

## Urinary Bladder Tumors: A comparative histopathological study in patients less than 40 years and more than 40 years

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### Abstract

**Introduction:** The effect of age on histopathology of the urothelial and non-urothelial bladder tumors has not been studied extensively in literature. This study was undertaken to gain knowledge about this aspect.

**Materials and Method:** A four year retrospective study, from January 2013 to December 2016 of bladder tumors was carried out in the department of pathology, Sri Ram Murti Smarak institute of medical sciences, Bareilly. The biological material came from TURBT specimens from patients hospitalized for bladder tumors in our institute.

**Results:** Of all the bladder tumors studied, urothelial tumors comprised 95%. A total of 172 urothelial tumors were detected in age category 40 years and above, as compared to 18 in age category below 40 years. Out of all the urothelial tumors in age category 40 years and above, 65.5% tumors were invasive. In age category 40 years and below, such tumors were 46.6%. All the non-urothelial tumors were detected to be histopathologically invasive and were nine times more common in above 40 year age category than in 40 years and below age category. On studying the non-urothelial variety of bladder tumors we detected that all of them were invasive histopathologically. Besides, these non-urothelial variety of bladder tumors were nine times more common in age group 40 years and above than in age category 40 years and below.

**Conclusion:** The incidence of bladder tumors of both urothelial and non-urothelial varieties is significantly lower in patients less than 40 years.

**Keywords:** Urothelial tumors, Adenocarcinoma, Squamous cell carcinoma, Urinary Bladder, TURBT

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### Introduction

Cancer of urinary bladder is the ninth most common cancer in the world<sup>(1)</sup> with its prevalence steadily increasing during the past few years.<sup>(2)</sup> Higher incidence has been reported in the developing countries as compared to the developed ones.<sup>(3)</sup> Male preponderance is seen worldwide, especially the elderly, with cigarette smoking, industrial chemicals like arylamines, and parasitic infestation by *Schistosoma haematobium* being the common risk factors. In the younger population, who for the purpose of this article are defined as 40 years or younger, the disease is considered uncommon.<sup>(4)</sup> Whether these younger patients have a better prognosis than their elderly counterparts has long been a matter of debate.<sup>(5-9)</sup>

More than 90% of the urinary bladder malignancies are represented by urothelial carcinomas.<sup>(10)</sup> Trans-urethral resection of bladder tumor (TURBT) provides the necessary material for histopathological examination as it allows assessment of degree of differentiation, depth of invasion, and other parameters required for diagnosis and prognosis assessment.<sup>(11)</sup> In this article we have compared histopathological findings of urinary bladder cancers (TURBT specimens) of younger (below 40 years) with elder (above 40 years) patients. To the best of our

knowledge, this is the largest histopathological study of bladder tumors from northern India.

### Materials and Method

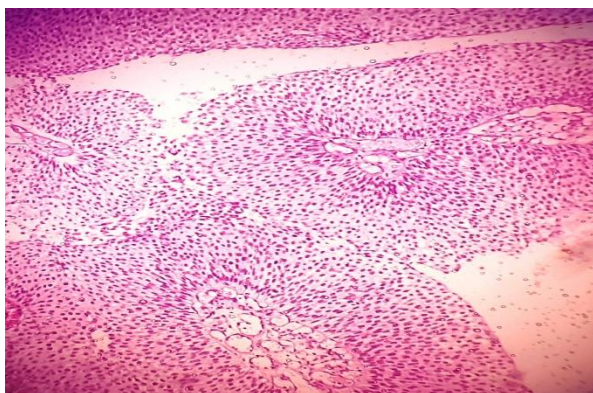
A four year retrospective study, from January 2013 to December 2016 of bladder tumors was carried out in the department of pathology, Sri Ram Murti Smarak institute of medical sciences, Bareilly. The biological material came from TURBT specimens from patients hospitalized for bladder tumors in our institute.

