

Evaluation of Bladder Wash Cytology and Its Correlation with Histopathology in Diagnosing Neoplastic Lesions of the Urinary Bladder

Rama Das¹, Pallabi Purakayastha², Partha Pratim Deb³

¹Associate Professor, Department of Pathology, North Bengal Medical College & Hospital, Siliguri, West Bengal, India

²Junior Resident, Department of Pathology, North Bengal Medical College & Hospital, Siliguri, West Bengal, India

³Assistant Professor, Department of Urology, North Bengal Medical College & Hospital, Siliguri, West Bengal, India

Corresponding Author: Pallabi Purkayastha

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ABSTRACT

Background: Urinary cytology is a proven non-invasive diagnostic modality used in The Paris System (TPS) for detecting urothelial carcinoma especially high-grade lesions. Bladder wash cytology (BWC) offers better cellularity than voided urine samples, and could improve the diagnostic accuracy.

Objectives: To assess the diagnostic value of the BWC using TPS, to compare the cytological results with the histopathological results in suspected patients of urinary bladder neoplasms.

Methods: This study was an observational study that was carried out in a tertiary care hospital from 2023 to 2025 with 82 participants having urinary bladder lesion. Before transurethral resection or biopsy, bladder washings were collected and processed by conventional cytospin methods. The cytology interpretations were compared with Histopathological diagnosis. The statistical analysis was done using SPSS version 30.

Results: Seventy-eight cases were available in the form of histopathological correlation. The most frequent cytology diagnosis was high-grade urothelial carcinoma. BWC showed sensitivity of 98.2, specificity of 90.9, diagnostic accuracy of 96.1% and p value <0.0001.

Conclusion: BWC has highly diagnostic value for diagnosing high-grade urothelial carcinoma, and being a useful complement to histopathology in the assessment and follow-up cases of bladder neoplasm.

Keywords: Bladder wash cytology, The Paris System, Cytospin method, Urothelial carcinoma of bladder.

INTRODUCTION

Urothelial Carcinoma of the urinary bladder is most prevalent cancer of the urinary tract, contributing 75% cancer burden in males worldwide and having a high recurrence and progression rate [1]. Early and correct diagnosis is decisive especially in high-grade

urothelial carcinoma (HGUC) and carcinoma in situ which has a poor clinical outcome.

Since long days urine cytology has been extensively used in screening and monitoring cancerous lesions in the bladder as it is very specific to high-grade lesions [2]. Nevertheless, sensitivity of cytology is variable according to the type of specimen,

where voided urine has low cellularity. Better cellular yield is obtained from bladder washings during cystoscopy or before that from catheter specimen, and could lead to better diagnostic performance. Bladder washings could offer well preserved large sheet or three-dimensional clusters of urothelium, so better prediction of various grades of urothelial carcinoma [3].

The Paris System of Reporting Urinary Cytology was proposed to report uniformly and give importance on the identification of HGUC and reduction in the number of equivocal diagnoses [4,5,6]. Hence forth, the current study is designed to evaluate diagnostic capabilities of Bladder wash cytology (BWC) using The Paris system (TPS) 2022, to determine the various grades of urothelial carcinoma of urinary bladder and to correlate them with histopathology.

MATERIALS AND METHODS

This was a prospective observational study done in the Department of Pathology and Urology, in a tertiary care hospital in eastern part of India, during the period of last 2 years after getting approval from the Institutional Ethics Committee [IEC/NBMC/M-17/003/2025]. The informed consent was obtained from all the participants.

Study Population

Eighty-two patients who were having cystoscopy due to haematuria, or suspicion of mass in the bladder, or to monitor recurrence following transurethral resection of bladder tumour (TURBT) for surveillance that had been detected before were included. Cases of upper urinary tract malignancy, inadequate samples from bladder wash or those cases when no histopathological analysis had been made- were eliminated from the final analysis.

Sample Collection and Processing

Bladder washing samples were collected after using the 50-100 ml of sterile normal saline instilled in the bladder during or after cystoscopy. The saline was introduced and irrigated through the Foley's catheter and

repeated three times. The samples were processed within an hour of collection. The cytocentrifugation was done at 1500 rpm for 10 minutes and subsequently Papanicolaou stain was used to prepare the smears. The exfoliated epithelial cells after bladder wash were obtained in large sheet, fragments and preserved morphology.

