

Implementing the Paris System into Reclassifying Urine Cytology: A Descriptive Analysis

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Abstract: Background: The Paris system (TPS) is an attempt to standardize and validate the terminology used in Urine cytology reporting as it is an essential screening test for HGUC. This study was implemented to reclassify the archived cases at our institution using TPS to find consensus between the two and assess the clinical utility of TPS in classifying equivocal cases with 'Atypia'. Materials and Methods: Archived cases of two years (n=164) were reassessed and classified as per TPS and evaluated for Correlation with Histopathology (wherever available). Results: Category VI and V had good consensus, with 60% PPV for HGUC (Category VI) with histopathology diagnosis. Conclusion: Wide case range and correlation data required for accurate assessment, nevertheless TPS has been a successful tool in correctly classifying the equivocal cases of "Atypia" and HGUC, thus facilitating effective clinical management.

Keywords: The Paris System for Reporting Urine Cytology, TPS, High Grade Urothelial Carcinoma, HGUC, Atypia of Undetermined Significance, AUC

1. Introduction

Urine cytology, a microscopic evaluation of exfoliated cells; is a non invasive potentially useful screening modality for urothelial carcinomas and for surveillance of recurrence. The lack of strong consensus regarding a comprehensible classification system and the wide inter observer variability of cytology diagnoses potentiates the need for a standardized reporting system. Cytological inter observer variability in atypical specimens and the low sensitivity it bears in detecting low grade non - invasive lesions pose a diagnostic dilemma to the pathologist.^{1, 2, 3} To minimize the use of equivocal terminology as "atypical" or "suspicious"; Papanicolaou Society of Cytopathology in 2004 recommended to include 'atypical urothelial cells' as a diagnostic category, with a note to further classify it's cause as reactive or neoplastic. However there is no defined criteria to distinguish the two etiological entity making this category a wastebasket diagnosis.^{4, 5}

The Paris System (TPS) Working Group, in 2013 conceived a standardized platform on which to base cytologic interpretation of urine samples that includes specific diagnostic categories and cytomorphic criteria. The rational of this classification system had collectively improved the seminal paradigm shift and has helped to optimize the impact on patient care.⁶⁻¹¹

In our study we have attempted to reclassify the archived cases based on TPS guidelines and validate the utility and effectiveness of the system by correlating with histopathological data, wherever available.

2. Materials & Methods

The study design was retrospective, two year archived data from 2016 January to December 2017 was considered. All

the consecutive urine cytology cases; within the time frame; reported as Negative, Suspicious, Atypical or Positive for malignancy, were reassessed for their morphology and re - categorized according to TPS. All the slides available for study were well preserved and well stained by Papanicolaou stain.

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 concordance between the original report and these reclassified terminologies were then assessed using multiple statistical tools. Further the correlation of these reclassified cases with the histopathological diagnosis (wherever available only) were considered.

Prior reported cases were considered to be original system and TPS as the comparative system for ease of discussion. Ethical and research committee clearance were obtained for initiating this study.

Statistical Analysis

Categorical variables were reported as counts, relative frequencies and distribution along with Positive predictive values.

3. Results

A total of 164 cases of Urine samples were obtained during the study frame for cytological assessment. The age ranges of the cases were between 36 - 85 years with male predominance (90%). As per the original reporting system, 120cases (73%) were called negative, 27 cases (16.4%) as suspicious, 15 cases (9.1%) as positive and 02cases (1.2%) as papillary neoplasm (Table: 1). Distribution as per TPS

upon reclassification of these 164 cases were - 20 cases (12.1%) as Inadequate, 100 cases (60.9%) as NHGUC, 17 cases (10.3%) as AUC, 10 cases as SHGUC (6.0%), 02 cases as LGUN (1.2%) and 15cases (9.1%) as HGUC (Table: 2). In comparison to the original system, using the TPS resulted in significantly fewer cases being assigned to the AUC cytologic category (16.4% vs 10.3%). However, less cases were diagnosed as negative on cytology (60.9% of cases) using the TPS in comparison to the original system, in which there were 73 % cases which included the unsatisfactory samples as well. In comparison, no change was noted in the rate of HGUC and Papillary urothelial neoplasm using the original system and TPS, both of which showed consensus of 1.2 % and 91.4 % for Category V and VI, respectively.

