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Original Research Paper

Pathology

UTILITY OF THE PARIS SYSTEM OF URINE CYTOLOGY REPORTING: A GENERAL POPULATION CONTEXT

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ABSTRACT

BACKGROUND: The Paris system (TPS) for reporting urinary cytology is an exercise by experts in the field of urinary system pathology to streamline reporting of urine cytology smears on the lines of cervical cytology reporting system. The primary aim of our study was to find out cases of high-grade urothelial carcinoma (HGUC) using TPS in a general population.

MATERIALS AND METHODS: A retrospective study was done to classify as per TPS, all urine cytology smears prepared for various cases of suspected malignancy in the period between 01 Jan 2017 to 31 Mar 2019 at a tertiary care centre in India. All slide smears were reviewed by two experienced pathologists and reclassified into various categories as specified by TPS. Histopathology/biopsy reports, where available, were corroborated for correlation with final cytology reports.

RESULTS: A total of 661 Geimsa and PAP stained urine cytology smears from 121 patients (91 males and 30 females) were studied. A total of 11 cases were categorized as Category I, 88 as Category II, 03 as Category III, 09 as Category IV ,06 in category V and 04 as Category VI. There were no cases in category VII.

CONCLUSION: Consolidating on previous data from our published study the authors further highlight that TPS is an effective and objective tool for reporting urine cytology specimens and is recommended for early detection of HGUC cases. The detection rate of low-grade urothelial carcinoma (LGUC) by this system is low, in keeping with findings of other studies on this subject.

KEYWORDS : Urine Cytology, High Grade Urothelial Carcinoma, The Paris System

INTRODUCTION:

Urinary bladder carcinoma is one of the commonest malignancies in the western world with the United States of America (USA) reporting nearly 68000 new cases per year. Majority of cases are potentially detectable at an early stage when the disease is imminently treatable (1). It is more common in males, with a male: 1 female ratio of 3:1. Urine cytology has historically been used for screening, diagnosis and monitoring of cases of urothelial cancers since 1945 when famously Dr George Papanicolaou published his seminal work on cytology smears (2). From his five categories for reporting of cytology slides we have evolved today to seven categories as propounded by TPS; Figure 1. His classification was widely used until recently when studies indicated two divergent classes of urothelial cancers with totally different clinicopathological and molecular attributes. The LGUC are usually non-invasive and have low rate of progression to invasive carcinomas, of the order of 1-5% with very low disease related mortality. On the other hand, HGUC 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 lacking 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, the groundwork for TPS was done in a conference 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 of cervical and thyroid cytology. TPS has seven different diagnostic categories namely; Category I – Non-diagnostic or Unsatisfactory, Cate gory 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 furtherance of our previous retrospective descriptive study the authors have felt a need to adopt TPS as the sole reporting system of urine cytology at all centres across our country.

MATERIALS AND METHODS:

Objectives of this study included firstly, to classify all urine cytology samples received in the period between 01 Jan 2017 to 31 Mar 2019 at the department of pathology as per TPS and secondly to analyze the spectrum of various categories, and correlating it with biopsy findings, where available, in positive HGUC cases.

PROCEDURE:

All preserved smears of urine cytology from 01 Jan 2017 to 31 Mar 2019 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 (MST and PSM). All cases were reclassified into various categories as specified by TPS. In cases with differences of opinion between the two pathologists a final category was ascribed to the cases only after reaching a consensus opinion. 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. The slides were examined using Olympus Microscope model UMDOB3.

RESULTS:

A total of 661 Geimsa and PAP stained urine cytology smears from 121 patients (91 males and 30 females) were studied;

table 1. Eleven smears were discarded for poor quality of staining and lack of clinical details in requisition forms. A total of 11 cases were categorized as Category I, 88 as Category II, 03 as Category III, 09 as Category IV ,06 in category V and 04 as Category VI. There were no cases in category VII. Only 14 patients (11 male & 03female) for whom urine cytology sample were received, had undergone urinary bladder biopsy and their reports were available in records.

Statistical analysis: The mean age of the patients for whom samples were received was 60.3 years, median being 63.4 years and mode 61 years.

Table1: Total number of patients

Male	91
Female	30
Total	121

Of the 14 patients (excluding 1 biopsy for a recurrent case), for whom histopathological reports were also available in records, 11 were males and 03 females. 04 Biopsies were reported as HGUC (all males including one recurrence) and 09 were reported as LGUC and included 03 females. Four cases were of benign conditions including one case of cystitis cystica et gladularis and non-specific inflammation; table 2.

Table 2: Histopathological reports of available biopsy reports

DIAGNOSIS	MALE	FEMALE
HIGH GRADE UROTHELIAL CARCIOMA	4 (+1 * RECURRECE)	0
LOW GRADE UROTHELIAL CARCIOMA	6	3
TOTAL	10 +1*	3
OTHER BEINIGN CASES: DIVERTICULUM WITH SQUAMOUS METAPLASIA	1	
CYSTITIS CYSTICA ET GLANDULARIS	1	
NON SPECIFIC IFLAMMATION	1	
BENIGN PAPILLARY UROTHELIAL GROWTH	1	

DISCUSSION:

This study is one of the first descriptive retrospective studies of its kind from our country which sets to find out efficacy of TPS in reporting of urine cytology smears. Urine cytology remains one of the most widely used non-invasive investigations for the early diagnosis, screening and monitoring of urothelial carcinoma. It is best suited for a resource poor country like India. 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 (3). An average of nearly 6 smears for each patient were examined which is found to be adequate in most other studies for the purposes of screening and monitoring. We extended the period and number of cases examined for our study as compared to the previous one enhancing its validity and veracity.

