



DIAGNOSTIC UTILITY OF URINE CYTOLOGY IN URINARY BLADDER LESIONS WITH HISTOPATHOLOGICAL CORRELATION

KEYWORDS

Urine cytology, Urothelial carcinoma, Cytohistological correlation

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ABSTRACT **Background:** Urine cytology is primarily used for diagnosis of symptomatic patients, detection of cancer in high-risk patients and follow-up of patients with history of urinary tract neoplasia.

Aims & Objective: To find out the efficacy of urine cytology smear in detecting malignant lesions of the bladder in patients coming with bladder symptoms.

Materials and Methods: Voided urine samples were obtained from 160 symptomatic patients, urine cytology smears were made and analyzed. Out of 160 cases, bladder biopsy specimens were obtained for 84 cases and cytohistological correlative study was done.

Results: Cytohistological correlation revealed the overall sensitivity as 74.1%, specificity as 96.7%, accuracy as 82.1%, positive predictive value as 97.6%, negative predictive value as 67.4%.

Conclusion: Cytological examination of urine is more sensitive in detecting high grade urothelial carcinoma.

INTRODUCTION

Cytologic examination of a urine specimen is a simple, safe and inexpensive method that may uncover a hidden urothelial cancer. Since the entire mucosal surface including the farthest reaches of the urinary tract, is bathed in this easily obtainable fluid, in theory, urine is the perfect specimen to examine for evidence of tumor. Urinary cytology has its place as an additive diagnostic tool to cystoscopy.¹

Urinary cytology can detect most aggressive neoplasms as well as carcinoma in situ. Patients with negative cytologic findings have a very low risk of recurrence, while high-grade cytologic abnormalities predict an aggressive tumor course (Harving 1989). The accuracy of urine cytology depends on several factors that are mainly related to tumor grade, the nature of specimen, and sampling. It has long been known that urine cytology is accurate in the diagnosis of high-grade urothelial carcinoma (HGUC) with cytohistologic correlation reported as high as 98%.² In contrast, it carries a much lower diagnostic yield for low-grade urothelial neoplastic lesions that include papillary neoplasm of low malignant potential (PUNLMP) and low-grade papillary urothelial carcinoma (LGUC), with sensitivity and specificity values as low as 8.5% and 50% respectively.³

A variety of newer diagnostic techniques, including flow cytometry, image analysis/quantitative cytology, cytogenetics, immunology (e.g., blood group isoantigens and monoclonal antibodies to a variety of tumor-associated antigens) and molecular biology have been studied in an effort to increase diagnostic accuracy. However, at least for the moment, urinary cytopathologic examination remains one of the most clinically useful means of diagnosing urothelial cancer and predicting its biologic behavior and hence this study was carried out.

MATERIAL AND METHODS

A cross-sectional study was carried out in the department of pathology, tertiary care hospital, Tamilnadu India for a period of 2 years. 160 patients who came with bladder symptoms to the urology department in the 11 to 90 age group was included in the study. Three random voided urine samples were collected from each patient on 3 consecutive days and fixed in equal volume of 50% alcohol. The urine cytology smears were made after centrifugation, Papanicolaou

staining and Modified Hematoxylin and Eosin staining were done. The smears were analyzed and the cellular details were evaluated under light microscopy.

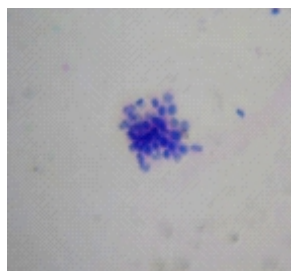
Out of 160 cases, bladder biopsy specimens were obtained for 84 cases, fixed in 10% neutral buffered formalin, processed, sections stained by Hematoxylin and Eosin as described by Bancroft in theory and practice of Histological Techniques.⁴

OBSERVATION AND RESULT

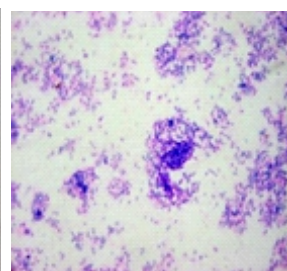
Results of 160 urine cytology smears study were shown in table-1 and malignant smear studies shown in fig-1.

