Journal of Pathology of Nepal (2022) Vol. **12**, 1881 - 1885

Journal of
PATHOLOGY
of Nepal

www.acpnepal.com

Original Article

Utility of reporting urine cytology samples as per the Paris system

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Keywords:

High-grade urothelial carcinoma;
Urine cytology;
Urothelial carcinoma;
The Paris system;

ABSTRACT

Background: Urinary tract cytology is an accurate test for the detection of urothelial malignancy especially high-grade urothelial carcinoma. The Paris System for Reporting Urinary Cytology was introduced to standardize urinary tract cytology reporting. We aim to evaluate the utility of reporting urinary cytology as per this system and correlate with histopathology.

Materials and Methods: This is a descriptive cross-sectional prospective study conducted on urine samples submitted for cytological examination at Kathmandu Medical College Teaching Hospital, Sinamangal, Nepal between 1st November 2020 to 31st July 2021. Ethical consent was taken from the Institutional Review Committee. Urine cytology was reported as per The Paris System for Reporting Urinary Cytology and correlated with the histopathologic diagnosis. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated for the high-grade and low-grade urothelial lesion.

Results: A total of 104 urine samples were evaluated. Biopsy specimens were available for 38 cases. Urine cytology consisted of 1.92% non-diagnostic cases, 69.23% negative for high-grade urothelial carcinoma, 5.76% atypical urothelial cells, 5.76% suspicious for high-grade urothelial carcinoma, 13.46% high-grade urothelial carcinoma, and 3.84% low-grade urothelial neoplasm respectively. Sensitivity, specificity, negative predictive value and positive predictive value were 90.48%, 82.35%, 86.37% and 87.5% respectively for high grade urothelial carcinoma and 40%, 93.9%,50% and 91.17% respectively for low grade urothelial lesions..

Conclusions: Our study shows that reporting urine cytology as per The Paris System for Reporting Urinary Cytology provides high sensitivity for the detection of high-grade urothelial lesions.

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Received : 12th December 2021 ; **Accepted** : 9th Feburary 2022

Citation: Dhakhwa R, Shrestha O, Thapa R, Pradhan S. Utility of reporting urine cytology samples as per the Paris system. J Pathol Nep 2022;12(1):1881-5. DOI:10.3126/jpn.v12i1.41443

INTRODUCTION

Urine cytology is easy to perform, non-invasive and remains an essential diagnostic tool in the screening and surveillance of urothelial carcinoma.[1-3] The performance of urine cytology depends on tumor grade. Its sensitivity is high for detecting high-grade urothelial carcinomas (HGUCs) but relatively low for low-grade lesions. In that regard, since HGUC cells can shed in the urine, even in carcinomas that are not seen by cystoscopy (ie, occult carcinomas), a positive urine cytology diagnosis is a clinically meaningful result even in the absence of tissue confirmation. Consequently,

patients with positive cytology and negative cystoscopy or biopsy results are usually investigated further and closely monitored because a significant percentage is eventually proven to harbor HGUC. [4-7]

Urine cytology is reported conventionally by allocating different diagnostic classes or groups based on available expertise and experience in different institution. The diagnostic criteria for each group are however not very clear. Moreover, urine cytology reporting is not uniform and highly subjective owing to the unavailability of consensus classification. The lack of standard diagnostic criteria and widely accepted terminology in urine cytology reporting has led to significant variability between reporting systems, and several classification schemes have been proposed to address this issue at different times.[8,9] In November 2015, The Paris System for Reporting Urinary Cytology (TPS) was published. TPS is a 7-tier classification, taking into account the adequacy of the specimens, and is based on strict cytomorphologic criteria which are believed to reduce subjectivity observed in reporting urine cytology using the conventional method. The seven diagnostic categories of TPS are as follows. [5,10-16]

i. Non-diagnostic or unsatisfactory

ii. Negative for high-grade urothelial carcinoma

iii. Atypical urothelial cells (AUC)

iv. Suspicious of high-grade urothelial carcinoma (SHGUC)

v. Low-grade urothelial neoplasia (LGUN)

vi. High-grade urothelial carcinoma (HGUC)

vii. Other malignancies, primary and metastatic

In our institution, we have been reporting urine cytology conventionally based on traditional guidelines. Recently we have adopted the TPS in our laboratory and we intend to evaluate its performance prospectively and aim to test the impact of implementing this system during the study period.

