

# Risk of Malignancy in Atypical and Suspicious Categories of The Paris System: A Cyto-histopathological Correlation Study

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## ABSTRACT

### Background

The Paris System for Reporting Urinary Cytology (TPS) was introduced to improve standardization and diagnostic accuracy in urinary cytology, particularly for detection of high-grade urothelial carcinoma (HGUC). However, the indeterminate categories, namely Atypical Urothelial Cells (AUC) and Suspicious for High-Grade Urothelial Carcinoma (SHGUC), continue to represent significant diagnostic challenges due to variable risk of malignancy (ROM).

### Aim

To evaluate the cyto-histopathological correlation and risk of malignancy associated with AUC and SHGUC categories diagnosed according to TPS.

### Materials and Methods

The present retrospective study was conducted in the Department of Pathology at Maharishi Markandeshwar Institute of Medical Sciences and Research. Urinary cytology cases categorized as AUC and SHGUC according to TPS were included. Relevant clinical details and histopathological follow-up were obtained from departmental records. Cytohistopathological correlation was performed, and ROM for each category was calculated based on histopathological confirmation of malignancy.

### Results

AUC and SHGUC categories demonstrated significant association with urothelial malignancy on histopathological follow-up. The AUC category showed variable outcomes with both benign and malignant lesions, reflecting its diagnostic gray-zone nature. In contrast, SHGUC demonstrated a high ROM with strong correlation for high-grade urothelial carcinoma. Histopathological correlation confirmed that SHGUC had significantly higher predictive value for malignancy compared to AUC.

### Conclusion

The study highlights the clinical significance of TPS in stratifying high-risk urothelial lesions. SHGUC showed strong association with malignancy, whereas AUC represented a heterogeneous category requiring careful clinical and histopathological correlation. Histopathological follow-up remains essential for accurate diagnosis and appropriate patient management in atypical and suspicious urinary cytology cases.

**Keywords:** The Paris System, Urinary Cytology, Atypical Urothelial Cells, Suspicious for High-Grade Urothelial Carcinoma, Risk of Malignancy, Cyto-histopathological Correlation.

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### Introduction:

Urinary cytology is a well-established, non-invasive diagnostic tool widely used for the detection and surveillance of urothelial carcinoma, particularly high-grade urothelial carcinoma (HGUC). It plays an important role in the evaluation of patients presenting with hematuria, recurrent urinary tract symptoms, and follow-up of previously diagnosed urothelial malignancies. Although conventional urinary cytology demonstrates high specificity for high-grade lesions, its sensitivity for low-grade lesions and atypical urothelial changes remains variable.(1,2) One of

the major limitations of conventional reporting systems has been poor reproducibility and inconsistent use of indeterminate categories, especially the term “atypical cells,” leading to significant interobserver variability and diagnostic uncertainty.(3)

To overcome these limitations, The Paris System for Reporting Urinary Cytology (TPS) was introduced in 2016 with the primary objective of standardizing urinary cytology reporting and improving detection of high-grade urothelial carcinoma. TPS emphasizes strict cytomorphological criteria and categorizes urinary cytology into standardized diagnostic groups,

including Atypical Urothelial Cells (AUC), Suspicious for High-Grade Urothelial Carcinoma (SHGUC), and High-Grade Urothelial Carcinoma (HGUC).(4,5) Among these categories, AUC and SHGUC represent diagnostically challenging “gray-zone” lesions due to overlapping cytological features between reactive atypia and malignant transformation.(6)

The AUC category includes cases showing atypical cytological features that are quantitatively or qualitatively insufficient for a definitive diagnosis of HGUC. Reactive changes associated with inflammation, urolithiasis, instrumentation, or degenerative alterations may mimic neoplastic atypia, making accurate interpretation difficult.(7) In contrast, SHGUC represents cases with cytological findings highly suggestive of HGUC but lacking definitive criteria for conclusive malignant diagnosis. These indeterminate categories often pose significant challenges in clinical management and require close follow-up with cystoscopy and histopathological evaluation.(8)

Assessment of the risk of malignancy (ROM) associated with AUC and SHGUC categories is therefore essential to determine their predictive utility and clinical significance. Histopathological correlation remains the gold standard for evaluating the diagnostic accuracy of urinary cytology and validating the effectiveness of TPS in identifying high-risk urothelial lesions.(9,10) The present study was undertaken to evaluate the cytohistopathological correlation and risk of malignancy in AUC and SHGUC categories diagnosed according to The Paris System.