Table - 1 Cytological diagnosis in 160 Urine samples

Sl. No.	Lesion	No. of cases		Total %
		Male	Female	
1	Normal	32	12	44 (27.5%)
2	Non specific cystitis	38	15	53 (33.1%)
3	Reactive	13	3	16 (10%)
4	Low grade UC	3	1	4 (2.5%)
5	High grade UC	39	2	41 (25.6%)
6	Squamous cell carcinoma	-	1	1(0.6%)
7	Adeno carcinoma	1	-	1(0.6%)
	Total	126	34	160(100%)



(a)



(b)

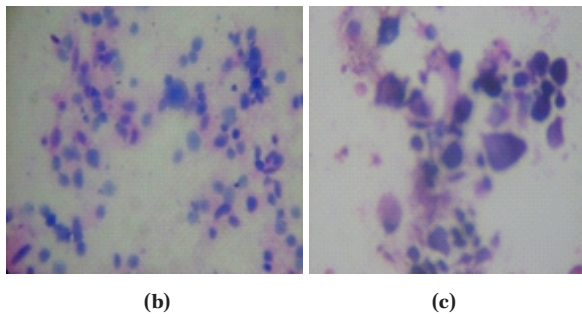


Fig.1 (a) Low grade urothelial carcinoma. Cells arranged in loose papillary clusters with increased nuclear/ cytoplasmic ration, Pap stain x40

(b)High grade urothelial carcinoma. Cellular smear in which cells are arranged in loose clusters as well as isolated cells, Pap stain x40

c) Squamous cell carcinoma. Cellular smear with large pleomorphic cells with hyperchromatic nuclei and eosinophilic cytoplasm H and E stain x40

(d) Adenocarcinoma. Pleomorphic tumour cells arranged in acinar pattern. H and E stain x100

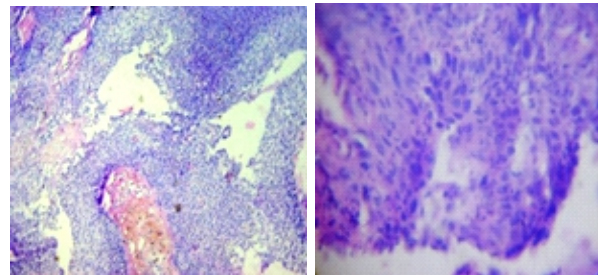
Histopathological diagnosis

Out of 160 cases, bladder biopsy specimens were obtained for 84 cases. Results were tabulated(Table-2) and histopathology images are shown in figure2.Bladder carcinoma was reported in 88% of patients aged >50 years.

Table-2 Histological diagnosis of bladder biopsy in 84 samples

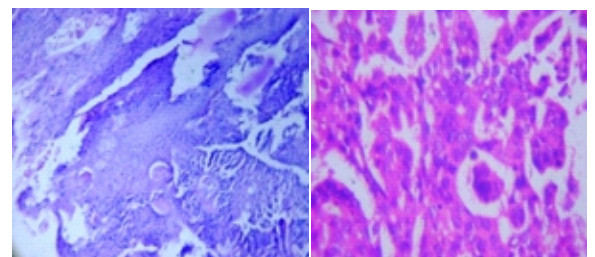
Sl. No.	Lesion	No. of cases		Total %
		Male	Female	
1	Normal	7	-	7 (8.3%)
2	Non specific cystitis	5	12	17 (20.2%)
3	TB cystitis	3	0	3 (3.6%)
4	Schistosomiasis	1	0	1(1.2)
5	Leiomyoma	-	1	1(1.2%)
6	Transitional cell papilloma	1	-	1(1.2%)
7	Urothelial carcinoma(UC)			
	Papillary GradeI (Low grade)	5	1	52 (61.9%)
	Invasive Grade II (High grade)	31	2	
	Invasive GradeIII (High grade)	12	1	

8	SCC	-	1	1(1.2%)
9	Adenocarcinoma	1	-	1(1.2%)
	Total	66 (78.6%)	18 (21.4%)	84 (100%)



(a)

(b)



(b)

(c)

Fig-2 (a)Urothelial carcinoma grade II. Relatively uniform cancer cells separated from each other by bands of connective tissue. H and E stain x40

(b) Urothelial carcinoma grade III. Cancer cells with variability in size of cells and marked nuclear abnormalities. H and E stain x40

(c) Squamous cell carcinoma. tumour cells with marked nuclear abnormalities and focal squamous differentiation. H and E stain x40

(d) Adenocarcinoma. Pleomorphic tumour cells with vesicular nuclei arranged in glandular pattern. H and E stain x40

For the cyto-histologic follow-up and correlation, histology was considered the “gold standard,” acknowledging the fact that this would create a certain bias owing to the possibility of sampling error, even in biopsy.⁵ In our study cytohistopathological correlation was done in 84 cases(Table-3).