Table 1: Distribution of original Cytology cases and categories

Original categories	Distribution	Frequency (%)
Negative	120	73 %
Suspicious	27	16.4 %
Positive	15	91.4 %
Papillary neoplasm	02	1.2 %

Table 2: Distribution of reclassified cases as per TPS categories

Reclassified categories (TPS)	Distribution	Frequency (%)
Inadequate	20	12%
NHGUC	100	60.9%
AUC	17	10.3%
SHGUC	10	6%
LGUN	02	1.2%
HGUC	15	91.4%

In our study only 22 cases had histopathological correlation available to calculate the positive predictive value of TPS categories. Biopsy were performed for those cases with strong clinical suspicion of malignancy or where resection was not possible. The cases on histopathology fell into two categories: Low grade and high grade carcinoma. Most of these cases had no deeper muscle biopsy to assess muscular invasion. Distribution of biopsy cases and its cytology categorization done as per TPS is depicted in Table: 3.

Table 3: Distribution on Histopathology and corresponding cytology categorization as per TPS

Histopathology (n=22)	Distribution	Cytology category	
		Cat II	02
Low Grade	09	Cat III	06
		Cat IV	01
		Cat I	01
High Grade	13	Cat IV	03
		Cat VI	09

Table 4: Positive Predictive Value of TPS categories in correlation with Histopathology.

Positive Predictive Value (%)	Cat - III	Cat - IV	Cat - VI
	35	30	60

4. Discussion

The clinical utility of any classification system depends on both its precision (reproducibility) and its diagnostic accuracy. The overall agreement by TPS demonstrated good

precision among NHGUC and HGUC diagnostic categories; an observation similar to the studies by Hassan et al² and Das et al.¹⁷

The current study demonstrates that implementing TPS improved overall performance of urine cytology in several aspects. Most importantly fewer cases were being assigned to the AUC category, an observation comparable to the study by Hassan et al². The terminology a typia was used to describe any cell with high N: C, irrespective of reactive or neoplastic nature. However, TPS considers additional cytologic features such as hyperchromasia, irregular nuclear membranes, or clumpy chromatin pattern to diagnose Atypia.¹³ To limit the diagnosis of AUCs to the strict minimum, it has also been recommended diagnosing cell clusters or tissue fragments as NHGUC provided cytologic atypia is lacking, an approach that we have already been practicing in the past and that is therefore unrelated to the observed change in the rate of “atypia” in our cohort.¹⁵

As per original reporting cases with low grade papillary features were placed under suspicious category or in to the negative category due to morphological overlap between low - grade urothelial carcinoma and reactive changes. Hence there was low sensitivity and low interobserver agreement for diagnosing low - grade urothelial neoplasm.¹⁶ This dilemma is now removed because of the definitive diagnosis of low - grade urothelial carcinoma based on the presence of cellular fragments with fibrovascular cores, with cells displaying a mild degree of atypia.²

One of the limitations of this study is extremely low number of cases available for histopathological correlation and a fairly biased interpretation of the Positive predictive values due to this. Surgical intervention with curative intent on these cases were minimal probably due to advanced patient age or lost to follow up or palliative mode of treatment given to higher stage malignancies. A larger time frame and sample size would have eliminated this confounding factor thus adding more relevance to assess the effectiveness of TPS.

Incorporating the findings of the current study with those of the literature not only indicate that the quantitative criteria proposed in TPS are valid but also point to the fact that the suspicious and positive categories are distinct and should probably not be lumped together at the cytologic and clinical levels.^{2, 12, 18 - 20.}

5. Conclusion

The Paris system of reporting seems to improve the performance of urine cytology by limiting the AUC category to cases that are more strongly associated with HGUC. To keep up the reproducibility in reporting and standardize the analysis in urine cytology implication of this novel system in to routine practice is a must.

