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Original Research Article

Diagnostic utility of the Paris system for urine cytology with histopathological correlation

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ABSTRACT

Background: Urothelial carcinoma (UC) is the second most common malignancy in the urogenital system. Urinary cytology is a non-invasive, cost-effective screening and monitoring technique for UC.
Methods: In this retrospective study, conducted from over a period of one year, 62 urine cytology sample s were evaluated utilizing. The Paris system (TPS) for reporting urinary cytology and correlated with histopathological findings where available.
Results: Urine cytological cases were divided in 5 categories as per TPS. The majority (46.77%) were negative for high-grade urothelial carcinoma (NHGUC), while 35.48% were unsatisfactory/non-diagnostic, indicating inadequate samples. 6.45% of cases were diagnosed as high-grade urothelial carcinoma (HGUC), and 4.83% were suspicious for high-grade urothelial carcinoma (SHGUC). Atypical urothelial cells (AUC) made up 6.45% of cases. No any case of low-grade urothelial neoplasm was found. Out of 62 total cases, histological correlation was available in 13. On histopathology 8 cases confirmed as UC which were diagnosed cytologically as HGUC (2 cases), SHGUC (1 case), AUC (3 cases) and NHGUC (2 cases). Two cases were nondiagnostic on cytology due to low cellularity were later reported as Sarcomatoid urothelial carcinoma with squamous component and Low-grade urothelial carcinoma each on histology. Remaining biopsies were inadequate where only necrosis and/or few atypical cells noted.
Conclusions: The study highlights the effectiveness of urine cytology in detecting high-grade lesions but emphasizes the challenges posed by unsatisfactory samples and the need for a multi-modal diagnostic approach, including cystoscopy and histopathology, to enhance diagnostic accuracy. The TPS framework offers a structured method for interpreting urinary cytology, critical for improving patient outcomes in urothelial carcinoma detection.

Keywords: Paris system, Urothelial carcinoma, Cytology

INTRODUCTION

At the 2013 International congress of cytology, the Paris system for TPS was introduced to standardize urinary tract cytology reporting. UC is the second most common malignancy of the urogenital system, following prostate cancers in male, ranking 11th in incidence in global cancer statistics, and in female it ranks as the 17th position. Urinary cytology is currently the most common technique used for screening and monitoring urothelial carcinoma. It is non-invasive and cost effective when compared to other modalities.[1-3] Urine cytology has high sensitivity for detection of high-grade urothelial carcinoma and thus it compliments cystoscopic examination. There is no doubt that cystoscopy with biopsy is gold standard for diagnosis of UC but it is an invasive procedure and cystoscopy has several limitations as a diagnostic method, more so for flat urothelial lesions.

The main purpose of urine cytology is to detect high grade urothelial carcinoma.[4] The Paris system for TPS guidelines provide cytomorphologic criteria for categorizing the cytology results. This system emphasizes the main objective of urine cytology, which is identifying HGUC,

other is surveillance, follow up of patients with known urothelial carcinoma to detect recurrence or progression and evaluation of haematuria, particularly painless haematuria. TPS also supports the use of ancillary techniques (e. g., UroVysion FISH) for indeterminate interpretations.[5,6] TPS has contributed to the formation of clearer and robust diagnostic criteria and ameliorated the correlation with the ROHM of each diagnostic category. In addition, it has changed the pathologist's diagnostic perception and has improved communication with clinicians. TPS has also been applied in specific settings, like upper urinary tract specimens and BCG-treated patients, as well as in specimens with different preparation techniques. Reviews of TPS report a decrease in the frequency of intermediate diagnoses and an acceptable interobserver variability.[6-8]

METHODS

This retrospective study was conducted in the Department of Pathology, Government Medical College, attached with a tertiary care hospital, over a one-year period. All voided mid-stream urine samples received for cytological evaluation during the study period were included in the study. A total of 62 voided mid-stream urine samples were collected and processed. All 62 samples were received for cytological evaluation.

