

Demographics, Clinical Presentation, Staging, Management and Outcome of Urinary Bladder Cancer in Qassim Region

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Abstract

Background: Urinary bladder cancer (UBC) is one of the most common cancers worldwide. According to the 2020 Cancer Incidence Report in Saudi Arabia, there were 348 cases of UBC recorded among Saudi nationals in 2020, with 291 cases (83.62%) occurring in males and 57 cases (16.38%) in females. This study aims to assess and evaluate the prevalence, incidence, clinical symptoms, and management of UBC in the Qassim Region.

Methods and Results: This retrospective study was conducted over 12 months at King Fahad Specialist Hospital in Buraidah, Saudi Arabia. The study population comprised all patients diagnosed with UBC between October 2017 and July 2024, with complete medical records, irrespective of age, gender, or nationality.

Of 75 UBC patients, 81.3% were males, most participants (68.0%) were above 60, and Saudis comprised 85.3%. Hematuria was the most common symptom, reported in 57.3% alone and in 10.7% of cases with other symptoms. Most patients underwent TURBT (89.3%), while 8.0% underwent radical cystectomy. Surgical margins were negative in 96.0% of patients, and recurrence was noted in 37.3%.

Histopathological analysis revealed that 97.3% of the tumors were classified as TCC. Squamous cell carcinoma and urothelial carcinoma with squamous differentiation accounted for 1.3% in each case. Most of the tumors were low-grade and non-muscle invasive. The most frequent stage was TaN0M0, reported in 44% of cases, followed by T1N0M0 at 37%. Less common stages included T1N1M0 and T2aN0M0, each accounted for 2% of the cases. Rarer stages, including TisN0M0, T2N2M0, and T3N0M0, each accounted for 1%.

Conclusion: This study reports the predominance of UBC in males and older populations, with TCC as the most common histological type. Hematuria is the primary symptom, reported in more than half of the patients, indicating its critical role in early diagnosis. A significant recurrence rate necessitates rigorous surveillance post-treatment. (**International Journal of Biomedicine. 2024;14(4):615-620.**)

Keywords: urinary bladder cancer • hematuria • transitional cell carcinoma • squamous cell carcinoma

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Abbreviations

ASIR, age-standardized incidence rate; SCC, squamous cell carcinoma; TURBT, transurethral resection of bladder tumors; TCC, transitional cell carcinoma; UBC, urinary bladder cancer.

Introduction

Urinary bladder cancer (UBC) emerges from the lining of the urinary bladder, has the highest recurrence rate, and is one of the most common cancers worldwide.¹ According

to research, UBC globally is the sixth most prevalent type of cancer in men and the 17th in women.² Globally, an estimated 213,000 people died from UBC, resulting in an age-standardized mortality rate of 1.9 per 100,000.³ The incidence of UBC is very high in most European and North American

countries.⁴ According to the data, the age-standardized incidence rate (ASIR for developing UBC in the Arab countries was 9.9/100,000, which is higher than the average global ASIR (6.5/100,000).⁵ Lebanon exhibited an ASIR of 30.1 per 100,000 people. This was followed by Egypt with an ASIR of 19.1 per 100,000, Iraq with 13.8 per 100,000, and both the UAE and Qatar with 12.2 per 100,000.⁵

According to the 2020 Cancer Incidence Report in Saudi Arabia, there were 348 cases of UBC recorded among Saudi nationals in 2020, with 291(83.62%) cases occurring in males and 57(16.38%) cases in females.⁶ In the male population of Saudi Arabia, UBC ranked as the eighth most common cancer, accounting for 4.70% of all newly diagnosed cancer cases, compared to 0.70% for females.⁶ A retrospective medical record review by Alghafees et al.⁷ examined 3,750 patients diagnosed with primary bladder tumors between January 1, 2008, and December 31, 2017, in Saudi Arabia. The study revealed an overall incidence rate of 1.4 per 100,000 individuals, with the mean age of UBC patients being 62.3 years.

Major non-modifiable risk factors for UBC include male sex, old age, family history of bladder cancer, or other cancerous syndromes, including Lynch syndrome, Cowden syndrome, or Peutz-Jeghers syndrome. Other modifiable risk factors included a history of a bladder infection, smoking, alcohol abuse, chronic use of indwelling catheters, exposure to chemotherapy, and toxin chemical exposures like arsenic, benzene fraction, and aromatic amines.^{8,9}

