

NEOPLASTIC AND NON-NEOPLASTIC LESIONS OF URINARY BLADDER SEVEN YEARS STUDY

HAYAT S. AHMED, BSC, MSC*
BASHAR A. AL-HASSAWI, MBCHB, FRCPath**
ABDULGHAFOOR SULAIMAN ABDULKAREEM, MBCHB, FICMS***

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ABSTRACT

Background and Objectives: Urinary bladder like any organ in the body that involved by many non-neoplastic and neoplastic lesions. These lesions are more disabling than being fatal. Bladder tumor is the seventh most common tumor worldwide. Although progress has been made in the field of non-invasive imaging, histopathological study of bladder biopsy is still the gold standard for tumor diagnosis, grading, staging and management. This study is conducted to clarify the pathological changes of various lesions in the urinary bladder biopsies that obtained by cystoscopy, and to categorize the bladder tumor according to WHO classification.

Subject and Method: All the subjects involved in this study were obtained from central laboratory and private laboratories in Duhok province, Kurdistan Region-Iraq, during a period extended from January 2009 to December 2015.

Results: Histologically 376 cystoscopic biopsies were studied. The males were 236 (76.1%) and females were 90 (23.9%); the male to female ratio was 3.1:1. Non neoplastic lesions accounted for 97 cases (25.8%), Neoplastic lesions accounted for 279 cases (74.2%). Of the total cases 9.4% of patients were presented by hematuria. Among the non-neoplastic lesions there were 87 (89.7%) inflammatory lesions, and the urothelial transitional cell carcinomas were the most common histopathological ones among the neoplastic lesions 278 (99.6%). Adenocarcinoma were found in three cases, squamous cell carcinoma in two, one with sarcomatoid carcinoma and metastatic lesion in one.

Conclusions: This study concludes that the most histopathological bladder lesions are neoplastic ones. The non-invasive low grade transitional cell carcinoma is the commonest type among bladder tumors and more frequently seen in males above age of 60, where's inflammatory lesions are more frequent non neoplastic diseases. Hematuria is the main presenting symptom of the patients with bladder lesions.

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Keywords: Urinary bladder, Urothelium, Carinoma, Hematuria..

The urinary bladder is a sac shaped hollow organ that sits on the pelvic floor posterior to the symphysis and anterior to the vagina in females or rectum in males. The wall of urinary bladder consists of main four layers which are mucosa, submucosa, muscular is and serosa. It's lined by transitional cells

epithelium called urothelium¹. Urine formed in kidney is transported to the bladder through the ureters, for storage until eliminating through the urethra. As the final urinary reservoir, the distensible bladder consist of a wall of smooth muscle, its normal capacity is about 250 CC of urine under normal conditions, and

*Assistant Professor, Department of Anatomy, College of medicine. University of Duhok, Iraq.

**Assistant Lecturer, Department of Anatomy, College of Medicine. University of Duhok, Iraq

***Assistant Professor, Department of surgery, College of Medicine. University of Duhok, Iraq

able to hold up 450 CC in extreme cases. The urinary bladder is the most common site of malignancy among urinary system organs and arises mainly from urothelium². Urinary bladder lesions whether neoplastic or non-neoplastic are common. These pathologies are more disabling than being lethal. The most common pathology affects the urinary bladder is bacterial inflammation either primary or secondary to lower urinary tract dysfunction³. Bladder tumor is the seventh most common tumor worldwide. Although progress has been made in the field of non-invasive imaging, histopathological analysis of submitted material is the mainstay for cancer diagnosis and treatment⁴.

This study conducted to clarify the pathological changes of various lesions in the urinary bladder biopsies, and to categorize the tumor grading according to WHO classification.

PATIENTS AND METHODS

All the subjects involved in this study were obtained from central laboratory and private laboratories in Duhok province, Kurdistan region -Iraq, during a period extended from January 2009 to December 2015. The paraffin embedded blocks (PEBs) of the patients containing the tissues were selected. Sections from the PEBs where obtained in a 4 microns thickness and to perform the Hematoxyline and Eosinstains. Categorize the neoplastic lesions according to WHO/ISUP 2004 classification⁵.

STATISTICAL ANALYSIS

Data were analyzed by using the statistical package for social science (SPSS) version

21.One way analysis of variance (one way ANOVA).

