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Research Article

# Histopathological Study of Urinary Bladder Cancer in a Group of Iraqi Patients from 2019 to 2024

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**Abstract:**

**Background:** Urinary bladder cancer (UBC) is the most common urinary tract malignancy, ranking tenth worldwide. In Iraq, UBC is ranked as the seventh most prevalent cancer among the top 10 cancers. Numerous established risk factors for bladder cancer, including genetic and hereditary factors, smoking and nicotine behaviors, occupational exposure to certain chemicals and pigments, and environmental pollution from drinking water contaminated with arsenic, may also be problems, as well as disorders including chronic cystitis, and infectious diseases like schistosomiasis. Urine cytology and cystoscopy are the gold standard for detecting UBC.

**Objectives:** To analyze and characterize urinary bladder cancer (UBC) diagnosed in a group of Iraqi patients.

**Cases and methods:** A total of 70 paraffin-embedded tissue blocks of bladder cancer were obtained from the archive of the Histopathology Unit of the Martyr Ghazi Al-Hariri/ Medical City, Al-Yarmouk Teaching Hospital, and several private laboratories in Baghdad, Iraq, for cases diagnosed between 2019 and 2024. Clinical data, in addition to the age and sex of the patients, were collected from the patients' clinical records. Histological examination was conducted to determine the tumor characteristics, including type, tumor age, sex, size, stage, and grade.

**Results:** The results revealed that 82.9% of UBC cases were males, and 62.9% were between the ages of 60 and 79 years. The most common tumor size was 2-5 cm, with stage T1 accounting for 80% of the total. A high tumor grade was observed in 60% of UBC cases. The most prevalent histological type observed was papillary urothelial carcinoma (77.1%).

**Conclusion:** UBC was found to be mainly a disease of males and older age. Papillary urothelial carcinoma was the most frequently seen, mostly at stage T1 and high grade, and more likely to be of a small or moderate size.

**Keywords:** Clinicopathological features; Histopathological study; Urinary bladder cancer.

## Introduction:

Among all malignancies, urinary bladder cancer (UBC) ranks tenth in the world. The International Agency for Research on Cancer states that there are 573,278 new cases and about 212,536 deaths globally per year (1). In Iraq according to Iraqi Cancer Registry (ICR) in 2022, UBC is the 7th most common cancer of top ten cancers among Iraqis (2).

UBC includes a spectrum of illnesses, from chronically recurrent and non-invasive tumors that can be controlled, to aggressive and advanced-stage illnesses that need invasive and multimodal treatment (3) It is a morphologically and genetically variable disease with a wide range of histological subtypes and associated molecular changes (4). It is a tumor that starts in the lining of the bladder when tissues grow strangely and sometimes spreads to the bladder muscles (5). According to histological features, UBC has three primary subtypes: Transitional cell carcinoma (TCC), which is the most prevalent subtype (>90%), squamous cell carcinoma (SCC; <5%), and adenocarcinoma, which is the least common among all UBC cases (<2%) (6).

Many established risk factors are connected with bladder cancer: Genetic and inherited risk factors, tobacco and other smoking habits, high body mass index (BMI), occupational exposure to specific chemical substances and pigments, diseases like schistosomiasis and chronic cystitis, and occupational exposure to tobacco products. In addition, side effects from anti-diabetic treatments (like pioglitazone), radiation therapy, chemotherapy (cyclophosphamide), and environmental pollution from drinking water contaminated with arsenic may also increase the risk (7). Moreover, UBC has been linked to the activity of the sex steroid hormone system, suggesting that androgens and estrogens have biological impacts on bladder cancer in both in vivo and in vitro studies (8). The phosphoinositide 3-kinase (PI3 kinase) /AKT signaling pathway is activated when androgen stimulates bladder cells, leading to regular molecular alterations and increased UBC activity (9). Urine cytology and

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cystoscopic biopsy are the gold standards for detecting UBC (1).

The present study aimed to review the records and histopathological specimens of a group of Iraqi patients with malignant urinary bladder cancers, to explore their relationship with some clinicopathological characteristics.

