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A RETROSPECTIVE STUDY OF URINE CYTOLOGY SAMPLES AS PER THE PARIS SYSTEM

Pathology

P Sengupta	MD Pathology & Nephropathologist, Department of Pathology , Command Hospital (Southern Command) , Pune
Atul Sahai	MD Pathology, Department of Pathology , Military Hospital Kamptee, Nagpur
PS Mishra*	MD Pathology & Oncopathologist, Department of Pathology , Command Hospital (Southern Command) , Pune *Corresponding Author
V Srinivas	MD Pathology & Oncopathologist, HOD & Consultant, Department of Pathology , Command Hospital (Southern Command) , Pune

ABSTRACT

Background: The Paris system (TPS) for reporting urinary cytology was published in 2016 with the goal of standardization of reporting urine cytology. The primary objective of this exercise was early detection of high grade urothelial carcinoma (HGUC).

Materials and methods: A retrospective study was done to classify as per TPS, all urine cytology samples received in the period between 01 Jan 2016 to 31 Dec 2016 at a tertiary care hospital. All preserved slides of urine cytology were retrieved from the archives, reviewed by two experienced pathologists (PSM&PSG) and reclassified into various categories as specified by TPS. Biopsy reports of patients, where available, were compared against the cytology reports.

Results: A total of 432 stained urine cytology smears (prepared from 200 urine samples) of 72 different patients (56 males and 16 females) were studied. A total of 24 samples were categorized as Category I, 159 as Category II, 07 as Category III, 02 as Category IV and 08 as Category VI. There were no cases in category V and VII.

Conclusion: TPS is an objective tool for reporting urine cytology specimens and is particularly useful in identifying HGUC cases. The detection rate of low grade urothelial carcinoma (LGUC) by this system is low, in keeping with findings of similar studies.

KEYWORDS

Urine Cytology; The Paris System; High Grade Urothelial Carcinoma.

Introduction:

Cancer of the bladder stands as the ninth most common cause of cancers worldwide. It is more commonly seen in males, with a male: female ratio of 3:1.[1] Urine cytology is utilized for screening as well as monitoring of cases of urothelial cancers since 1945 when Dr George Papanicolaou first demonstrated its use.[2] He offered 5 various categories for reporting of cases ranging from negative for malignancy to definitely malignant categories. His classification was widely used until recently when studies indicated two divergent classes of urothelial cancers with totally different clinicopathological and molecular findings.[2,3] The LGUC are usually non invasive and have low rate of progression to invasive carcinomas, of the order of 1-5% with low disease related mortality.[1,4] The other set is of HGUC which are invasive, frequently metastatic and have a high mortality rate. The HGUC cases are often found to have mutation of p53 gene in the tumor cells which are usually not seen in LGUC. It was observed that timely detection of these cases can change the course of their management and significantly improve their prognosis. In 2013 a conference was held In Paris which culminated in the formation of an objective system of reporting of urinary cytology, on the lines of The Bethesda System for reporting Cervical Cytology and Thyroid. This new system was named as 'The Paris system for reporting urinary cytopathology' and was published in 2016. TPS has seven different diagnostic categories namely; Category I – Non-diagnostic or Unsatisfactory, Category II - Negative for High Grade Urothelial Carcinoma (NHGUC), Category III – Atypia, Category IV- Suspicious for High Grade Urothelial Carcinoma (SHGUC), Category V- Low Grade Urothelial Neoplasia (LGUN), Category VI - High Grade Urothelial Carcinoma (HGUC) and Category VII of other non-urothelial malignancies both primary and metastatic.

Since the advent of this new reporting system, there has been a paradigm shift in the reporting of urine cytology in most of the western cancer care centres. However, the same enthusiasm has not been seen in most of the South Asian countries and response has been much of skepticism. There is a perceived need to adopt this new method of urine cytology reporting in order to achieve its objectives. In this retrospective descriptive study the authors have attempted to classify as per TPS, all the samples received fof urinary cytology at our hospital in the year 2016.

