

## Histomorphological pattern of urinary bladder mass with their clinical correlation

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### Abstract

**Background:** Urinary bladder tumours are common lesions in man and woman. Mortality and morbidity depend on the grade and stage of tumour at the time of diagnosis. Early diagnosis is associated with good prognosis, but there are limited data in Bangladesh about such practice.

**Objective:** The aim of the study is to see the histomorphological pattern of urinary bladder tumors in different age groups and to see the pattern of presentation of various urinary bladder tumours.

**Methodology:** A total 150 cases, clinically, sonographically and/or cystoscopically suggestive of urinary bladder tumor were included in this study. Specimens were collected after surgical resection in a container containing 10% formalin. The specimens were processed by paraffin embedding method and stained by routine Haematoxylin and Eosin stain for microscopic examination. The results of this study were calculated by standard statistical formula.

**Results:** This study focuses mostly on the histological examination of the specimen of urinary bladder mass with their clinical findings. The microscopic type of 150 cases of urinary bladder tumor was: 143 (95.33%) were papillary urothelial carcinoma, 4 (2.66%) were adenocarcinoma, 2 (1.33%) were squamous cell carcinoma and 1 (66%) was carcinosarcoma. The main clinical presentations were haematuria, irritative voiding of urine and flank pain.

**Conclusion:** Papillary urothelial carcinoma stage T2 are much more common in Bangladesh. Regarding association with risk factor, smoking plays very important part for making bladder tumour.

**Key words:** Histopathology, urinary bladder tumor

### Introduction

Urinary bladder tumour is a disease of middle aged and elderly person. It is 3 to 4 times more common in men than in women.<sup>1</sup> In case of male it is the second most common genitourinary malignancy after prostate.<sup>2</sup> The median age at diagnosis for urothelial carcinoma is 65 years in males and 71 years in females.<sup>3</sup> It is the 4th most common cancer in male but 8th most common cancer in female.<sup>4</sup> Moreover the incidence of bladder cancer increases directly with age. Mortality from bladder cancer is also higher in elderly persons.<sup>5</sup> Diagnosis is made most often on the basis of the findings of cystoscopy, tumor biopsy, and urine cytology.<sup>6</sup>

Common risk factors for bladder cancer are smoking, exposure to polycyclic aromatic hydrocarbons, chronic cystitis, pelvic irradiation and schistosomiasis.<sup>7,8</sup> Among these, cigarette smoking is recognized as the main cause of

bladder cancer and accounts for about 50% of cases in developed countries.<sup>9</sup> The relation between Schistosomiasis and bladder cancer is well established. The common presenting symptoms are painless haematuria, irritative voiding of urine, urinary frequency, urgency and dysuria. In the early stage, clinical findings are almost insignificant, but in advance stage of the disease flank pain, pelvic mass, bone pain, dependent edema, weight loss etc are usually present.<sup>10</sup> As haematuria and irritative voiding symptoms are the two most common presenting features, the standard evaluation for these includes urine culture, cytology, ultrasonography, intravenous urography (IVU), cystoscopy and cystoscopic biopsy.<sup>11</sup> Tumor grades are also important prognostic variables as low grade tumors have better prognosis than high grade.<sup>12</sup> Staging, in addition to grade is critical in assessment of blad

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der neoplasm.<sup>13</sup> Appropriate pathologic staging of bladder cancer remains an important factor for appropriate prognostic and therapeutic stratification of patients.<sup>14</sup>

Urinary bladder tumor is common in Bangladesh. Therefore this study was carried out to determine the pattern of bladder tumour in relation to clinical features.

