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Reviews Of Progress

A PROSPECTIVE STUDY ON COMPARISON OF URINARY CYTOLOGY WITH HISTOPATHOLOGICAL EXAMINATION IN BLADDER TRANSITIONAL CELL CARCINOMA

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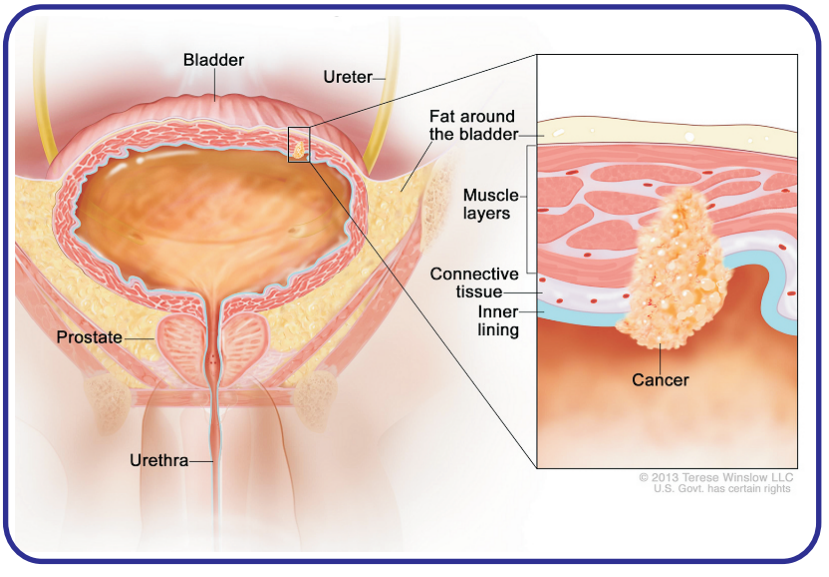
ABSTRACT

iBladder cancer accounts for 7% of all cancers in male and 2% of all cancers in female. Urinary cytology has prominent role in the multidisciplinary diagnostic approach to bladder cancer. It is used as a valuable adjunct to cystoscopy and biopsy for diagnosis and follow up of patients with bladder cancer. Urine cytology remains gold standard for bladder cancer screening. It is the test against which all others are compared when evaluating potential bladder tumor markers. It has excellent specificity with few false positive cases.

Cytological examination of voided urine is a non-invasive screening test for bladder tumors, which can be carried out in remote areas of the country. By cytology one can even classify type and grade malignancy.

Key words: Urinary cytology , urological malignancies , management of patients .



INTRODUCTION :

In 1945 Papaniculoau and Marshall recommended cytological examination of urinary sediment for diagnosis and follow up of patients with urological malignancies. The prognostic value of conventional cytology to monitor patients with superficial bladder carcinoma is well established. While cystoscopy and biopsy are optimum for diagnosis of visible disease, entire bladder mucosa can be sampled by cytology, enabling detection of occult urothelial abnormalities.

Traditionally cytological examinations have been used to detect in situ and early invasive bladder cancer in high-risk population and in conjunction with cystoscopy and biopsy to diagnose new or recurrent bladder tumor. Cytology also has been used to identify persistent tumor after transurethral resection.

Urine Cytological examination is a simple, safe, and inexpensive method to detect hidden urothelial tumours. Urinary tract tumours are often multifocal. Indications for urine cytology

examinations are 1) detection and diagnosis of tumours, carcinoma in situ, inaccessible lesions in ureters, pelvis, diverticuli, 2) Screening of high risk patients (chemical or metal exposure, smokers) 3) Monitor tumours and therapy.

Cystoscopy remains the standard for the diagnosis and surveillance of bladder tumors, allowing the lesions to be mapped and sampled. However, cystoscopy cannot explore whole bladder urothelium, and cannot diagnose all carcinoma in situ cases or lesions of upper urinary tract. Thus, it must be combined with urinary cytology, particularly in search for tumor cells from high-grade lesions, wherever their location in the urinary tract.

Urine cytology can detect bladder tumor before it can be detected cystoscopically. Urine cytology is still indispensable in the management of patients with transitional cell carcinoma. It remains as a gold standard for bladder cancer screening. All Ultrasound detected bladder neoplasm will be screened by urine cytology collected randomly. Urine cytology will be corroborated with histopathological examinations

AIM OF THE STUDY

1.To Correlate Urine cytology with Histopathology of the Bladder Transitional Cell Carcinoma.
2.To Study the Role of Urinary Cytology in the diagnosis of Bladder Transitional Cell Carcinoma.
3.To Find out the Correlation between the Grading by Urine cytology and Histopathology.

