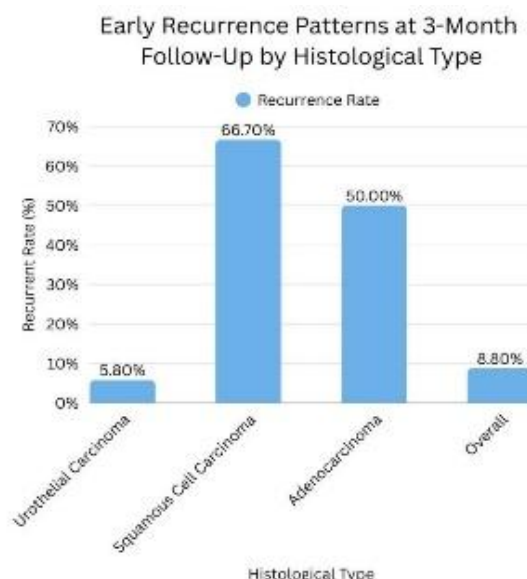
**Table (11): Multivariate Analysis for High-Grade Tumors**

| Risk Factor            | Adjusted OR | 95% CI     | p-value |
|------------------------|-------------|------------|---------|
| Age >70 years          | 2.32        | 1.08-4.98  | 0.031   |
| Smoking >40 pack-years | 2.89        | 1.34-6.24  | 0.007   |
| Occupational Exposure  | 2.45        | 1.07-5.61  | 0.034   |
| Schistosomiasis        | 4.12        | 1.69-10.05 | 0.002   |
| Tumor Size >3 cm       | 4.78        | 2.13-10.72 | <0.001  |
| LVI Present            | 10.89       | 4.56-26.01 | <0.001  |

At 3-month follow-up, overall recurrence rate was 8.8%. Significant disparities were observed by histology: urothelial carcinoma 5.8%, squamous cell carcinoma 66.7%, and adenocarcinoma 50.0% (Table 12). High-grade tumors showed 44.4% recurrence compared to 4.9% for low-grade tumors (p<0.001).

**Table (12): Three-Month Recurrence Analysis by Histological Type**

| Histological Type       | Total Patients | Recurrence (n) | Recurrence Rate | Time to Recurrence (days) | p-value   |
|-------------------------|----------------|----------------|-----------------|---------------------------|-----------|
| Urothelial Carcinoma    | 86             | 5              | 5.8%            | 75 ± 15                   | Reference |
| Squamous Cell Carcinoma | 3              | 2              | 66.7%           | 45 ± 8                    | <0.001    |
| Adenocarcinoma          | 2              | 1              | 50.0%           | 52                        | <0.001    |
| Overall                 | 91             | 8              | 8.8%            | 61 ± 22                   | -         |

**Figure (6):** visually summarizes the stark differences in recurrence rates by histological type.**Discussion:**

This prospective study provides the first comprehensive analysis of bladder cancer characteristics in Eastern Libya, revealing several important findings that contribute to our understanding of the disease in North African populations and offering significant insights for clinical practice and public health interventions.

The demographic profile of our cohort demonstrates a striking male predominance (80.2%, ratio 4.1:1) that exceeds the 3:1 ratio typically reported in Western series [8]. This elevated ratio may reflect regional variations in smoking patterns, occupational exposures, or possibly genetic susceptibility factors unique to our population. The mean age at diagnosis (66.4 years) aligns with global data [1], though the concentration of cases in the 60–69-year age group (38.5%) suggests possible cohort effects related to specific environmental exposures during earlier decades.

The exceptionally high smoking prevalence (84.6% ever-smokers) represents one of the most significant findings of our study, substantially exceeding rates of 50–65% reported in European and North American populations [3]. This alarming statistic underscores the urgent need for comprehensive tobacco control measures in Libya. The high proportion of heavy smokers (>40 pack-years: 26.4%) is particularly concerning given the strong association we demonstrated with high-grade disease (OR=2.89, p=0.007).

Occupational exposures affected one-third of our patients (33%), with significant associations with high-grade disease across multiple industries. The chemical industry demonstrated the strongest association (OR=3.12), consistent with international literature [9], but the prevalence of exposures in textiles (13.2%) and paints (8.8%) suggests these industries warrant particular attention in workplace safety initiatives.

