

*Research Article*

## Urinary Bladder Carcinoma Pattern at Urology Minia University Hospital

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### Abstract

**Introduction:** Bladder cancer is one of the most common malignancies occurring worldwide. Bladder cancer develops predominantly in males with a ratio male: female (3:1). In developed countries, Urothelial cell carcinoma (UCC) is the predominant bladder tumor (>90%) of cases. In Egypt, previous research has reported a significant decrease in squamous cell carcinoma (SCC) over the past 30 years but the overall bladder cancer incidence is steady due to increase in UCC and this has been explained due to decrease in S.haematobium (SH) with increase in smoking. **Aim of the work:** Through a study that will be conducted at Urology and Nephrology Minia university hospital we will report the patterns (clinically, radiologically, and histo-pathologically) of bladder cancer patients presented to our institution in the period between 2020-2021. **Patients and Methods:** Our study is a prospective clinical study conducted on 120 patients who attended to our outpatient clinic at Nephrology and Urology Minia University Hospital in the period from February 2020 to March 2021. We included all patients presented to our institution with bladder mass, while patients who received chemotherapy or radiotherapy, or did Previous cystoscopic resection with intravesical therapy; were excluded from our study. **Results:** This study was conducted on 120 with bladder cancer. Male: female ratio was 5:1 with median age of 59.73 years. About 80 cases were from rural area. The main presenting symptom was gross hematuria with clots in about 72% of cases. During this study, sensitivity of urine cytology was 32.5 % and noticed that it increased mainly with high grade tumors. We did complete TURBT in 50 cases for masses with size lower than 3 cm and histopathology of all resected tumors showed that, about 78 cases were UCC, 36 were SCC and 6 were ADC. About 62.5% of cases were high grade tumors. During this study, we assessed correlation between urine cytology and tumor grading and the relation was statistically significant but on the other hand, the relation between cytology and tumor staging was statistically insignificant.

**Key Words** UCC: Urothelial cell carcinoma, SCC: squamous cell carcinoma, SH: S.haematobium, TURBT: transurethral resection of bladder tumor, ADC: adenocarcinoma.

### Introduction

Bladder cancer is one of the most common malignancies occurring worldwide. Bladder cancer develops predominantly in males with a ratio male: female (3:1). In developed countries, Urothelial cell carcinoma (UCC) is the predominant bladder tumor (>90%) of cases. In Egypt, previous research has reported a significant decrease in squamous cell carcinoma (SCC) over the past 30 years but the overall bladder cancer incidence is steady due to increase in UCC and this has been explained due to decrease in S.haematobium (SH) with increase in smoking (Parkin et al., 2005). The most common presenting symptom is painless hematuria, seen in >80% of patients. Others may also present with irritative symptoms such

as dysuria, frequency or urgency. Symptoms of metastases such as bone or flank pain are rare.

A complete history and physical examination should be undertaken, together with laboratory tests evaluating full blood counts and renal function. Bladder ultrasonography most frequently gives an initial suspicious image, but final diagnosis of bladder cancer is based on cystoscopy and evaluation of the resected tissue. (Hodges SC 2017) (DeGEORGE et al., 2017).

Most of the time, treatment of bladder cancer is based on the tumor's clinical stage. Stage means how deep it is thought to have grown into the bladder wall and spread beyond the bladder. Other factors, such as the size of the tumor,

grade and performance state. Treatment options are TUR and intra vesicle injection of BCG, mitomycin or chemotherapy for stage 0, for invasive bladder cancer not metastatic, radical cystectomy is the standard treatment, followed by chemotherapy and radiotherapy. (DeGEORGE et al., 2017)

## Patients and Methods

### Study Design:

Our study is a prospective clinical study conducted on 120 patients who attended to our outpatient clinic at Nephrology and Urology Minia University Hospital in the period from March 2020 to March 2021.

### Inclusion criteria:

All patients presented to our institution with bladder mass will be included in our study.

### Exclusion criteria

- 1- Patients who received chemotherapy or radiotherapy.
- 2- Previous cystoscopic resection with intravesical therapy.

### Methodology:

Patients were assessed on the baseline of complete bladder mass diagnosis, confirmation of surgical indication and fitness for surgery, the study was approved by ethical committee. A consent was signed by the patient explaining potential outcome and possible complications of the procedure, then admitted patients were assigned to certain hospital number.