MATERIALS AND METHODS

1.Study group :

70 Patients who were admitted in Department of Urology, Kilpauk Medical College and Govt. Royapettah Hospital in coordination with Department of Pathology , patients presented with lower urinary tract symptoms (LUTS) due to bladder transitional cell carcinoma detected by ultrasonography were included in the study

2.Study design : Prospective clinical study

3.Study period : One Year from February 2014 to January 2015

4.Materials :

Freshly voided urine samples are collected for cytological examination. Cystoscopy was performed in all patients using rigid cystoscope and details of growth are noted. Material was obtained from TURBT biopsy , Radical Cystectomy specimen

Freshly voided urine samples are collected usually 3 hours after first morning void. Samples are immediately mixed with 95 % alcohol and kept in refrigerator till centrifuged. Approximatedly 100ml of urine are centrifuged at 2500 revolution/min for 20 min. Multiple smears are prepared from sediment and slides are fixed in 95% alcohol immediatedly.

Smears are stained with papanicolaou stain and haematoxylene and eosin stain. Interpretation of exfoliative cytology of urinary sediments are classifieds as Negative, Atypia, Suspcious, Positive.

Biopsies taken are processed routinely and 3-5 u thick sections are cut.

H & E Staining was done on tissue section for morphological evaluation & lesions are histologically classified as Low grade, High grade & No malignancy

Inclusion criteria

- Patients with Bladder Neoplasms detected by ultrasound
- Symptomatic patients with LUTS and hematuria

Exclusion criteria

- Patients who already undergone biopsy
- Other causes of Hematuria like RCC, Upper tract TCC

OBSERVATION AND RESULTS

70 patients of urinary bladder neoplasms diagnosed by ultrasonography were studied for comparative evaluation of urinary cytology with Histopathological correlation . The findings in these patients have been presented as

- Clincal Data
- Ultrasonography and Cystoscopic Findings
- Cytology and Histopathological Report

Table : 1 Age /Sex wise Distribution

AGE	MALE	FEMALE
30-39	2	-
40-49	10	2
50-59	24	7
60-69	16	3
70-79	5	-
80-89	1	-

Among our study group, Most common Age Group – 50-59 Years (42%). Male to Female Ratio was 4:1. Since age and Sex distribution are not statistically significant (>0.05), it means that there is no difference between the Urine Cytology Findings groups. In other words the groups contain subjects with the same basic demographic characteristics.

TABLE 2: CLINICAL FEATURES

CLINICAL PRESENTATION	NO OF PATIENTS
Hematuria, Dysuria, Frequency	34
Hematuria & Dysuria	22
Hematuria & Frequency	10
Dysuria & Frequency	4

By conventional criteria, association between Clinical Features Distribution and Urine Cytology Findings is considered to be not statistically significant since p 0-936.

Statisticial Analysis

Smoking	Urine Cytology -ve	%	Urine Cytology +ve	%
Smoking -ve	6	33.33	11	21.15
Smoking +ve	12	66.67	41	78.85
Total	18	100.00	52	100.00
Chi Square Statistic			1.08	
Degrees of Freedom			1	
P value Chi Square Test			0.299	

By conventional criteria the association between Smoking Status and Urine Cytology Findings is considered to be not statistically significant since p > 0.05.

CHART :4 URINE CYTOLOGY

In our study group, urine cytology were positive for cancer cells in 44(63 %), Suspicious in 8, (11%), Atypical in 4 (6%), Negative in 14(20%) patients

TABLE : 3 ULTRASONOGRAPHIC FINDINGS

TYPE OF LESION	NO OF CASES	PERCENTAGE
HYPOECHOGENIC	44	60%
MIXED ECHOIC	16	17%
HYPERECHOIC	6	8%
ISOECHOIC	4	5%
TOTAL	70	100%

Ultrasound Findings	Urine Cytology -ve	%	Urine Cytology +ve	%
Hypoechogenic	8	44.44	36	69.23
Mixed Echoic	6	33.33	10	19.23
Hyperechoic	4	22.22	2	3.85
Isoechoic	0	0.00	4	7.69
Total	18	100.00	52	100.00
Chi Square Statistic			9.12	
Degrees of Freedom			3	
P value Chi Square Test			0.028*	

By conventional criteria the association between Ultrasound Findings and Urine Cytology Findings is considered to be statistically significant since $p < 0.05$

Statitiscial Analysis

Location of Lesions	Urine Cytology -ve	%	Urine Cytology +ve	%
Lateral Wall	12	66.67	26	50.00
Posterolateral Wall	3	16.67	13	25.00
Base & Neck ofBladder	2	11.11	8	15.38
Dome of bladder	1	5.56	2	3.85
Anterior Wall	0	0.00	3	5.77
Total	18	100.00	52	100.00
Chi Square Statistic			2.39	
Degrees of Freedom			4	
P value Chi Square Test			0.664	

By conventional criteria the association between Location of Lesions and Urine Cytology Findings is considered to be not statistically significant since $p > 0.05$.

