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URINE CYTOLOGY IN BLADDER WALL THICKENING: A TERTIARY CARE EXPERIENCE USING THE PARIS SYSTEM

Oncopathology

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ABSTRACT

Background: The Paris system (TPS) for reporting urinary cytology was published in 2016 with the goal of standardization of reporting urine cytology. The primary objective of this exercise was early detection of high grade urothelial carcinoma (HGUC) in bladder thickned wall patients. **Materials And Methods:** A hospital-based observational study was done to classify as per TPS, all urine cytology samples received in the period between January 2021 to March 2024 at a tertiary care hospital. All preserved slides of urine cytology classified into various categories as specified by TPS. Immunohistochemistry reports of cell blocks of patients, where available, were compared against the cytology reports. **Results:** A total of 48 stained urine cytology smears (prepared from 60 urine samples), (29 males and 19 females) were studied. A total of 12 samples were categorized as Category I, 22 as Category II, 12 as Category III, 09 as Category IV and 05 as Category VI. There were no cases in category V and VII. **Conclusion:** TPS is an objective tool for reporting urine cytology specimens and is particularly useful in identifying HGUC cases in bladder thickned wall patients. The detection rate of low grade urothelial carcinoma (LGUC) by this system is low, in keeping with findings of similar studies.

KEYWORDS

Urine cytology, Paris System, Urothelial carcinoma

INTRODUCTION

Bladder cancer is the 9th most common cancer worldwide, with male:female ratio of 3:1.[1] Urine cytology has been used for screening and monitoring urothelial cancers since 1945 when Dr. George Papanicolaou first demonstrated its utility.[2] He proposed five categories for reporting cases, ranging from negative for malignancy to definitely malignant. This classification was widely used until recent studies revealed two distinct classes of urothelial cancers with differing clinicopathological and molecular features.[2,3] Low-grade urothelial carcinomas (LGUC) are usually non-invasive, with a low progression rate (1–5%) to invasive carcinomas and minimal disease-related mortality.[1,4] In contrast, high-grade urothelial carcinomas (HGUC) are invasive, frequently metastatic, and associated with high mortality. HGUC often harbors p53 gene mutations, typically absent in LGUC. Timely detection of HGUC can significantly improve management and prognosis. In 2013, a conference in Paris led to the development of an objective urinary cytology reporting system, modeled after the Bethesda Systems for cervical and thyroid cytology. Published in 2016, The Paris System (TPS) includes seven diagnostic categories: I – Non-diagnostic/Unsatisfactory, II – Negative for High-Grade Urothelial Carcinoma (NHGUC), III – Atypia, IV – Suspicious for High-Grade Urothelial Carcinoma (SHGUC), V – Low-Grade Urothelial Neoplasia (LGUN), VI – High-Grade Urothelial Carcinoma (HGUC), and VII – Other Malignancies (primary and metastatic).

Objectives:

1. To classify all urine cytology samples as per Paris system for reporting urine cytology.
2. To analyze spectrum of various categories, and correlating it with Immunohistochemistry Findings, here available, in positive and doubtful HGUC cases.

MATERIALS AND METHODS:

The study design was hospital-based observational study, three years data from 1st Jan 2021 to 31st Mar 2024 was considered. All consecutive urine cytology cases; within the time frame; reported as Negative, Suspicious, Atypical or Positive for malignancy, were assessed for their morphology and categorized according to TPS. All the slides available for study were well preserved and well stained by Papanicolaou stain, Hematoxylin and Eosin (H&E) and May-Grünwald-Giemsa (MGG), Cases reported as negative were to be categorized as I, II of TPS. Atypical /dysplastic or suspicious for atypical to be categorized as III and those cases reported suspicious for malignancies or positive for malignancy to be Categorized as IV, V or VI of TPS. The recorded data were entered into Microsoft Excel and analyzed using appropriate statistical tests. Ethical and research committee clearance were obtained for initiating this study.