RESULTS

During a period of study from January 2009 – December 2015, 376 patients were included in the study with median age of 57 years (range 8 months- 90 years). There were 236 male (76.1%) and 90 female (23.9%); male to female ratio 3.1:1 (Table 1). There was no significant difference between age and incidence of neoplastic or non-neoplastic lesions in males, while in females the differences were significant. The non-neoplastic lesions were frequently seen in age group below 40 years, while the neoplastic lesions were more common above the age of 60 (Table 2).

Table 1: The Distribution of Bladder Lesions According to Gender of the Patients

Sex	Non neoplastic lesions		Neoplastic		Total	
	No.	(%)	No.	(%)	No.	(%)
	Male	50	51.5	236	84.6	286
Female	47	48.5	43	15.4	90	23.9
Total	97	100	279	100	376	100

Table 2: Mean age Distributions of Patients According to the Gender and Pathology

Sex	Non Neoplastic Lesions Mean Age	Neoplastic Mean age	P-value
Male	55.42	61.52	0.1 Not significant
Female	37.30	60.72	0.04 Significant
Total	47.08	61.45	

Clinical presentation

Table 3 shows the different clinical presentation of patient with bladder lesions and indications for endoscopy and biopsy, of both non neoplastic and neoplastic lesions. The hematuria was the commonest symptom and difficulty of micturition was

least symptom in both neoplastic and neoplastic diseases.

Table 3: Clinical Symptoms of Patients Presented to the Cystoscopy Biopsy

Symptoms	Non neoplastic lesions		Neoplastic		Total	
	No.	(%)	No.	(%)	No.	(%)
Hematuria	44	45.4	104	37.3	148	39.4
Urinary tract symptoms	20	20.6	34	12.2	54	14.4
Dysuria	12	12.4	40	14.3	52	13.8
Urinary retention	8	8.2	33	11.8	41	10.9
Lower abdominal pain	7	7.2	37	13.3	44	11.7
Difficulty of micturation	6	6.2	31	11.1	37	9.8
Total	97	100	279	100	376	100

Histopathological findings

Table 4, reveals the frequency of different pathological findings from patients subjected for bladder biopsy. Among non neoplastic the inflammatory lesions (Figure 1) were 87 cases (89.7%) and it was statistically significant. The neoplastic

lesions were 278 (99.6%), and benign tumors were very rare (0.4%). Regarding the whole cases the neoplastic lesions were the common findings (74.2%) in comparison to non-neoplastic ones (25.8%).

Table 4: Frequency of Neoplastic and Non-Neoplastic Lesions of Urinary Bladder Biopsies

Pathology	Histopathological findings			P-value
	Type of lesion	No.	(%)	
Non neoplastic lesions	Inflammatory	87	89.7	0.001 (Significant) *
	Polyps	2	2.1	
	Metaplasia	8	8.2	
Total		97	100	
		97/376	25.8	
Neoplastic lesions	Benign	1	0.4	0.001 (significant)**
	Malignant	278	99.6	
Total		279	100	0.001 (significant)***
		279/376	74.2	

*The inflammatory lesions are significantly more common than other non-neoplastic lesions.

**The malignant tumors are significantly more common than other benign tumors.

***The neoplastic lesions are significantly more common than other non-neoplastic lesions

Distribution of patients with bladder carcinoma according to their types

Table 5, shows that TCC was the commonest malignant bladder tumor, and affecting males more than females; 62.5% and 37.5% respectively. Histopathologically 268 patients (96.4%) had transitional cell carcinoma (TCC). The TCC found in males more than females,

However only five patients found to have adenocarcinoma and two patients had SCC. One case had primary sarcoma and other one case diagnosed as secondary, all were males (Figure 7). These two cases were proved by using immunohistochemistry, the markers were used are cytokeratin, vimentin, CK 20 and CK7.

NEOPLASTIC AND NON-NEOPLASTIC LESIONS OF URINARY BLADDER

Table 5: The Histopathological Findings of Bladder Cancer.