### *All patients will be evaluated at baseline as follows: -*

- **Medical history:** detailed medical history with a special emphasis on lower urinary tract symptoms (LUTS), previous medical treatment if present.
- **Surgical history:** whether open or endoscopic surgery.
- **Physical examination**
  - 1- General examination
  - 2- Abdominal examination.
  - 3- Genital examination.
  - 4- DRE.
- **Laboratory investigation:**
  - 1- Urine analysis.
  - 2- Complete blood culture.
  - 3- Renal function tests.
  - 4- Liver function tests.
  - 5- coagulation profile.
  - 6- Urine cytology.

- **Imaging:**

- **Pelvi-abdominal ultrasound. CT urography commenting** on (size, site of mass) and the condition of upper system.
- **MRI (if needed).**

- **Surgical technique:**

### **Pre-operative preparation:**

Emphasis on patient medical history and evaluation of coagulation profile of all patient is done due to prevalence of chronic liver diseases and possible azotemia also increased risk of cardiovascular diseases in old age and subsequent anticoagulant therapy, patient on aspirin therapy is ordered to discontinue treatment 1 week before operation

All patients received preoperative antibiotics; patients with indwelling Foley catheters are presumed to be infected regardless of culture results and should be routinely given broad-spectrum antibiotic coverage before surgery. Culture-specific antibiotics are preferred; patient presented with UTIs is treated preoperatively.

All patients have CBC, blood hemoglobin and hematocrit value preoperatively.

### **Intra operative procedure:**

- The procedure was performed under spinal anesthesia, all cases underwent initial diagnostic cystoscopy using 22 Fr (Karl Storz) cystoscope to visualize urethra and prostate (in men), identify the ureteric orifices and site, size and multiplicity of the masses (Fig.5).
- Then we introduced resectoscope (26 Fr) (Karl Storz) with continuous wash with adapted 30° lens system and Olympus camera head connected to monitor, using Glycine 1.5 % for irrigation with monopolar generator
- KLS martin maximum diathermy with the power setting at 120 for cutting and 80 for coagulation and active working element to do complete resection of the mass if accessible or take multiple TUR biopsies (Fig.4, 5).
- Bimanual Examination under anesthesia was done to all cases.
- Then a wide caliber urethral catheter was inserted.

**All patients will be assessed during post-operative period as follows:**

Patient who did not develop any immediate post-procedure complications will be discharged after 24 h of monitoring.

- Within 2-5days, urethral catheter was removed if there was no hematuria.
- Within 7 days the results of histopathology will appear.
- Data were checked, entered, and analyzed using SPSS (version 15, special package for social science). Data were expressed as mean  $\pm$  SD for quantitative variables, number and percentage for qualitative ones. Chi-squared ( $\chi^2$ ) with  $P < 0.05$  as statistically significant.

**Results**

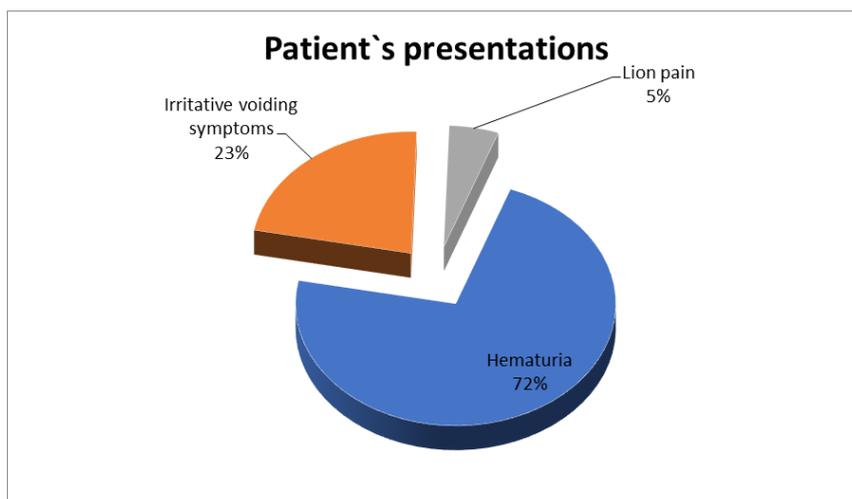
Our study is a prospective clinical study, conducted at Nephrology and Urology Minya University Hospital. We involved in our study all cases presented with urinary bladder mass at our outpatient clinic in period from February 2020 to march 2021. All cases had diagnostic cystoscopy with biopsy or total resection.