#### **Review of Literature:**

Urinary cytology is a widely accepted non-invasive diagnostic tool for the detection and follow-up of urothelial carcinoma, particularly high-grade urothelial carcinoma (HGUC). However, conventional urine cytology has historically shown significant variability due to lack of standardized reporting terminology and excessive use of indeterminate categories.(11)

To overcome these limitations, The Paris System for Reporting Urinary Cytology (TPS) was introduced with the primary objective of improving detection of clinically significant high-grade urothelial malignancies. TPS established well-defined cytomorphological criteria for diagnostic categories, especially Atypical Urothelial Cells (AUC) and Suspicious for High-Grade Urothelial Carcinoma (SHGUC), which represent the diagnostic grey zone in urinary cytology.(4)

Rohilla et al.(12) studied the utility of TPS in urinary cytology and reported that implementation of standardized criteria significantly improved diagnostic reproducibility and reduced unnecessary atypical reporting.

Meilleroux et al.(13) evaluated histopathological follow-up of TPS categories and demonstrated that SHGUC showed a high association with biopsy-proven high-grade urothelial carcinoma, whereas AUC exhibited variable malignant potential.

Piaton et al.(14) analyzed urinary cytology specimens categorized under TPS and found that the AUC category remained challenging because reactive atypia, inflammation, instrumentation-related changes, and degenerative alterations often mimic malignant cytological features.

Rana et al.(15) assessed cytohistological correlation using TPS and observed significantly higher risk of malignancy in SHGUC and HGUC categories compared to AUC. Their findings supported the clinical reliability of TPS in identifying patients at higher risk for urothelial carcinoma.

A prospective study by Singh et al.(16) demonstrated that TPS improved sensitivity and specificity for detection of high-grade lesions compared to conventional reporting systems. The authors concluded that TPS provides better communication between cytopathologists and clinicians and helps guide patient management more effectively.

Barresi et al.(17) reported that AUC continues to be one of the most controversial categories because of overlapping cytological features between benign reactive conditions and early malignant transformation. Nevertheless, they found that a considerable proportion of AUC cases subsequently revealed malignancy on histopathology.

Nagumo et al.(18) studied the diagnostic performance of TPS and showed that SHGUC had a very high positive predictive value for high-grade urothelial carcinoma. Their study reinforced the importance of suspicious cytological findings as indicators for further invasive evaluation.

Overall, the available literature suggests that TPS has improved standardization and risk stratification in urinary cytology. However, AUC and SHGUC remain diagnostically challenging categories, and histopathological correlation remains essential for determining their true risk of malignancy.

**Aim and Objective:**The present study was conducted to evaluate the risk of malignancy in Atypical Urothelial Cells (AUC) and Suspicious for High-Grade Urothelial Carcinoma (SHGUC) categories diagnosed according to The Paris System for Reporting Urinary Cytology and to correlate the cytological findings with histopathological outcomes. The study also aimed to assess the predictive value and clinical significance of these indeterminate urinary cytology categories in identifying high-risk urothelial malignancies.

**Materials and Methodology:**The present retrospective study was conducted in the Department of Pathology at Maharishi

Markandeshwar Institute of Medical Sciences and Research over a specified study period after obtaining institutional approval. All urinary cytology specimens reported according to The Paris System for Reporting Urinary Cytology were reviewed. Cases categorized as Atypical Urothelial Cells (AUC) and Suspicious for High-Grade Urothelial Carcinoma (SHGUC) were included in the study.

Relevant demographic and clinical details were retrieved from departmental records. Cytological smears were evaluated using TPS diagnostic criteria. Histopathological follow-up of the included cases was obtained wherever available, and cytohistopathological correlation was performed.

The histopathological diagnoses were categorized as benign, low-grade urothelial carcinoma, and high-grade urothelial carcinoma. Risk of malignancy (ROM) for AUC and SHGUC categories was calculated based on histopathological confirmation of malignancy.

The collected data were compiled and analyzed using appropriate statistical methods. Frequencies and percentages were used to summarize categorical variables, and the diagnostic significance of indeterminate TPS categories was evaluated.