Statisticial Analysis

Type of Lesions	Urine Cytology -ve	%	Urine Cytology +ve	%
Pedunculated	9	50.00	17	32.69
Sessile	9	50.00	35	67.31
Total	18	100.00	52	100.00
Chi Square Statistic			1.72	
Degrees of Freedom			1	
P value Chi Square Test			0.190	

By conventional criteria the association between Type of Lesions and Urine Cytology Findings is considered to be not statistically significant since p > 0.05.

TABLE 4: COMPARISON OF HISTOLOGY WTIH URINARY CYTOLOGY

HISTOLOGY	CYTOLOGY		TOTAL
	POSITIVE	NEGATIVE	
LOW GRADE	16	7	23
HIGH GRADE	36	9	45
NEGATIVE	0	2	2
TOTAL	52	18	70

Statisticial Analysis

Histological Diagnosis	Urine Cytology -ve	%	Urine Cytology +ve	%
Negative	2	11.11	0	0.00
Low Grade	7	38.89	16	30.77
High Grade	9	50.00	36	69.23
Total	18	100.00	52	100.00
Chi Square Statistic			6.82	
Degrees of Freedom			2	
P value Chi Square Test			0.033*	

P value - Significiant

Statistical Significance

• In simple terms, the incidence of High Grade Histological Positivity is 50% in Urine Cytology –ve Group compared to 69.23% in Urine Cytology +vegroupwith a p-value of 0.033 according to Chi-Squared test.

• This indicates that there is a true difference among the study groups and the difference is significant and has not occurred by chance.

TABLE 5: COMPARISON OF URINARY CYTOLOGY WITH TUMOUR STAGING

URINE CYTOLOGY	PTa,	PTis	PT1	PT2 & Above
Positive	4	15	12	21
Negative	6	6	2	4
Total	10	21	14	25

Statisticial Analysis

Tumour Staging	Urine Cytology -ve	%	Urine Cytology +ve	%
Pta	6	33.33	4	7.69
Ptis	6	33.33	15	28.85
PT1	2	11.11	12	23.08
PT2 & Above	4	22.22	21	40.38
Total	18	100.00	52	100.00
Chi Square Statistic			8.44	
Degrees of Freedom			3	
P value Chi Square Test			0.038*	

By conventional criteria the association between Tumour Staging and Urine Cytology Findings is considered to be statistically significant since $p < 0.05$.

TABLE :6 COMPARISON OF URINE CYTOLOGY WITH DIFFERENT HISTOLOGY

HISTOLOGY	URINARY CYTOLOGY	
	POSITIVE	NEGATIVE
TCC	52	16
ADENOCARCINOMA	0	2
TOTAL	52	18

Statisticial Analysis

Type of Tumour	Urine Cytology -ve	%	Urine Cytology +ve	%
TCC	16	88.89	52	100.00
Adenocarcinoma	2	11.11	0	0.00
Total	18	100.00	52	100.00
Chi Square Statistic			5.95	
Degrees of Freedom			1	
P value Chi Square Test			0.015*	

By conventional criteria the association between Types of Tumour and Urine Cytology Findings is considered to be statistically significant since $p < 0.05$.

Accuracy Statistics

Histological Diagnosis	Positive	Negative	Total
Urine Cytology +ve	52	0	52
Urine Cytology -ve	16	2	18
Total	68	2	70

Accuracy Statistics	
Sensitivity	96%
Specificity	26%
Positive Predictive Value	76.5%
Negative Predictive Value	90%
Likelihood Ratio +ve	1.13
Likelihood Ratio -ve	0.00
Diagnostic Effectiveness	0.77
Prevalence	0.74

• Sensitivity of Urine Cytology study findings is High, meaning that malignancy +ve test result often occurs in those with malignancy
• Specificity of Urine Cytology study findings is extremely low, meaning that malignancy –ve test very rarely occurs in those without malignancy
• The diagnostic effectiveness or diagnostic accuracy is very high. It means that the overall value of Urine Cytology studyin detecting malignancy as a combined screening and case-finding test is good
• Prevalence of this condition is very common

ANALYSIS & RESULTS

In our Prospective clinical study, totally 70 patients were included those who are presented with Lower urinary tract symptoms due to Bladder TCC detected by ultrasound. Age of patient ranged from 40 to 89 . Most common age group - 50-59 years (49%). Male to Female ratio – 4:1

The main clinical presentations were hematuria , dysuria & increased frequency of micturition . Most patients about 34, presented with features of hematuria, dysuria, & Frequency of micturition. 22 patients presented with hematuria & dysuria, 10 patients with hematuria & frequency of micturition . Only 4 patients presented with dysuria & frequency of micturition.