The age of our patients ranged from 23: 83 years and mean( $\pm$ SD) patient age was 59.73( $\pm$ 12.43), 99(82.5%) of our cases were males while 21(17.5%) were females and regarding patients' occupation, 54 patients were employees and 48 patients were farmers. Most of our patients were from rural area (Table 2).

**Table 1: Demography of cases**

CHARACTERISTIC	CASES (N =120)
<b>Age (years)</b>	
Mean $\pm$ SD	59.73 $\pm$ 12.43
<40	12(10.0%)
40-60	36(30.0%)
>60	72(60.0%)
<b>Gender</b>	
Male	99(82.5%)
Female	21(17.5%)
<b>Occupation</b>	
Employee	54(45.0%)
Farmer	48(40.0%)
Worker	12(10.0%)
House wife	6(5.0%)
<b>Residence</b>	
Urban	40(33.8%)
Rural	80(66.3%)

Eighty-seven patients were presented with hematuria as a main complaint while twenty-seven were presented with irritative symptoms. Fourty four cases (36.2%) were with hydronephrosis which was mainly unilateral while the majority of cases were with no hydronephrosis .



**Fig 1: Common complaints of cases**

Transitional cell carcinoma (TCC) was most common histopathological pattern in our study 78(65%) of cases while Squamous cell carcinoma (SCC) was about 36(30%) of cases and Adenocarcinoma was about 6(5%) of cases. Regarding tumor grading, 75 (62.5%) of masses were with high grade nature while according to tumor staging, stages 1,2,3,4 were 24.9%, 21.6%, 29.1%, 24.1% respectively (Table 2).

Our study revealed that about 28 (77.78%) of SCC masses were high grade tumors, 43 (55.12%) of TCC masses were high grade tumors and 4 (66.67%) of adenocarcinoma masses are high grade tumors and on the other hand, 35 (44.88%) of TCC were low grade tumor, 2 (33.3%) of adenocarcinoma were low grade tumors and 8 (22.22%) of SCC were low grade tumors (Table 2).

**Table (2): histopathological characteristic and staging of tumor among cases**

Characteristic	cases (n =120)
<b>histopathological pattern</b>	
Adeno carcinoma	6(5.0%)
SCC	36(30.0%)
TCC	78(65.0%)
<b>Histopathological grade</b>	
Low	45(37.5%) divided into: SCC = 8(22.22%) TCC = 35(44.88%) Adenocarcinoma = 2(33.3%)
High	75(62.5%) divided into: SCC = 28 (77.78%) TCC = 43(55.12%) Adenocarcinoma = 4(66.67%)
<b>TNM staging</b>	
1	30(24.9%)
2	26(21.6%)
3	35(29.1%)
4	29(24.1%)

## Discussion

An estimated 80,470 new cases of urinary bladder cancer (61,700 men and 18,770 women) were diagnosed in United States in 2019 with approximately 17,670 deaths (12,870 men and 4,800 women) occurring in the same period (Siegel RL, et al., 2019). Bladder cancer, the sixth most common cancer in the United States, is rarely diagnostic in individual younger than 40 years of age. Given that the median age at diagnostic is 73 years (cancer stat facts, 2019).

In Egypt, the relative frequency of bladder carcinoma is 10.1% of all cancers according to the latest National Cancer Institute registry (5 Xu Y, et al., 2017).

Bladder cancer is one of the most common malignancies occurring worldwide. Bladder cancer develops predominantly in males with a ratio male: female (3:1). In developed countries, Urothelial (transitional cell) carcinoma is the predominant bladder tumor (>90%) of cases. In Egypt, previous research has reported a significant decrease in SCC over the past 30 years but the overall bladder cancer incidence is steady due to increase in TCC and this has been explained due to decrease in *S. haematobium* with increase in smoking (Parkin DM, Bray F, Ferlay J, Y. L. 2002) (Zheng, S. Amr, D. A. Saleh et al., 2012).