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Annexures

(Photographic Plates)

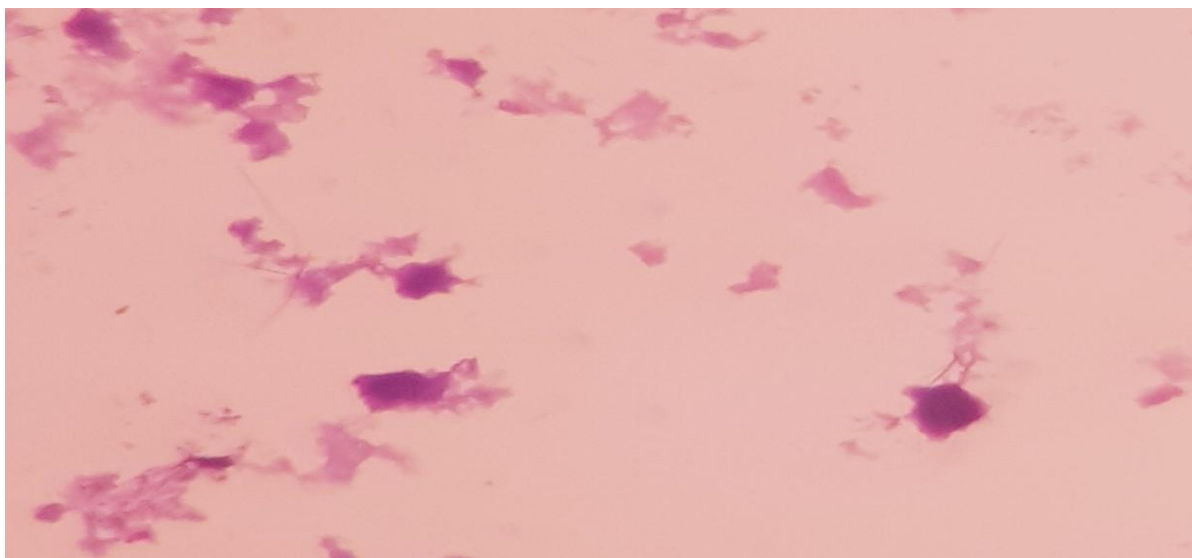


Figure 1: Degenerated cells – Category I

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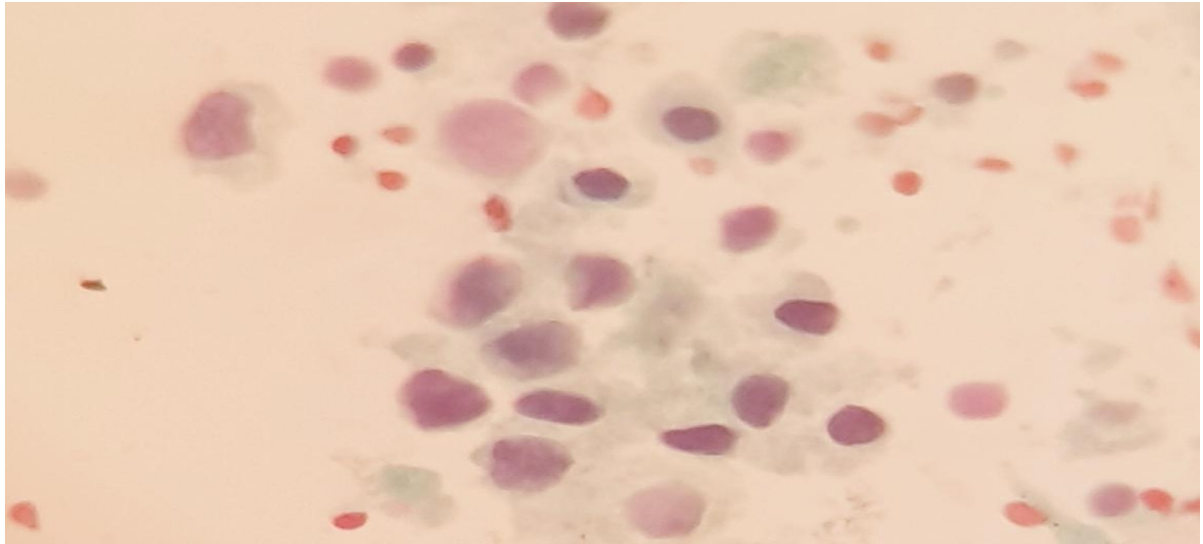


