

# Histological Spectrum of Urothelial Lesions – Experience of A Single Tertiary Care Institute

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## ABSTRACT

**Introduction:** Bladder cancer is the 7th most common cancer worldwide, Urinary bladder carcinoma accounts for about 3.2% of all cancers worldwide and is considerably more common in males than in females with a ratio of about 5:1. Non-neoplastic lesions usually encountered in the bladder are chronic non-specific cystitis, granulomatous cystitis, metaplastic conditions and malakoplakia. Aim of the present study was to analyse the histopathological features of various lesions in bladder biopsies and to study the frequency of different pathological lesions of urothelial carcinomas in biopsies and cystectomy specimen at a tertiary care institute.

**Material and Methods:** All the data was retrieved from the archives of Department of Pathology over a period of 3 years from August 2012 to July 2015, and the results were assessed according to their histology as biopsy is the gold standard for diagnosis and categorization.

**Results:** During this period, total cases were 38 among which 31.5% were non-neoplastic lesions and 68.5% were neoplastic lesions. Of the neoplastic lesions 84.6% were urothelial carcinomas of varying grade and 15.4% were squamous cell carcinomas. The male to female ratio was 5:1. The commonest age group was seen in the 41-60 years. Out of 26 cases of urothelial carcinomas, six (23%) were low grade and eighteen (77%) were high grade neoplasms.

**Conclusion:** Neoplastic lesions were more common than non-neoplastic lesions which were more common in the elderly age with prevalence in males.

**Keywords:** Urothelial lesions, Bladder carcinoma, Non-neoplastic lesions, Neoplastic lesions.

carcinomas in biopsies and cystectomy specimen at a tertiary care institute.

## MATERIAL AND METHODS

The present study was approved by the Institute Ethical Committee.

**Source and method of collection of data:** This was a three year study conducted in the Department of Pathology, Guntur Medical College, Guntur from August 2012 to July 2015. All patients who visited the Surgery/Urology outpatient department and presenting with signs and symptoms pertaining to urinary system like haematuria, dysuria etc. were included in the study. Cystoscopic bladder biopsies were performed. The biopsies were preserved in 10% formalin.

**Inclusion Criteria:** All cystoscopic biopsies taken from the urinary bladder and renal pelvis, received in Department of Pathology, Guntur Medical College, Guntur were considered for the study.

**Exclusion Criteria:** Inadequate bladder biopsy was defined as that biopsy which could not be interpreted by the pathologist due to an inadequate tissue content or poor preservation during its transfer to the pathology department, or biopsy of bladder cancer lacking muscular tissue for pathologic staging.

Gross examination was done, the tissues were processed for paraffin blocking. Four micron sections were cut and are stained with haematoxylin and eosin. The histological features were studied and relevant findings were noted.

## STATISTICAL ANALYSIS

Microsoft office 2007 was used to generate tables. Results of the study are based on descriptive statistics and presented as mean and percentage.

## RESULTS

38 urinary bladder biopsies were studied which included patients of all age groups, ranging from 9-76 years. The maximum number of cases were seen in between 4<sup>th</sup> to 6<sup>th</sup> decades of life with maximum cases seen in 41-60 years of age with 16 cases

## INTRODUCTION

Diseases of the urinary bladder both non-neoplastic and neoplastic are responsible for significant morbidity and mortality. Despite the improved methods of diagnosis and treatment, they pose biologic and clinical challenges. Cystoscopy is the primary diagnostic tool for patients who are suspected of having bladder tumours, which allows a direct visualization of the bladder mucosa and biopsies of the suspected lesions. An accurate diagnosis of urinary bladder lesions requires simultaneous data from urology, radiology and surgical pathology labs. The non-neoplastic lesions especially cystitis constitute an important source of symptoms and signs. These diseases are more disabling than lethal. Neoplastic lesions are responsible for significant morbidity and mortality. Bladder tumor is the seventh most common tumor worldwide. Urothelial carcinoma is the commonest type accounting for 90% of all primary tumors of the bladder.<sup>1</sup>

Aim of the present study was to analyse the histopathological features of various lesions in bladder biopsies and to study the frequency of different pathological lesions of urothelial

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(42%) The least number of cases were seen in the extremes of age groups. In the present study there were 28 male patients (73.6%) and 10 females (26.3%) (Table-1). Among the 38 cases, 12 were non- neoplastic and 26 were neoplastic lesions (Table-2).

Of the 12 non-neoplastic lesions, there were 8 cases of non-specific cystitis, two cases of exostrophy showing metaplastic changes and one case of Cystitis glandularis (Table-3).

Among the neoplastic lesions most of the cases were in the 5th and 6th decade of life with as many as 16 cases (42%) together and more than half of them were males. Of the 26 neoplastic lesions, 22 cases were papillary urothelial carcinomas and four cases were squamous cell carcinoma. Of the 22 papillary urothelial carcinomas, 6 cases were low grade papillary urothelial carcinomas, 8 were high grade urothelial carcinomas and 7 cases were high grade urothelial carcinoma showing squamous differentiation and one case of high grade urothelial carcinoma of ureter. Of the 6 low grade papillary urothelial neoplasms, 3 were non-invasive and 3 were invasive carcinomas (Table-4).

In the present study 69.3% were non-invasive and 30.7 % were invasive tumors with a male to female ratio of 5:1 with a higher incidence in 4<sup>th</sup> to 6<sup>th</sup> decade of life. Inflammatory lesions were common in younger age group, whereas the neoplastic lesions were common in the older age group with a predominance in males.