**Materials and Methods:**

Collection of specimens: A total of 70 paraffin-embedded tissue blocks of malignant UBCs with their information collected from the archive of the Histopathology Unit of the Department of Martyr Ghazi al-Hariri Hospital/ Medical City, Al-Yarmouk Teaching Hospital, and some private laboratories in Baghdad, Iraq, for patients diagnosed between 2019 and 2024. Patient's medical records were used to retrieve information about gender, tumor size, stage, grade, and histological type. The type of biopsy was transurethral resection of bladder tumor (TURBT).

Preparation and staining of specimens: All sections were stained with hematoxylin and eosin (H&E) according to the general protocol of staining and prepared for microscopic examination.

Statistical analysis: The Statistical Packages for Social Sciences (SPSS; version 26) was used to analyze data. The Pearson Chi-square test with Yates' adjustment or the Fisher Exact test was conducted. Data was presented in simple measures of frequency, percentage, mean, standard deviation, and range.

**Results:**

Patients' ages ranged from 29 to 90 years, with the highest frequency of UBC occurring in the age group of 60-79 years (62.9%), Figure 1. There were 58 males (82.9%) and 12 females (17.1%) in the study group, Figure 2.

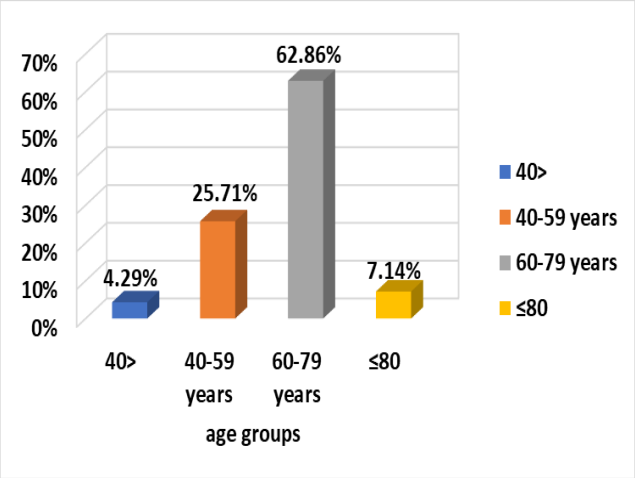



**Figure 1: Age distribution of the study group**

The cases were categorized according to the American Joint Committee on Cancer (AJCC) guidelines. T1 stage was the most frequent (80%), Figure 3. According to the World Health Organization's tumor grading, 40% of the UBC cases were low grade and 60% of the cases were high grade, Figure 4.