Histopathology	Sex				P value	
	Male	%	Female	%		
SCC	2	0.9	0	0		
TCC	228	97	40	93		
Type	Adenocarcinoma	3	1.3	2	4.6	0.001 Significant*
	Sarcoma	1	0.4	0	0	
	Metastatic Carcinoma	1	0.4	1	2.4	
	Total	235	100	43	100	

* Statistically the neoplastic lesions are more common than females, especially the TCC.

Distribution of transitional cell carcinoma according to the tumor grade and other parameters

Histopathological grading results of the patient's tumors found to be low grade in 183 patients (68.2%) (Figure 2, 3) while 85 patients had high grade (31.8%) as

shown in Table 6 (Figure 4). This difference was statistically significant. Other parameters that include muscle invasion (Figure 6) vascular invasion and necrosis (Figure 5), the negative cases were more frequent and statistically significant.

Table 6: Frequency of Different Parameters in TCC.

Histopathology	TCC	Sex		Total		P-Value
		Male	Female	No.	%	
Grade	Low	151	32	183	68.3	0.08
	High	77	8	85	31.7	significant
Muscle invasion	+VE	50	5	55	20.5	0.08
	-VE	178	35	213	79.5	significant
Vascular invasion	+VE	18	0	18	6.7	0.05
	-VE	210	40	250	93.3	significant
Necrosis	+VE	24	1	25	9.3	0.08
	-VE	204	39	243	90.7	significant

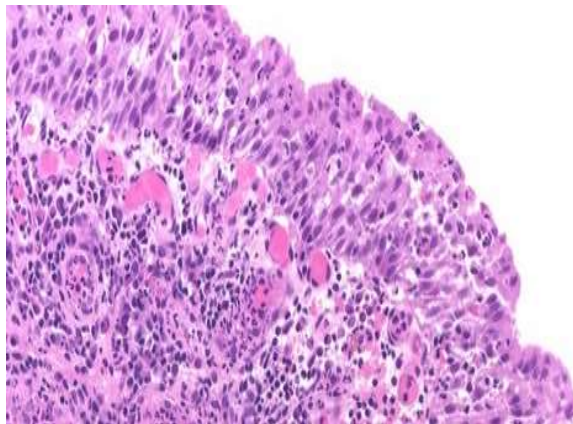


Figure 1: Cystitis with Mild Dysplasia

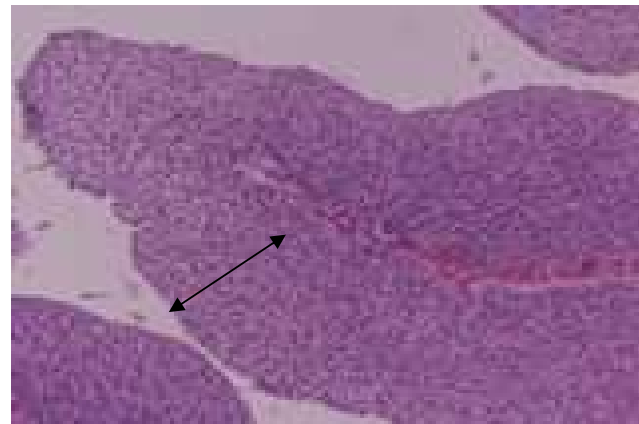


Figure 2: Low Grade TCC with Papillary Configuration with Mild Cellular atypia, but it Showing Loss of Polarity and Multilayering (arrow) (H&E x100).



Figure 3: Low grade TCC Showing Fibrovascular Core Line by Neoplastic Transitional Cells with Mild A Typia (arrow). (H&E x 400).

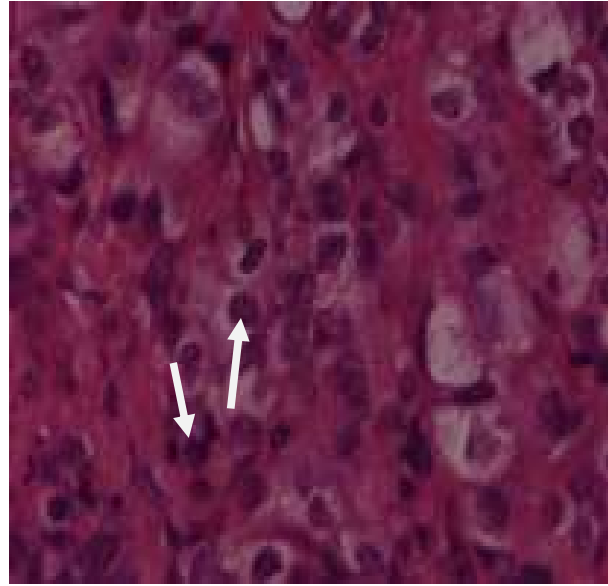


Figure 4: High Grade TCC Showing Marked A Typia, note the Hyperchromasia, Pleomorphism (arrows). (H&E x 400)

