

## A Comparison of Urinary Cytology and Histopathological Study in Urinary Bladder Transitional Cell Carcinoma at Our Institute in a Prospective Study

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Conflict of interest: Nil

### Abstract:

**Background:** Urine cytology is a standard diagnostic test to aid in diagnosis of bladder cancer. It detects the exfoliated cells from urinary tract and helps identify the presence of malignancy. The prognostic value of conventional cytology to monitor patients with superficial bladder carcinoma is well established. The study aims to correlate urine cytology with histopathology of the bladder transitional cell carcinoma and to study the role of urinary cytology in its diagnosis.

**Methods:** 70 Patients admitted in Department of Urology, SCB Medical College and Hospital, Cuttack were prospectively studied. 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. Smears are stained with papanicolaou stain and haematoxyline and eosin stain. Biopsies taken are processed routinely and 3-5 u thick sections are cut. H & E Staining was done on tissue section. Lesions are histologically classified as Low grade, High grade & no malignancy

**Results:** 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. Overall value of Urine Cytology study in detecting malignancy as a combined screening and case-finding test is good.

**Conclusions:-**Voided urine cytology correlates with histological diagnosis in more than 60% of cases. 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. 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

**Keywords:** Urinary Cytology, Histopathology, Transitional Cell Carcinoma, Urinary Bladder, Malignancy.

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### Introduction

Bladder cancer is three times more common in male than female and twice as common among whites compared to blacks. Bladder cancer was first noted in man worked in aniline dye industry in 1895. Common age group is 65 to 70 years old. Most of patients are older than 50 years of age. [1]

It accounts for 7% of all cancers in male and 2% of all cancers in female. Cytology 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 In 1945 Papanicolaou 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. [2]

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. [3]

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. [4]

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.

#### Aims 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.

#### Materials and Methods

**1. Study Group:** 70 Patients admitted in Department of Urology, SCB Medical College and Hospital, Cuttack between January 2021– December 2022 was studied in coordination with

Department of Pathology. Patients presenting 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. Material:** 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. Approximately 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 immediately.

Smears are stained with papanicolaou stain and haematoxyline and eosin stain. Interpretation of exfoliative cytology of urinary sediments are classified as Negative, Atypia, Suspicious, 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

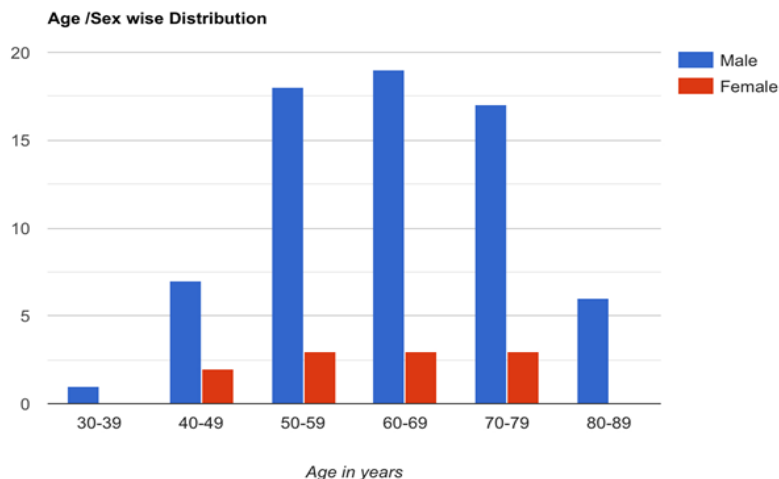
- Patients who already undergone biopsy other causes of Hematuria like RCC, Upper tract TCC.