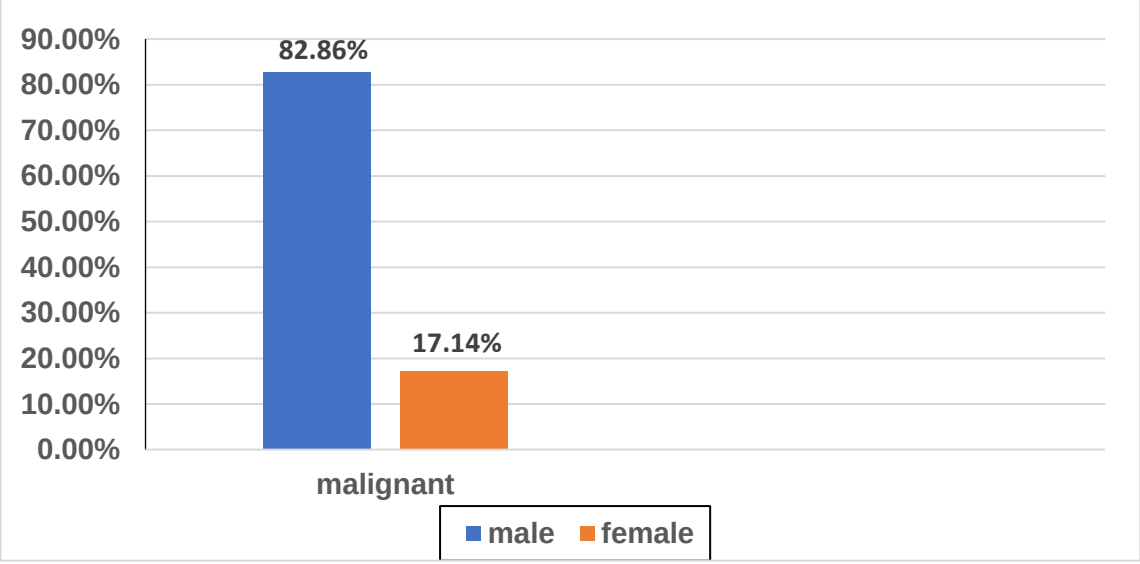



**Figure 2: Distribution of study group by gender**

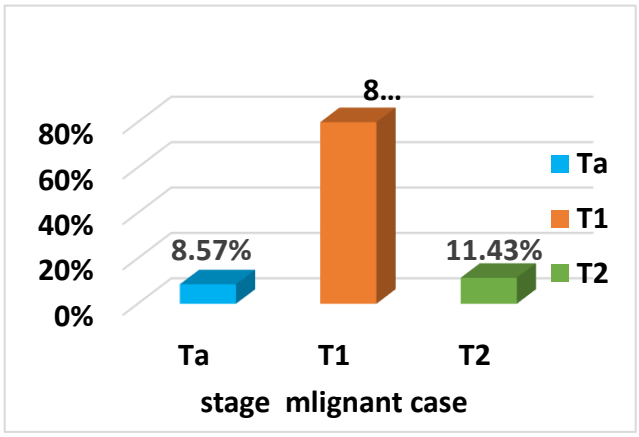



**Figure 3: Distribution of UBC cases according to pathological stage**

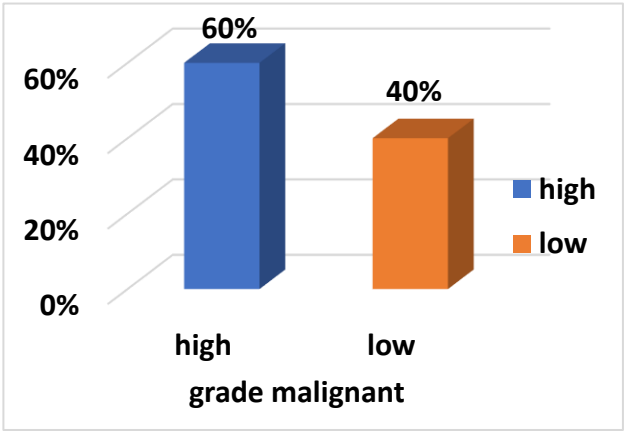



**Figure 4: Distribution of UBC cases by tumor grade**

Histologically, the most common cell type of UBC cases was papillary urothelial (77.1%, 54 cases), papillary with squamous differentiation (17.1%, 12 cases), and invasive urothelial type (5.7%, 4 cases), Figure 5. The photomicrographs of the bladder tissue sections for malignant cases stained with H&E are presented in Figure 6.

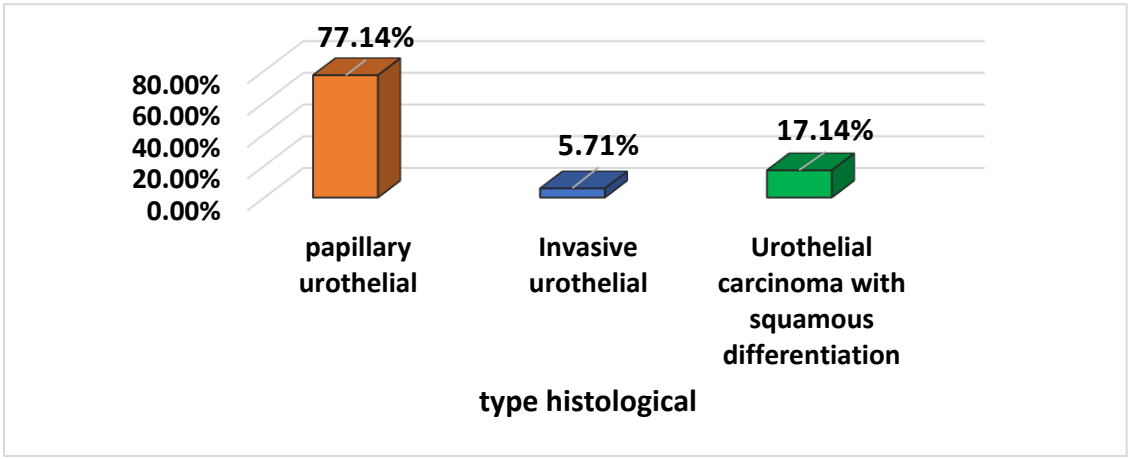
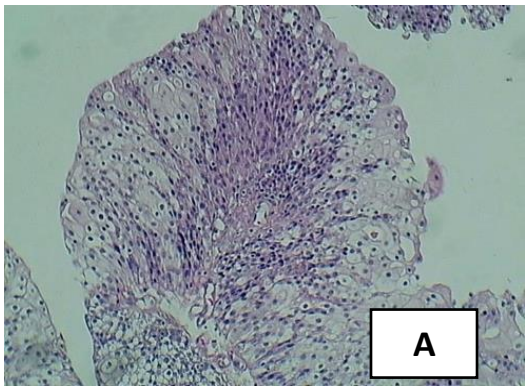
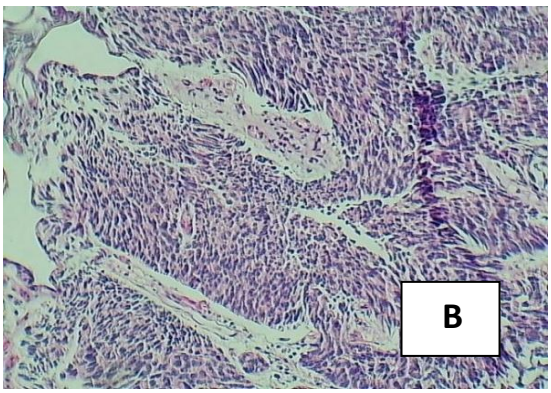