RESULTS AND OBSERVATION

Table 1: Age Distribution of Urothelial Lesions in Urine cytology

AGE GROUP	FREQUENCY	PERCENTAGE
20-40	9	18.75
41-60	14	29.17
>60	25	52.08
TOTAL	48	100.00
MEAN ± SD	58.02 ± 2.14	

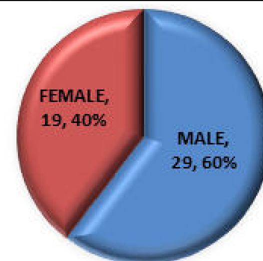

Figure 1: Gender Distribution of Urothelial Lesions in Urine Cytology

Table 2: PARIS System Grading of Urothelial Lesions in Urine Cytology

PARIS SYSTEM GRADING	FREQUENCY	PERCENTAGE
NHGUC	22	45.83
AUC	12	25.00
SHGUC	9	18.75
HGUC	5	10.42

Table 3: Clinical Features and PARIS System Grading of Urothelial Lesions

CLINICAL FEATURES	PARIS SYSTEM GRADING			
	NHGUC	AUC	SHGUC	HGUC
BLADDER WALL THICKENING (n=20)	10	5	3	2
HEMATURIA (n-16)	2	4	4	5
BURNING MICTURATION (n=21)	10	8	1	2

Bladder wall thickening (n=20) is mostly associated with NHGUC (50%) and less with high-grade lesions (10%). Hematuria (n=16) shows a higher association with HGUC (37.5%). Burning micturition (n=21) is mainly linked to NHGUC (47.62%) and AUC (38.10%). Hematuria indicates high-grade lesions, while Bladder wall thickening

and Burning micturition suggest lower-grade lesions.

Table 4: Clinical features and PARIS System Grading of Urothelial Lesions

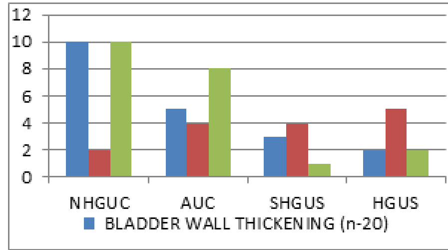

Table 5: PARIS System Grading and Immunohistochemical (IHC) Diagnosis of Urothelial Lesions

PARIS SYSTEM GRADING	IHC DIAGNOSIS				
	HIGH GRADE NON INVASIVE PAPILLARY UROTHELIAL CARCINOMA	HIGH GRADE UROTHELIAL SQUAMOUS CELL CARCINOMA	INVASIVE UROTHELIAL CARINOMA	LOW GRADE NON INVASIVE PAPILLARY UROTHELIAL CARCINOMA	UROTHELIAL SQUAMOUS PAPILLOMA
NHGUC	0	0	1	0	0
AUC	1	0	0	0	0
SHGUC	1	1	0	0	1
HGUC	1	0	0	4	0

Screening Test (PARIS System Classification) v/s Gold Standard Test for Urothelial Carcinoma

The PARIS system shows 100% accuracy in identifying HGUC for Grade 5 cases, confirmed by IHC. For Grades 3 and 4, it detects both HGUC and non-HGUC lesions, highlighting the need for IHC confirmation. This demonstrates PARIS's reliability for high-grade cases but limited specificity in lower grades.

Photograph

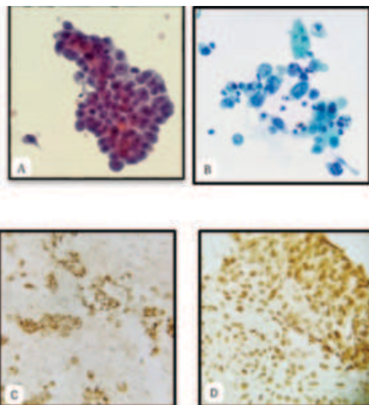

Figure 2:

A. PAP Stain: Category III, AUC
B. PAP Stain: Paris System Category V, HGUC
C. CK20 (C) Positivity in Malignant Urothelial Cells
D. GATA3 (N) positivity in Malignant Urothelial Cells

DISCUSSION

Our study is the first hospital-based observational study of its kind from India which addresses the pressing need of evaluating TPS for urine cytology reporting in bladder wall thickned patients. Urine cytology remains one of the most widely used non-invasive investigations for the early diagnosis and monitoring of urothelial carcinoma. It is best suited for a resource poor country like ours.[1-3] The primary objectives of study were to categorize urothelial lesions based on the PARIS system, correlate cytopathological findings with clinical features, and evaluate the cytodiagnosis of atypical urothelial cells (AUC). To achieve these aims, urine samples were collected from spontaneous voided urine specimens.