**Methods**

This study was carried out at the Department of Pathology, Khulna Medical College, Khulna during the period of January 2015 to December 2017. A total of 150 cases of urinary bladder tumors of all ages and both sexes were collected, 82 cases were collected from KMCH, had full clinical information. The remaining 68 cases were collected from other private Hospital in Khulna City. Clinically, sonographically and/or cystoscopically suggestive cases of urinary bladder tumor were included in this study. Fresh specimens of surgically resected and transurethral resection of bladder tumor (TURBT) were collected along with a completed clinical proforma which was filled after taking history from patients attendants. The fresh specimens were collected in a container containing 10% formalin and it is labeled with name of the patient, address, identification number, type of specimen, date and place of operation. Among 150 cases of urinary bladder tumor 145 (96.66%) were collected by transurethral resection of bladder tumor (TURBT) and 5 (3.33%) were collected by cystectomy. If the specimen was a TURBT one, it was embedded as such and if it was a cystectomy specimen, the representative sections were taken. After over night fixation in 10% formalin, all the grossed specimens were submitted for routine processing and paraffin embedding. For microscopic examination paraffin sections were stained with hematoxylin and eosin method. Routine stained sections were first examined under low power and then under high power magnification. The following features were noted: the number and size of the lesion, grade of tumour, configuration (papillary or solid), depth of penetration, presence of muscle invasion, lymphatic invasion, blood vessel invasion, the presence and extent of cancer tissue in the perivesical fat or adjacent structures.

**Results**

This study was undertaken to observe the histomorphological pattern of urinary bladder tumor in a group of patients with their clinical findings and to compare the findings with those of other countries. The age range was from 25 years to 95 years with a mean age of 58.5 years. The

patients were divided into 8 groups (Figure 1). Out of 150 cases maximum number (43, 28.7%) of patients belonged to age group 55-64 years, these were followed by 42 (28%) cases who were in 45-54 years group, 31 (20.7%) in 65-74 years group, 11 (7.3%) in 75-84 years group, 9 (6%) in 35-44 years group, 7 (4.7%) in 85-94 years group, 6 (4%) in 25-34 years group, 1 (66%) in 95-104 years group.

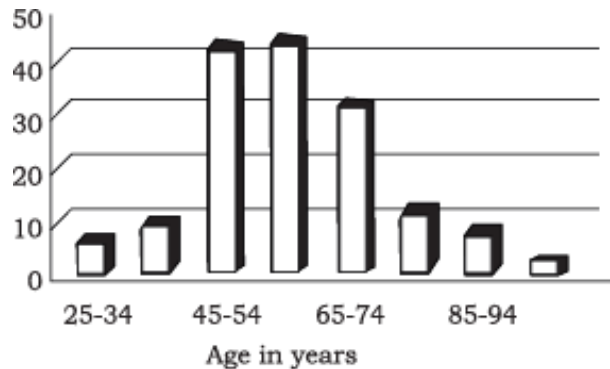


Figure 1 : Age distribution of study population

In this study out of 150 cases, 143 (95.3%) cases were male and 7 (4.7%) cases were female with M:F ratio of 20.4: 1. Sex distribution in relation to mean age were shown in Table-1.

**Table I**

Sex distribution in relation to mean age (<58.5 and >58.5) years

Age (years)	Male (%)	Female (%)
<58.5	89(59.3)	2(1.3)
>58.5	54(36.0)	5(3.3)
Total	143 (95.3)	7 (4.7)

Almost all 139 (92.7) patients had haematuria. Along with haematuria 57 (4%) had irritative voiding symptoms and 29 (19.3%) complained of flank pain. Most of the patients had other symptoms (burning during micturition, hesitancy) prior to haematuria but they came to the doctor when haematuria started as is shown in Figure 2.

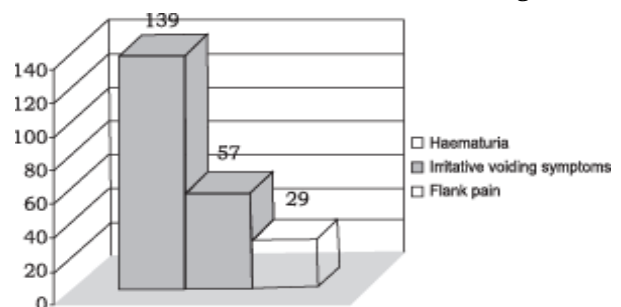


Figure 2 : Main clinical presentations of the patients

Site distribution of tumor was done by direct visualization with cystoscopic examination or by ultrasonography was as follows: 65 (43.3%) cases were in lateral wall, 53 (35.3%) were in posterior wall, 12 (8%) were in neck, 9 (6%) were in trigone and 11 (7.3%) cases had no information about site.