## DISCUSSION

The urinary bladder and renal pelvis are more common sites for urothelial carcinomas, than the ureters and urethra<sup>2</sup> In general, the prevalence of bladder tumours in developed countries is approximately 6-times higher compared to developing countries. Urinary bladder lesions, non-neoplastic and neoplastic are collectively responsible for significant morbidity and mortality throughout the world. Cystoscopy is the primary diagnostic tool for the patients, who are suspected of having bladder tumors, which allows a direct visualization of the bladder mucosa and biopsies of the suspected lesions.

Bozzoni in 1805 described the first cystoscope consisting of a metal tube which on the extravescicle end applied a spark plug through which the vesicle field was illuminated and limited at the other end of the tube. The first bladder biopsy forceps were independently described by Young and Manon in 1929 by which it was possible to extract portions of tumor tissue.<sup>3</sup> The role of pathologist is just not limited to its diagnosis, but also gives additional information that can have impact on the treatment and outcome of the patient.

Most common non-neoplastic lesions of the bladder, renal pelvis and urethra are chronic non-specific cystitis with histological variants like follicular, eosinophilic and xanthogranulomatous types, Granulomatous cystitis, metaplastic changes and malakoplakia.

In the present study there were 9 cases of chronic non-specific cystitis, whose ages ranged from 16 years to 62 years. Microscopic picture showed edematous lamina propria and infiltration by chronic inflammatory cells with overlying normal urothelium which were similar to the study done by SriKouSthubha where 84% of the non-neoplastic lesions were inflammatory lesions.

We have one case of Von Brunn's nest with cystitis cystica was

Age	Male	Female	Total	Percentage (%)
1-10	2		2	5.2%
11-20	1	1	2	5.2%
21-30	1	1	2	5.2%
31-40	4	3	7	18.4%
41-50	6	2	8	21%
51-60	6	2	8	21%
61-70	6	1	7	18.4%
71-80	2	-	2	5.2%
Total	28	10	38	100

**Table-1:** Distribution of Urothelial lesions

Type of Lesion	No. of cases	Percentage (%)
Non-Neoplastic	12	31.5%
Neoplastic	26	68.4%
Total	38	100

**Table-2:** Distribution of Lesions

Diagnosis	No. of cases	Percentage (%)
Chronic non-specific Cystitis	9	75%
Metaplastic changes	2	16.6%
Cystitis glandularis	1	8.3%
Total	12	100%

**Table-3:** Distribution of Non-neoplastic lesions

Diagnosis	No. of cases	Percentage (%)
LGPUN	6	23%
HGPUN	9	34.6%
HGPUN with squamous differentiation	7	26.9%
SCC	4	15.3%
Total	26	100%

**Table-4:** Distribution of Neoplastic lesions

noticed in a 39 year old male, in the region of trigone, in which the urothelium showed a solid invagination into the lamina propria, some of them had lost connection with the surface urothelium.

In the present study, bladder carcinoma was more common in males when compared to females with a ratio of 5:1 which is comparable to the studies done by Johansson SL et al in where it ranges from 3:1 to 4:1.3. The incidence was less in females because of less exposure to industrial carcinogens and a few women who smoke when compared to men.

In the present study, 19 cases of urothelial carcinoma of varying grades and 07 cases of High grade papillary urothelial neoplasm (HGPUN) showing squamous differentiation were seen out of a total 38 cases. Squamous differentiation within an urothelial carcinoma occurs in approximately 21% of urothelial carcinomas of the bladder and in 44% of tumors of the renal pelvis. The frequency increases with tumor grade and stage.<sup>4,5</sup> Patients with urothelial carcinomas containing abundant squamous differentiation may have a worse prognosis, possibly because they are typically associated with a higher grade urothelial carcinoma. Also, some studies have shown that tumors with squamous differentiation may be more resistant to systemic chemotherapy and radiation treatment.<sup>5-7</sup>

In most of the studies, less than 10% of low grade carcinomas invade, but as many as 80% of high grade urothelial carcinomas

are invasive.<sup>8</sup> In the present study, out of 06 low grade Urothelial carcinomas only 3 cases (50%) showed lamina propria invasion and out of 16 high grade Urothelial carcinomas 10 (62.5%) showed lamina propria invasion and muscular invasion.

Urothelial carcinomas are known to exhibit a variant or divergent differentiation like squamous, glandular, micropapillary, sarcomatoid, nested, microcystic, small cell, clear cell, lymphoepithelial, rhabdoid, lipid rich, plasmacytoid and undifferentiated types. Mentioning about a note on differentiation in histopathology report is useful as it has both prognostic and therapeutic implications.

Squamous cell carcinoma (SCC) of the bladder arises frequently in the setting of chronic irritation, whether the source of the irritation is smoking, schistosomiasis, or other causes of repetitive trauma.<sup>9</sup> These conditions, however, do not appear to be important in the pathogenesis of urothelial carcinoma with squamous differentiation.<sup>12</sup> The prevalence of SCC varies in different parts of the world, accounts for 3-7% in the United States but as much as 75% in Egypt where schistosomiasis is endemic.<sup>11</sup> In the present study, SCC constituted 15.3% which was on higher side when compared to western countries and it could be due to smoking because all the cases of SCC were seen in males in the present study.

In this study we found that the Urothelial carcinomas with squamous differentiation were present in more aggressive carcinomas with moderate or poor differentiation and with deeper invasion.

## CONCLUSION

In the present study chronic non-specific cystitis constitutes the bulk of the non-neoplastic lesions and maximum number of neoplastic lesions were Urothelial origin. Urothelial carcinoma displays many forms, and some of these variant morphologies may pose diagnostic difficulties because of their similarity to other malignancies and / or benign lesions. Additionally, it is important to recognize the variants that are associated with different outcomes from conventional urothelial carcinoma. For these reasons, familiarity with the diverse morphology of urothelial carcinoma is not simply an academic exercise but is important in providing quality care for patients as they have prognostic significance.

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