



Correlation of Urine Cytology for Urothelial Carcinoma as per Paris System with Histopathology

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Abstract

Objectives: This study aims to evaluate the diagnostic accuracy of urine cytology for urothelial carcinomas as per the Paris System and its histopathological correlation.

Methods: A cross-sectional study was conducted over 1 year (July 2018 – June 2019). The study population comprised patients presenting with haematuria/dysuria and had radiological findings suggestive of bladder tumor. Preoperative, early morning, midstream, voided urine samples were collected and processed for three consecutive days. The cytospin smears were stained with Papanicolaou stain and reported as per the Paris system. These results were then correlated with gold standard test i.e. Histopathology of TURBT as per WHO classification 2016⁽⁴⁾. Relevant statistical tests were utilized for data analysis.

Results: 40 cases were studied. According to the reporting criteria of the Paris System, 62.5% cases were positive for malignancy and 37.5% cases were negative for malignancy. On histopathology, 82.5% cases were positive for urothelial carcinoma and 17.5% cases were negative for urothelial carcinoma. The sensitivity of urine cytology was calculated to be 75%, specificity of urine cytology was 87.5% and the positive predictive value was 96%.

Conclusion: Urine Cytology as reported by the Paris System will lead to uniform and unequivocal reporting of urothelial carcinoma.

Introduction

The incidence of bladder cancer is ranked 11th in global cancer statistics and seventh in malignancy for male tumors⁽¹⁾. Among urogenital tumors, it is only second to prostate cancer with significant morbidity and mortality. The presence of neoplastic cells in urine was first described by

Sanders in as early as 1864⁽⁵⁾. However, urinary oncology gained popularity when Papanicolaou and Marshall in 1945 mentioned it in a publication⁽⁵⁾.

Urine cytology has high sensitivity for detection of high grade urothelial carcinoma and thus it compliment 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⁽²⁾.

The main purpose of urine cytology is to detect high grade urothelial carcinoma. With this principle in mind The Paris System (TPS) Working group proposed a standardized reporting system in 2013. It also included specific diagnostic categories and cytomorphological criteria for reliable diagnosis of HGUC. So, In late 2015, the consensus group published their guidelines, known as The Paris System (TPS) for reporting urine cytology.⁽³⁾

Material and Methods

A cross-sectional study was conducted over 1 year (July 2018 – June 2019). The study population comprised patients presenting with haematuria/dysuria and had radiological findings suggestive of bladder tumor. Preoperative, early morning, midstream, voided urine samples were collected and processed for three consecutive days. The cytospin smears were stained with Papanicolaou stain and reported as per the Paris system. These results were then correlated with gold standard test i.e. Histopathology of TURBT as per WHO classification 2016⁽⁴⁾. Test thresholds were selected for cytology and histopathology. Relevant statistical tests were utilized for data analysis.

Selections of thresholds for reporting

Since multiple diagnostic categories were present on cytology as per the Paris System so we used SHGUC (Suspicious for High Grade Urothelial carcinoma) as threshold for considering urine cytology to be positive. Both the categories SHGUC (Suspicious for High Grade Urothelial Carcinoma) and HGUC (High Grade Urothelial carcinoma) had similar cytologic criteria regarding cellular morphology and differed only with respect to variation in cellularity.

The other categories under the Paris System i.e. NHGUC (Negative for High Grade Urothelial

carcinoma), AUC (Atypical Urothelial cells), LGUN (Low Grade Urothelial neoplasm) and Non diagnostic, clearly denotes the absence of morphologically high grade/ malignant cells, hence, in this study these categories are grouped together and considered negative for malignancy, as shown in table no.1.

Table no. 1. Cytology categories as per selected threshold

Urine cytology results	Diagnostic categories as per selected threshold
Positive for Malignancy	<ul style="list-style-type: none"> ▪ Suspicious for High grade carcinoma (SHGUC) ▪ High grade Urothelial Carcinoma (HGUC)
Negative for malignancy	<ul style="list-style-type: none"> ▪ Atypical Urothelial cells(AUC) ▪ Negative for high grade urothelial carcinoma (NHGUC) ▪ Low grade urothelial neoplasm (LGUN) ▪ Non- diagnostic.

The histological condition was assessed whether histological high grade morphology was present or absent. The selection of threshold of high grade in histopathology was according to WHO classification 2016 as shown in table no. 2.

Table no. 2. Diagnostic categories in Histopathology as per selected threshold

Histopathologic results	Diagnostic histopathology categories considered as per threshold
Positive for Urothelial Carcinoma	<ul style="list-style-type: none"> • Infiltrating urothelial carcinoma. • High Grade Papillary Urothelial Carcinoma. • Low Grade Papillary Urothelial Carcinoma.
Negative for Urothelial Carcinoma	<ul style="list-style-type: none"> • Papillary Urothelial Neoplasm of Low Malignant Potential • Inverted Papilloma. • Benign (cystitis, reactive change)

Results

40 cases were studied. According to the reporting criteria of the Paris System, 62.5% cases were positive for malignancy and 37.5% cases were negative for malignancy as in table no. 3. On histopathology, 82.5% cases were positive for urothelial carcinoma and 17.5% cases were

negative for urothelial carcinoma as shown in table no. 4. The sensitivity of urine cytology was calculated to be 75%, specificity of urine cytology was 87.5%, the positive predictive value was 96% as shown in table no. 5.