Out of 70 cases, 74% were smokers, remaining 26% were non-smoker. The smokers were found to be more prone to develop neoplastic lesion in bladder. Urine cytology were positive for cancer cells in 44(63%), suscipious in 8(11%), Atypical in 4(6%), and negative in 14 (20%). For comparative study with histopathological correlation, positive cytology & were suscipious grouped as Positive, Atypical & Negative were grouped as Negative.

Lesions in ultrasound in bladder TCC were mostly hypoechoic of which some were irregular, some lobulated and some pedunculated. Most of lesions are multiple & few are single. Hypoechoic lesion were followed by mixed echoic, few hyperechoic in decreased order of frequency.

Statisticaly incidence of USG hypoechogenic lesionsis 44.44% in Urine Cytology –ve Group compared to 69.23% in Urine Cytology +vegroup with a p-value of 0.028 according to Chi-Squared test. This indicates that there is a true difference among the study groups and the difference is significant and has not occurred by chance

In cystoscopy, lesions were mostly situated in lateral wall in 38 cases, followed by Postero-lateral, base & neck of bladder, dome of bladder and anterior wall respectively. The association between location of Lesions and Urine Cytology Findings is considered to be not statistically significant since $p > 0.05$.

Our study shows Most of lesions are pedunculated (40%), followed by sessile (60%). Multiple tumours are present in 28 cases, single tumours in 48 cases. Likewise, tumour size < 2cm present in 10 cases, 2-5cm seen in 44 cases, > 5cm in 16 patients. Cytopositivity was found to more with single , large & sessile tumours than multiple, small pedunculated tumour. Size of tumour increase with increase in cytopositivity. When tumour size >5cm & above there is about 90-100% cytopositivity was observed . the association between Number & size of Tumours and Urine Cytology Findings is considered to be not statistically significant since $p > 0.05$.

In our study group, among 70 cases, 68 cases were confirmed histologically, of which 24 cases of low gradw TCC, 44 cases of High grade TCC, only 2 cases are histologically negative.

Out of 68 cases of histologically proved TCC, 52 cases were correctly diagnosed by urine cytological examination. Only 16 cases have cytological negative, 2 cases cytological negative due to benign disorder like papillary cystitis. Among cytological negative 16 cases, 10 cases were diagnosed as low grade in histopathology

Histological confirmed High grade TCC in 44 patient, of which 36 patient were detected cytological i.e (86%) detected by cytology. Histological confirmed low grade TCC occur in 24 patients of which 16 patients were detected cytologically (58%). Finally histological confirmed TCC occur in 68 patients on which 52 patients were diagnosed cytologically (76%). Statistically the incidence of High Grade Histological Positivity is 50% in Urine Cytology –ve Group compared to 69.23% in Urine Cytology +ve group with a p-value of 0.033 according to Chi-Squared test. This indicates that there is a true difference among the study groups and the difference is significant and has not occurred by chance. Statistically P value- 0.033 is significiant

In our study group, consists of 10 patients of PTa, 21 patients of carcinoma in situ PTis, 14 patients invaded subepithelial connective tissue PT1, 25 patients have muscle invasive PT2 & above. Urine cytology was positive in 4 cases of PTa, 15 cases of Tis, 12 cases of PT1, 21 cases of PT2 & above. In 6 cases of PTa, 6 cases of PTis, 2 cases of PT1, 4 cases of PT2 & above staging were found to have urine cytology negative. About 80% of noninvasive Tumour had negative urine cytology. Statisticially the incidence of PT 2 and above Tumour Staging is 22.22% in Urine Cytology –ve Group compared to 40.38% in Urine Cytology +ve groupwith a p-value of 0.038 according to Chi-Squared test. This indicates that there is a true difference among the study groups and the difference is significant and has not occurred by chance Cytopositivity increases with increase in Grade & Stage of tumour.

Out of 70 patients histologically , 68 patients had varying grades of Bladder Transitional cell carcinoma, 2 Patients had adenocarcinoma . Incidence of T-cell Carcinoma type is 88.99% in

Urine Cytology –ve Group compared to 100% in Urine Cytology +ve groupwith a p-value of 0.015 according to Chi-Squared test.

DISCUSSION

Urine cytology is a non invasive method of detection, diagnosis and follow up of bladder transtitional cell carcinomas. Urine cytology involves exfoliated cells from lining of urinary tract. Specimen collected from voided urine and should be processed immediately or refrigerated as soon as possible. It can be useful investigation for individuals with hematuria, has been own draw backs.

Urine cytology relies on neoplastic cells being shed in urine. High grade tumours like CIS are more likely to shed abnormal cells into urine. Sensitivity rates are higher for high grade tumours. Low grade tumours are less likely to shed cells into urine and less sensitivity. Exfoliated cells are usually shed in clusters rather than single cells. False positive due to stones, infections, instrumentation and chemo/radiotherapy.

