

Clinicopathological Spectrum of Urothelial Carcinoma – A Study from Tertiary Care Set Up

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ABSTRACT

Background: Urothelial carcinoma is the most common malignancy encountered in genitourinary tract. Urinary bladder cancer is the 7th most common malignant tumor worldwide. It is a disease of older age group. **Objective:** To determine the demographic characteristics of urinary bladder cancer and to analyze the cases of urothelial carcinoma according to gender, age, grade, invasion, histologic subtype, presenting complaints and pathologic stage of specimens. **Study Design:** Retrospective study. **Settings:** Pathology Department of Faisalabad Medical University from Department of Urology of Allied Hospital Faisalabad Pakistan. **Duration:** Three years (January 2015-December 2018). **Methodology:** Total 305 cases were included in this study. **Results:** 226 were male patients (74%), and 79 (26%) were females. Majority of the patients (62%) with urothelial carcinoma in this study were in their 5th and 6th decade of their life. Only 27 patients (8.8%) were below 40 years. Of total cases 149(48%) were of low grade, 150(49%) were of high grade and only 6 cases (2%) fell under the category of lesion named PUNLMP. 151(49%) cases were detrusor muscle invasive and 151(49%) were non-invasive and only 3 (1%) cases were found in which no muscle biopsy was identified. 99% of patients were diagnosed with commonest type of tumor that is transitional cell carcinoma, while only 3 (1%) cases were of transitional cell carcinoma with squamous differentiation. Painless visible hematuria was the most common presenting complaint (96%) followed by dysuria (3%) and storage symptoms (1%). Majority patients lie under the pathologic stage pT1(50%) then in pT2(48%). A significant correlation was found between gender and a grade of tumor. Female patients (60%) presented with higher grade and aggressive disease. Patients of younger age group (below 40) were diagnosed with low grade carcinoma. **Conclusion:** Urothelial carcinoma is a disease of elderly people with a significant predominance of male patients. Painless hematuria is the most common presenting symptom.

Keywords: Urothelial carcinoma, Tertiary care, Clinicopathological spectrum.

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INTRODUCTION

Urinary bladder cancer is ranked at number 10th among the most common cancers worldwide. According to Global Cancer Statistics 549,393 new cases of bladder cancer were reported in year 2018 and of them about 200,000 patients died of this disease.¹ Bladder cancer carries a greatest lifetime treatment cost per patient. Due to complex nature of disease, higher rates of recurrence and progression, it requires a multimodality treatment, that makes it one of the most costly cancers.² Tobacco smoking, occupational(dye, arsenic, aromatic amines) and environmental carcinogens are the well-known risk factors for development of urothelial carcinoma.³ Pioglitazone, which is an oral hypoglycemic drug, is thought to be associated with the development of

urothelial carcinoma.⁴ The spectrum of urinary bladder is versatile but majority of the cases are of transitional cell carcinoma followed by squamous cell carcinoma and adenocarcinoma.⁵ Stage and Grade of bladder tumors are the most important factors for evaluation of the prognosis of the disease.⁶ In 1998, WHO/ISUP proposed a classification system according to which papillary neoplasms of urinary bladder are classified as, PUNLMP, Low grade and High grade. 2016 WHO classification system continues to recommend the same grading system. The introduction of term PUNLMP emphasizes the importance of very low-grade nature of lesion which requires clinical follow up. The psychological, financial and emotional implications that come with a diagnosis of cancer can be avoided by using this term.⁷

This study aims in analyzing the clinicopathological spectrum of urothelial carcinoma regarding the age, sex, grade, invasion and pathological stage and to compare our results with local and international reports. Due to higher prevalence of bladder cancer in Pakistan this study will assist the clinicians to update their management guidelines.

METHODOLOGY

Study Design: Retrospective study.

Settings: Pathology department of Faisalabad Medical University Faisalabad Pakistan.

Duration: Three years from Jan-2015 to Dec-2018.

Sample Technique: Non-probability convenient.

Sample Size: 305 patients.