It has been reported that 80% of patients with UBC present with intermittent, gross, and painless hematuria as the predominant symptom.¹⁰ Some patients with UBC present with irritative and obstructive symptoms, including urgency, frequency, hesitancy, dysuria, and difficulty in voiding; these symptoms are accompanied by invasive UBC or carcinoma in situ. In some cases, UBC may present with abdominal pain, pelvis pain, and iliac vein compression, which presents with lower extremity edema.¹¹ The most important and indicative symptom is hematuria; according to some research studies, it correlates with a higher grade of disease.¹²

A diagnostic workup is important for patients who present with gross hematuria. Cystoscopy is the gold standard for diagnosing UBC with urine cytology to analyze urine samples for cancerous cells. Imaging studies of the upper urinary tract are included in the diagnostic workup to identify the spread of cancer.¹³

Staging of UBC involves assessing the depth of tumor invasion, particularly whether it has invaded the muscle layer, which is crucial for treatment decisions.¹⁴ For staging purposes, transurethral resection of bladder tumors (TURBT) is an important diagnostic procedure; the correct way is to obtain muscle tissue to diagnose accurate pathology.¹⁵ Although diagnostic TURBT often lacks muscle tissue, which can result in a misleading diagnosis and make it difficult for doctors to confirm muscle invasion; confirming muscle invasion is important as it indicates high-grade neoplasm and a bad prognosis.¹⁶

Urinary bladder cancer constituted 3.9% of new cancer diagnoses among males and 0.9% among females in Saudi Arabia.⁶ In the Al-Qassim region, 13 new cases of UBC

were diagnosed among Saudi nationals in 2020, consisting of 10 (76.92%) males and 3 (23.07%) females. Investigating UBC within the Al-Qassim region is essential for addressing prevalent knowledge gaps. Although UBC ranks as the ninth most diagnosed cancer globally, there exists a substantial deficiency in comprehensive data concerning its prevalence, risk factors, and characteristics that are specific to the Al-Qassim region. This lack of data underscores the pressing necessity for targeted research initiatives to bridge these gaps and inform interventions specifically tailored to the unique context of the region.

This study aims to assess and evaluate the prevalence, incidence, clinical symptoms, and management of UBC in the Qassim Region.

Materials and Methods

This retrospective study was conducted over 12 months at King Fahad Specialist Hospital in Buraidah, Saudi Arabia. King Fahad Specialist Hospital is a tertiary care facility in the Qassim region of Saudi Arabia to which all tumor cases in the Qassim region are referred. The study population comprised all patients diagnosed with UBC between October 2017 and July 2024, with complete medical records, irrespective of age, gender, or nationality.

Patients with incomplete medical records were excluded from the analysis. A pre-designed, standardized data-collection checklist was employed to extract data from the medical records. The collected data encompassed patients' demographics, clinical characteristics, histopathological features, and treatment outcomes. To ensure data quality and reliability, the researchers verified the accuracy of the extracted data through random checks.

The study was approved by the Qassim Region Research Ethics Committee (QREC).

Statistical analysis was performed using statistical software package SPSS version 26.0 (SPSS Inc, Armonk, NY: IBM Corp).

Results

Of 75 UBC patients, 81.3% were males, most participants (68.0%) were above 60, and Saudis comprised 85.3%. Common comorbidities included hypertension (13.3%), diabetes mellitus (12.0%), and cystitis cystica (5.3%) (Table 1). Incidental findings accounted for 18.7% of cases. Hematuria was the most common symptom, reported in 57.3% alone and in 10.7% of cases with other symptoms, followed by irritative voiding symptoms (Table 2).

Most patients underwent TURBT (89.3%), while 8.0% underwent radical cystectomy. A combination of both procedures was performed in 2.7% of cases (Table 3). Urinary diversion was performed for 10.7% of patients.

Histopathological analysis revealed that 97.3% of the tumors were classified as TCC. Squamous cell carcinoma and urothelial carcinoma with squamous differentiation accounted for 1.3% in each case. Most of the tumors were low-grade and non-muscle invasive. Necrosis was observed in 14.7% of

the cases, while metastasis was rare, occurring in only 4.0%. Surgical margins were negative in 96.0% of patients, and recurrence was noted in 37.3% (Table 4).

Table 1.

Demographic and clinical characteristics of the study participants.

Characteristics		n (%)
Sex	Male	61 (81.3)
	Female	14 (18.7)
Age, years	30-40	3 (4.1)
	41-50	7 (9.3)
	51-60	14 (18.7)
	> 60	51 (68.0)
Nationality	Non-Saudi	11 (14.7)
	Saudi	64 (85.3)
Associated disorders	Cystitis cystica	4 (5.3)
	Diabetes mellitus	9 (12.0)
	Hypertension	10 (13.3)
Smoking	No	57 (76.0)
	Yes	17 (22.7)
	Ex-smoker	1 (1.3)

Table 2.

Incidental and symptomatic findings in the study patients.