Cytological Evaluation

Cytological interpretation was done based on The Paris System and was classified as: Negative for HGUC (NHGUC), Atypical Urothelial Cells (AUC), Suspicious for HGUC (SHGUC), High-Grade Urothelial Carcinoma (HGUC), low grade urothelial neoplasm (LGUN)- (5). There were cases of SHGUC and HGUC which were viewed as positive of malignancy.

Histopathological Evaluation

A study of transurethral resection of the bladder tumor or biopsy specimens was conducted on available seventy-eight cases and were grouped under the WHO/ISUP 2022 classification [6]. The gold standard for diagnosis of bladder carcinoma was considered to be histopathology.

Statistical Analysis

The SPSS version 30 was used to find out statistical analysis. Sensitivity, specificity, Positive predictive Value (PPV), Negative Predictive Value (NPV) and accuracy of BWC were estimated. Diagnostic performance was assessed using ROC curve analysis. Association between the cytological and histopathological findings was measured using the Chi-square test and Fisher's exact test, as appropriate. The p-value of less than 0.05 was taken as statistically significant.

RESULTS

Among 82 patients of BWC, 78 cases of adequate BWC could be matched with biopsy tissue for histopathological examination. The age range of the patients was from 31 years to above 70 years; maximum incidence (31.7%) was found 61-

70 years age group (Fig-1). There existed a strong male predominance at a male-to-female ratio of about 4:1. (Table.1)

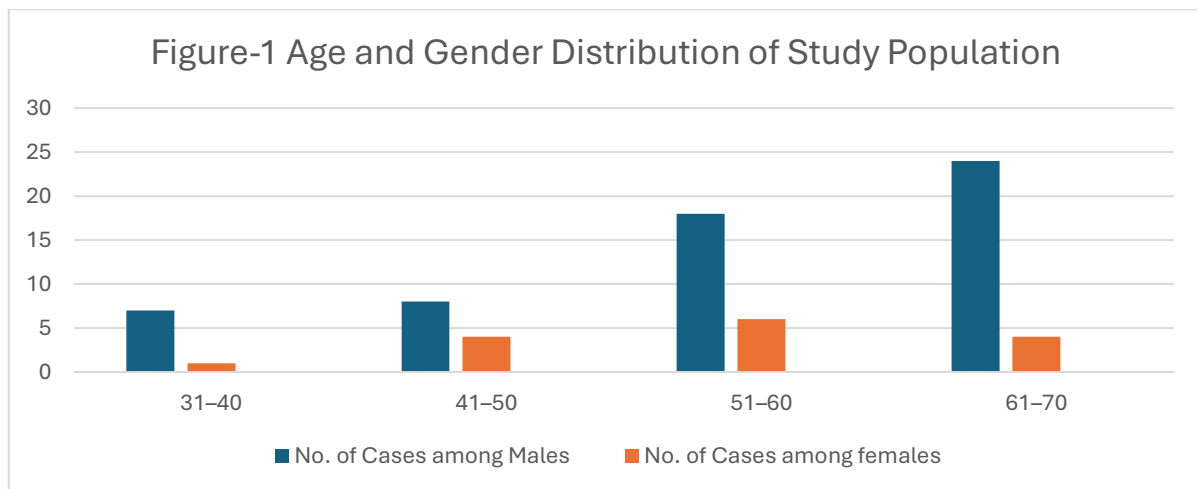


Table1. Age distribution and Male – Female ratio of the study

Age Group (years)	No. of Cases among Males	No. of Cases among females
31-40	7	1
41-50	8	4
51-60	18	6
61-70	24	4
>70	9	1
Total	66	16

The bladder wash samples were collected and processed at earliest by conventional cytopspin method. The cytological examination was done according to The Paris System. Poor samples were of minor percentage of cases. The cytological examination led to the following distribution: High-Grade Urothelial Carcinoma (HGUC) made up the largest category comprising 36 cases (43.9%). Suspicious for High-Grade

Urothelial Carcinoma - (SHGUC) was 16 cases (19.5%). Negative for High-Grade Urothelial Carcinoma (NHGUC) was 18 (21.9 %). Atypical Urothelial Cells (AUC) were detected in 6 cases (7.3%). Low Grade urothelial neoplasm was found in 2cases only (2.4%). There were 4 cases (4.8%), which are unsatisfactory samples- considered as Nondiagnostic. (Fig-2)