Inclusion criteria we followed were all the TURBT specimens received in the department of Pathology, Sri Ram Murti Smarak Institute of Medical Sciences, Bareilly. All autolysed specimens and inadequate biopsies were excluded from the study. These specimens were processed using 10% formalin fixation, paraffin embedding, followed by Haematoxylin and Eosin staining. A total of 190 urothelial and 10 non-urothelial bladder tumors were studied during this time period. The slides were studied and classified according to WHO/ISUP histological classification of tumors of urinary tract 2004 (Table 1).<sup>(12)</sup>

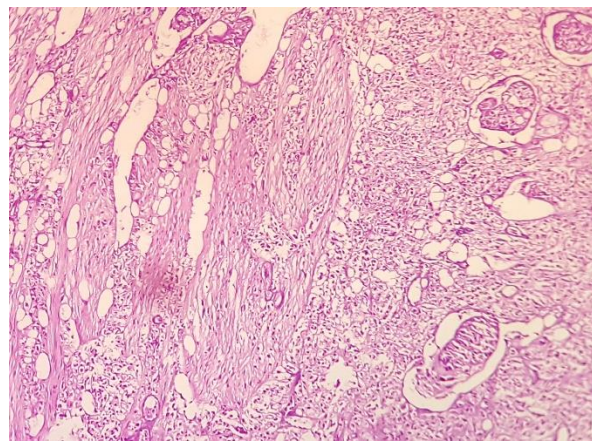
**Table 1: Simplified 2004 World Health Organization Histologic Classification of Urothelial Tumors\***

<b>Noninvasive Urothelial Neoplasm</b>
Papillary type
<ul style="list-style-type: none"> <li>• Urothelial papilloma, including inverted type</li> <li>• Papillary urothelial neoplasm of low malignant potential (PUNLMP)</li> <li>• Low-grade, papillary urothelial carcinoma (LGPUC)</li> <li>• High-grade, papillary urothelial carcinoma (HGPUC)</li> </ul>
Nonpapillary type
<ul style="list-style-type: none"> <li>• Urothelial carcinoma in situ</li> </ul>
<b>Invasive Urothelial Carcinoma</b>
*Excerpted from Eble et al, <sup>(12)</sup> 2004.

The microphotographs of the representative cases of low grade non invasive papillary urothelial carcinoma and high grade invasive urothelial carcinomas from our study are given in Fig. 1 (A. Low grade papillary urothelial carcinoma, B. High grade papillary urothelial carcinoma).



**Fig. 1a: Low grade papillary urothelial carcinoma**



**Fig. 1b: High grade papillary urothelial carcinoma**

**Results**

The results were tabulated as shown in Tables 2 and 3. The age range of patients detected with tumors of urinary bladder was from 21 years to 89 years. It was in the 51 to 70 years category that the peak incidence of these tumors was detected. The percentage of males was found to be 88.5%. Male to female ratio was 3.8:1 in age category above 40 years. The same ratio was 5:1 in the below 40 years age category. In above 40 years age category, there were 182 patients, as compared to 18 patients in the below 40 years age category. Youngest patient was a 21 year female with papillary urothelial neoplasm of low malignant potential (PUNLMP).

**Table 2: Distribution of patients with urothelial tumors by age and tumor type**

	Less than 40 years				More than 40 years			
	Total	%age	Male	Female	Total	%age	Male	Female
Papilloma	1	5%	1	-	-	-	-	-
PUNLMP	2	11%	1	1	7	4%	6	1
LGPUC	7	39%	6	1	73	42%		
• LGPUC; non invasive	6	(86%)	5	1	45	(62%)	35	10
• LGPUC; lamina invasive	-	-	-	-	20	(27%)	17	3
• LGPUC; muscle invasive	1	(14%)	1	-	8	(11%)	6	2
HGPUC	8	45%	7	1	92	54%	82	10
• HGPUC; non invasive	2	(25%)	2	-	12	(13%)	9	3
• HGPUC; lamina invasive	2	(25%)	1	1	14	(15%)	13	1
• HGPUC; muscle invasive	4	(50%)	4	-	66	(72%)	60	6
Total	18	100%	15	3	172	100%	136	36