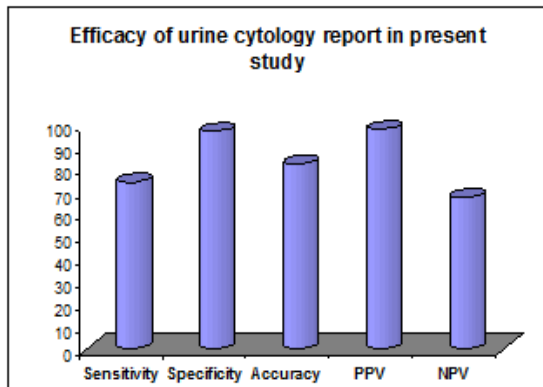
Table-3 Comparison of cytological diagnosis of urine with histopathological diagnosis

Cytological diagnosis	Final histopathological diagnosis																				Total		
	Normal		TB cystitis		Schistosomiasis		Non specific cystitis		Leiomyoma		Transitional cell papilloma		Urothelial carcinoma			Squamous cell carcinoma		Adenocarcinoma					
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F			
Normal	1		1				3	4					1		6	1	2	1					20
Nonspecific cystitis	1		1				1	7					1		2								13
Reactive	4		1		1		1	1		1	1												10
Low grade UC													3	1									4
High grade UC	1														23	1	10						35
SCC																					1		1
Adenocarcinoma																					1		1
Total	7		3		1		5	12	1	1	1		5	1	31	2	11	1		1	1		84

Coming to the efficacy of urine cytology in detecting bladder malignancy,

True positive cases were 40
False positive cases were 1
True negative cases were 29
False negative cases were 14

So the over all sensitivity was 74.1%, specificity was 96.7%, accuracy was 82.1%, positive predictive value was 97.6%, negative predictive value was 67.4%. (Diagram-1)



(Diagram-1)

DISCUSSION

Urinary cytology is extremely valuable and is often the test used for diagnosis; suggestive urine cytology findings should encourage the urologist to perform a cystoscopy and possibly bladder biopsy. False negativity may also be due error in screening or some of the urothelial carcinomas, such as low grade tumours rarely shed malignant cells.

The overall sensitivity in the detection of bladder cancer by different study groups was ranging from 50% to 97%.^{6,7} The present study indicates the sensitivity to be of 74.1%.

In Murphy WM et al (1984) the sensitivity of Low-grade UC and High-grade UC was 0-73% and 95% respectively.⁸ The sensitivity of Low-grade UC and High-grade UC in our study was 62.7% and 74% respectively.

In both of these studies, the sensitivity of urine cytology in detecting High -grade UC was more than Low-grade UC indicating that High-grade UC shed malignant cells more readily. Urine cytology has relatively low sensitivity and high specificity, particularly for well differentiated bladder tumors.⁹

In Weigner HG et al study (1993) the proportion of positive malignant cases detected by cytology for Urothelial carcinoma grade I was 31%, grade II-44%, grade III-72%, for Squamous cell carcinoma-75% and Adenocarcinoma-63%.

In our study, the proportion of positive malignant cases detected by cytology for Urothelial carcinoma grade I was 66.7%, grade II-72.7%, grade III-76.9%, for Squamous cell carcinoma-100%, Adenocarcinoma-100%. 14 cases were found to be false negative. Low grade urothelial tumors rarely shed cells in urine.

There was 1 false positive case in our study. It may be due to inadequate biopsy or misinterpretation of benign process. False positivity may be due to bladder calculi or recent catheterization or recent surgery in the urinary tract which may dislodge cluster of urothelial cells which may mimic urothelial carcinoma.

CONCLUSION

In summary, a correlative study of urine cytology and

histopathological examination of bladder lesions revealed the overall sensitivity of 74.1%, specificity of 96.7% and accuracy of 82.1%. The sensitivity of Low-grade UC and High-grade UC is 62.7% and 74% respectively indicating that High-grade UC shed malignant cells more readily than Low-grade UC.

The false negative and false positive cases in this study, can be minimized by proper collection of urine samples, proper fixation and staining methods, screening, interpretation and obtaining previous history of bladder stones, chemotherapy/radiotherapy and recent urinary tract instrumentation and surgery. Since bladder carcinomas were reported more in >50 years age group, this test may be useful in screening such patients for bladder carcinoma.

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