

Original research article

Diagnostic Value of Combined Cystoscopy and Urine Cytology in Urothelial Neoplasia

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Abstract

Objectives: Urine cytology is an essential modality for the detection of urothelial neoplasia. It has various indications that generally fall in two principal groups: in the evaluation of patients with genitourinary symptoms, especially hematuria, and as a surveillance tool for patients with a history of bladder cancer. We undertook this study to evaluate the role of cytology in detection of urothelial carcinoma and to estimate the reliability of combined cystoscopy and urine cytology examination in cases of urinary bladder neoplasm

Materials and methods This prospective, analytical study was conducted at a tertiary care superspeciality teaching hospital in Patna . Sixty patients with hematuria from urology outpatient department and indoor patient were included in the study.

Results: Of the 60 patients presenting with haematuria, cystoscopy findings were available for 48 cases. In 12 cases cystoscopy reports could not be obtained. In our study the commonest age group of patients presenting with haematuria was 60-69 years and more in males. All the cases with abnormal cytology had abnormal cystoscopic findings except one case, where although cystoscopy was normal, urine cytology was reported as category4 .There was low concordance between cystoscopy and cytology

Conclusions: Urine cytology is still a useful test in detecting bladder cancers, despite its limitations of having low sensitivity. When used appropriately, cytology complements cystoscopy as they target different types of lesions.

Keywords: Cytology, Carcinoma, Urothelial

Introduction

Urine cytology is an essential modality for the detection of urothelial neoplasia. It has various indications that generally fall in two principal groups: in the evaluation of patients with genitourinary symptoms, especially hematuria, and as a surveillance tool for patients with a history of bladder cancer. Carcinoma of the urinary bladder, the fourth most common cancer in men and ninth most common cancer in women, results in significant morbidity and

mortality¹. It has excellent specificity with few false-positive cases. The chronic nature of bladder cancer necessitates long-term surveillance in patients after initial diagnosis.

Early diagnosis of the bladder cancer is very difficult because there is no distinct associated symptom.² Hematuria is one of the most common presenting symptom; however, 90% of individuals with hematuria do not have bladder cancer.³ Cystoscopy has been proven quite successful in surveillance and follow-ups of patients with previously diagnosed bladder cancer. In conjunction with cystoscopy, urine cytopathology helps identify precancerous and cancerous cells in the urine. Urinary cytology has relatively high specificity, especially in detecting carcinoma in situ and high-grade, flat lesions that can be difficult to detect on cystoscopy.^{4,5}

Aims and Objectives

To evaluate the role of cytology in detection of urothelial carcinoma in patients presenting with haematuria and as a surveillance tool for patients with a history of bladder cancer To estimate the reliability of combined cystoscopy and urine cytology examination in cases of urinary bladder neoplasm

Methodology:

Type of study and study design : It is a prospective , analytical study.

Study population: This study was conducted at a tertiary care superspeciality teaching hospital in Patna over a period of two months

Sample size: 60 cases were included

Inclusion criteria: Patients with hematuria, any age, and any gender from urology outpatient department and indoor patient were included in the study.

Exclusion criteria: Abdominal mass, history of prostatism, urinary tract infection, anorexia, weight loss, or proteinuria were excluded in the study.

Specimen collection and Handling

The types of cytologic specimens were as follows: voided urine and catheterized urine.

Urine Cytology-Procedural Overview

Voided urine cytology is the standard noninvasive method for diagnosis in the detection of bladder carcinoma. Cytology is used to assess morphologic changes in intact cells. Exfoliated urothelial cells are viewed using microscopy. At least 100 mL of a freshly voided specimen is usually sufficient for urine cytology.

The first morning sample were not used, because cells sitting in the urine overnight tend to become distorted and are difficult to analyze. If the urine is very dilute, the number of cells may be insufficient, necessitating a larger urine volume.

Catheterized specimens were labeled as such, as cellular findings may be altered by instrumentation. Laboratory specimen preparation methods include cytocentrifugation where aliquots of urine was centrifuged to concentrate the cells, as urine normally contains few cells. The slides were stained by the Papanicolaou method and examined under a light microscope. By this method, the cytoplasm of transitional cells stained greenish-blue and the nuclei are

purple. If malignancy was reported, the degree of cellular atypia and other cytologic features were noted.