Cases with available histopathological follow-up were included for cyto-histological correlation. 13 cases were available for histopathology correlation. Samples that were improperly collected, grossly contaminated, or otherwise unsuitable for cytological processing were excluded from the study. Each urine sample first underwent gross examination, followed by centrifugation for preparation of conventional smear and staining with hematoxylin and eosin (H&E), Papanicolaou, and Giemsa stains. Microscopic findings were recorded for every sample, and all cases were finally categorized according to the Paris system for reporting urinary cytology (TPS). Categories of the Paris system for reporting urinary cytology (TPS): unsatisfactory/non-diagnostic, negative for high grade urothelial carcinoma (NH GUC), atypical urothelial cells AUC, SHGUC, HGUC & low-grade urothelial neoplasm (LGUN). Data were entered into Microsoft Excel and analysed using descriptive statistical methods. The findings were presented using tables. The study was approved by the institutional ethics committee.

RESULTS

Total 62 urine cytological sample were studied based on The Paris system for reporting urinary cytology. Table No. 1 shows the distribution of urine cytological diagnosis according TPS. Out of 62 sample, 22 cases (35.48%) were in unsatisfactory/non -diagnostic and 29 cases were (46.77%) NH-GUC categories, AUC and HGUC were identified in 4 cases each, making up 6.89% of the total.

Suspicious for high -grade urothelial carcinoma (SHGUC) accounts for 4.83% (3 cases). No any case of LGUC was observed. Table no 2 shows demographic characteristics of the present study, there was male predominance and Male to female ratio is 4.5:1. Out of 62 urine cytology samples, the maximum number of cases were seen in the 61-70 years age group, followed by 41-50 and 51-60 years. Malignancy was observed in patient with more than 40 years of age.

Table 1: Urine cytological diagnosis as per the Paris system.

Sr. No	Lesion	No. of cases	Total %
1	**Unsatisfactory/Non diagnostic**	22	35.48
2	**Negative for high grade urothelial carcinoma**	29	46.77
3	**Atypical urothelial cells**	4	6.45
4	**Suspicious for high-grade urothelial carcinoma**	3	4.83
5	**High-grade urothelial carcinoma**	4	6.45
6	**Low grade urothelial neoplasm**	0	0
Total		62	100

Table 2: Age wise distribution of all urine cytology sample.

Sr. No	Lesion	<41	41-50	51-60	61-70	71-80	>80	Total
1	**Unsatisfactory/Non diagnostic**	6	7	3	8	-	-	24
2	**Negative for high grade urothelial carcinoma**	3	2	5	7	7	-	24
3	**Atypical urothelial cells**	-	-	1	2	-	1	4
4	**Suspicious for high-grade urothelial carcinoma**	-	1	1	-	-	-	2
5	**High-grade urothelial carcinoma**	-	1	1	1	1	-	4
6	**Low grade urothelial neoplasm**	-	-	-	-	-	-	**0**
Total		9	11	11	18	8	1	62

Table 3: Correlation between cytological diagnosis of urine with histological diagnosis.

Histology	Cytology					
	Non diagnostic	NHGUC	AUC	SHGUC	HGUC	Total
Inconclusive/Inadequate	-	-	1	-	1	2
Invasive UC	-	2	2	-	1	5
HGUC	-	-	1	1	1	3
Sarcomatoid UC	1	-	-	-	-	1
Non-invasive LGUC	1	-	-	-	-	1
Atypical cells among necrotic areas	-	-	-	1	-	1
Total	2	2	4	2	3	13

Total 13 bladder biopsy samples were available for follow up histopathology which were compared with urine -based cytological diagnoses. While there was a general correlation, discrepancies were observed. Whenever uncertainties arise during histopathology examination, immunohistochemistry was utilized for diagnosis. Table 3 shows the correlation between urine cytological diagnosis and histological diagnosis according to the Paris system for reporting urinary cytology. Out of 13 histologically confirmed cases, 2 cases were reported as non-diagnostic for evaluation on cytology, later on histopathology follow up one reported as Sarcomatoid urothelial carcinoma with squamous component and other one as non-invasive low grade urothelial carcinoma. Two cases reported on cytology as negative for high grade urothelial carcinoma (NH-GUC), which were later on confirmed histopathogically as invasive urothelial carcinoma.