**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

- Clinical 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	-

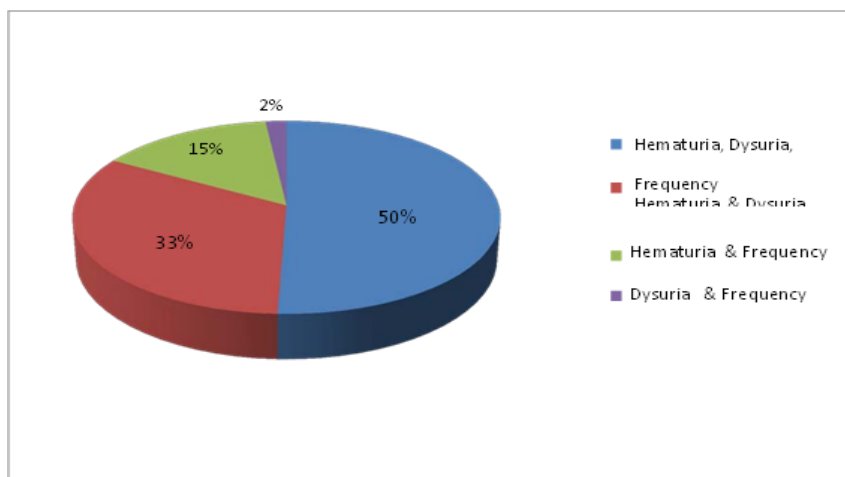


**Chart 1: Age /Sex wise Distribution**

Among our study group, Most common Age Group – 60-69 Years. Male to Female Ratio was 5:1. 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



**Chart 2: Clinical features**

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

**Table 3: Smoking history**

Smoking History	No of Patients	Percent
Smoker	49	70%
Non-Smoker	21	30%
Total	70	100%

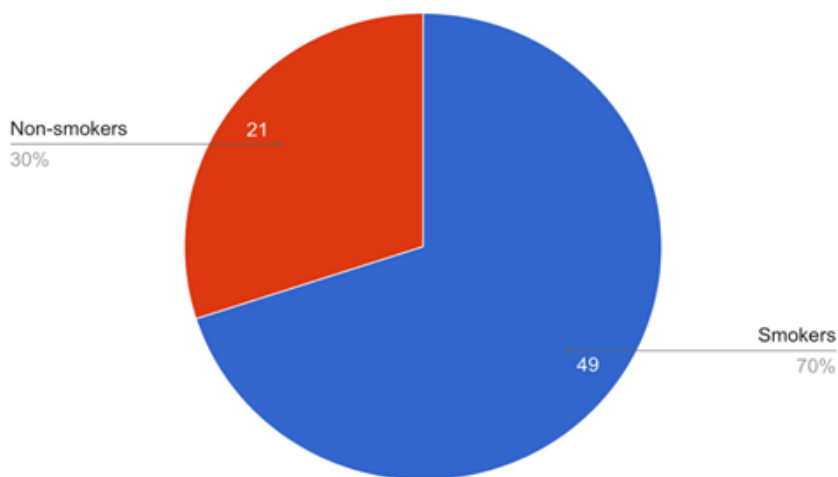


Chart: 3 Smoking history

Table 4: Urine cytology

Urine Cytology Results	No o f Cases
Positive	44
Suspicious	8
Atypical	4
Negative	14