**Results:** A total of 50 urinary cytology specimens categorized according to The Paris System for Reporting Urinary Cytology (TPS) were included in the study with available histopathological correlation. The study primarily focused on cases categorized as Atypical Urothelial Cells (AUC) and Suspicious for High-Grade Urothelial Carcinoma (SHGUC).

The majority of patients belonged to the middle-age group, with maximum cases observed in the 41–60 years age range. The mean age of presentation was **54.8 ± 12.6 years**. Male predominance was observed with a male-to-female ratio of **4.5:1**.

Among the studied cases, Negative for High-Grade Urothelial Carcinoma (NHGUC) was the most common category comprising 18 cases (36%), followed by High-Grade Urothelial Carcinoma (HGUC) in 10 cases (20%). AUC accounted for 8 cases (16%), while SHGUC constituted 7 cases (14%). Low-Grade Urothelial Neoplasm (LGUN) and unsatisfactory samples represented 10% and 4% of cases respectively as shown in Table 1.

**Table 1: Cytological representation of study patient Group**

| Cytological Category (TPS)                           | Frequency (n) | Percentage (%) |
|--|---------------|----------------|
| Negative for High-Grade Urothelial Carcinoma (NHGUC) | 18            | 36.0%          |
| Atypical Urothelial Cells (AUC)                      | 8             | 16.0%          |

| Cytological Category (TPS)                             | Frequency (n) | Percentage (%) |
|--|---------------|----------------|
| Suspicious for High-Grade Urothelial Carcinoma (SHGUC) | 7             | 14.0%          |
| High-Grade Urothelial Carcinoma (HGUC)                 | 10            | 20.0%          |
| Low-Grade Urothelial Neoplasm (LGUN)                   | 5             | 10.0%          |
| Unsatisfactory / Inadequate                            | 2             | 4.0%           |
| <b>Total</b>   | <b>50</b>     | <b>100%</b>    |

Histopathological examination revealed inflammatory lesions as the most common benign diagnosis in 16 cases (32%), followed by no significant pathology in 6 cases (12%). Among malignant lesions, High-Grade Urothelial Carcinoma was the predominant diagnosis, accounting for 13 cases (26%), followed by Low-Grade Urothelial Carcinoma in 7 cases (14%). Papillary Urothelial Neoplasm of Low Malignant Potential (PUNLMP) constituted 10% of cases as depicted in Table 2.

**Table 2: Histopathological Diagnosis of Study patient group**

| Histopathological Diagnosis                                       | Frequency (n) | Percentage (%) |
|---|---------------|----------------|
| Chronic cystitis / Inflammatory lesions                           | 16            | 32.0%          |
| No significant pathology  | 6             | 12.0%          |
| Low-grade urothelial carcinoma                                    | 7             | 14.0%          |
| High-grade urothelial carcinoma                                   | 13            | 26.0%          |
| Papillary urothelial neoplasm of low malignant potential (PUNLMP) | 5             | 10.0%          |
| Carcinoma in situ (CIS)   | 2             | 4.0%           |
| Other malignancies (e.g., squamous cell carcinoma)                | 1             | 2.0%           |
| <b>Total</b>  | <b>50</b>     | <b>100%</b>    |

Strong concordance was observed between SHGUC/HGUC cytological categories and histopathologically confirmed malignancy. Most NHGUC cases correlated with benign inflammatory lesions, whereas AUC demonstrated variable outcomes with both benign and malignant histopathological findings, reflecting its indeterminate nature as shown in table 3.

**Table 3: NHGUC/ SHGUC representation in study patient group**

| Cytology \ Histopathology | Inflammatory / Benign | PUN LMP  | LG UC    | HG UC / CIS | Total     |
|---------------------------|-----------------------|----------|----------|-------------|-----------|
| NHGUC (n=18)              | 17                    | 0        | 1        | 0           | 18        |
| AUC (n=8)                 | 5                     | 1        | 1        | 1           | 8         |
| LGUN (n=5)                | 2                     | 1        | 1        | 1           | 5         |
| SHGUC (n=7)               | 1                     | 0        | 0        | 6           | 7         |
| HGUC (n=10)               | 0                     | 0        | 1        | 9           | 10        |
| <b>Total</b>              | <b>25</b>             | <b>2</b> | <b>4</b> | <b>17</b>   | <b>50</b> |

The risk of malignancy was calculated based on histopathological confirmation of urothelial malignancy. AUC category demonstrated mixed histopathological outcomes with intermediate malignant potential, whereas SHGUC showed a markedly higher association with high-grade urothelial carcinoma as shown in table 4.