Objective:

1. To classify all urine cytology samples received in the period between 01 Jan 2016 to 31st Dec 2016 at the Department of Pathology as per the Paris system for reporting urine cytopathology
2. To analyze the spectrum of various categories, and correlating it with biopsy findings, here available, in positive HGUC cases.

Materials and methods:

All preserved smears of urine cytology of the year 2016 (01 Jan to 31 Dec) were retrieved from the archives of the department of pathology. All cases comprised of at least one smear each stained with Giemsa and Pap stains respectively. The slides were reviewed by two experienced pathologists, one of them an oncopathologist (PSM) & other nephropathologist (PSG). All cases were reclassified into various categories as specified by TPS. A total of 432 stained slides (203 urine samples) belonging to 72 different patients were analyzed. 03 urine cytology samples were discarded as the age and other details were not found in the records. Corresponding biopsy reports, where available, of the cases reported as suspicious or positive for HGUC were matched with the cytology findings for verification and corroboration of the cytologic diagnosis. Only 08 patients (07 male & 01 female) for whom urine cytology sample were also sent, had their biopsy reports in the records. The slides were examined using Olympus Microscope model UMDOB3.

Results:

A total of 432 stained slides of 200 samples of 72 different patients (56 males and 16 females) were analyzed.

Table 1: Sex distribution of patients

Male	56
Female	16
Total	72

Statistical analysis:

The mean age of the patients for whom samples were received was 59.4 years, median being 59 years and mode 76 years. For males the mean, median and mode were 60.6, 58.5 and 76 years respectively while for females the mean, median and mode were 55.3, 59 and 47 years respectively.

Table 2 : Mean, median and mode of age of patients

	Male	Female	Combined
Mean	60.5	55.3	59.38

Median	58.5	59	59
Mode	76	47	76

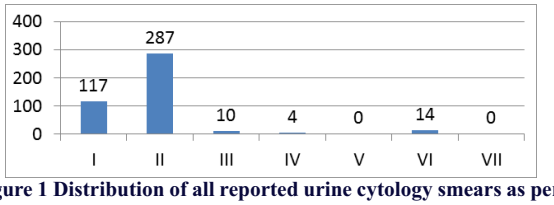

Figure 1 Distribution of all reported urine cytology smears as per TPS (Total = 432).

A total of 24 samples were categorized as Category I, 159 as II, 07 as III, 02 as IV and 08 as VI. There were no cases belonging to categories V and VII. The percentage of category I samples was 12% of total samples. The category of atypia (Category III) also comprised of a small proportion i.e. 3.5% of the total samples submitted for cytology. Category IV cases were only 1%. Category V cases were nil in our study. However the category VI cases were of the order of 4%.

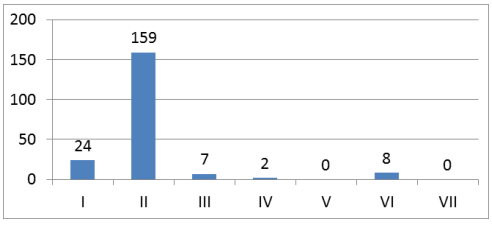

Figure 2 Distribution of samples as per the Paris System urine cytology reporting (n=200)

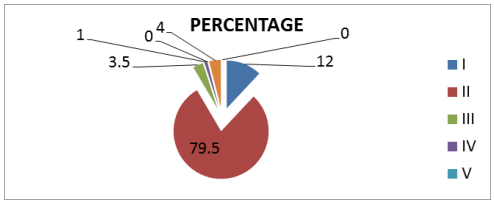

Figure 3 Pie-diagram of distribution of patients as per the Paris system of urine cytology (n=72)