The most common presenting symptom is painless haematuria, seen in >80% of patients. Others may also present with irritative symptoms such as dysuria, frequency or urgency. Symptoms of metastases such as bone or flank pain are rare. A complete history and physical examination should be undertaken, together with laboratory tests evaluating full blood counts and renal function. Bladder ultrasonography most frequently gives an initial suspicious image, but final diagnosis of bladder cancer is based on cystoscopy and evaluation of the resected tissue (Hodges SC 2017).

Urinary bladder cancer (UBC) is predominantly a disease of male gender as described in the textbook (Bray et al., 2013). Recent individual researches from around the world also confirm this observation, such as from studies conducted in Pakistan (Mubarak et al., 2014), Netherlands (Ploeg et al., 2010), Malaysia (Kong et al., 2010) and Nigeria (Anunobi et al.,

2010). We also found a predominance of male gender in our UBC cases with a M:F ratio as high as 5:1; however recently Rambau et al., from Tanzania found a predominance of females in their UBC cases (Rambau et al., 2013). This is probably due to the presence of more cases of SCC in their cohort, which comprised a schistosomiasis-infested population. Mallin et al., from their recent study of UBC and comparison between race and gender found more cases of muscle-invasive UBC in females than males (Mallin et al., 2011).

Our study included a total of 120 patients. The median age at diagnosis was 59.73 years, which is lower than the median age at diagnosis in developed countries which was 73 years (cancer stat facts, 2019). A multicenter retrospective study conducted on Egyptian UBC patients treated at NCI, Cairo University and Medical Oncology and Hematology department, Zagazig University showed similar median age at diagnosis which was 62 years (Haggag R, et al., 2014).

Most of the classical literature and historical age-related data of UBC point towards a higher frequency in elderly patients. Mubarak et al., from Southern Pakistan have reported a mean age of 57.5 years (Mubarak et al., 2014). whereas Mansoor et al., in their study on superficial bladder cancers, observed a median age of 62 years (Mansoor et al., 2011). Kong et al., from Malaysia found slightly higher figures of 65 years (Kong et al., 2010).

The mean age reported from Nigeria is towards the lower end 51.3 years (Anunobi et al., 2010). The Tanzanian study of schistosomiasis-associated UBC also quotes a lower mean age figures of 54.3 year (Rambau et al., 2013). The schistosomiasis-associated UBC has been classically associated with young age group; this has recently been confirmed from an Egyptian study by Salem and Mahfouz. But they found an increase in the mean age of UBC patients by about 10 years; probably because of a decrease in the incidence of schistosomiasis (Salem and Mahfouz, 2012).

Our results showed that bladder cancer more common in males with percentage 82.5% which was consistent with data from cancer statistics, 2019 (Siegel RL, et al., 2019). Another study

done by Lavery et al., and conducted on 129 patients, had found that 102 of cases were males while 27 of cases were females (Lavery et al., 2017).

In another study performed by Karsiyakali et al., 145 (88.4%) of study group were males and 19 (11.6%) were females with a mean age of  $66.46 \pm 10.57$  (Karsiyakali et al., 2020).

In our study most of our patients 66.5% (n=80) were from rural area. while in Shah et al., the (85.4%) were urban, 320 cases (9.5%) were large towns, and 172 cases (5.1%) were rural (Shah et al., 2020).

Our study showed that 72.5% (n=87) were presented with hematuria as a main complaint while 22.5% (n=27) were presented with irritative symptoms, which is similar to study done by Cohen and Brown (Cohen and Brown, 2003) also, Rafique et al., reported that hematuria, seen in 78.6% of the patients (Rafique et al., 2006).

TCC is the most common type of UBC as observed in the textbooks and WHO data (Bray et al., 2013). In our study, TCC was most common histopathological pattern with a percentage of 65% (n= 78) while SCC was about 30% (n=36) and Adenocarcinoma was about 5% (n= 6). Similar high percentages of TCC have been reported in the recent literatures. Martin et al., reported in a study conducted on 1238 patients (975 male, 263 female) that 577 (47%) had UC, 174 (14%) UCV, 398 (32%) SCC, and 89 (7%) ADC, and the median age was 54 (20-87) (Martin et al., 2018).