Table 6: Comparison Of Mean Age And Age Range In Urothelial Lesion Studies

Study	Mean Age (± SD)	Age Range
Our Study	58.02 ± 2.14 years	Predominantly >60
Bantita	66 years	Not specified
Phruttinarakorn et al.[5]		
Aakriti Kundlia et al.[6]	62.8 ± 11.7 years	Majority >60 years
Thameem A[7]	62 years	Primarily 61-70 years
Rai S et al.[8]	Median 62 years	17–87 years
Mari Yamasaki et al.[9]	73.5 years	26–93 years

Table. 7: Comparison Of Male-to-female Ratio In Urothelial Lesion Studies

Study	Male-to-Female Ratio
Our Study	1.5:1
Bantita Phruttinarakorn et al.	1.4:1
Parag Gupta et al.[10]	8.6:1
Aakriti Kundlia et al.	3.64:1
Rai S et al.	2.3:1

Clinical Features of Urothelial Lesions

Our study using the PARIS reporting system found burning micturition (43.75%) and abdominal pain (41.67%) as the most common symptoms of urothelial lesions. Hematuria, a key diagnostic indicator, was present in 33.33% of cases. Less frequent symptoms included weight loss, fever, urinary retention, vomiting, and flank pain (4.17%–10.42%).

Comparing with other studies, Aakriti Kundlia et al. reported hematuria in 85% of cases, particularly in neoplastic lesions, reinforcing its diagnostic significance. They also found dysuria and abdominal pain important, though abdominal pain was less common than in our study. Thameem A et al. observed painless gross hematuria as the most common presentation, followed by dysuria, differing from our study where burning micturition was more prevalent.

Additionally, Emin Özbek[12] highlighted early bladder wall thickening detection as crucial for cancer diagnosis and intervention, aligning with our finding it requires further evaluation rather serving as a standalone diagnosis.

These variations emphasize the need for comprehensive symptom evaluation. While hematuria remains a critical diagnostic feature, symptom prevalence differs across studies.

Paris System Grading Of Urothelial Lesions In Cytological Examination

In our study, urothelial lesions classified by the PARIS system were distributed as follows: 45.83% Non-High Grade Urothelial Carcinoma (NHGUC), 25.00% Atypical Urothelial Cells (AUC), 18.75% Superficial High-Grade Urothelial Carcinoma (SHGUC), and 10.42% High-Grade Urothelial Carcinoma (HGUC). NHGUC was the most common, with fewer high-grade lesions.

Bantita Phruttinarakorn et al. reported 76.1% of cases as negative for HGUC, 6.1% as HGUC, and 2.7% as SHGUC, showing a lower prevalence of high-grade lesions than our study, possibly due to demographic or methodological differences. Aakriti Kundlia et al. found 32% classified as negative for HGUC, 21% as HGUC, and 25% as AUC, aligning with our AUC rate but showing a higher HGUC proportion. Rai S et al. reclassified 20% of "atypical cells – suspicious for malignancy" as SHGUC and 33% of AUC as NHGUC, suggesting a higher rate of high-grade lesions. Straccia et al.[11] found 38.5% of SHGUC cases confirmed as HGUC, reinforcing the importance of accurate cytological grading. Mari Yamasaki et al. observed fewer SHGUC and HGUC cases in the TPS group than the CS group, suggesting the PARIS system might under represent high-grade lesions. Overall, our study shows a high proportion of NHGUC and AUC, but variability in high-grade lesion prevalence across studies highlights the need for standardized diagnostic criteria and further research to refine grading systems.

Table 8: Comparisons of Diagnostic Performance Metrics for High-Grade Urothelial Carcinoma (HGUC) Across Different Studies

Diagnostic Metric	Our Study	Bantita Phruttin arakorn et al.	Rai S et al.	Mari Yamasaki et al.	Malviya et al.[12]
Sensitivity	50%	63%	83.33%	56%	95%
Specificity	100%	92.80%	89.40%	97.80%	Not reported

Positive Predictive Value (PPV)	100%	89%	87.50%	93.30%	Not reported
Negative Predictive Value (NPV)	88.37%	73.10%	85.70%	80%	Not reported
Accuracy	89.58%	78.50%	86.52%	Not reported	86.20%

CONCLUSION:

This study, conducted in a tertiary care hospital, assessed the effectiveness of the Paris System (TPS) in urine cytology for categorizing urothelial lesions. TPS standardized reporting, improved diagnostic consistency, and facilitated better communication among clinicians, especially in cases of bladder wall thickned patients. It effectively differentiated Non-High Grade and High-Grade Urothelial Carcinomas, showing strong correlation with histopathology and IHC. The study highlights TPS as a valuable tool for accurate diagnosis and management of urothelial neoplasms, supporting its routine clinical use.

Conflicts Of Interest:

The authors have no conflict of interests to disclose.

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