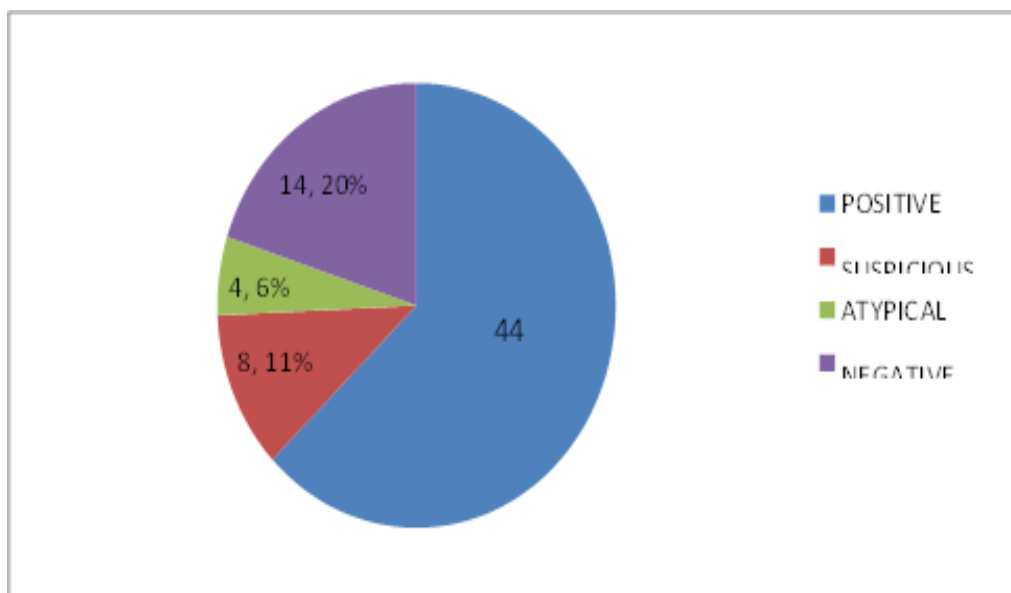
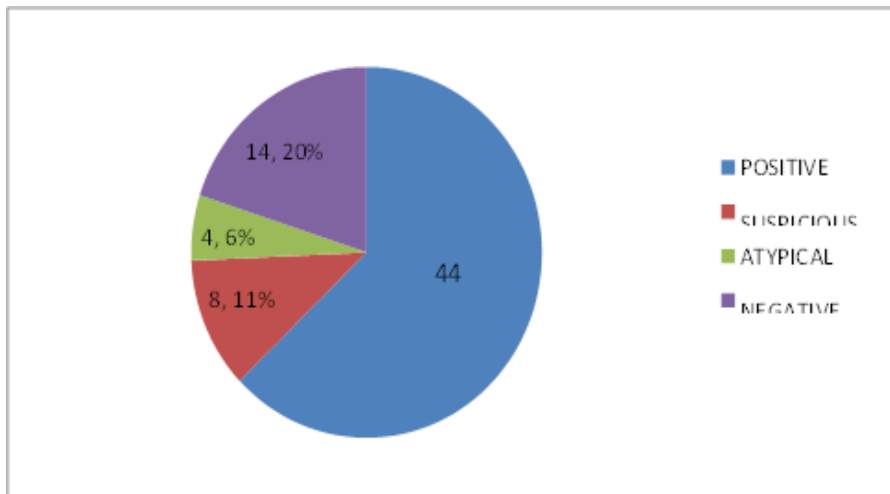


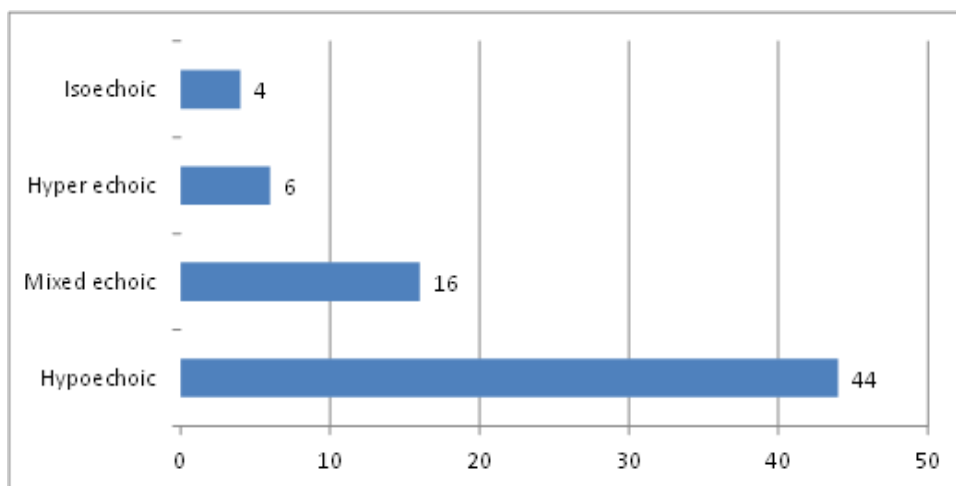
Chart 4: Urine cytology

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.