Cytology specimens were interpreted without access to any clinical information.

Urine cytology Reports were scored as following

: 0 = inadequate or no specimen

1 = benign

2 = atypical probably benign

3 = atypia of uncertain significance

4 = atypia suspicious of malignancy

5 = malignant.

We considered the urothelial cells in voided specimens as atypical when they exhibited a nuclear/ cytoplasmic (N/C) ratio exceeding 50%.⁷ The atypical, reactive category was reserved for the atypical cases, in which the cells were in cell clusters and had bubbly cytoplasm with intact and smooth nuclear membranes, with a conspicuous nucleolus. On the other hand, the atypical, unclear category was used when the urothelial cells, even if single or few, appear to be degenerated but display a high N/C ratio, intact and irregular nuclear membranes with clumpy chromatin and/or a dark India ink chromatin pattern

Cystoscopy

Cystoscopy, a relatively short, minimally traumatic office procedure performed with local urethral anesthesia, Cystoscopy is the primary modality for the diagnosis of bladder carcinoma because of its low risk . Men were evaluated with a flexible cystoscope. In women, cystoscopy was performed using a flexible cystoscope or a rigid cystoscope because the female urethra is relatively straight.

Ethical considerations: Institutional Ethics Committee (IEC) approval was obtained by the Institute ethical committee (Ref No. 815/ Acad /dated 25.07. 2017)

Observations and Results:

Of the 60 patients presenting with haematuria, cystoscopy findings were available for 48 cases. In 12 cases cystoscopy reports could not be obtained. In our study the commonest age group of patients presenting with haematuria was 60-69 years and more in males. (**Table 1**). Of the 60 patients, 18 were known cases of bladder cancer on follow up, of which in 8 cases no cystoscopy reports were available, remaining 10 cases had abnormal cystoscopy , and 5 cases showed positive findings on urine cytology(2 cases- category 3; and 3 cases – category 5)

All the cases with abnormal cytology had abnormal cystoscopic findings except one case, where although cystoscopy was normal, urine cytology was reported as category4.

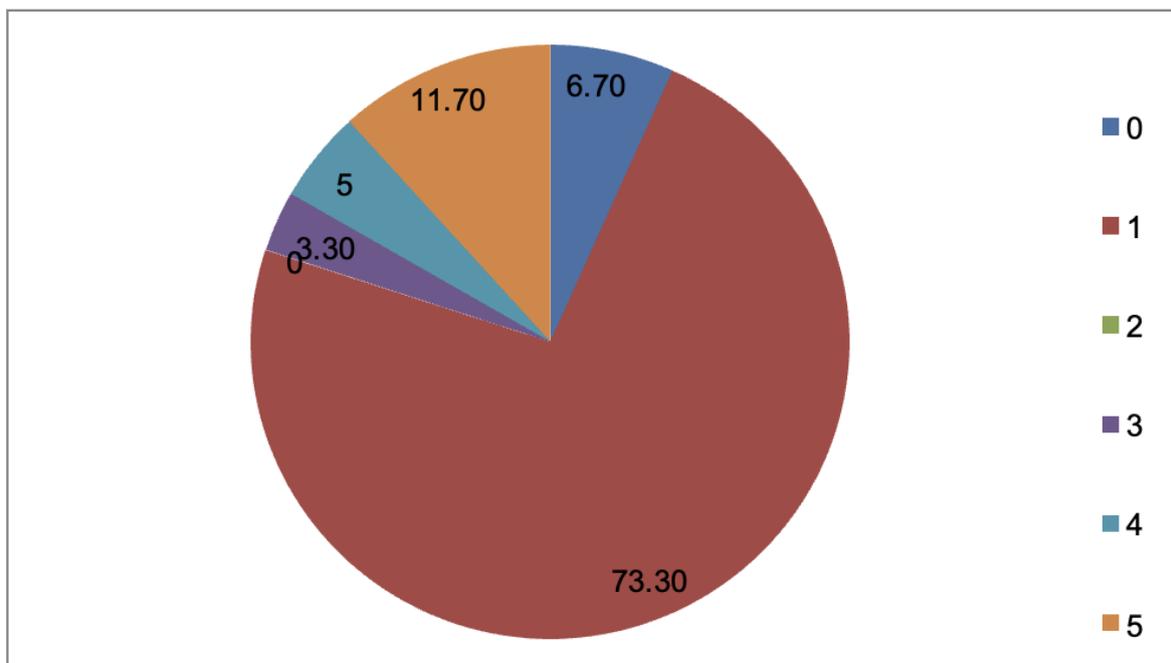
Scoring was done for urine cytology reports, cases were categorized into category 0 to 5. In our study, 4 (6.7%) patients were in category 0 (Inadequate or no specimen) as the smears showed few degenerated cells only without adequate urothelial cells. 44 (73.3%) patients were in category 1 (benign). Non e of the cases were in category 2(atypical probably benign) , 2 (3.3%) patients were in category 3 (atypia of uncertain significance), 3 (5%)patients were in category 4 (atypia suspicious of malignancy) and 7 (11.7%) patient was in category 5 (malignant). (**Table-2, Fig 2**). (**Fig3**) There was low concordance between cystoscopy and cytology (**Tables 3 & 4**).