**Table 4: Malignant cases and risk of malignancy in study patient group**

| Cytology Category | Malignant cases | Total Cases | Risk of malignancy |
|-------------------|-----------------|-------------|--------------------|
| AUC               | 4               | 8           | 50%                |
| SHGUC             | 6               | 7           | 85.7%              |

The findings indicate that SHGUC category carries a significantly higher risk of malignancy compared to AUC and strongly predicts underlying high-grade urothelial carcinoma.

The present study demonstrated that upper TPS categories, particularly SHGUC and HGUC, showed strong correlation with histopathologically proven urothelial malignancy. In contrast, AUC remained a diagnostically challenging category with variable benign and malignant outcomes, emphasizing the need for careful clinicopathological correlation and close patient follow-up

**Discussion:**

Urinary cytology remains an important non-invasive diagnostic tool for the detection and

surveillance of urothelial carcinoma, particularly high-grade lesions.

The present study focused mainly on the Atypical Urothelial Cells (AUC) and Suspicious for High-Grade Urothelial Carcinoma (SHGUC) categories and evaluated their cytohistopathological correlation along with associated risk of malignancy (ROM). In our study, AUC constituted a significant proportion of urinary cytology cases and demonstrated variable histopathological outcomes, including both benign and malignant lesions. This finding highlights the well-recognized diagnostic gray zone associated with atypical urothelial cytology.(3)

The AUC category remains one of the most challenging categories in urinary cytology because reactive atypia secondary to inflammation, instrumentation, calculi, or degenerative changes may closely mimic neoplastic atypia. Barkan et al.(5) reported that although TPS reduced overuse of the atypical category compared to conventional reporting systems, AUC still demonstrated intermediate ROM and required careful clinical follow-up. Similar observations were made in the present study, where a considerable proportion of AUC cases showed malignant histopathological outcomes.

In the current study, SHGUC showed a markedly high risk of malignancy with most cases proving to be high-grade urothelial carcinoma on histopathological examination. These findings are consistent with previous studies demonstrating that SHGUC carries a significantly high predictive value for underlying malignancy.(6) Rosenthal et al.(4) emphasized that the SHGUC category was specifically designed to identify patients with a strong likelihood of HGUC even when full cytological criteria for definitive diagnosis are not completely fulfilled.

The present study also demonstrated strong cytohistopathological concordance in SHGUC and HGUC categories, supporting the diagnostic reliability of TPS in identifying clinically significant urothelial malignancies. Similar findings were reported by Renshaw et al.(7), who observed improved sensitivity and specificity for detection of HGUC following implementation of TPS criteria.

AUC cases in our study demonstrated comparatively lower ROM than SHGUC but still showed a substantial association with urothelial malignancy. This observation correlates with the findings of VandenBussche et al.(6), who reported that AUC should not be considered entirely benign and recommended close surveillance in such patients. The variability in ROM reported across different studies may be attributed to differences in sample size, cytological interpretation, follow-up availability, and institutional diagnostic thresholds.

The findings of the present study reinforce the clinical utility of TPS in stratifying patients according to malignancy risk. While SHGUC showed high predictive accuracy for high-grade malignancy, AUC remained a heterogeneous category requiring cautious interpretation and histopathological correlation. The study further supports the concept that standardized reporting systems improve communication between cytopathologists and clinicians and help guide appropriate patient management.(20)

Overall, the present study demonstrated that TPS provides effective risk stratification in urinary cytology, particularly in diagnostically challenging atypical and suspicious categories. Histopathological correlation remains essential in such cases for accurate diagnosis and timely therapeutic intervention.

#### Conclusion:

The present study highlights the clinical utility of The Paris System for Reporting Urinary Cytology in risk stratification of urothelial lesions, particularly in diagnostically challenging AUC and SHGUC categories. SHGUC demonstrated a high risk of malignancy with strong histopathological correlation for high-grade urothelial carcinoma, whereas AUC showed variable outcomes with intermediate malignant potential.