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 60.3 years which is similar to other studies on urothelial cancers. The average age for the females 58 years while for males it was 62.5 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 (5). 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 by previous methods. The reports as per TPS for all these cases changed to HGUC, possibly signifying more objective approach by TPS as compared to the previous system. Most other studies have also come out with higher objective reporting categories while employing TPS in their studies (5,6). There were no samples reported as unsatisfactory by previous reporting system while in our study, nearly 09 % of the samples were reported as category I or inadequate. 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. In three smears unavailability of clinical input on requisition form rendered them inadequate for reporting. Most of the cases were in category II of TPS, comprising of approximately 73% of the total samples which is in accordance with the published literature (7). The category of atypia (Category III) comprised of just 03 cases or 2.4% which is a significant deviation from our previous study possibly due to increased sample size and better sample handling and minimizing of preanalytical fallacies by the staff (8). However, it was within the low range of most other studies as recorded in available literature (9). Reporting rate of atypia ranging from 1.3-23.2% has been recorded by various institutions (1,2,9). 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. Category IV cases were 09 or about 7.5% of total 121 cases which is significantly more than our previous study, although it still is consistent with findings of other studies (3,10). Category V consisted of 06 cases which is similar to our previous report and in line with world literature (10). Category VI or HGUC cases were 04 or 3.3%, which is a significant detection rate of HGUC in general population; however, the same cannot be said of screening test in high risk cases. Our study consisted of all urine samples from patients who represented general population as cytology was asked for to detect infections, inflammation or malignant cells (3,6,7,11). Most other studies have addressed cytology reporting in high risk cases or tested value of TPS as screening tool for HGUC; our study though incorporating the said objective was still aimed at general population thereby increasing its scope to scrutiny in future. This also perhaps is the most important limitation of our study.
No cases were reported in category VII, which is consistent with our conventional knowledge that non-urothelial and secondary malignancies of urinary bladder account for lesser than 5% of all cases (12). Our study has added advantage of representing pan-India population with all ethnic and regional being represented in our cases making it possibly first such study from this sub-continent.

CONCLUSION:

TPS, after its recent adoption by some centres has been proven to be an important screening, diagnostic and monitoring tool for urothelial malignancies. While most cases in our study were non-neoplastic benign conditions, TPS did prove to be critical in identifying suspicious and frank HGUC cases in general population vis-à-vis previous reporting system, re-iterating a felt need by authors to adopt it as the sole reporting system for urine cytology by all institutions. More studies are required to further establish importance of TPS in urine cytology reporting.

CONFLICTS OF INTEREST:

The authors have none to disclose.

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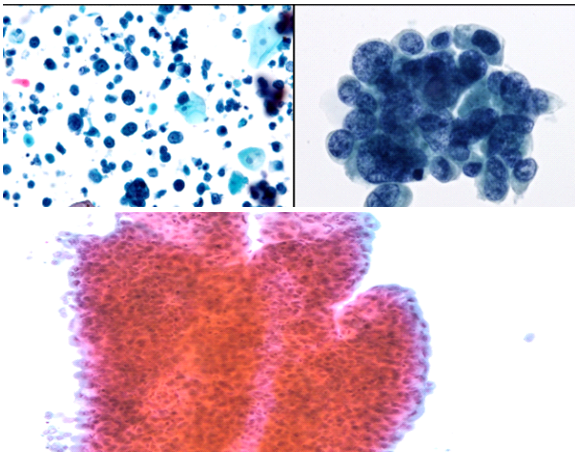
Figure 1 : History of urine cytology reporting systems

Cytologic Classification						Histologic Classification	
Papanicolaou 1947[9] (Papanicolaou Classification System)	Koss 1985[10]	Murphy 1984[11]	Ooms & Veldhuizen 1993[12]	Layfield et al 2004[13] (Papanicolaou Society of Cytopathology)	Hopkins Template*	Mostofi & Torloni 1973[8] (WHO†)	Epstein 1998[14] (WHO/ISUP)
I	Benign cells, ATY 1 cells, few clusters	Negative	Negative	Negative	NUAM	Papilloma TCC, grade 1	Papilloma PUNLMP LGUC
II							
III	Clusters, nuclear elongation, few ATY 2 cells	Dysplastic cells	Atypical, significance uncertain	Atypical urothelial cells	AUC-US	TCC, grade 2	
		Suspicious	Suspicious		AUC-H		
IV	Malignant tumor cells, many ATY 2 cells	Malignant cells	Neoplastic cells present	Urothelial carcinoma	Urothelial carcinoma		HGUC
V						TCC, grade 3	

Abbreviations: ATY 1, atypical cells with hyperchromasia and predominantly round or oval contours; ATY 2, cells with hyperchromasia and nuclear membrane abnormalities; AUC-H, atypical urothelial cells cannot exclude high-grade urothelial carcinoma; AUC-US, atypical urothelial cells of uncertain significance; HGUC; high-grade papillary urothelial carcinoma; ISUP, International Society of Urological Pathology; LGUC, low-grade papillary urothelial carcinoma; NUAM, no urothelial atypia or dysplasia identified; PUNLMP, papillary urothelial malignancy of uncertain malignant potential; TCC, transitional cell carcinoma; WHO, World Health Organization.
See Table 7.

(reproduced with permission)

Figure 2



High Grade Urothelial Carcinoma (upper panel); Low Grade Urothelial Carcinoma (lower photograph)

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