Table no. 3. Number of cases as per selected threshold for urine cytology.

Categories	No. of cases (n=40)	Percentage
Positive for Malignancy	25	62.5
Negative for Malignancy	15	37.5

Table no. 4. Number of Histopathology cases as per selected threshold

Categories	No. of cases (n=40)	Percentage
Positive for Urothelial Carcinoma	33	82.5
Negative for Urothelial Carcinoma	7	17.5

Table .5. Statistical analysis in this study

Sensitivity	75%
Specificity	87.5%
Positive Predictive Value	96%
Negative Predictive Value	46.6%

Discussion

Urine contains cells that are exfoliated from entire urinary tract. Thus, urine cytology is a non-invasive and inexpensive test for detection of Urothelial Carcinoma compared to histopathology. Over the years, several investigators have published classification schemes for urine cytology and first classification was given by Papanicolaou and Marshall in 1945⁽⁵⁾. Following this Koss gave a classification which was based on 1973 WHO classification of bladder tumors. He very nicely dealt with the problem faced by Papanicolaou on atypical cells and mentioned the morphological changes seen in atypical cells.

More recently in 1984, Murphy and colleagues gave a classification that described Grades of tumors on the basis of morphological changes in tumor cells but he found it difficult to separate low grade lesion from reactive change⁽⁵⁾.

Age and Sex distribution

The mean age for urothelial carcinoma in various studies ranged from 62 to 69 years. In our study also the mean age for UC was found to be 65 years similar to different studies.

In all the studies there has been male preponderance in cases of urothelial carcinoma. In literature, Male to Female ratio ranged from 2-7 :1 and in present study also there is male preponderance with M:F ratio of 4.7 : 1.

Urine Cytology Result

In different studies the percentage of cases diagnosed as HGUC varied widely from 11.1% to 38.8%. In our study we found 35% of cases as HGUC and this finding was similar to observation of Soumitra Das et al⁽⁶⁾.

In literature for category SHGUC, cytologically there has been a wide variation in proportion of cases under this category i.e. from 6% to 27.7% and in present study 27.5% cases were diagnosed under this category which was close to observation of Soumitra Das et al⁽⁶⁾.

Similarly, proportion of cases under category NHGUC ranged from 13.8% to 52.2%. In our study only 12.5% cases were under this category. Such a variation can be explained partially by relatively small sample size.

On cytological examination no case of LGUN was found in our study and in other studies also LGUN was uncommon as shown in table 10. However in one study (Sharada Rai et al⁽⁷⁾) 5.6% of cases were under this category.

Similarly in the literature, cases under AUC category ranged from 11% to 26% and in our study it was 22.5% which is well within this range.

Histopathology Result

In present study LGUC comprised minority of cases i.e. 20%. In different studies LGUC cases ranged from 19.4% to 26.8%. However, for HGUC category Mohannad Hassan et al⁽⁹⁾ and Sharada Rai et al⁽⁷⁾ found the percentage of cases of HGUC on histopathology to be 56% and 40% respectively. Somaye zare et al⁽⁸⁾ and Soumitra

das et al⁽⁶⁾ has relatively lesser number of HGUC cases i.e. 26.3% and 5.5% respectively. In present study number of cases under HGUC comprised 50% of cases which is well within this range. Such a variation may be due to the difference in number of cases and duration of the study.

There has been wide variation in number of cases under infiltrating urothelial carcinoma category. Soumitra Das et al⁽⁶⁾ reported 58.3% of cases under this category. In our study 12.5 % cases were reported under this category whereas Mohannad Hassan et al⁽⁹⁾ and Somaye zare et al⁽⁸⁾ didn't report any case under this category.

Statistical Analysis

The sensitivity of diagnosing UC in literature varies from 70% to 86.9%. In our study the sensitivity was found to be 75%, which was well within this range. Similar observation was seen by Sharada Rai et al⁽⁷⁾.

In our study specificity i.e. 87.5% was found close to Sharada rai et al⁽⁷⁾. In different studies this value ranged from 69.2% to 89.4%.

Various studies found PPV to vary from 62.3% to 87.5%. However, in our study PPV was quite high at 96%. This value shows that there is good chance of detecting HGUC on urine cytology as per TPS. NPV was found to be less at 46.6%, this may be because of small sample size and poor preservation of cells which came out to be negative on cytology (AUC) but positive on histopathology.

Conclusion

Urine cytology as reported by the Paris system will lead to uniform and unequivocal reporting of urothelial carcinoma.

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