Urine cytology reported as suscipous of malignancy require further evaluation. Most of these studies shows that outcome of patients having atypical urine cytology shows that less than 50% of individuals are 30% are found to have malignancy. It requires further follow up, currently large number of patients are subjected to unnecessary investigations with time and resources lost.

Patients were selected on basis of clinical features and ultrasonographic features. Only those cases diagnosed as urinary bladder lesions by USG were included in the study. Out of 70 cases, age of the patients ranged from 40-80 years and most of the patients were in sixth decade of life. The male to female ratio was 4:1.

The most common clinical presentations were hematuria, dysuria and increased frequency of micturition followed by presented with hematuria & dysuria, hematuria and frequency of micturition.

Most of the patients in the study were smokers. Out of 70, smokers were majority in about 74%. So there was strong association between smoking and bladder neoplasms

The lesion in ultrasonography were mostly hypoechoic (42), of which some where irregular, lobulated, pedunculated. Some of the lesions were multiple and few are single. This was followed by mixed echoic masses, hyperechoic and isoechoic lesions. Its Clinical Significance, incidence of USG hypoechogenic lesionswas meaningfully 24.79 percentage points more in Urine Cytology +ve group compared to Urine Cytology –ve group In our study Urine Cytology Positivity leads to 1.56 times increase in occurrence of USG hypoechogenic lesions.

Urine samples are freshly whole voided post ambulatory specimen, collected randomly and processed immediatedly. After detection of growth by USG, cytology as a screening technique.

To detect malignant lesions by cytology depend upon morphological features of atypical cells namely cellularity, clusters, papilla, alteration in cell type, shape, size, comet cells, necrosis, nuclear membrane irregularity, high N:C ratio and nuclear hyperchromasia Urine cytology were positive for cancer cells in 44(63%), suscipious in 8(11%), Atypical in 4(6%), and negative in 14 (20%). For comparative study with histopathological correlation, positive cytology & were suscipious grouped as Positive, Atypical & Negative were grouped as Negative.

The macroscopic appearance of growth in bladder cystoscopy were mainly sessile followed by pedunculated. About 48 cases are single and 28 cases are multiple. Most of lesions were situated in lateral walls, namely right and left lateral walls. The remaning were located in

postero lateral, base & neck and dome of bladder. The patients who have lesions in base and neck of bladder presented with increased frequency of micturition.

Likewise, tumour size < 2cm present in 14%, 2-5cm seen in 62%, > 5cm in 22% patients. Cytopositivity was found to more with single , large & sessile tumours than multiple, small pedunculated tumour. Size of tumour increase with increase in cytopositivity. When tumour size >5cm & above there is about 90-100% cytopositivity was observed .

In our study group, among 70 cases, 97% were confirmed histologically, of 34% which of low grade TCC, 63% of High grade TCC, only 2 cases are histologically negative.

Out of 68 cases of histologically proved TCC, 72% were correctly diagnosed by urine cytological examination. Only 25% cases have cytological negative, 2 cases cytological negative due to benign disorder like papillary cystitis. Among cytological negative ,38% were diagnosed as low grade in histopathology.

Histological confirmed High grade TCC in 44 patient, of which 86% patient were detected cytological . Histological confirmed low grade TCC occur in 24 patients of which 58% patients were detected cytologically . Finally histological confirmed TCC occur in 68 patients on which 76% patients were diagnosed cytologically. It's Clinical Significance the incidence of High Grade Histological Positivity was meaningfully 19.23 percentage points more in Urine Cytology +ve group compared to Urine Cytology –ve group . Urine Cytology Positivity leads to 1.38 times increase in occurrence of High Grade Histological Positivity. Our study conclude that Urine Cytology Positivity can predict an increasing trend of High Grade Histological Positivity

In our study group, Urine cytology was positive in 7% cases of PTa, 28% cases of Tis, 23% cases of PT1, 40% cases of PT2 & above.. About 80% of noninvasive Tumour had negative urine cytology. Its Clinical Significance the incidence of PT 2 and above Tumour Staging was meaningfully 18.16 percentage points more in Urine Cytology +ve groupcompared to Urine Cytology –ve group. Urine Cytology Positivity leads to 1.82 times increase in occurrence of PT2 and above Tumour Staging. Our study conclude that Urine Cytology Positivity is detrimental in nature and can lead to an increasing trend of Higher levels of tumour staging

Out of 70 patients histologically, 68 patients had varying grades of Bladder Transitional cell carcinoma, 2 Patients had adenocarcinoma. Its Clinical Significance the incidence T-cell Carcinoma type was meaningfully 11.1 percentage points more in Urine Cytology +ve group compared to Urine Cytology –ve group. Urine Cytology Positivity leads to 1.12 times increase in occurrence of T-cell Carcinoma type. Our study group conclude that Urine Cytology Positivity is detrimental in nature and can lead to an increasing trend of Transtitional cell Carcinoma type

Stromal invasion by urothelial carcinoma proceeds in two stages, invasionof lamina propria and invasion of muscle layer. Muscle invasion found in 25 cases

Urothelial bladder malignancies diagnosed by combination of cystoscopy and biopsy, with cytology as a screening procedure. Accuracy of cytological diagnosis depend upon experience and vary from cone cytologist to another. Cytological findings alone cannot be diagnostic in many cases, they require clinical and radiological findings also.