Table 1: Age-wise distribution of the patients

Age group (yrs)	Number of patients
21-30	1
31-40	4
41-50	8
51-60	44
61-70	29
71-80	15
>80	3

MATERIALS AND METHODS

This was a descriptive cross-sectional study conducted among patients from 1st November 2020 to 31st July 2021. The institutional review committee of Kathmandu Medical College and Teaching Hospital provided the ethical approval (reference number:305202002). Using convenience sampling technique, urine samples and histopathology specimens submitted to the Department of Pathology for evaluation during the study period were included in the study. Urine samples submitted to the Department of Pathology for cytological evaluation were studied using routine technique and cytocentrifuge slide preparation (CytoSpin; Thermo Fisher Scientific, Villebonsur-Yvette, France). Two smears prepared from the centrifuged and cytospin preparation were stained by May Grunwald Giemsa (MGG) and Papanicolaou stain. Cytology was evaluated as per the TPS, with cytological diagnoses classified as per the TPS. Whenever available, histological diagnoses from concomitant bladder biopsies were also collected for correlation purposes. Histopathologic diagnosis was taken as the gold standard for the evaluation of the overall performance of cytology.

Relevant demographic data were obtained from the requisition form provided with the specimen. Data were entered and analyzed using the Statistical Package for the Social Sciences version 23. Statistical analysis was carried out with calculation of sensitivity and specificity, positive and negative predictive values. Positive urinary cytology (for high-grade urothelial carcinoma) included cases categorized as SHGUC and HGUC. For statistical analysis samples categorized as AUC were also taken as positive. Samples with a histological diagnosis of low-grade lesions were also correlated with cytological findings.

RESULTS

Altogether 104 urine specimens were evaluated during the period of study. The majority of patients were male (64; 61.53%) with a male: female ratio of 1.6:1. The median age was 60 years old (range 28-82). (Table 1)

Cytological diagnoses according to TPS categories were as follows: 2 (1.92%) cases classified as non-diagnostic/ unsatisfactory, 72 (69.23%) as negative for high-grade urothelial carcinoma, 6 (5.76%) as atypical urothelial cells, 6 (5.76%) as suspicious for high-grade urothelial carcinoma and 14 (13.46%) as positive for high-grade urothelial carcinoma and 4 (3.84%) as low-grade urothelial lesions.

Histological specimens were available for 38 (36.8%) cases. Histological diagnoses from biopsies were as follows: 12 (31.57%) benign urothelial tissue, 21 (55.26%) as high-grade urothelial carcinoma, 5 (13.15%) as low-grade papillary urothelial carcinoma.

DOI: 10.3126/jpn.v12i1.41443

Table 2: Correlation between urine cytology and histopathology

Historical diagnosis	Cytological diagnosis (TPS categories)						
	Non-diagnostic	NHGUC	AUC	SHGUC	LGUN	HGUC	Total (n=38,100%0
Benign urothelial tissue	1	8	1	0	1	1	12 (31.57%)
LGUN	0	2	1	0	2	0	5 (13.15%)
HGUC	0	1	4	5	1	10	21 (55.26%)

A cyto-histological correlation was performed for 38 cases (Table 2). For high-grade urothelial carcinoma, when considering HGUC, SHGUC, and AUC as positive cytology for histological correlation purposes, a total agreement between cytological diagnosis and histology was achieved in 19 out of 21 cases (90.47%). Disparity occurred in 5 cases (3 false-positive and 2 false negatives), with an overall sensitivity and specificity of 90.48% and 82.35% respectively. PPV was 86.37% and NPV was 87.5%. For the three false-positive cases, a meticulous review of both cytological and histological slides was performed. Cytology showed marked nuclear atypia favoring a diagnosis of HGUC however histological features showed normal urothelial mucosa only. For the two false-negative cases, smears were sparsely cellular hence no obvious atypical cells could be identified.

For low-grade urothelial carcinoma, a total agreement between cytological diagnosis and histology was achieved in 2 out of five(40%) cases. Sensitivity, specificity, PPV, and NPV were calculated as 40%, 93.9%, 50%, and 91.18% respectively for the low-grade lesion.