Table1: Age and sex distribution of patients with haematuria.

Age (yrs)	M	F
15-29	2	1
30-39	1	1
40-49	3	3
50-59	13	3
60-69	16	4
70-79	8	3
80-90	2	-

Table 2: Urine cytology reports- Scoring (n=60)

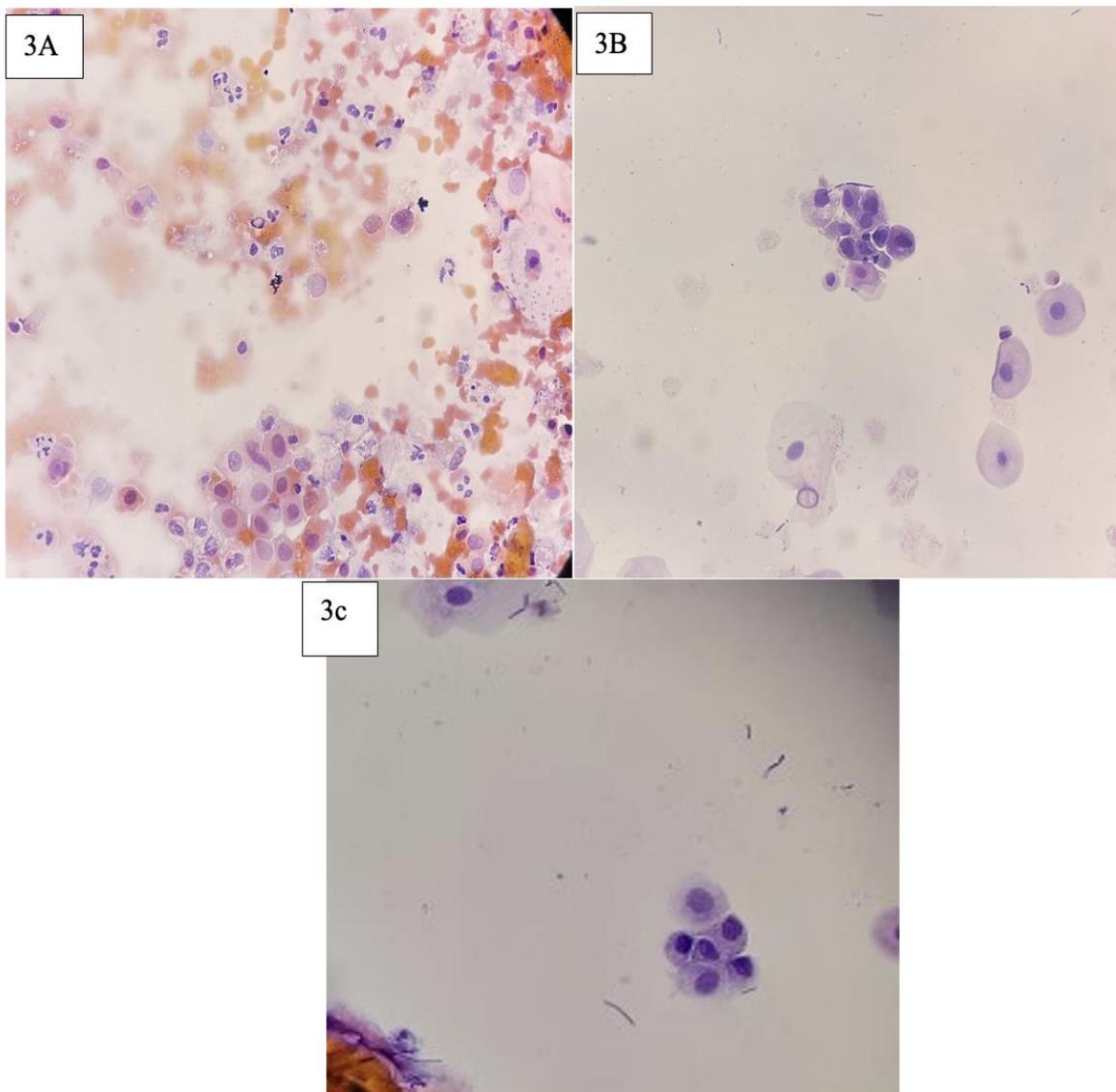
Diagnostic Category	Number of cases	% of cases
0 = inadequate or no specimen	4	6.7%
1 = benign	44	73.3 %
2 = atypical probably benign	0	0
3 = atypia of uncertain significance	2	3.3%
4 = atypia suspicious of malignancy	3	5%
5 = malignant	7	11.7%