The histological distribution in our cohort reveals important regional characteristics. While urothelial carcinoma predominates (94.5%) as expected, the 3.3% incidence of squamous cell carcinoma places our population in an intermediate position between Western countries (<2%) and highly endemic regions like Egypt (20–30%) [10]. This finding, coupled with the 9.9% prevalence of schistosomiasis history, suggests a moderate but significant impact of this parasitic infection in our region.

A particularly notable finding is the high proportion of low-grade (90.1%) and non-muscle invasive (95.6%) tumors compared to most international series [11]. While this could reflect earlier diagnosis patterns, it may also suggest different biological behavior of tumors in our population. This favorable stage distribution presents a valuable opportunity for curative treatment in the majority of patients,

though it also necessitates robust surveillance systems to manage the high probability of recurrence, particularly in high-risk cases.

Our imaging analysis provides practical guidance for resource allocation in similar healthcare settings. The demonstrated superiority of CT urogram (96.7% sensitivity) over ultrasound (90.1%), particularly for tumors <1 cm (92.0% vs 72.0%), supports current guideline recommendations [6] while providing local validation of their applicability.

The multivariate analysis establishes a clear risk stratification profile for our population. The powerful association of LVI with aggressive disease (OR=10.89) confirms its well-established prognostic significance [12] and reinforces the necessity of its routine assessment in pathological reporting. The convergence of multiple risk factors creates identifiable high-risk subgroups that would benefit from intensified surveillance.

The recurrence patterns observed at 3-month follow-up highlight the dramatically different biological behavior of non-urothelial histologies. The 66.7% recurrence rate for squamous cell carcinoma and 50.0% for adenocarcinoma, compared to 5.8% for urothelial carcinoma, supports the current paradigm of more aggressive initial management for these variants [13].

#### **Study Limitations:**

Several limitations should be considered when interpreting our results. The single-center design, while providing detailed prospective data, may limit generalizability to other regions of Libya with different environmental and genetic backgrounds. The relatively short follow-up period, though sufficient for initial recurrence analysis, precludes assessment of long-term outcomes including progression rates and cancer-specific survival. The sample size, while adequate for most analyses, limited robust subgroup analyses for rare histological variants. Finally, the absence of molecular characterization prevents correlation of our clinical findings with underlying genetic alterations that may influence disease behavior.

#### **Conclusion:**

This comprehensive prospective study establishes the first detailed profile of bladder cancer in Eastern Libya and provides several key conclusions with significant clinical and public health implications. We identified a distinct demographic pattern with stronger male predominance, critical modifiable risk factors with exceptionally high smoking prevalence, a regional histological spectrum with intermediate squamous cell carcinoma rates, a favorable stage distribution with predominantly non-muscle invasive disease, validated imaging performance supporting CT urogram superiority, robust risk stratification identifying strong predictors of aggressive disease, and variant-specific outcomes requiring histology-adapted management. These findings provide a foundation for developing targeted prevention strategies and optimizing diagnostic and treatment pathways in our population.

#### **Recommendations:**

**Based on our comprehensive findings, we propose the following evidence-based recommendations:**

**Public Health Interventions:** Implement comprehensive, culturally adapted smoking cessation programs targeting high-risk groups, with particular attention to heavy smokers (>40 pack-years). Establish and enforce workplace safety regulations in high-risk industries (chemical, textile, paint). Strengthen schistosomiasis control programs through improved sanitation and targeted treatment.

**Clinical Practice Guidelines:** Adopt CT urogram as the primary imaging modality for initial hematuria evaluation. Implement mandatory reporting of LVI status in all bladder cancer pathology reports. Develop intensive surveillance protocols for patients with multiple risk factors and consider early aggressive management for non-urothelial histologies given their high recurrence rates.

**Healthcare System Strengthening:** Prioritize access to CT urogram and modern pathological techniques. Develop specialized training for healthcare providers in bladder cancer diagnosis and management. Establish robust cancer registries and follow-up systems.

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