**Figure 5: Distribution of UBC cases based on histological types**



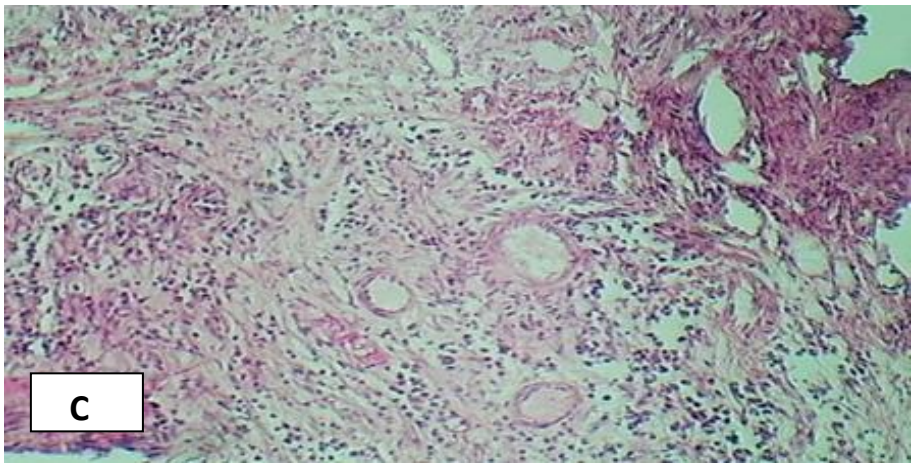



**Figure (6): H&E stained UBC tissue sections:**
**(A) papillary urothelial carcinoma(40X).**
**(B) Invasive urothelial carcinoma (40X)**
**(C)Urothelial carcinoma with squamous differentiation (10X)**

The UBC masses were classified according to size into three groups: < 2 cm, 2-5 cm, and > 5 cm. The 2-5 cm size was the most frequent (45.9%) followed by the < 2 cm (42.9%), Figure 7.