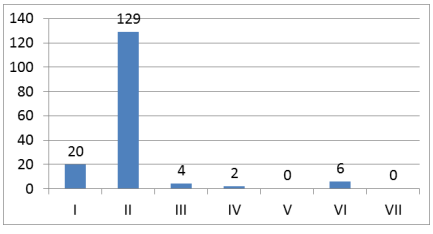

Figure4: Distribution of categories of samples of the male cases as per TPS (n=161)

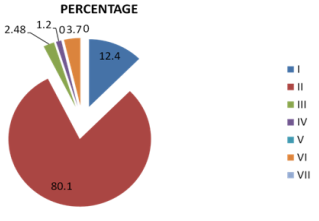

Figure 5: Categories allotted to samples of male patients as a percentage

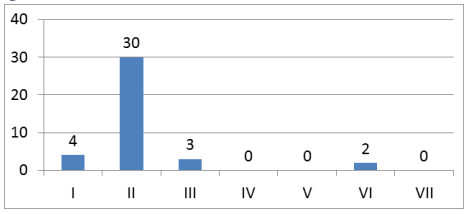

Figure 6 Distribution of categories as per TPS; female patients (n=39)

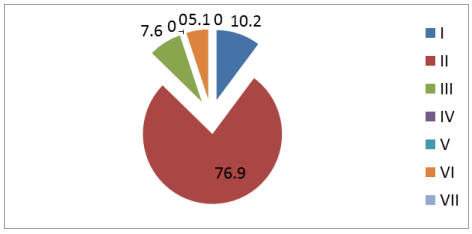

Figure 7 Percentage distribution of categories as per TPS; female patients (n=39

On histopathological correlation of available cases (Total 18); all 07 cases of high grade muscle invasive urothelial carcinoma on tissue diagnosis were also reported as

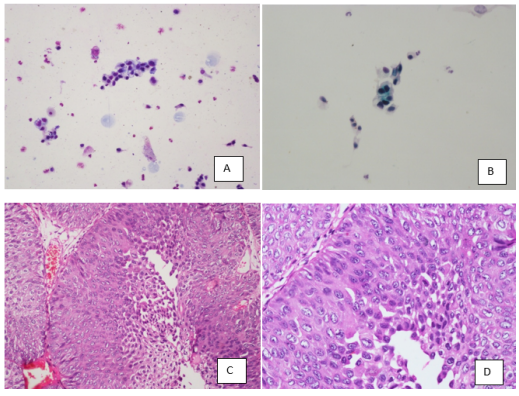

Figure 8:. A&B; 100X Giemsa and Papanicolaou cytological photomicrographs of HGUC. C&D; H&E photomicrograph (100&200X) of HGUC

HGUC: high grade urothelial carcinoma; H: Hematoxylin; E: Eosin.

category IV (suspicious for HGUC or category VI (HGUC) on cytology reporting by TPS. Though, 02 of these cases were reported as LGUC on conventional reporting previously. Of two cases of LGUC on biopsy, categories by TPS were category III and category IV in both cases respectively. Of rest of 09 cases belonging to various benign diagnostic categories, the cytology report by TPS ranged from category I (5 cases), category II (03 cases) and category III (01 case).Previous reports of these cases on cytology were mostly inadequate (07) or atypia (02).

Table 3

TPS Category	Histopathological diagnosis (n=18)	No of cases
I	Benign	5
II	Benign	3
III	LGUC; Benign	1+1
IV	HGUC; LGUC	2+1
V		0
VI	HGUC	5
VII	-	0

Histopathological correlation of cases (n=18)

Efforts to correlate the findings with cystoscopy were inconsistent due to lack of record keeping for cystoscopy reports and loss of some patients on follow up.

Discussion:

Our study is one of the first descriptive retrospective studies of its kind from India which addresses the pressing need of evaluating TPS for urine cytology reporting. Urine cytology remains one of the most widely used non-invasive investigations for the early diagnosis and monitoring of urothelial carcinoma. It is best suited for a resource poor country like ours[1-3].