Inclusion Criteria: Blocks and clinical data, of 305 histologically diagnosed cases of urothelial carcinoma received from Allied & Hospital, between Jan 2015 and Dec 2018, were included in the study already received.

Exclusion Criteria: Patients who received chemotherapy and radiotherapy were excluded from the study.

Data Collection Procedure: Total 305 cases of urothelial carcinoma obtained after transurethral resection of bladder tumor (TUR-BT), were evaluated. The urothelial tumors were classified and graded according to 2004 World health organization/International society of urological pathologist (WHO/ISUP). Pathological Staging was assessed according to American joint commission on cancer/Union for international cancer control AJCC/UICC). According to which pT0, pT1 are those tumors which haven't invaded the underlying detrusor muscles, and are limited to lamina propria only. These tumors are considered low grade tumors while all detrusor muscle invasive tumors (pT2) were considered to be high grade lesions.⁸ Patient's record was evaluated for age, gender, procedure, tumor configuration, histologic subtype, histologic grade, pathologic stage and presenting symptoms. The data was analyzed using SPSS 20 and results were obtained in tabulated form as frequencies, percentages and ratio.

RESULTS

The study included 305 cases of urothelial carcinoma. 226(74%) were male and only 79(26%) were females, with male to female ratio of 3:1. (Figure 1)

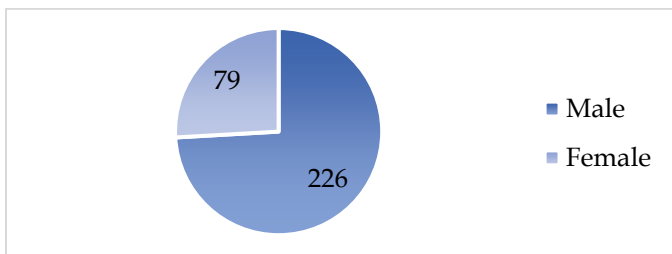


Figure 1: Frequency distribution of the cases of urothelial carcinoma regarding gender

238 (78%) of the cases were above the age of 50 years with the mean age of 63 years. (Figure 2)

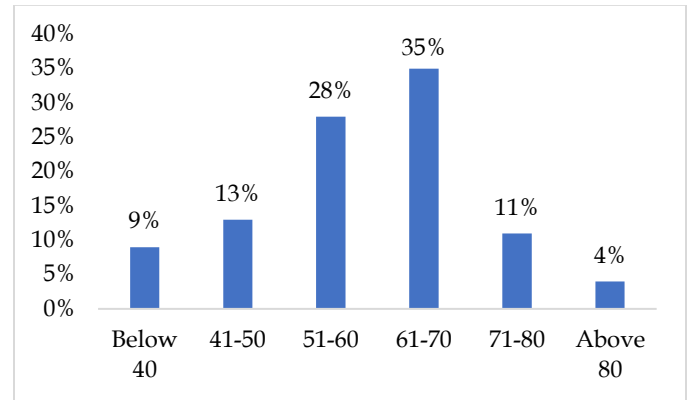


Figure 2: Frequency distribution of the cases of urothelial carcinoma regarding age

Histologically, 99 % tumors were pure TCC and 3(1%) cases were TCC with foci of squamous differentiation. No squamous cell carcinoma or adenocarcinoma of urinary bladder was reported in last three years. (Figure 3)

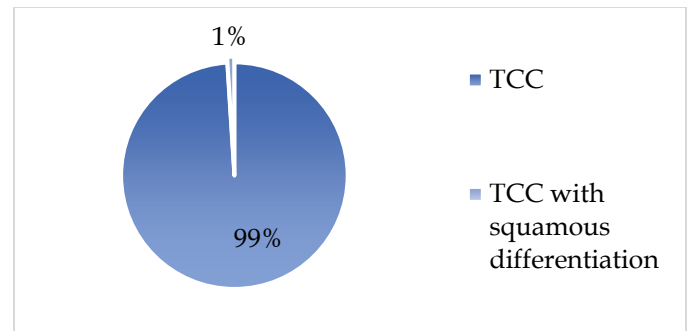


Figure 3: Frequency distribution of cases of urothelial carcinoma regarding Histologic subtype