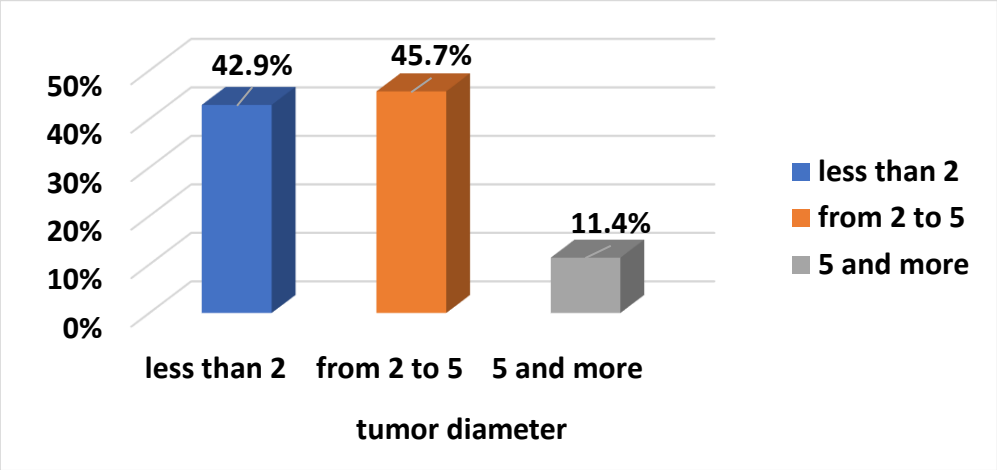



**Figure (7): Distribution of the UBC cases by tumor diameter**

**Discussion**

The highest frequency of UBC in the 7th and 8th decades of age in the current study is consistent with a recent investigation in Iraq that reported that the maximum number of UBC cases occurred between 70 and 79 years of age, accounting for 32.5% of the cases (10). Other studies in Iraq indicated that patients aged 61 to 70 years were the most frequent (56.7%) of the disease (11). Studies from Egypt reported the majority of UBCs to be above the age of 60 years (60.0%) (12). According to a study from India, those between the ages of 60 and 79 years had the highest rate of UBC (43%) (13). Hussein's study in Iraq found that the mean age of UBC cases was 56 years (14). An investigation from southeastern Iran indicated that the highest rate of UBC was 35% among individuals under 55 years of age (15). In Tanzania, Yohana's study indicated that UBC patients had a mean age of 55 years (16). Nearly two-thirds of all cancer diagnoses in the US afflict persons over the age of 65, and patients over 65 have a 15-fold higher risk of mortality than those under 65 (17). The findings of the current study suggest that UBC is a disease that is most prevalent in older people. The finding of the current study that males constituted more than 80% of the cases is consistent with those of Hussein's study from Iraq, which found that 83% of patients were males (14). Another study in Iraq by Alyasiri found that 74.6% of the patients were males with a male-to-female ratio of 4:1 (10). In contrast, a study in Tanzania by Rambau et al. found that 48.6% of patients were males (18). The reason for men being more likely than women to develop bladder cancer may be that a higher proportion of men smoke and are exposed to carcinogenic chemicals at work (19). These chemicals attack base pairs and break DNA strands in bladder epithelial cells. One of the main risk factors for UBC is smoking, and the harm increases with smoking intensity and duration (20). Furthermore, sex hormones and their receptors have been connected to the distinct behaviors of UBC in men. It is well known that estrogenic hormones

suppress bladder tissue carcinogenesis, while androgens are strongly associated with bladder cancer, leading to more bladder cancer in males than females (21).

The finding of the present study that 80% of total cases were at stage T1 of the disease agrees with the results of Mohammed et al. study in Iraq, who found that stage T1 was reported in 65.3% of the cases (22). Moussa and El-Sheshtawy from Egypt found that the highest percentage of their cases were stage T1 (52.4%) (23). Diana et al. from Italy reported that only 19% of their patients were within stage T1 (24). Abdel-Rahman et al. from Egypt, found that stage T1 was detected in 35% of their cases (25).

The T-stage of the lesion has a significant influence on the prognosis of UBC. Bladder tumors identified as T1 according to the 2018 American Joint Committee on Cancer (AJCC) staging classification are those that infiltrate the lamina propria (subepithelial connective tissue), but not the muscularis propria (MP) (26).

In the present study, tumor grading was done according to the 2004/2016 WHO grading system. The finding that 60% of malignant cases were with high grade concurs with the finding of a study from Saudi Arabia by Al-Maghradi, with 53.8% having high grade UBC (27), and a study from Egypt by Abdelrahman et al., with 60% of patients having high grade (28). A study from China by Wang *et al*. reported that 46.1% of their cases were in high grades (29) and a study from the UK by Mariappan et al. reported that 47% of their cases were high-grade (30).

The finding of the current study that the most frequent histological type was papillary urothelial cancer (77.1%) agrees with the findings of another in Iraq by Abbas et al. that 79.0% of patients were papillary urothelial (31). In Jordan, a study by Al-Saraireh et al. reported that 76.9% of patients had papillary urothelial cancer (32). However, in Tanzania, Yohana et al. reported that only 37% of patients had papillary urothelial cancer (16).