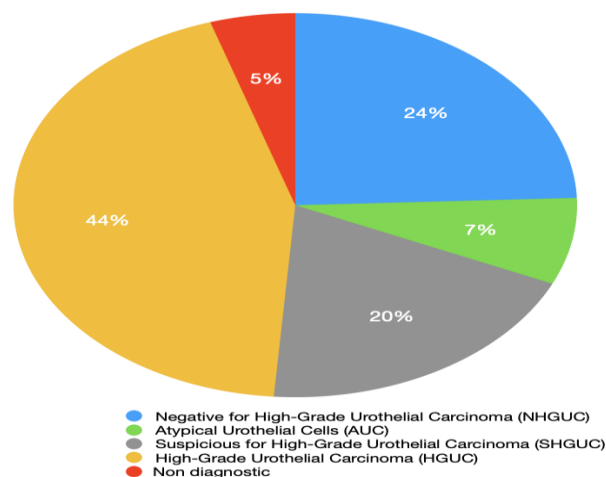


Fig-2. Cytological Diagnosis of Bladder Washings (The Paris system)

It is characterized by a preponderance of high-grade lesions in BWC, which means that the specimens of bladder wash are most

frequently collected in patients with the high clinical suspicion of malignancy during cystoscopy.

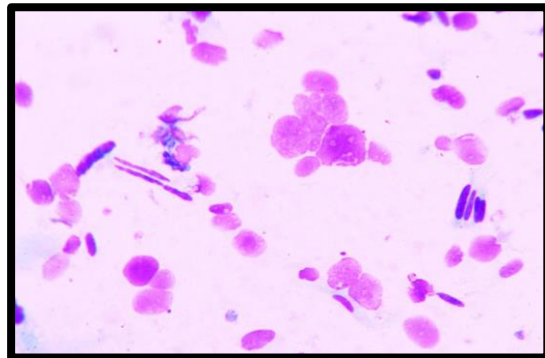
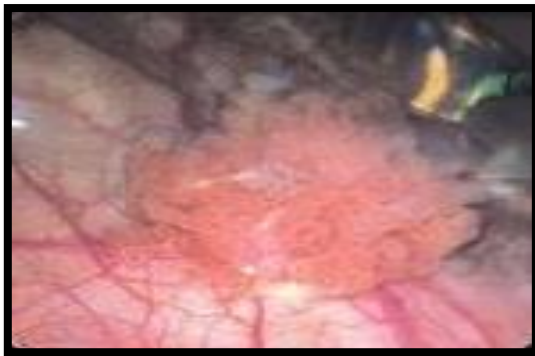


Fig-3. Cystoscopy typically shows a raised, cauliflower like lesion with papillary projection in the urinary bladder wall surrounded by increased vascularity.

Fig-4. The smear shows non superficial, non-degenerated urothelial cells with high N/C ratio (>0.7). The individual cell cells shoe marked nuclear pleomorphism, nuclear hyperchromasia. prominent nucleoli (H & E stain,40X)

Out of a total number of 78 cases, fifty-six cases (71.80 %) were identified as neoplastic lesions, of which Invasive urothelial carcinoma (44.8%) was the most common findings on histopathological examination. The 22(28.2%) cases were not neoplastic lesions (Table2). This prevalence coincides with previous estimates of the high

prevalence of HGUC in symptomatic or high-risk patients undergoing bladder wash cytology. The lesions of Papillary urothelial neoplasm of low malignant potential (PUNLMP) and non- invasive papillary urothelial carcinoma -low grade finally diagnosed on histopathology (Fig-5, 6) were reported as NHGUC during cytology.

Table 2. Histopathological Diagnosis of Urinary Bladder Lesion

Histopathological Diagnosis	No. of Cases (n=78)	Percentage (%)
Neoplastic:	56	71.80
PUNLMP	1	1.28
Non-invasive papillary urothelial carcinoma- Low grade	6	7.69
Non-invasive papillary urothelial carcinoma- High grade	14	17.94
Invasive Urothelial Carcinoma	35	44.87
Non neoplastic -	22	28.20