96% patients presented with the complaint of painless macroscopic hematuria while only 3% presented with dysuria and 1% patients presented with irritative bladder symptoms. (Figure 4)

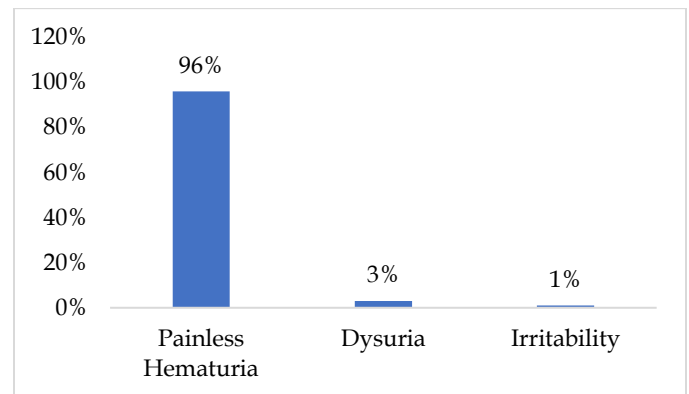


Figure 4: Frequency distribution of the cases of urothelial carcinoma regarding presenting complaints

According to histological grade 6(2%) cases were of PUNLMP, 149(48.9) were of low-grade urothelial neoplasm and 150(49.2) were of high grade. (Table 1)

Table 1: Frequency distribution of cases of urothelial carcinoma regarding grade

Grade	Frequency	percentage
PUNLMP	6	2%
Low grade	149	49%
High Grade	150	49%

Cases showing muscle invasion were similar to those with no muscle invasion,151(49%). In 3 cases no detrusor muscle was identified. (Table 2)

Table 2: Frequency distribution of cases of urothelial carcinoma regarding pathologic stage

Pathologic stage	Frequency	Percentage
pT0, pT1.	155	51%
pT2	151	49%

A significant co-relation was found between grade of tumor and a gender. High grade tumors were more common among women. (Table 3)

Table 3: Co-relation between cases of urothelial carcinoma with respect to gender of patient and grade of tumor

Gender	Grade		
	Low Grade	High Grade	PUNLM
Male	121	104	1
Female	28	46	5
Total	149	150	6

P value =0.001(significant)

High grade tumors were more prevalent among older age group than younger. (Table 4)

Table 4: Co-relation between cases of urothelial carcinoma with respect to age and gender

Age	Grade		
	Low	High	PUNLMP
Below 40	15	9	2
41-50	74	52	2
51-60	53	84	2
61-71	7	5	0
Total	149	150	6

P value= 0.007(Significant.)

DISCUSSION

This is the largest study conducted on urinary bladder cancer in the Faisalabad District. This study will add to the knowledge on urinary bladder cancer. Urinary bladder cancer is a common morbid and expensive health problem affecting older patients.⁹

According to one study conducted on urinary bladder cancer in Saudi Arabia shows, the mean age of presentation of the patients with urothelial carcinoma is 61 years,¹⁰ while in our neighboring country India, the age of patients presented with urothelial carcinoma is 60 years.¹¹ Our results are similar to them in this aspect as the mean age of presentation in our population is 63 years. According the study conducted in King Edward Medical College, Mayo hospital showed the similar results with mean age calculated is 59 years.¹¹ The mean age calculated in Sindh Institute of Urology and Transplant, is 57.5 years.¹² Association of higher age with the development of urothelial carcinoma is due to additive effect of environmental exposure to carcinogen especially cigarette smoke or occupational exposure. In addition, aging causes accumulation of several cellular events that may lead to cancerous development which is enhanced by difficulty in emptying the bladder completely which increases the contact time of carcinogen with the bladder mucosa. Furthermore, because of bothering voiding symptoms, older people might drink less water which further increases the exposure time of carcinogens.¹³