**Table 3: Distribution of patients with non-urothelial tumors by age and tumor type**

	Less than 40 years			More than 40 years		
	Total	Male	Female	Total	Male	Female
Adenocarcinoma	1	1	-	6	6	-
Squamous Cell Carcinoma	-	-	-	1	1	-
Spindle cell sarcoma	-	-	-	1	1	-
High grade undifferentiated carcinoma	-	-	-	1	1	-
Total	1	1	-	9	9	-

There is low incidence of all categories in less than 40 year population, but our only case of transitional cell papilloma was found only in less than 40 years category. The most prevalent tumor in both the age groups was high grade papillary urothelial carcinoma (HGPUC), but when we compare the two age categories, its incidence was more in age category 40 years and above. Coming to the second most prevalent type of urothelial carcinomas, it was detected that low grade papillary urothelial carcinoma (LGPUC) occupied this place in both the age groups. Papillary urothelial neoplasm of low malignant potential (PUNLMP) was more common in the younger patients. There was a higher percentage of non-invasive tumors of both high and low grade in the younger age category. Of all the urothelial tumors, 39% were invasive and 61% were non-invasive in age category below 40 years whereas 63% urothelial tumors were invasive and 37% were non-invasive in the age category above 40 years.

The age of patients diagnosed with non-urothelial bladder tumors (Table 3), ranged from 40 to 85 years. The incidence of such tumors was uniformly distributed in the above 40 years age group. Only one patient aged 40 years could be categorized in the 40 years and below age group. There was no female patient having non-urothelial bladder tumor. All tumors in both the age group were histopathologically aggressive.

## Discussion

There have been a number of comparative studies on urothelial tumors in younger and older age groups.<sup>(13,14)</sup> The findings of this study were consistent with those of previously published reports. According to most of the studies, the carcinoma of bladder is a disease of the elderly with marked male predominance.<sup>(13-15)</sup> In our study, the incidence of urothelial tumors was 10.1 times more common in patients in age category 40 years and above when compared to those in age category below 40 years. We observed that the benign disease is more common in the younger age group, in this study, 71% bladder tumors were non-invasive in age category below 40 years when compared to only 37% in the age category 40 years and above. The only case of transitional cell papilloma in our study was also detected in the age category 40 years and below. The exact cause for this difference is not known at present and needs to be ascertained by further studies. This may help in altering the treatment

prognosis in invasive cases which at present is not very satisfactory.

However, there were some differences we noted in our study. Compared to 1% to 2.4% incidence of tumors reported in literature,<sup>(13,14)</sup> in our study, 9.5 % of the tumors of urinary bladder were detected in the younger age category.

The increased incidence of tumors of urinary bladder was detected in more than 40 years age category was detected in both the urothelial and non-urothelial varieties of tumors of urinary bladder. We found that the incidence of non-urothelial bladder tumors was nine times in the age category 40 years and above, i.e., out of the ten non-urothelial tumors (listed in Table 3), only one was found in age category 40 years and below.

The effect of age on the histopathological findings of bladder tumor is poorly investigated and understood. Maybe prolonged exposure to carcinogens like smoking in older age leads to formation of more malignant varieties. Besides, genetic factors may also play a role in higher incidence of invasive carcinomas in older age.<sup>(13)</sup>

There were some limitations of our study. It is purely a histopathological study, so we cannot comment much on the natural history of the disease in our patients. Then, our study does not have specimens of radical surgeries for invasive bladder cancers as such surgeries were not being performed in our institute during the study period.

## Conclusion

The incidence of bladder tumors of both urothelial and non-urothelial varieties is significantly lower in patients less than 40 years. Histopathologically less aggressive varieties of urothelial bladder tumors like papilloma, papillary urothelial neoplasm of low malignant potential, and noninvasive low grade papillary urothelial carcinoma were found to be more frequent in the below 40 year age group. The tumors occurring in patients in age category 40 years and above tend to be invasive.

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