There was a predominance of males in our study with a sex ratio of 3.5:1 (M: F) consistent with the available literature on urothelial carcinomas. On an average, 6 smears for each patient were examined

totaling to 434 for 72 patients; implying approximately 3 urine samples each for a patient. This is in keeping with widely accepted standard clinical practice followed the world over for suspected urothelial carcinoma cases as well as for the monitoring of proven cases[4]. The average age of patients in our study was 59 years which is consistent with medical literature on urothelial cancers. The average age for the females 53 years while for males it was 60.5 years which again is in line with occurrence of urothelial carcinomas a little earlier in females as described in most of other studies and texts[2,4].

On scrutiny of the cytopathological reports of the urine sample maintained in the departmental archives the authors found that 2 samples were reported as HGUC while one of the cases was reported as suspicious. There were no samples reported as unsatisfactory while in our study, 12 % of the samples were reported as category I. Few of the cat I may have been earlier adequate, however as the sample volume of urine specimen was not known, any sample which failed to demonstrate 10 well visualized preserved urothelial cells was considered inadequate. Few slides were poorly stained/ had air bubbles/ other artifacts for which the authors considered them inadequate in this study.

Maximum number of cases were in the category II, comprising of 79.5% of the total samples which is in accordance with the published literature. The category of atypia (Category III) also comprised a fair proportion, 3.5% of the total samples submitted for cytology. However it was within the limits as noted in various other studies. A rate of atypia ranging from 1.9-23.2% has been recorded by various institutions.[6] Urine cytology is a widely accepted method for follow up of high grade urothelial lesions, however it can be combined with other ancillary investigations like fluorescent in-situ hybridization (FISH) to increase its sensitivity especially for Category III cases.[2,8] Category IV cases were only 1% in our study and it was noted that once malignant cells were evident they usually were numerous in a particular sample. Category V cases were nil in our study, with none of the examined samples revealing papillae with fibro vascular cores, again stressing the low rate of detection of LGUC on urinary cytology which is in conformity with the available literature.[2,7] However the category VI cases were of the order of 4% which correlates well with the detection of HGUC on voided urinary samples, making it an efficient and inexpensive tool for detection and follow up of patients which are likely to progress to invasive urothelial carcinomas. Esposti et. al. reported recognition of 68% cases of urothelial cancers from bladder washings and voided urine cytology samples.[2] Out of the total biopsied cases 4/18 were reported as HGUC , contributing to 22.22 % of the total while LGUC were 9/18 contributing to 50% of the total. In the event that only cases of urothelial carcinomas are considered, a total of 13 cases, HGUC comprised of 30.8 % while the majority were low grade comprising of 69.2% which is in accordance with the available literature.[7]

Category VII was not allotted to any of the samples, again corroborating with the findings in other studies that other non urothelial primary malignancies of the bladder comprise less than 5 % of all malignancies of the organ. [2] Cancers of the cervix, rectum and prostate can secondarily , however, involve bladder in advanced stages.[8]

For the cases with histopathological reports available, a lower rate of cat II cases (5.3%) was observed; while a higher no. of cat III (7.1%) and category VI (10.71%) cases points towards relatively higher sensitivity and specificity of urine cytology for detection of HGUC. Also noted was a higher rate of cat I cases, more than double, 25% for biopsy cases as compared to 12% for total cases, which again stresses the importance of reporting unsatisfactory /inadequate samples when necessary, because cases with HGUC may be having more obscuring features in the form of hemorrhage/ concomitant urinary tract infection with presence of RBCs / pus cells etc.[9]

Conclusion:

TPS is an objective tool in urine cytology for identification of HGUC cases. Its usefulness as both screening and monitoring tool has been well established. The detection rate of low grade urothelial carcinoma (LGUC) by this system is relatively low, in keeping with findings of similar studies. Reporting of inadequate or category I cases is important to optimize the efficacy of this system. Lastly, clinical laboratories need to validate their own urine cytology findings by rigorously employing TPS.

Conflicts of interest: The authors have no conflict of interests to disclose.

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