Vaidya et al., from Nepal reported the TCC percentages to be as high as 97.6% (Vaidya et al., 2013). Mubarak et al., from Pakistan reported a frequency of 94.3% TCC (Mubarak et al., 2014). A recent study analyzing the cancer registry of Netherlands found more than 90% urothelial cancers in their population cohort of more than 28 thousand patients (Ploeg et al., 2010). Kong et al., from Malaysia also reported TCC to be present in 90.4% (Kong et al., 2010). The reports from the schistosemiasis-endemic African countries are different. Although TCC is still a predominant tumor, in the study from Nigeria, the frequency percent-

tage is only 61.5% (Anunobi et al., 2010). Rambau et al., from Tanzania found more SCC (55.1%) than TCC (40.5%) in keeping with association of SCC with that of endemic schistosomiasis in the (Rambau et al., 2013). The apparent increase in the frequency of TCC in Egypt, during the 10 years period of study by Salem and Mahfouz, was also attributed to a decrease in the incidence of schistosomiasis (Salem and Mahfouz, 2012).

Histological grading of the tumors was done according to WHO (2004)/ISUP grading of urothelial neoplasms (Epstein, 1999).

In our study 62.5% (n=75) of masses were of high-grade nature while 45(37.5%) were of low grade, this was closely similar to study from Nepal which has reported more than half the cases 52.2% (n=120) as high grade. In contrast the study from El-Siddig et al., has reported that two-thirds of cases to be in low-grade (i.e. grade I and II) category and only one-third cases were high grade (El-Siddig et al., 2017).

The Malaysian researchers also found about 1/3 high-grade cases (32.5%) in the superficial TCC (Kong et al., 2010). The Southern Pakistani study has observed this ratio to be approximately 3/4 low grade to 1/4 high grade, i.e. they found more percentages of well-differentiated TCC (Mubarak et al., 2014).

Also in a study performed by Laishram et al., it was reported that low grade papillary urothelial carcinoma was (53.85%) were more common than high grade with (34.61%) (Laishram et al., 2012).

Similar results by Ahmed et al., who was also reported where 44% were low grade and 29.5% were high grade (Ahmed et al., 2002).

The reason why in our study most of cases was of high grade may be attributed mainly to the advanced age of patients at time of presentation, this was similar to the study performed in Jordan (Amman city) by Al Khader et al., which reported that advanced age was significantly associated with high tumor grade where 57(58.2%) and 5(5.1%) of high-grade tumors were found in the age groups 65-84 and >84 years, respectively (Al Khader et al., 2019).

In our study, according to tumor staging, stages 1,2,3,4 were 24.9%, 21.6%, 29.1%, 24.1%

respectively and other study revealed most bladder cancers (75–80%) do not involve the muscle wall of the bladder and are usually treated by telescopic removal of the cancer (transurethral resection of bladder tumor [TURBT]). This is often followed by instillation of chemotherapy or vaccine-based therapy into the bladder (Guidance, 2017).

El-Siddig et al., has reported that superficial TCC was predominant (70%) and only about 30% cases of TCC were muscle invasive (El-Siddig et al., 2017). Another study by Laishram et al., has found that early stage (PTa, PT1) tumors comprised 73.07% of the cases which is similar to findings by Kong et al., (71.8%) (Kong et al., 2010) (Laishram et al., 2012).

The figures observed by the Nepalese scientists were 35% showed muscle invasion (Vaidya et al., 2013). Slightly higher percentage of 38% muscle invasive were observed by Mubarak et al., from Southern Pakistan (Mubarak et al., 2014).

#### Conclusion & Recommendation

- (1) Urinary bladder cancer is more common in males more than females.
- (2) Painless hematuria is the commonest presentation of ub cancer patients.
- (3) In our environment, TCC is the commonest histopathological pattern of urinary bladder cancer and high-grade tumors have higher percentages.
- (4) Urine cytology has low sensitivity in diagnosis of ub cancer but becomes more valuable in tumors with large size and high-grade nature.
- (5) TURBT and histopathology analysis is the primary and sure modality for diagnosis of bladder cancer.

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