Figure 2: Cells with N: C >0.5 Reactive change –Category II

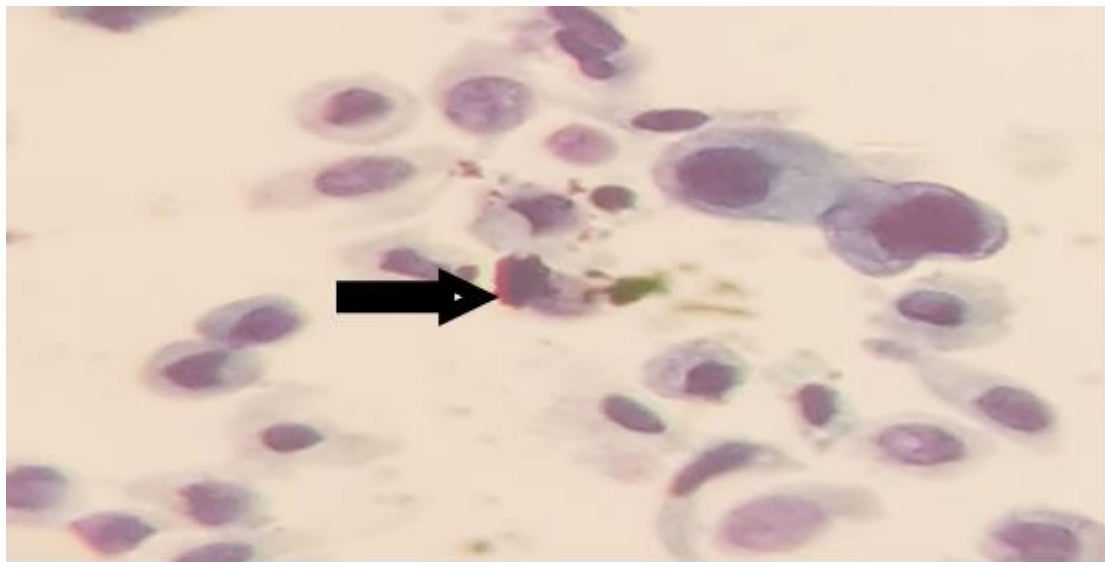


Figure 3: Atypical urothelial cells, (Arrow showing cell in mitosis) –Category III