Symptoms	n (%)
Incidental	14 (18.7)
Hematuria	43 (57.3)
Hematuria, irritative voiding symptoms	4 (5.3)
Hematuria, irritative voiding symptoms, occasional discharge and pain	1 (1.3)
Hematuria, loin pain	1 (1.3)
Hematuria, suprapubic/rectal/perineal pain	3 (4.1)
Irritative voiding symptoms	5 (6.7)
Irritative voiding symptoms, bilateral testicular pain	1 (1.3)
Irritative voiding symptoms, clots	1 (1.3)
Irritative voiding symptoms, dysuria	1 (1.3)
Right flank pain	1 (1.3)

Table 3.

Surgical management of UBC patients.

Management		n (%)
Type of surgery	TURBT	67(89.3)
	Radical cystectomy	6 (8.0)
	Both	2 (2.7)
Urinary Diversion	No	67 (89.3)
	Yes	8 (10.7)

Table 4.

Tumor histopathological characteristics and clinical outcomes of UBC patients.

Characteristics		n (%)
Histopathological type	Squamous cell carcinoma	1 (1.3)
	Transitional cell carcinomas	73 (97.3%)
	Urothelial carcinoma with squamous differentiation	1 (1.3)
Grade	High-grade tumor	29 (38.7)
	Low-grade tumor	46 (61.3)
Muscle invasion	No	65 (86.7)
	Yes	10 (13.3)
Necrosis	No	64 (85.3)
	Yes	11 (14.7)
Metastasis	Multiple	1 (1.3)
	Non	72 (96.0)
	Single	2 (2.7)
Surgical margin	Negative	72 (96.0)
	Positive	3 (4.0)
Recurrence	Yes	28 (37.3)
	No	47 (62.7)

The most frequent stage was TaN0M0 (non-invasive papillary carcinoma), reported in 44% of cases, followed by T1N0M0 (tumor invasion into connective tissue without lymph node involvement or metastasis) at 37%. Less common stages included T1N1M0 (tumor with regional lymph node involvement) and T2aN0M0 (muscle-invasive tumors without lymph node involvement), each representing 2% of the cases. Rarer stages, including TisN0M0, T2N2M0, and T3N0M0, each accounted for 1% (Figure 1).

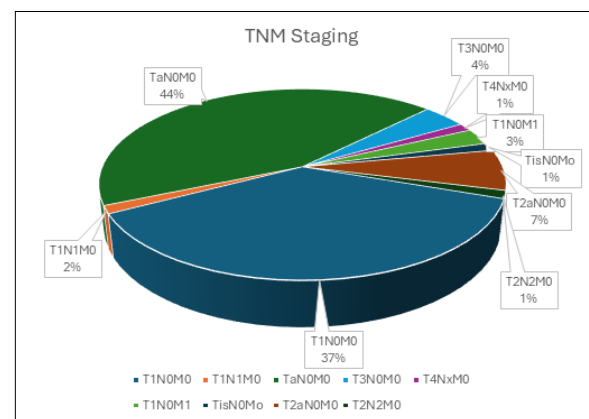


Fig. 1. Distribution of TNM staging among UBC patients.

Discussion

According to Sung et al.,¹⁷ there were 573,000 UBC cases worldwide in 2020, which accounted for 3% of all cancer cases. Halaseh et al.¹⁸ reported that UBC was 4 times more prevalent in males than females, with 9.5 and 2.4 incidence rates per

100,000 cases for males and females, respectively. However, UBC is also observed to be more significantly common in females in Hungary.¹⁹ Occupational and environmental exposure, including alkylating agents, arsenic, aniline dyes, and tobacco smoke, might be the factors behind this 4-fold higher prevalence in males.²⁰ Other risk factors contributing to UBC may be conditions such as chronic infections, pelvic radiation, congenital bladder disorders, Lynch syndrome, Cowden disease, and genetic predisposition such as mutations in the retinoblastoma (*RBI*) gene.²¹

In the current study, the most common risk factors reported in patients were hypertension, diabetes mellitus, and cystitis cystica. A large-scale cohort study found a positive association between hypertension and the risk of UBC, indicating a 32% increased risk for individuals with hypertension.²² Moreover, in patients with high-risk UBC undergoing BCG immunotherapy, hypertension was found to be a significant prognostic factor for cancer recurrence.²³ Furthermore, according to a systematic review, a statistically significant association was found between the use of angiotensin II receptor blockers and UBC (RR = 1.07, 95% CI 1.03-1.11); however, no such association was observed with other antihypertensive medications. (24) A case-control study indicated that the risk of UBC positively correlates with the duration of diabetes (OR = 1.92 for 1-5 years, 1.63 for 5-10 years, 2.39 for 10-15 years, and 2.58 for ≥ 15 years).²⁵ Furthermore, a cohort study corroborated this positive association between diabetes and UBC in women.²⁶