Two cases initially diagnosed as atypical urothelial cells through cytology was later confirmed as one high-grade urothelial carcinoma and another invasive urothelial carcinoma histologically. 3 cases were reported as HGUC on cytological evaluation, later on histological correlation, 1 case corresponded to invasive urothelial carcinoma, 1 case to high-grade urothelial carcinoma and 1 case to inconclusive/inadequate histology. 2 cases were reported as suspicious for SHGUC on cytology, which were later on histological examination, 1 case was confirmed as high-grade urothelial carcinoma, while 1 case showed atypical cells among necrotic areas.

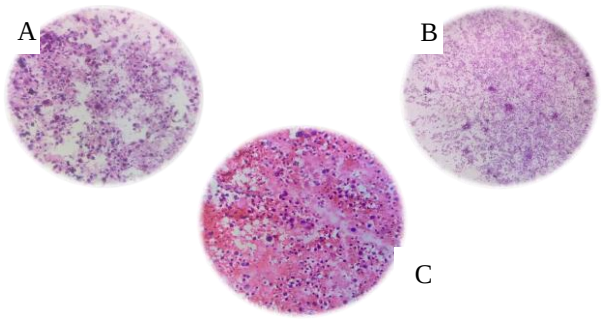

Figure 1 (A-C): Urine cytology: HGUC, enlarged nuclei with high N:C ratio (>0.7), hyperchromasia, clumped chromatin & irregular nuclear border.

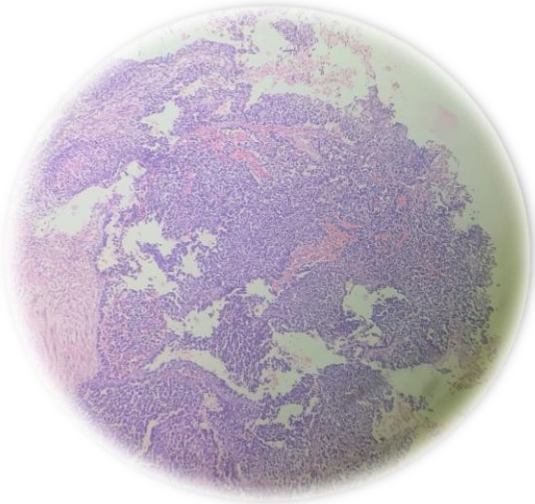

Figure 2: Urothelial carcinoma HP examination.

DISCUSSION

The study reaffirms the utility of urine cytology in detecting high-grade urothelial carcinoma, particularly when using the Paris system. However, the high rate of unsatisfactory/non-diagnostic cases suggests that sample quality remains a critical factor in the effectiveness of cytological evaluation. The unsatisfactory or non-diagnostic category, representing 35.48% (22 cases) of the total samples. This indicates a significant proportion of samples where a definitive diagnosis could not be established, possibly due to delayed transport of samples, leading to cellular degeneration and loss of diagnostic details.

Additionally, improper or false collection techniques contributed to poor sample quality. Some samples were obtained from catheterized patients, which showed significant bacterial and fungal overgrowth, further hampering cytological interpretation. It can be reduced through a multidisciplinary approach. Similarly, 46.77% (29 cases) of the samples were negative for high-grade urothelial carcinoma. This category encompasses cases where no malignant features were identified, providing reassurance for the absence of high-grade malignancies.[1]

Atypical urothelial cells were observed in 6.45% (4 cases). This category is crucial as it represents cases where the cells exhibit abnormal features that are not diagnostic of malignancy but may warrant further investigation due to the potential risk of progression to high-grade lesions. Suspicious cases comprised 4.83% (3 cases). These cases present cytological features concerning for malignancy but fall short of a definitive diagnosis, indicating the need for close follow-up or additional diagnostic procedures, such as cystoscopy and biopsy. High-grade urothelial carcinoma was identified in 6.45% (4 cases). This category represents definitive cases of high-grade malignancy, underscoring the effectiveness of urine cytology in detecting aggressive forms of urothelial carcinoma.