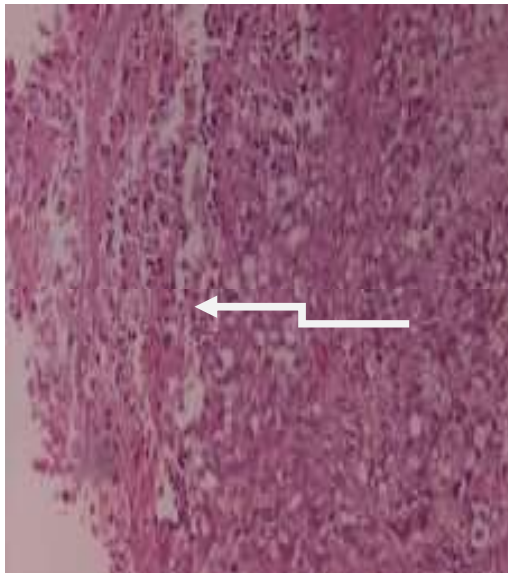


Figure 5: High grade TCC; absence of Papillary Projection with Area of Necrosis (arrow). (H&E x 400)

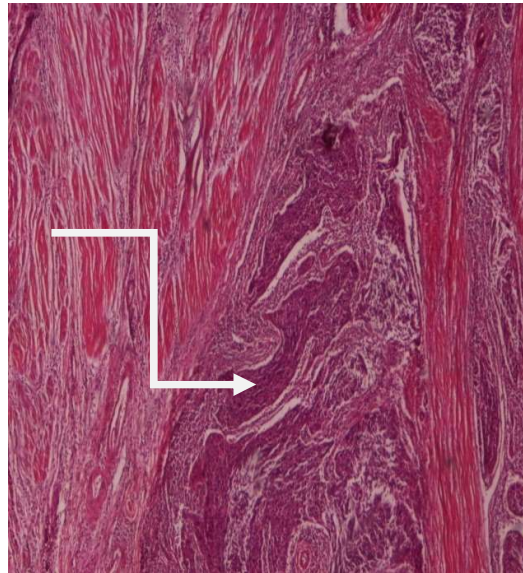


Figure 6: SCC: Nests of Neoplastic Cells Invading Deep Stroma with Necrosis (H&E:x100)



Figure7: Squamous Cell Carcinoma Showing Neoplastic Cells with Marked Keratinized Cells (H&E;x40).

DISCUSSION

Bladder biopsies is an important tool in the diagnosis of urinary bladder lesions whether neoplastic or non-neoplastic lesions. The histopathological study of the bladder biopsies gives the definite diagnosis and hence proper management. In the present study (76.1%) were males and (23.9%) were females; therefore the male to female ratio was 3.1:1. Similar finding was seen in several studies of cystoscopic biopsies. Boudreaux K et al 2009⁶, showed (1.38:1) Cheng L et al 1999⁷, showed (4:1), 19, Gupta P et al 2009⁸, showed (8.6:1) and Matalka I et al 2008⁹, showed (10:1). The reason for higher incidence in males could be attributed to different carcinogenic factors like smoking, environmental factors, dietary exposure, anatomical difference, Genetic differences and hormonal factors. Inflammatory lesion; mainly chronic nonspecific cystitis (89.7%) was the most common lesion among the non-neoplastic lesion and (23.6%) among the whole cystoscopic biopsies. Shruthi et al 2015¹⁰, showed (35%) of cystitis and another study done by Rauniyar et al 2001¹¹ showed (44%) of cystitis.

Bladder carcinoma is more common in elderly males. The sex incidence of bladder tumor in our study was 84.6% male and 15.4% in female. Patients were above 60 years (mean age; 61.4 years). This is compatible to other studies (Table7).