Urine cytology is used for diagnosis of clinical symptomatic patients, detection of tumours in high risk patients those who exposure to industrial chemicals, smoking. Cytology only complements, does not replace cystoscopy and biopsy. Cytology useful in detection in small or hidden lesions like diverticulum, ureters, rensl pelvis, urethra.

Incidence of urothelial carcinoma increases, so demand for urine cytology increases. Clinical history is important to minimse false positive . urine cytology sensitivity increases with

grade of tumour

To conclude that sensitivity of urine cytology was 96% where as specificity was 26%. Sensitivity for high grade tumous was higher than low grade tumours. Its Diagnostic Significance, Sensitivity of Urine Cytology study findings is High, meaning that malignancy +ve test result often occurs in those with malignancy. Specificity of Urine Cytology study findings is extremely low, meaning that malignancy –ve test very rarely occurs in those without malignancy.

The PPV of Urine Cytology study findings aremodest, meaning false positives are little common in those who screen positive. The NPV of Urine Cytology study findings is very high, meaning false negatives are rare in those who screen negative.

LH ratio for positive test is high, meaning that the test is more indicative of malignancy. It is good in ruling-in malignancy .LH ratio for negative test is not very low, meaning that it is more likely the negative test result is to occur in a patient than in a subject without disease. It is not good in ruling-out malignancy

The diagnostic effectiveness or diagnostic accuracy is very high. It means that the overall value of Urine Cytology study in detecting malignancy as a combined screening and case-finding test is good. Prevalence of this condition is very common. Our study shows that cyto- histological correlation was 76%.

Although specificity for urine cytology is low, its high sensitivity shows still a valuable tool in diagnosis of bladder carcinoma, where newer modalities have not yet been established. Larger studies may be required to better study specificity and sensitivity of urine cytology.

CONCLUSION

- Cytological examination of urine specimen is valuable as an aid in the diagnosis of bladder tumors.
- Voided urine cytology correlates with histological diagnosis in more than 60% of cases.
- The accuracy is more with high grade tumors
- Urine cytology grading correlates in most cases with histopathological grading.
- The voided urine cytology is not only of diagnostic, but also of prognostic value; positive cytology of high grade presumably identifies patients at high risk for high grade and invasive tumours.
- Cystoscopy is essential in diagnosing low grade tumors which were mostly missed by voided urine cytology.
- Voided urine cytological study can be a valuable adjunct to the clinician in the evaluation of suspected urothelial malignancy, as it is simple, non-invasive and with good accuracy in the diagnosis of TCC.

BIBLOGRAPHY

1. A Desgrippes,V. Izadifar, J. Assailly ,E. Fontaine and D. Beurton : Diagnosis and prediction of recurrence and progression in superficial bladder cancer with DNA image cytometry and urinary cytology. British Journal of Urology International, 85, 434 - 436, 2000.

2. Ahmad orandi and Mehdi Orandi: Urine Cytology in the detection of bladder tumor recurrence. The Journal of Urology 116: 568 - 569, 1976.

3. A.Saad ,D.C. Hanbury , T.A.McNicholas ,G.B. Boustead ,S.Morgan and A.C.Woodman : A Study comparing various noninvasive methods of detecting bladder cancer in urine. British Journal of Urology International,89,39 - 373, 2002.

4. Asitava Mondal, Dipak K Banerjee : The Reliability of Urinary Cytology in the Detection of Tumours of Urinary Bladder. Journal of Indian Medical Association, 90: 265 - 267, 1992

5.Culling C.F.A : Exfoliative Cytology and chromosome techniques.Handbook of Histopathological and