Majority of patients presented with urinary bladder cancer are males, In our study male to female ratio calculated is 3:1. Which is much similar to the ratio calculated among patients of urothelial carcinoma in United States which is 4:1, in Spain it is 6.7:1 and in Italy it is 7:1.¹⁴ In the studies conducted in different areas of Pakistan showed similar results, 5.7:1 in Hyderabad,¹⁵ 4:1 in Kashmir,¹⁶ 5.3:1 in Central Punjab.¹⁷ The reason for this increased incidence of bladder cancer in males is explained by influence of sex hormones and urination habits and reduced occupational exposure.¹⁸ Other possible reason for this decreased incidence can be attributed to the social trends of our population that females avoid exposing the diseases of genital tract to someone else.¹⁹

Transitional cell carcinoma is the most common histological subtype of urinary bladder cancer.²⁰ Our study showed similar results where TCC constitutes 99% of all cases. Our results are in total agreement with a work done by Ahmed and co-workers in AFIP, who have reported 91.1% of TCC, Similar results are obtained from a study done in Nepal reported 94.8%TCC. No pure Squamous cell carcinoma is reported in our study, most obvious reason for this is that squamous cell carcinoma of urinary bladder is more common in some Africans and Middle East where schistosomiasis is more prevalent,

leading cause of squamous cell carcinoma of urinary bladder.²¹

In our study the low grade and high-grade tumors, muscle invasive and non-invasive tumors were equal in number. Our results are different in these aspects from others. A study conducted in Hyderabad showed a greater prevalence of high-grade tumors followed by low grade and then by PUNLMP.¹⁵ Our results are in contrast to another study done in Shoukat Khanam Memorial hospital, which reported more cases of high grade than low grade tumors.²²

Urinary bladder cancer is rare in younger patients, and presents as low grade and low stage tumors and behaves in indolent manner.²³ The significant co-relation was found in our study (p value=0.007), that majority of patients who presents at younger age have low grade disease. These results are similar to the study done in New York which reported the same results.²⁴ This is opposite to the common belief that biological behavior of many tumors are aggressive but urinary bladder cancer presents in younger age with low grades and superficial tumors. The probable reason for this can be explained by the observation that younger patients lack genetic instability.

Female gender has a survival advantage in many other tumors but this does not seem to true in case of urinary bladder cancer.²⁵ Women presents with more advanced bladder cancer and have worst oncologic outcomes. Female gender is now considered as an independent prognostic factor for recurrence and mortality due to bladder cancer.²⁶

According to one series reported showed that bladder tumor occurring in women is associated poorer response to BCG (Bacillus Calmette Guerin) and early recurrence of tumor.²⁷ The probable reason for this is explained in the terms of symptoms. Painless hematuria is a main presenting complaint of bladder tumor, in male patients these symptoms may quickly seek attention and leads to immediate referral to urologist followed by proper cystoscopic evaluation while the same symptoms in females may be misdiagnosed as urinary tract infections which further delays the diagnosis and management of tumor.²⁸

Women presents with bladder cancer at older age than males, the possible reason for this is thought to be protective effects of estrogen but once this protective effect is lost it may lead to development of more aggressive and invasive tumors.²⁶ Similar results are observed in our study that showed more female patients are with high grade urothelial carcinoma and all those women were in there 6th or 7th decade of life. Our results in this aspects are similar to the study done Marks and co-workers who reported that females presents with more aggressive cancer biologic behaviors and they experience poorer outcome.²⁹

CONCLUSION

Transitional cell carcinoma is the most common histologic subtype of urinary bladder. Male above the 50 years are most commonly affected. Females usually presents at older age than males but possess a higher grade and aggressive disease course. Urothelial carcinoma is very common among the population of the Faisalabad District. The possible reason for this is due to the fact that Faisalabad is the main industrial city of Pakistan and development of urothelial carcinoma is much associated with occupation of the patient.

LIMITATIONS

All data collected in the study was retrospective. The sample size was small. No follow-up patients were included so comment about recurrence of tumor could not be established.

SUGGESTIONS / RECOMMENDATIONS

More elaborative study should be done as urothelial carcinoma is a huge emerging burden on health care system.

CONFLICT OF INTEREST / DISCLOSURE

There was no conflict of interest involved.

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No.

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