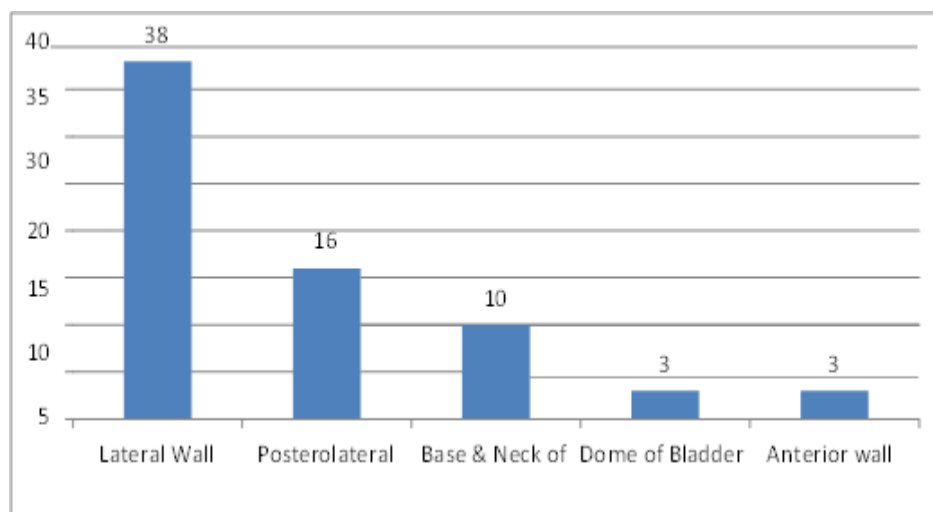


**Table 5: Ultrasonographic Findings**

Type of Lesion	No of Cases	Percentage
Hypoechoic	44	60%
Mixed Echoic	16	17%
Hyperechoic	6	8%
Isoechoic	4	5%
<b>Total</b>	<b>70</b>	<b>100%</b>