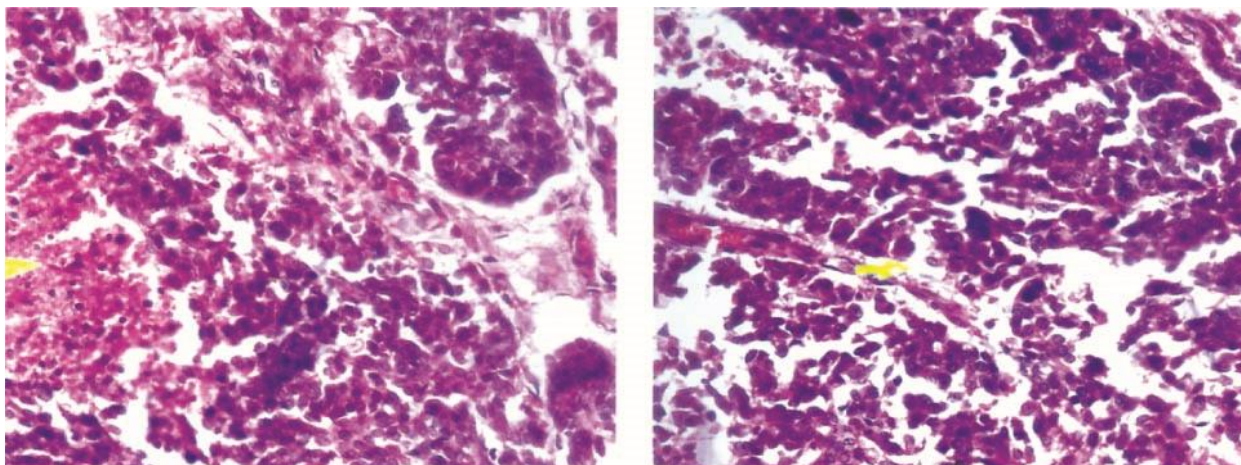


Figure 3 : Photomicrograph showing (a) high grade and (b) low grade papillary urothelial carcinoma

The microscopic type of urinary bladder tumor were: 143 (95.3%) were papillary urothelial carcinoma, 4 (2.7%) were adenocarcinoma, 2 (1.3%) squamous cell carcinoma and 1(0.7%) carcinosarcoma. The remaining 7 cases included adenocarcinoma, squamous cell carcinoma and carcinosarcoma and all of them were male. On microscopic examination, 72 (50.3%) bladder tumors were of high grade and 71(49.7%) were low grade. In 7(4.7) cases grading were not done because of these 4 were adenocarcinoma, 2 were squamous cell carcinoma and 1 was carcinosarcoma. Staging of urinary bladder tumor was done in 93 cases. In the remaining 57 (38%) cases staging was not possible as muscularis propria was absent. The maximum number of cases (57, 38%) were in stage T2, 32 (21.3%) were in stage T1 and 4 (2.7%) were in stage Ta. Out of 150 cases of urinary bladder tumors 94 (62.7%) were smoker, 30 (20%) were non smoker and 26 (17.3%) had no information about it.

### Discussion

Bladder cancer is one of the most common human cancers, constituting about 6% and 2% of all cancers among males and females, respectively. Over 90% of all bladder cancers are transitional cell carcinomas, with most of the remainder being squamous cell carcinomas. Smoking and occupational exposure to aromatic amines and other agents are most prominent among the risk

factors identified. Inflammation of the bladder may play some role in bladder cancer development. The association between inflammation and cancer appears to be stronger for squamous cell than for transitional cell carcinoma.<sup>15</sup>

In this study, histomorphological pattern, grade and stage of tumor with their clinical findings were compared with reported studies of many workers.<sup>16-31</sup>

The mean age in this study of the cases was 58.5 years; the age range was 25-95 years with male to female ratio of 20.4:1. Maximum number of cases 43, 28.7%) were seen in 55-64 years age group. Olivier found mean age at diagnosis of urinary bladder tumor was in the 70-74 years age group for both males and females & the mean age of urinary bladder tumor in this study is relatively more frequent in lower age group. It was observed during the present study that there is male preponderance among urinary bladder tumor patients. Out of 150 patients 143 (95.3%) were male and 7 (4.7%) were female. In a study Carrion found that 47000 men and 16000 women were diagnosed with bladder cancer in United States, in that year with a male: female ratio was 3.0:1.9 The ratio is quite different from the present study,

Haematuria was the commonest presenting symptoms in this study. The other presenting complaints, irritative voiding in 57 (38%) and flank pain in 29 (19.3%). Basler et al found that 80% of patients with bladder cancer had haematuria.<sup>6</sup> In this present study, it is significantly higher than above mentioned study.