Table 7: Comparison of Mean Age, Number of Cases with Other Studies

Authors	Study Period	Total cases studied	Mean age (years)
Zhang <i>et al</i> ⁽¹²⁾	2006-2010	658	61.9
Gupta <i>et al</i> ⁽⁸⁾	2001-2008	561	60.2
Biswas <i>et al</i> ⁽¹³⁾	2007-2009	88	65 .0
Pudasaini <i>et al</i> ⁽¹⁴⁾	2012-2013	18	60.6
Matalka <i>et al</i> ⁽⁹⁾	1994-2000	115	60.6
Alberto <i>et al</i> ⁽¹⁵⁾	1993-2005	153	65.9
Present study	2009-2015	278	61.4

The rising incidence with age may be explained by the accumulation of somatic mutations associated with the emergence of malignant neoplasms. In addition, the observed impairment in the immune system in such ages, due to senescent decline in the immune surveillance, might lead to accumulation of cellular DNA mutation that could be regarded as an additional significant factor in the development of such malignancies¹⁶.

In the current study the grade of tumor revealed; 68.3% of cases are of low grade, while high grade was 31.7%, where the high grade usually associated with muscle invasion vascular invasion and necrosis. These in agree with other study done by Dhafer A et al 2011¹⁷, who reported low and high grade 62%, 38% respectively. Other comparable results to this study showed 76% low grade and 24% high grade¹⁸. However disagreement result with other study in neighboring country like Iran, they reported most of their patients had high grade malignancy 89.7%¹⁹. Other study revealed 29.7% of low grade and majority were high grade²⁰. Most of the bladder tumor types were primary carcinoma and only one case was secondary and one other case was sarcoma, both cases were proved by using tumor markers.

Hematuria is the most common presentation of patients with bladder diseases. In this study, 39.4% patients were presented with hematuria. Other studies revealed more than 60% of patients of urinary bladder tumor had hematuria^{14, 21}.

This study concludes that most biopsies conduct histopathology lab are neoplastic lesions. The noninvasive low grade

transitional cell carcinoma is the commonest type among bladder tumors and more frequent in males, above age of 60 years. Whereas inflammatory lesions are more frequent among non-neoplastic diseases. Hematuria is the main presenting complaints of the patients with bladder lesions.

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پوخته

گرێکین پیس و بیین نه پیس بیین میزلدانکی، فه کولینه کا 7 سالی

نیشتهکی و نارمانج میزلدانک ئەندامهکی گرنج یی سیستمی زهراقی یه کو تووشی گهلهک گرێکین پیس و بیین نه پیس دبیت. ئەهه گرێکه گهلهک د ئالۆزن لی کیم جارن دکوزهکن. گرێکا میزلدانکی دهیه ههژمارتن ههفتهم بهربهلافتین گرێک ل سهرانسهری جیهانی. سههرای پێشکهفتن پزیشکی د بوارێ پشکنین وینهگرتنی بی کو لهش بهیته برین و فه کرن، لی هیشتا خواندنن هیستوپاتولوژی بو بایوبسیین میزلدانکی دهینه ههژمارتن پیهههین زهرین بو پشکنین و دهستنشانکرن و په دانان و قوناغکرن و چره سهرکرنان فان جوهره گرێکان.

ریکین ظه کولینی: ئەهه فه کولینه هاتیه ئەنجامدان ژ پێخه مهت خواندنا گوهرینین پاتولوژی بیین بایوبسیین گرێکین جودا جودا بیین میزلدانکی ئەههین ب ریکا ئامیرئ سایتوسکوپ هاتینه وهگرتن، ههردیسان ژ بو فافارتنا گرێکین میزلدانکی ل دوپف فافارتنا ریکخراوا ساخله میا جیهانی.