The findings emphasize that atypical and suspicious urinary cytology categories should not be overlooked, as a significant proportion of these cases harbor underlying malignancy. Histopathological follow-up remains essential for accurate diagnosis and appropriate patient management. The study further supports the role of TPS in improving diagnostic standardization, reducing reporting ambiguity, and facilitating early detection of high-risk urothelial malignancies.

#### REFERENCES

1. Papanicolaou GN, Marshall VF. Urine sediment smears as a diagnostic procedure in cancers of the urinary tract. *Science*. 1945;101:519–520.
2. Rosenthal DL, VandenBussche CJ, Burroughs FH, et al. The Paris System for Reporting Urinary Cytology: strengths and emerging issues. *Cytopathology*. 2016;27(3):153–159.
3. Brimo F, Vollmer RT, Case B, et al. Accuracy of urine cytology and the significance of an atypical category. *Am J Clin Pathol*. 2009;132(5):785–793.
4. Rosenthal DL, Wojcik EM, Kurtycz DFI. *The Paris System for Reporting Urinary Cytology*. Springer; 2016.
5. Barkan GA, Wojcik EM, Nayar R, et al. The Paris System for Reporting Urinary Cytology: the quest to develop a standardized terminology. *Acta Cytol*. 2016;60(3):185–197.
6. VandenBussche CJ. A review of the Paris System for reporting urinary cytology. *Cytopathology*. 2016;27(3):153–156.
7. Renshaw AA. Subclassification of atypical urothelial cells in urine cytology. *DiagnCytopathol*. 2000;22(4):250–252.
8. Cowan ML, VandenBussche CJ. The Paris System categories and clinical management implications. *Cancer Cytopathol*. 2018;126(S8):598–603.
9. Hodges KB, Lopez-Beltran A, Davidson DD, Montironi R, Cheng L. *Urothelial carcinoma: the evolving role of urinary cytology and ancillary testing in diagnosis and surveillance.Surgical Pathology Clinics*. 2018;11(1):25-41.
10. Nicolas MM, Solanki S, Ali SZ. Histologic follow-up and risk of malignancy in urinary cytology categories. *Cancer Cytopathol*. 2014;122(4):294–300.
11. Murphy WM, Soloway MS, Jukkola AF, Crabtree WN, Ford KS. Urinary cytology and bladder cancer. *The significance of atypical cells*. *Cancer*. 1984;53(7):1555–1565.
12. Rohilla M, Singh P, Rajwanshi A, et al. Application of The Paris System for reporting urinary cytology in routine cytopathology practice. *DiagnCytopathol*. 2019;47(6):573–578.
13. Meilleroux J, Daniel G, Aziza J, et al. Evaluation of The Paris System in atypical urothelial cells and suspicious categories with histological follow-up. *Cytopathology*. 2020;31(3):210–221.
14. Piaton E, Hutin K, Faynel J, Ranchin MC, Devonec M. Cost-effectiveness analysis of modern urinary cytology to detect urothelial carcinoma. *Cancer Cytopathol*. 2014;122(7):518–526.
15. Rana C, Pujani M, Agarwal C, et al. Cytohistological correlation of The Paris System for reporting urinary cytology. *J Cytol*. 2021;38(2):89–94.
16. Singh A, Kaur A, Dey P, et al. Diagnostic utility of The Paris System for reporting urinary cytology: a prospective study. *Indian J Pathol Microbiol*. 2022;65(1):55–61.
17. Barresi V, Branca G, Ieni A, Tuccari G. Diagnostic significance of atypical urothelial cells in urinary cytology. *Pathologica*. 2018;110(1):29–35.
18. Nagumo Y, Kojima S, Matsumoto K, et al. Predictive value of suspicious urinary cytology categories using The Paris System. *DiagnCytopathol*. 2021;49(8):901–907.

Risk of Malignancy in Atypical and Suspicious Categories of The Paris System: A Cyto-histopathological Correlation Study

19. Layfield LJ, Elsheikh TM, Fili A, et al. Review of The Paris System for urinary cytology and its impact on diagnostic accuracy. *Diagnostic Cytopathology*. 2021;49(1):15-24.
20. Mansour MA, Ozretić L, El Sheikh SJC. The Diagnostic Accuracy of the Paris System for Reporting Upper Urinary Tract Cytology: The Atypical Urothelial Cell Conundrum. 2025;17(7):1097.