Site distribution were as follows: lateral wall-65 (43.3%) and posterior wall-53 (35.3%). In a study of 1000 cases Ordonez observed the location were

as follows: lateral wall (37%), posterior wall (18%), trigone (12%), neck (11%), ureteric orifices (10%), dome (8%), and anterior wall (4%).<sup>10</sup> In both the studies lateral wall involvement is higher than other location. Among the five cases of cystectomy, two had multifocal lesion.

On histologic examination, papillary urothelial carcinoma were 143 (95.3%), adenocarcinoma were 4 (2.7%). Oosterlinck found in their study that histopathologically >90% of bladder cancer were urothelial carcinoma, approximately 5% were squamous cell carcinoma, and <2% were adenocarcinoma.<sup>11</sup> This study regarding histopathological diagnosis is nearly similar to the present study.

One case of carcinosarcoma was a 67 years old male, nonsmoker, presented with the complaints of intermittent frank urethral bleeding, increased frequency, pain and burning during micturition. Carcinosarcoma is a rare tumor of urinary bladder with fewer than 1000 documented cases reported to date.<sup>12,13</sup>

Grading is a method by which pathologists evaluate the growth pattern of a tumor in an attempt to predict its biological potential. High grade tumors are the most aggressive and the most likely to progress into the muscle of the bladder wall.<sup>14</sup> In the present study 72 (48%) were of high grade, 71(47%) were of low grade. Holmang et al (2011) showed that out of 363 patients. 95 (26.2%) were papillary urothelial neoplasm of low malignant potential, 160 (44.0%) were low grade, and 108 (29.8%) were high grade. In the present study high grade tumors were almost equal to low grade tumors.

Staging of bladder cancer is based on how deeply a tumor has penetrated the bladder wall. Stages Ta and Tis (in the urothelium) and stage T1 (in the lamina propria) are the non-muscle invasive stages. Most Ta tumors are low grade, and most do not progress to invade the bladder muscle. Stage T1 tumors are much more likely to become muscle invasive.<sup>16</sup> In the present study 57 (38%) cases, were in stage T2, 32 (21.3%) were in stage T1 and 4 (2.7%) were in stage Ta Marco showed in a study of 130 patients, 63 (48.5%) were in stage Ta, 30 (23.0%) were in stage T1, 25 (19.2%) were in stage T2 and 12 (9.2%) were in stage T3.<sup>17</sup> Staging pattern of the present study is significantly differing from that in study mentioned above.

Stage and grade are important prognostic criteria in stages Ta, T1 urothelial carcinoma of the bladder. Since therapy depends mainly on these tumor characteristics. The choice of chemotherapy, immunotherapy or conservative follow-up may depend on stage and grade.<sup>17</sup> In

this study 27 (18%) had squamous differentiation and all of these were of high grade and 8 (5.3%) had glandular differentiation. Humphrey observed that squamous differentiation of overall cases occurs in 21% of urothelial carcinomas and glandular differentiation in 6% of all urothelial carcinomas. Squamous differentiation may be associated with a poor response to surgery, radiation, and chemotherapy, while the clinical significance of glandular areas is uncertain.<sup>20</sup>

A close association between smoking and bladder cancer was observed in this study: 94 (62.7%) were smokers and 30 (20%) were non smoker. In a study in Sri Lanka showed that cigarette smoking is the single most important cause of bladder cancer, accounting for 25% to 65% of all cases.<sup>21</sup> Jankovic recognized that cigarette smoking is the main cause of bladder cancer and accounts for about 50% cases in developed countries.<sup>22</sup> Other risk factors such as occupational exposure, drug exposure, radiation etc could not be evaluated due to lack of information in these regards.

There are some limitations in this study: sample size was not so large to conduct a quality study, this study was conducted in only two hospitals in the southern area of Bangladesh which may not be representative for the whole country.

## Conclusion

Papillary urothelial carcinoma was the most frequent tumour and most of these present in the stage 2. Regarding risk factor, smoking has similar contribution in relation to other countries.

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