In present study, out of 9 cases of histopathology confirmed UC, 2 cases (22.2%) reported on cytology as HGUC, 1 case (11.1%) was SHGUC, 3 cases (33.3%) were AUC, 2 cases (22.2%) were NHGUC and one case (11.1%) was unsatisfactory on cytology. In Jaiswal et al study out of 20 cases of histologically confirmed uc, 16 cases (80%) reported on cytology as HGUC, 3 cases (15%) were suspicious and one case (5%) was NHGUC on cytology reporting. In Gaikwad et al study out of 32 cases on histology follow up, 18 cases (56.2%) reported as HGUC on cytology, 6 cases (18.7%) were SHGUC, 1 case (3.1%) was AUC, 2 cases (6.25%) were NHGUC and 1 case (3.1%) was unsatisfactory. The study by Kafle et al also showed that out of 57 cases, 4 cases (7.02%) each were HGUC, SHGUC, and AUC, while 40 cases (70.17%) were NHGUC.

Among the four cases categorized as AUC on cytology, histopathological follow up revealed HGUC in one case and invasive urothelial carcinoma in two cases, while one case was reported as inadequate. Stringent criteria of AUC significantly improve the detection of HGUC by increasing diagnostic sensitivity, minimizing false negative results and aiding in the early identification of clinically significant malignancy.[2,9,10]

In the present study, AUC, SHGUC, and HGUC showed almost 100% correlation with malignancy on histopathological examination after excluding cases with inadequate biopsy material. Similar findings have been observed in the studies by Rai et al and Arya et al who also observed a 100% positive predictive value for HGUC. However, the predictive values for AUC and SHGUC differed across studies. Rai et al reported PPVs of 12.5% for AUC and 64.3% for SHGUC, while Arya et al reported 25% and 77.5%, respectively. Overall, HGUC showed consistently high predictive value across studies, whereas the performance of AUC and SHGUC appeared to be more variable.[11,12] The most concerning false negative are those where cytology misses more aggressive forms of cancer, such as invasive UC or HGUC, emphasize the limitations of cytology as a sole diagnostic tool. It highlights the need for confirmatory histological diagnosis in cases where cytology is negative or inconclusive, especially when clinical suspicion for malignancy remains high.

Several factors that may contribute to false negative in urine cytology are inadequate or non-representative samples can lead to non-diagnostic results, as seen in the sarcomatoid UC case. Not all tumors shed malignant cells into the urine, especially low-grade tumors, which may not be detected through cytology. Subjectivity in interpretation cytological assessment involves a degree of subjectivity, and subtle malignant changes might be overlooked, particularly in AUC or NHGUC categories.

The findings emphasize the importance of categorizing urine cytology results accurately, as atypical and suspicious cases require vigilant monitoring to prevent the progression of undetected malignancies. While urine cytology is non-invasive and cost-effective, it should be complemented by cystoscopic examination, especially in cases with suspicious or atypical findings. Repeat sampling is recommended in clinically suspicious cases which are reported inclusive on cytology evaluation.

CONCLUSION

The Paris system provides a structured approach to urine cytology reporting, particularly for identifying high-grade urothelial carcinoma. However, the limitations in detecting low-grade lesions and the significant proportion of unsatisfactory samples highlight areas for improvement in sample collection and processing techniques. The study underscores the need for a multi-modality approach in the diagnostic workup of urothelial carcinoma.

In routine screening, it is critical to avoid false negative diagnosis of flat lesions or sample with low cellularity. For patients with a high clinical suspicion of urothelial carcinoma, a negative cytology should not be the endpoint; repeat urine cytology sample and biopsy should be done as indicated. Cystoscopic biopsy is more reliable for malignancy, especially in detecting low grade or rare aggressive cancers.

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