Graph 1:

Table 3: Summary of Cystoscopy and cytology findings (n= 48 cases)

	Abnormal cystoscopy	Normal cytology
Number of cases	27	27
	Normal cystoscopy	Normal cytology
Number of cases	8	8
	Abnormal cystoscopy	Abnormal cytology
Number of cases	12	12
	Normal cystoscopy	Abnormal cytology
Number of cases	1	1



Legends

3A &B = Atypia suspicious of malignancy Photomicrograph showing urothelial cells with moderate nuclear enlargement and nuclear irregularity (Smear, Pap 400x magnification)

3C = Malignant Photomicrograph showing urothelial cells with moderate to marked nuclear enlargement and nuclear irregularity (Smear, Pap 400x magnification)

Table 4: Agreement between Cystoscopy findings and urine cytology (n=48 cases)

		Cytology		Total
		Abnormal	Normal	
Cystoscopy	Abnormal	12	27	39
	Normal	1	8	9
Total		13	35	48

Percentage agreement = 41.67%.

Kappa coefficient is 0.09 which indicates there is poor agreement between the cytology and cystoscopy.

Discussion:

Most patients with bladder cancer present with gross or microscopic haematuria. Cystoscopy aided by cytology is the mainstay for the diagnosis of bladder cancer. According to a study done by S. Pedamullu et al.,⁶ positive cytology was found in 87 out of 169 cases (51%), suspicious cytology in 17 cases (10%), atypical in 2 cases (1.1%) and negative cytology in 57 out of 169 patients (34%). In our study, positive cytology was found in 7 out of 60 cases (11.7%), which is much lower than that reported by them. This could be attributed to the possibility of low grade urothelial tumors for which cytology has low sensitivity. Ideally, three sequential voided urine samples should have been processed but we processed and examined only one urine sample.

Urine cytology is a useful screening investigation in the management of urothelial carcinoma. However, a negative result does not rule out malignancy. This test lacks sensitivity for low grade superficial tumors⁸.

This group of tumors comprise the majority of transitional cell carcinomas. In our study the commonest age group of patients presenting with haematuria was 60-69 years and more in males. According to Brimo et al.,⁹ overall, the atypical category constituted 23.2% of all urine cytologic cases. Of those cases, 59.3% (410/691) and 40.7% (281/691) belonged to the atypical, reactive and the atypical, unclear categories, respectively and in (5.5% of cases) a malignant diagnosis was made. In a study done by Naveen Setal,¹

Combined cystoscopy and urine cytology had a specificity of 92.3% and a sensitivity of 100% with a necessity of cystoscopic biopsy if cytology or cystoscopy or both reported positive findings for the detection of bladder recurrence. In our study poor agreement was seen between cytology and cystoscopy, percentage agreement was 41.67%.

Conclusions:

Urine cytology is still a useful test in detecting bladder cancers, despite its limitations of having low sensitivity. This study helps us to understand the usefulness of combined cystoscopy and cytology in the diagnosis of bladder tumor. When used appropriately, cytology complements cystoscopy as they target different types of lesions. Both should be performed when suspecting urothelial neoplasia.

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