ئههجام: 376 بایوبسیین بیین هیستوپاتولوژی هاتنه خواندن. ههژمارا رهگهزی نیر 236 (76.1) کهس بوون و رهگهزی می 90 (%23.9) بوون. ریزا ههقه بهرکرن رهگهزی نیر بو می 3.1:1 بوو. گرێکین نه پیس ل دهه 97 (%25.8) حالهتان هاتنه دبیتن و گرێکین پیس ل دهه 279 (%74.2) حالهتان هاتنه دبیتن. ههردیسان (%39.4) ژ سهرجه می گشتی یی حالهتان، حالهتی میزخوینی (ههبوونا خوینی دنا میزی) ههبوون. ل دهه حالهتان گرێکین نه پیس، 87 (%89.7) تووشی ههوانان ببوون. ل دهه حالهتین گرێکین پیس، 278 (%99.6) په نهجه شیرا ته خا نافخوینی میزلدانکی ههبوو په نهجه شیرا گرێکین لیمفاوی دنا شانیهین نخافتنی بیین میزلدانکی ل دهه سی حالهتان هاتنه دبیتن، دوو حالهت ژ جوړئ سارکینوما خانیهین پیهلهکی بوون کو ئیک ژوان سارکینوما سارکوماتیدی و حالهتهکی ژی گرێکا میتاستاتیکی بوو.

دهرئههجام: ئەهه نجامین فی فه کولینی دیاکرن کو پتریا بایوبسیین ب ریکا هیستوپاتولوژی دهینه خاندن ل تاهیههه ژ جوړئ گرێکین پیسن سارکینوما خانیهین شانیهین نخافتنی بیین په لیا نزم ژ بهرلافتین گرێکین میزلدانکی بوو پتر ل دهه رهگهزی نیر بیین ژیی وان د سهه 60 سالی دا ههبوو. لی لی گرێکین ژ جوړئ ههوانی پتر ل دهه گرێکین نه پیس ههبوون. میزا ب خوین ئاریشا ههره سهههکی بوو ل دهه کهسین تووشی گرێکین میزلدانکی بووین.

الخلاصة

الأمراض الورمية وغير الورمية للمثانة دراسة سبعة سنوات

الخلفية والهدف:

المثانة مثل أي عضو في الجسم ممكن أن يتعرض الى امراض ورمية أو غير ورمية. هذه الأمراض هي معوقة للمريض وليست مميتة على الغالب، أورام المثانة تصنف على أنها سبع ورم من ناحية الشيوخ بين أورام الجسم. بالرغم من تقدم الطرق التشخيصية غير المؤذية، تبقى الخزعة النسيجية هي الطريقة القياسية في تشخيص الورم وقياس مقدار انتشاره ودرجة ونوع الورم وبالتالي طرق العلاج. إجريت هذه الدراسة من أجل معرفة تردد أمراض المثانة، وكذلك نوع الاورام التي تصيب المثانة بحسب تصنيف منظم الصحة العالمية، ومقارنتها مع الدراسات الاخرى.

المواد والطرق:

هذه الدراسة تضمنت 376 خزعة نسيجية اخذت من مختبر الصحة المركزي وبعض المختبرات الاهلية في مدينة دهوك خلال فترة تمتد من يناير 2009 إلى ديسمبر 2015. وجرت دراسة الشرائح مصبغة باستعمال الهيماتوكسيلين والأوسين.

النتائج:

من بين 376 حالة كان عدد الذكور 236 حالة (76.1 في المائة) والإناث 90 حالة (23.9 بالمائة). بنسبة الذكور للإناث 3.1:1. الامراض غير الورمية كانت 97 حالة (25.8 بالمائة) في كانت الورمية 279 حالة (74.2 بالمائة). وكانت النسبة الأعلى 39.4 بالمائة ممن كان سبب أخذ الخزعة هو التبول الدموي. من بين الحالات غير الورمية كانت نسبة الحالات اللألتهايبية 87 حالة (89.7 بالمائة)، في حين كان سرطان المثانة (TCC) 278 حالة (96.4 بالمائة)، ثلاث حالات من نوع السرطان الغددي وحالتين من سرطان الخلايا الحرشفية.

الاستنتاجات:

هذه الدراسة أثبتت أن الحالات الورمية للمثانة هي الاكثر شيوعا في الخزعة المأخوذة من بطانة المثانة. وأن نوع (TCC) هو الأكثر ويصيب الذكور فوق 60 سنة بشكل أكبر. الحالات الإلتهايبية هي الأكثر شيوعا بين الحالات غير الورمية. التبول الدموي هو السبب الرئيسي لأخذ الخزعة النسيجية