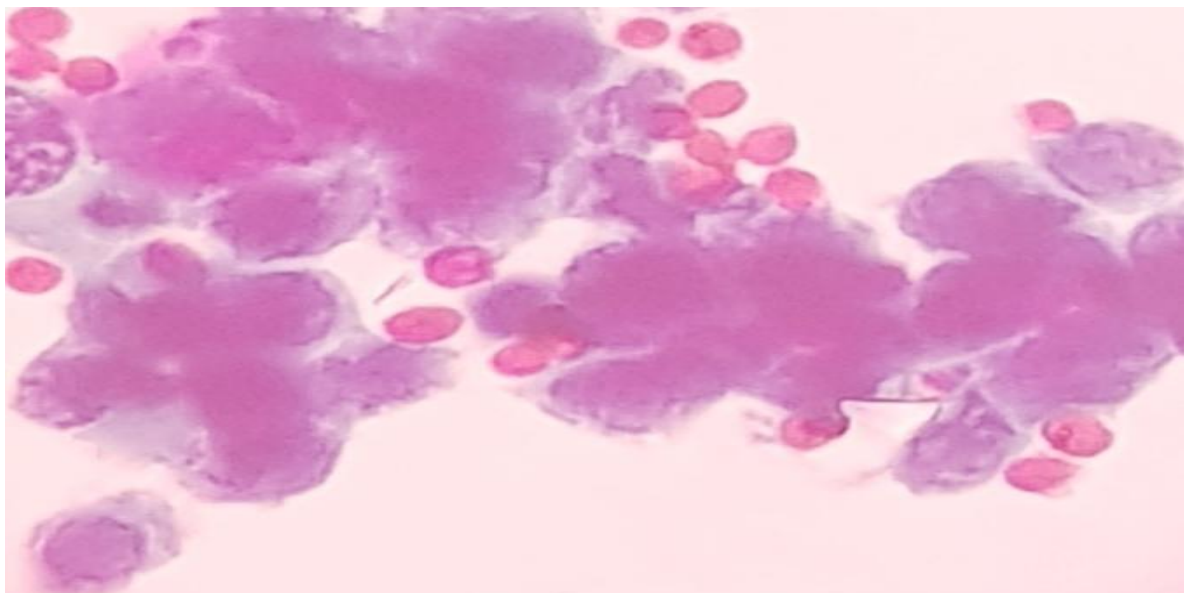


Figure 4: Clusters of atypical cells forming vague Papillary pattern –Category V

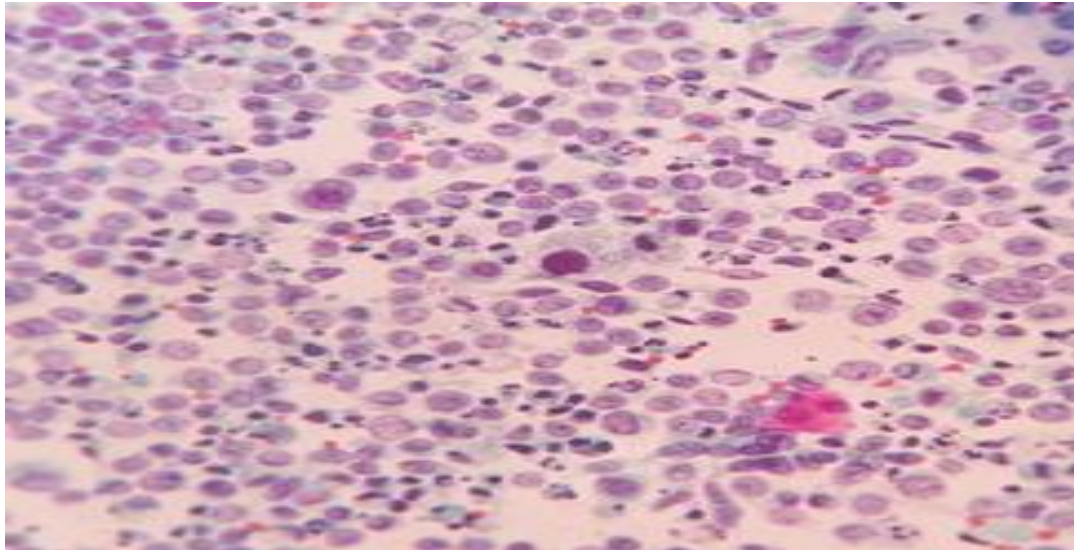


Figure 5: Cellular smears showing degenerated cells admixed with malignant cells –Category VI

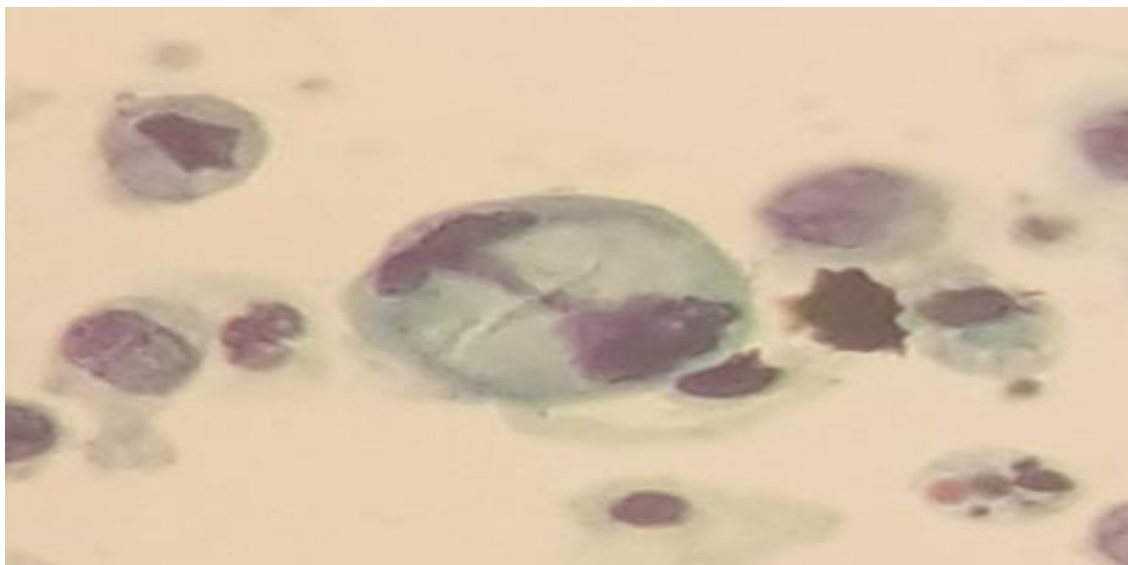


Figure 6: Cell exhibiting mitosis and pleomorphism (HGUC) –Category VI