Histochemical techniques. Ed: 3, page-492, Pub:Butterworths, 1974
6. David M. Schwalb, Harry W. Herr and William R. Fair: The Management of Clinically Unconfirmed Positive Urinary Cytology. The Journal of urology 150: 1751-1756, 1993.
7. DiBonito L, Musse MM, Dudine S, et al: Cytology of Transitional-Cell Carcinoma of the Urinary Bladder: Diagnostic Yield and Histologic Basis. Diagn Cytopathol 8: 124-127, 1992.
8. Edward M Messing, Urotherial tumors of the Urinary tract. Campbell's Urology, Walsh Retik, Vaughan Wein: Ed: 8, Vol: 4,page 2754.Pub:Saunders,2002.
9. E. Piaton ,K Hutin ,J Faynel, M-C Rachin and M Cottier : Cost efficiency analysis of modern cytocentrifugation methods versus liquid based (Cytyc Thinprep) processing of urinary samples. Journal of Clinical pathology 57: 1208-1212, 2004
10. Farrow GM: Urine Cytology in the Detection of Bladder Cancer: A Critical Approach. J Occup Med 32: 817-821, 1990.
11. Felix.M.Brown : Urine Cytology Is it still the gold standard for screening? Urologic Clinics of North America 27: 25 - 37, 2000.
12. Frable WJ, Paxson L, Barksdale JA, et al: Current Practice of Urinary Bladder Cytology. Cancer Res 37: 2800-2805, 1977.
13. Harry Suprun and Wilhelm Bitterman: A Correlative Cytohistologic Study on the Interrelationship Between Exfoliated Urinary Bladder Carcinoma Cell Types and the Staging and Grading of These Tumors. Acta Cytolgica 19: 265-273, 1975.
14. Helene G. Wiener, G. Peter Vooijs, Bep van't Hof-Grootenboer : Accuracy of Urinary Cytology in the Diagnosis of Primary and Recurrent Bladder Cancer. Acta Cytolgica 37: 163- 169, 1993
15. H.G.Wiener, CH Mian, A. Haitel , A Pycha, G. Schatzl and M Marberger. Can urine bound diagnostic tests replace cystocopy in the management of bladder cancer. The Journal of Urology 159: 1876 - 1880, 1998.
16. Jae Y. Ro , Gregg A.. Staerkel and Alberto G. Ayala: Cytologic and Histologic Features of Superficial Bladder Cancer. Urologic Clinics of North America 19: 435-453, 1992
17. J.N.Eble, R.H.Young: Tumor of the Urinary tract; Diagnoistic Histopathology of tumors; Christoper D.M. Fletcher, Ed: 2, Vol: 1, 516-517, Pub: Churchill Livingstone, 2000.
18. Jonathan I. Epstein: The lower Urinary Tract and Male Genital System. Robbins and Cotran Pathologic Basis of Disease. Vinay Kumar, Abul K Abbas, Nelson Fausto. Ed: 7, 1028 - 1033, Pub: Saunders, 2004.
19. Juan Rosai: Urinary tract (Bladder). Rosai and Ackerman's Surgical Pathology. Juan Rosai. Ed: 9, Vol: 1, 1327 - 1337, 2913-2914. Pub: Mosby, 2004.
20. Kannan V: Papillary Transitional-Cell Carcinoma of the Upper Urinary Tract: ACytological Review. Diagn Cytopathol 6: 204-209, 1990
21. Kenneth B Cummings, Joseph G. Baron and W. Steven Ward. Diagnosis and staging of Bladder cancer. Urologic Clinics of North America 19: 455 - 465, 1992.
22. K.J.Hastie ,R Ahmad and C.U Moisey: Fractionated Urinary Cytology in the Follow-up of Bladder Cancer.British Journal of Urology 66: 40-41, 1990
23. Lage JM, Bauer WC, Kelley DR, et al: Histological Parameters and Pitfalls in the Interpretation of Bladder Biopsies in Bacillus Calmette-Guerin Treatment of Superficial Bladder Cancer. J Urol 135: 916-919, 1986.
24. Leopold G. Koss, Daniel Deitch, Ramesh Ramanathan and Andrew B. Sherman: Diagnostic Value of Cytology of Voided Urine. Acta Cytolgica 29: 810-816, 1985
25. Lucien E.Nochomovitz, Nabia E. Metwalli, Prabodh Gupta: The renal pelvis, ureter, urinary bladder