In our study, the susceptibility to UBC was age-related, making it more prevalent in older populations above 60. It has been reported that 90% of new UBC diagnoses in the United States occur in individuals aged 55 years or older, with the average age at diagnosis being 73 years.²⁷ Aging is associated with physiological changes that can influence cancer development, including a decline in immune function, reduced DNA repair capacity, and the accumulation of genetic damage from prolonged carcinogen exposure.²⁸ Elderly patients often have multiple comorbidities that complicate treatment decisions and are at increased risk of treatment-related toxicities, leading to poorer disease outcomes compared to younger patients. Interventions like radical cystectomy or chemotherapy may be less tolerated in older adults due to their health status and physiological reserve.²⁹ Notably, the UBC incidence rate is lower in Middle Eastern countries than in more developed industrialized Western Europe and North American countries.³⁰

In the current study, around one-fifth of patients were diagnosed incidentally through procedures such as examinations of urine cytology, use of imaging tools, or cystoscopy for other health issues. The most common symptom in this study, reported by more than half of the patients, was hematuria. This finding aligns with previous studies that have identified visible or gross hematuria as the most common presentation of UBC, serving as a hallmark symptom in its diagnosis.³¹ The presence of hematuria cannot distinguish between the causes of renal cell carcinoma and UBC.³² Abdominal pain and irritative voiding symptoms were also significant in underscoring the diverse UBC presentation,

sometimes leading to diagnostic delays if attention is not paid. Hematuria is reported to affect three-quarters of patients compared to irritative voiding symptoms, accounting for less than 10%.³³ It is also stated that obstructions, urinary tract infections, and irritative urinary symptoms have low frequency in bladder TCC.³⁴

Histopathological findings of this study have revealed the prevalence of TCC in most patients, accounting for 98.7%. TCC is also reported to be the most frequent type of cutaneous metastasis, with a 90% prevalence.³⁵ The necrosis in 11% of the patients indicates the disease's aggressive nature. A relatively high percentage of low-grade cancer cases, accounting for 61.3%, along with a significant proportion of non-muscle invasive cancers, comprising 86.7%, indicates the presence of a potentially less aggressive disease within the study population. Specifically, 44% of the patients were classified as TaN0M0, 37% exhibited T1N0M0, while only 2% were reported as T1N1M0 and T2aN0M0, respectively.

In 2020, a study on the US population also revealed the high frequency of Tis/TaN0M0 among the low incidence of 1.5% of UBC in a young population between 18 and 39 years.³⁶ A high percentage of 5-year survival rates was also observed in these low-grade cancer cases, which suggests the prompt diagnosis and treatment of UBC in young adults.³⁶ This observation makes the epidemiology of UBC unique in the Qassim region, inviting further investigation into possible genetic and environmental factors.

Most patients, accounting for 89.4%, underwent TURBT as a primary treatment, reflecting the best medical and surgical practices in non-muscle invasive UBC management following European Association of Urology guidelines.^{37,38} In the current study, 8% of the patients underwent radical cystectomy, which is the treatment of choice for an invasive tumor. Moreover, a significantly high recurrence rate of 37.3% is reported. In comparison, the surgical margins for 96% of the patients were negative, consistent with previous studies reporting 15%–61% of cases with a 1-year recurrence rate and 31%–78% with a 5-year recurrence rate, necessitating rigorous surveillance after treatment.³⁹

The comprehensive analysis of UBC's epidemiology, complexity, and management in the Qassim region provides a basis for future studies and emphasizes potential developments in personalized patient care.

The current study's limitations include its retrospective design, small sample size, single-center setting, and the potential introduction of selection bias due to incomplete medical records. Consequently, the findings may not be generalizable. However, understanding these patterns can help healthcare professionals implement tailored treatment strategies and improve early diagnosis.

Conclusion

This study reports the predominance of UBC in males and older populations, with TCC as the most common histological type. Hematuria is the primary symptom, reported in more than half of the patients, indicating its critical role in early diagnosis. A significant recurrence rate necessitates

rigorous surveillance post-treatment. The majority of low-grade, non-muscle invasive tumors, along with the presence of necrosis in some cases, suggest an aggressive form of the disease. Further research is needed to investigate the factors contributing to the relatively lower prevalence of UBC in Middle Eastern countries than in Western populations. Future studies should focus on molecular and genetic factors, as well as environmental exposures that influence the development of urinary bladder cancer.

Competing Interests

The authors declare that they have no competing interests.

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