**Chart 5: Ultrasonographic findings**



**Chart 6: Location of lesions in cystoscopy**

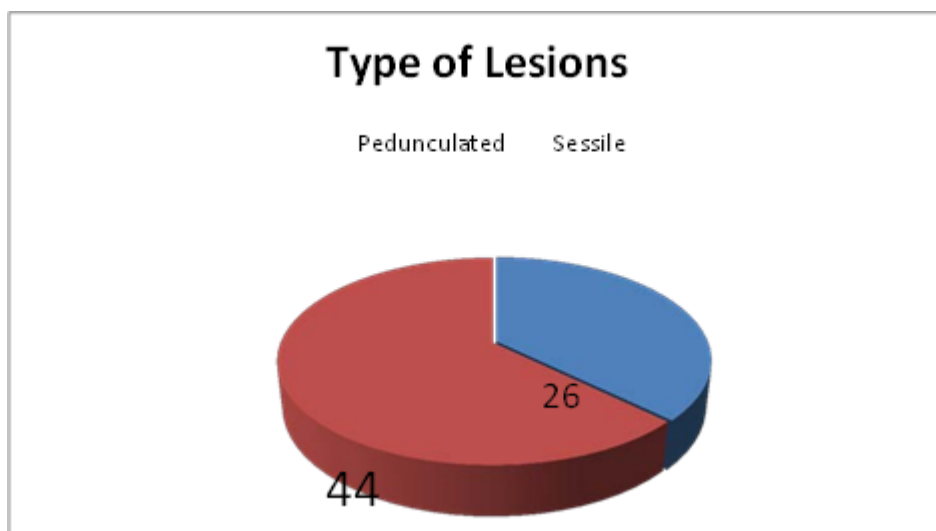


Chart 7: Type of lesions in cystoscopy

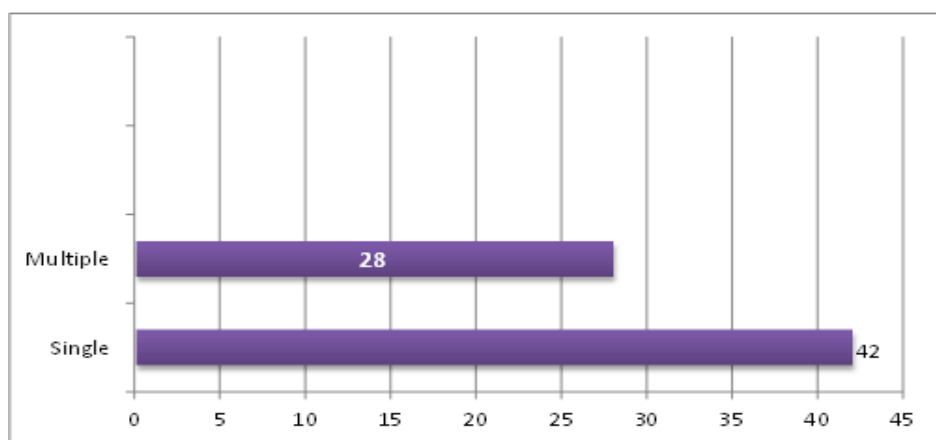


Chart 8: Numbers of tumours in cystoscopy

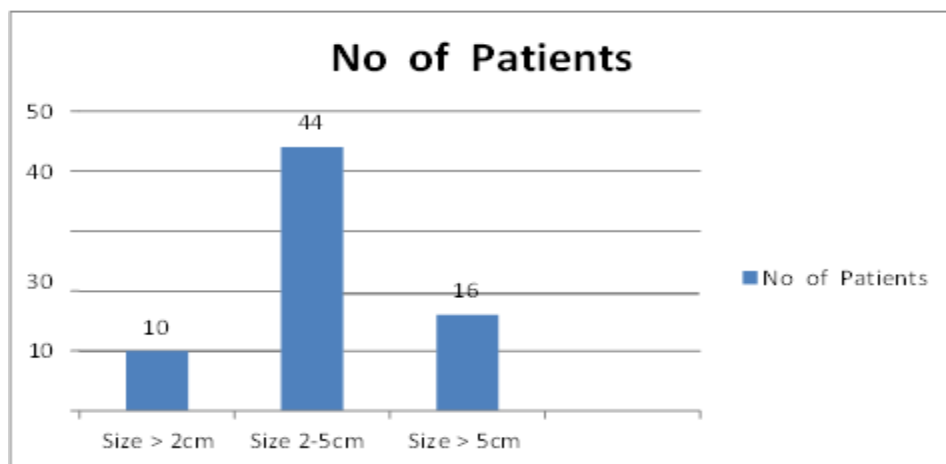


Chart 9: Size of tumour at cystoscopy

Table 10: Comparison of histology with urinary cytology

Histology	Cytology		Total
	Positive	Negative	
Low Grade	16	7	23
High Grade	36	9	45
Negative	0	2	2
<b>Total</b>	<b>52</b>	<b>18</b>	<b>70</b>