The finding of the current study that the percentage of the tumor size (2 – 5) cm was 45.9% is in agreement with those of Yazdi et al., who reported that 46.6% of patients had a tumor size of 2-5 cm (33). Ibrahim et al. from Iraq found that only 12% of patients had a tumor size of ≥5 cm (34). Cases < 2 cm in size constituted 42.9% of the total, which corresponds with the study of Yazdi et al. from Iran, who found that 40% of patients had a tumor size of < 2 cm (333).

**Conclusion**

UBC was found to be mainly a disease of males and older age. Papillary urothelial carcinoma was the most frequently seen, mostly at stage T1 and high grade, and more likely to be of a small or moderate size.

**Limitation**

The current investigation had some limitations as it relied on recorded data, which posed certain challenges in interpreting the findings due to incomplete information regarding patient history, tumor staging, and treatment management. It is important to admit that such difficulties are unavoidable in retrospective studies, especially in a country like Iraq, where medical services are provided by both the Ministry of Health and private hospitals. Nevertheless, the data collected from this study can contribute to formulating a better understanding of the national prevalence of urinary bladder cancer

**Authors' declaration:**

We confirm that all the Figures in the manuscript are ours. Besides, the authors have signed an ethical consideration approval (Ethical Clearance). The project was approved by the local ethical committee in the College of Science, according to the guidelines on biomedical research. The license has the code number CSEC/0124/0009 and is dated January 24, 2024.

**Conflicts of Interest:** None.

**Funding**: None.

**Authors' contributions:**

Study conception & design: Zahraa D. Salman and Dr. Ban J. Mohamad; Literature review: Zahraa D. Salman; Data acquisition: Zahraa D. Salman; Data analysis & interpretation, manuscript preparation: Zahraa D. Salman and Dr. Ban J. Mohamad.

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## الدراسة النسيجية لسرطان المثانة في عينة من المرضى العراقيين من عام 2019 الى 2024

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**الخلاصة:**
**خلفية البحث:** سرطان المثانة البولي (UBC) هو الورم الخبيث الشائع في المسالك البولية ويحتل المرتبة العاشرة بين الأورام الخبيثة الأكثر شيوعًا في جميع أنحاء العالم. وفي العراق، يحتل سرطان المثانة البولي المرتبة السابعة من السرطانات العشرة الأوائل. هناك العديد من عوامل الخطورة المؤكدة لسرطان المثانة بما في ذلك العوامل الوراثية والجينية، التبغ والتدخين، التعرض لمواد كيميائية معينة والاصباغ والامراض مثل التهاب المثانة المزمن، والاصابات المعدية مثل البلهارسيا.
**هدف الدراسة:** تقييم خصائص سرطان المثانة البولي التي تم تشخيصها في عينة من المرضى العراقيين.
**المنهجية:** تم جمع 70 كتلة نسيجية لسرطان المثانة مطمورة في شمع البرافين مع بياناتها من أرشيف وحدة التشريح المرضي لمستشفى الشهيد غازي الحريري/ مدينة الطب، مستشفى اليرموك التعليمي، وبعض المختبرات الخاصة في بغداد-العراق. تم الحصول على المعلومات الخاصة بالعمر والجنس والنوع النسيجي للورم وحجم الورم ومرحلته ودرجته من التقارير السريرية للمرضى.
**النتائج:** كشفت النتائج أن 82.9% من حالات سرطان المثانة البولي كانت من الذكور، وأن 62.9% كانوا في سن (79-60) عامًا. كان حجم الورم السائد من 2 إلى 5 سم، وكانت المرحلة T1 هي الأكثر شيوعًا بنسبة 80٪ من مجموع العينات. تم تسجيل الدرجة المرتفعة من الورم في 60٪ من المرضى وكان سرطان الظهارة البولية الحليمي هو النوع النسيجي الأكثر شيوعا بنسبة 77.1% .
**الإستنتاجات:** وُجِد أن سرطان المثانة البولي هو مرض يصيب الذكور وكبار السن بشكل أساسي. وكان سرطان الخلايا الحرشفية الحليمية هو الأكثر شيوعًا، وغالبًا ما يكون في المرحلة T1 والدرجة المرتفعة، ومن المرجح أن يكون حجمه صغيرًا أو متوسطًا.
**الكلمات المفتاحية:** المظاهر السريرية المرضية ;دراسة نسيجية ;سرطان المثانة البولي.،