and urethra. Priniciples and practice of surgical pathology and cytopathology: Steven G. Silverberg, Ronald A DeLellis, William J Frable. : Ed 3, Vol 3,2209-2213., Pub: Churchill Livingstone Inc, 1997.
26. Marilyn Gamble and Lan Wilson. The Hematoxylins and Eosin. Theory and practice of Histological Techniques, John D Bancroft, Marilyn Gamble, Ed: 5, page 130. Pub: Churchil Livingstone, 2002.
27. Meyer M. Melicow. The Role of urine in a patient with a bladder neoplasm. The Journal of Urology 127: 660 - 664, 1982.
28. Misra v, Gupta SC, Tandon SP, Gupta AK, Sircar S: Cytohistological study of Urinary bladder neoplasms. Indian J Pathol Microbiol 43: 303-309, 2000
29. MMTR - Madras Metropolitan Tumor Registry. National Cancer Registry Program. Indian Council of Medical Research, Cancer Institute, Chennai 2005
30. M.N.EL-Bolkainy: Cytology of bladder carcinoma. The Journal of Urology 124: 20 - 22, 1980.
31. Murphy WM: Falsely Positive Urinary Cytology: Pathologist's Error or Preclinical Cancer? J Urol 118: 811-813, 1977.
32. Nathan Lieberman, Philip G. Cabaud and Frank C. Hamm: Value of the Urine Sediment Smear for the Diagnosis of Cancer. 89: 514-519, 1963.
33. Niels Harving, Hans Wolf and Fleming Melsen: Positive Urinary Cytology After Tumor Resection: An Indicator for Concomitant Carcinoma In Situ. The Journal of Urology 140: 495- 497, 1988.
34. Peter Anthony Berlac and Hans Henrik Holm: Bladder Tumor control by abdominal ultrasound and urine cytology. The Journal of Urology,147:1510-1512,1992.
35. Planz B, Jochims E, Deix T, Caspers HP, Jakse G, Boecking A. The role of urinary cytology for detection of bladder cancer. Eur J Surg Oncol. 31:304-308,2005
36. P.N. Cowen: False Cytodiagnosis of Bladder Malignancy due to Previous Radiotherapy.British Journal of Urology 47: 405-412, 1975.
37. Richard M DeMay American Society of Clinical Pathologists. Chicago. ASCP Prees:1999
38. Rife CC, Farrow GM, Utz DC: Urine Cytology of Transitional Cell Neoplasms. Urologic Clinics of North America 6: 599-612, 1979
39. Robert A. Badalament , Dane K Hermansen , Mark Kimmel et al : The Sensitivity of Bladder Wash Flow Cytometry, Bladder Wash Cytology, and Voided Cytology in the Detection of Bladder Carcinoma. Cancer 60: 1423-1427, 1987.
40. Sanjay Ramkumar, Jalaluddin Bhuiyan, Jennifer A Besse, Steven G. Roberts, Peter C. Wollan, Michael L. Blute and Dennis J O'Kane. Comparison of screening methods in the detection of Bladder cancer. The Journal of Urology 161: 388-394,1999.
41. Sheldon Bastacky, Stackey Ibrahim, Sharon P.Wilczynski and William M. Murphy : The Accuracy of Urinary Cytology in Daily Practice: Cancer Cytopathology 87: 118 - 128, 1999.
42. Stephen S Raab, Julia C.Lenel, Michael B. Cohen : Low Grade Transitional Cell Carcinoma of the Bladder. Cytologic Diagnosis by Key Features as Identified by Logistic Regression Analysis. Cancer 74: 1621-1626, 1994.
43. Tawfik Zein, Zev Wajsman, Lenore S. Englander, Marie Gamarra, et al: Evaluation of bladder washings and urine cytology in the diagnosis of bladder cancer and its correlation with selected biopsies of the bladder mucosa. The Journal of Urology 132: 670 - 671, 1984.
44. Uma A.Shenoy, Thomas V. Colby and G. Berry Schumann : Reliability of Urinary Cytodiagnosis in Urothelial Neoplasms. Cancer 56: 2041- 2045, 1985
45. Vaidehi Kannan, Shikha Bose: Low Grade Transitional Cell Carcinoma and Instrument Artifact: A Challenge in Urinary Cytology.Acta Cytolgica 37: 899-902, 1993.
46. V.Poulakis, U.Witzsch, R. DE Vries, H-M. Altmannsberger et al. A comparison of urinary nuclear

matrix protein - 22 and bladder tumor antigen tests with voided urinary cytology in detecting and following bladder cancer: the prognostic value of false-positive results: British Journal of Urology International 88: 692- 701, 2001
47. Wallace DMA, Smith JHF, Billington S, et al: Promotion of Bladder Tumours by Endoscopic Procedures in an Animal Model. British Journal of Urology 56: 658-662, 1984.
48. Weldon TE, Soloway MS: Susceptibility of Urothelium to Neoplastic Cellular Implantation.Urology 5: 824-827, 1975.
49. William M Murphy, William N Crabtree, Alina F Jukkola and Mark S. Soloway: The Diagnostic Value of Urine Versus Bladder Washing in Patients With Bladder Cancer.The Journal of Urology 126: 320-322, 1981.
50. William M Murphy, Mark S Soloway , Alina F Jukkola , William N. Crabtree and Kimball S. Ford: Urinary Cytology and Bladder Cancer: The Cellular Features of Transitional Cell Neoplasms. Cancer 53: 1555-1565, 1984.
51. William M Murphy: Current Status of Urinary Cytology in the Evaluation of Bladder Neoplasms. Human Pathology 21: 886-896, 1990.
52. William N. Crabtree, William M Murphy : The Value of Ethanol as a Fixative in Urinary Cytology. Acta Cytolgica 24: 452-455