DISCUSSION

Urinary tract cytology is the most commonly used test for screening and monitoring of urothelial carcinomas. It is an accurate test for the detection of urothelial malignancy especially HGUC, which has the potential for invasion, metastasis, and an aggressive course.[1,2] Introduction of TPS has led to standardized reporting of urinary cytology.[14] In our context the utility of TPS has not been studied and reporting of urinary cytology is still based on the conventional method in most of the institutes and is highly subjective. We evaluated the utility of TPS for diagnosing high and low-grade urothelial carcinoma and correlated it with histopathologic diagnosis. In our study, the frequency of each diagnostic TPS category was comparable to other studies. Non-diagnostic samples were low compared to other studies. This might be because many of our samples were bladder washing and hence yielded high cellularity and were less contaminated with non-urothelial cells.[14-16]

As per TPS, the percentage of cases diagnosed as HGUC varied widely from 2.7% to 35% in various studies.[17-19] In our study the frequency of cases diagnosed as HGUC was 13.46% and SHGUC was 5.76%. The percentage of HGUC and SHGUC was significantly lower in the study done by de Paula et al who reported 2.7% of cases to be HGUC and SHGUC each. Their study included a larger sample size of 1660 urine specimens as compared to a small sample size in ours. As reported in their study and several others, we did not have major diagnostic difficulties for categorizing HGUC and SHGUC as the smears were cellular with prominent nuclear atypia.[15-17]

The frequency of the AUC category was relatively low in our study as compared to several studies done in India.[18,19] While labeling cases as AUC, we stuck to the strict criteria as described in TPS which might have decreased their proportion. Moreover, many studies have shown that the application of the TPS has decreased the number of cases signed out as AUC as compared to the conventional system.[20,21] In our study, only four cases (3.84%) qualified as LGUN on cytology. In the study done by Rai et al, 5.6% of cases were signed off as LGUN while Jamwal et al did not find any cases of LGUN.[18,19]

Histopathologic specimens were available in 36.53% cases of the total cytological specimens included in the study. When considering only high-grade lesion as positive for cyto-histological correlation, sensitivity and specificity of cytology was 90.48% and 82.35% respectively and a PPV and NPV of 86.37% and 87.5% respectively. The sensitivity and specificity of urine cytology range from 20 to 97.3% and 74-99.5% respectively in various studies.[1,17,22,23] Our study shows high sensitivity and specificity of urine cytology for detecting HGUC as compared to other studies. Our sensitivity and specificity have increased significantly as we included HGUC, SHGUC, and AUC category as positive cytology for high-grade urothelial carcinoma as opposed to other studies where they have taken only HGUC and SHGUC as positive cytology. Three cases in which we reported positive on cytology however showed normal urothelial tissue on histology. On review of these three cases, we found convincing nuclear atypia to qualify as HGUC despite having negative histology. Cases with negative biopsy with a positive cytology sample do not always indicate a false-positive diagnosis, as urine cytology detects carcinoma in situ and allows sampling of the entire urinary tract thus detecting malignancy from the upper urinary tract as well; cystoscopy may remain negative in these situations. On the other hand, the reasons for false-positive cytology includes reactive atypia due to inflammation, intravesical calculi, and chemotherapy.[24] In our cases, no clinical features or cystoscopic findings of calculi, inflammation, and chemotherapy were present. Hence, the patients were advised for a close follow-up in suspicion of an occult

DOI: 10.3126/jpn.v12i1.41443

urothelial malignancy.

TPS is not very useful in the diagnosis of LGUN. When low-grade urothelial carcinomas were considered as a positive histological diagnosis, the sensitivity dropped down to 40% only. Five cases were diagnosed as low-grade urothelial neoplasm on histology. Of these five cases two were reported as negative and one as AUC due to presence of mild nuclear atypia which was likely due to regenerative changes as seen on histology. Low-grade papillary urothelial neoplasms do not demonstrate notable atypia and make it difficult to diagnose on cytologic grounds. Besides, the criteria for detecting LGUN are strict as per TPS and requires visualization of unequivocal fibrovascular cores, which we did not encounter in our two false-negative cases for LGUN.[6,17]

The present study highlights the role of TPS in the diagnosis of high-grade urothelial carcinoma while its utility for the low-grade lesion is limited. The major drawback of our study is the inclusion of a small number of cases over a short period. The inclusion of a larger number of cases and a longer follow-up period could provide a clearer picture regarding the utility of TPS in routine practice.

CONCLUSIONS

Urine cytology reported as per TPS has a high sensitivity for detecting high-grade urothelial carcinoma. However, sensitivity for detecting low-grade urothelial neoplasm is low.

Conflict of interests: None

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