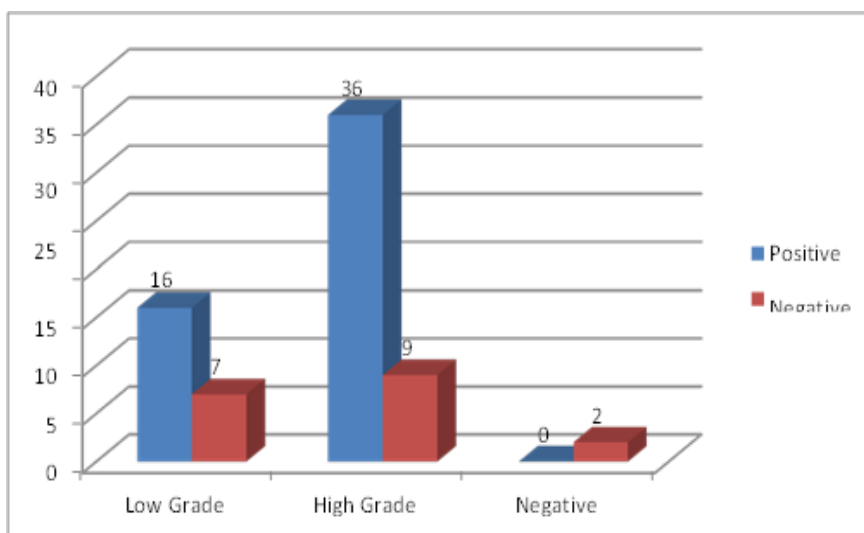


Chart 10 : Comparison of histology with urinary cytology

Statistical Analysis

HistologicalDiagnosis	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 - Significant

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 +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

Table 11: Comparison of urinary cytology with tumour staging

URINE CYTOLOGY	PTa,	PTis	PT1	PT2 & above
Positive	4	15	12	21
Negative	6	6	2	4
<b>Total</b>	<b>10</b>	<b>21</b>	<b>14</b>	<b>25</b>

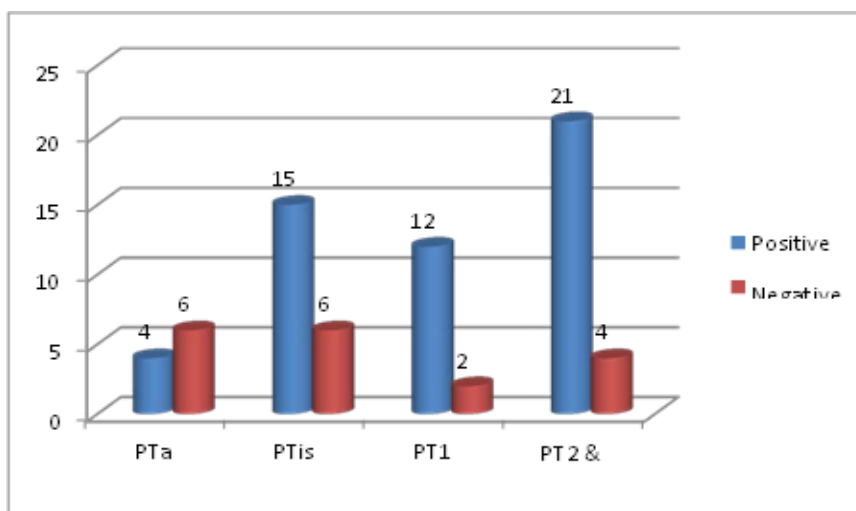


Chart 11: Comparison of urinary cytology with Tumour staging

### Accuracy Statistics

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

Accuracy Statistics	
<b>Sensitivity</b>	96%
<b>Specificity</b>	26%
<b>Positive Predictive Value</b>	76.5%
<b>Negative Predictive Value</b>	90%
<b>Likelihood Ratio +ve</b>	1.13
<b>Likelihood Ratio -ve</b>	0.00
<b>Diagnostic Effectiveness</b>	0.77
<b>Prevalence</b>	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 study in detecting malignancy as a combined screening and case-finding test is good.
- Prevalence of this condition is very common.

### Discussion

Urine cytology is a noninvasive method of detection, diagnosis and follow up of bladder transitional 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.

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 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 seventh decade of life. The male to female ratio was 5:1.

The most common clinical presentations were hematuria, dysuria and increased 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), this was followed by mixed echoic masses, hyperechoic and isoechoic lesions. Its Clinical Significance, incidence of USG hypoechoic lesions was 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 hypoechoic lesions.

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%), suspicious in 8(11%), Atypical in 4(6%), and negative in 14 (20%). For comparative study with histopathological correlation, positive cytology & suspicious 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 remaining 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 patients, 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 group compared 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.

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, renal pelvis, urethra.

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

To conclude that sensitivity of urine cytology was 96% whereas specificity was 26%. Sensitivity for high grade tumours 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.

### 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.
- 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.

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