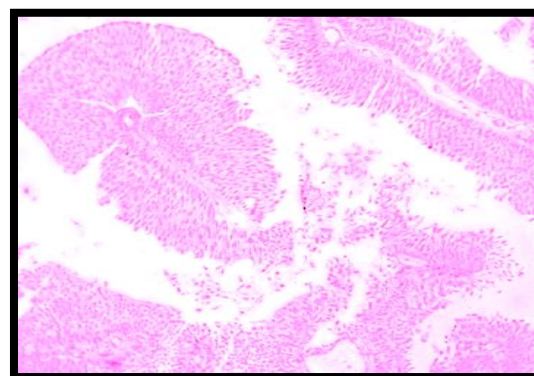
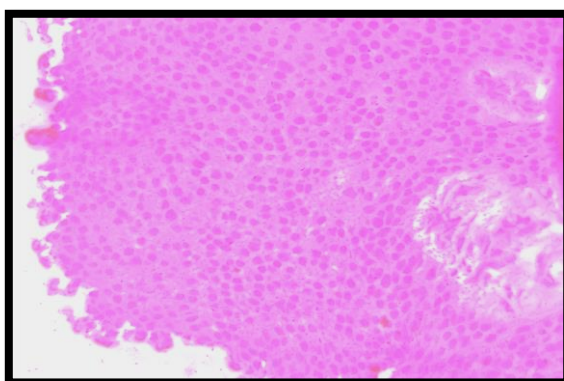


Fig-5The sections showing histopathological features of hyperplastic urothelium with preserved polarity, maintaining orderly maturation of basal cells to umbrella cells without atypia ((PUNLMP, H&E stain 40X).

Fig-6. The sections showing papillary structures with fibrovascular core lined by neoplastic urothelium with disordered architecture, cytological pleomorphism, and crowded overlapping cells. (Non invasive low grade urothelial carcinoma (H&E stain, 20x).

Cytological and histopathological diagnoses were correlated against each other in 78 cases. The 36 HGUC cases diagnosed on BWC were identical to 35 cases of urothelial carcinoma on histopathology. The non-neoplastic cytological findings of 18 cases NHGUC was similar to 17 cases non-neoplastic histomorphology. The 2 cases of LGUC came out as 1 case of urothelial carcinoma, but 1 case diagnosed as non-

neoplastic on histopathology examination. These results indicated a good level of agreement. Good predictive value of neoplasia was also exhibited by AUC and SHGUC categories (Fig-7,8). Overall, True positives cases were 56, True negatives-20, False positives-2 and False negative- 1. This implies that bladder wash cytology has great diagnostic concordance, especially in lesions of high grade cytomorphology. (Table 3).

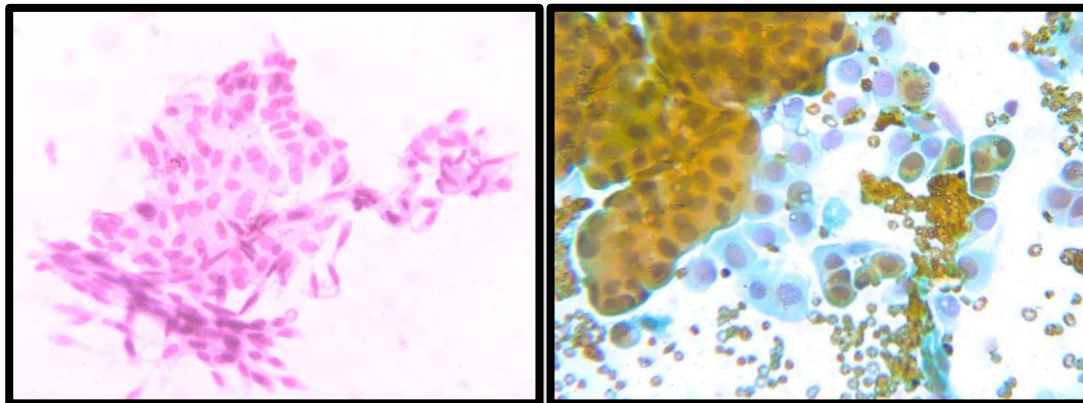


Fig-7. The smear shows non superficial and non-degenerated urothelial cells with high N/C ratio (> 0.5). The individual cells show mild nuclear hyperchromasia with coarse clumped chromatin of AUC.

Fig-8. The smear shows aggregates and singly scattered atypical urothelial cells with mild to moderate hyperchromasia, coarse chromatin and irregular nuclear membrane

Table 3. Correlation of BWC and Histopathological diagnosis (N=78)

Cytological Diagnosis	HP-neoplastic	HP-non neoplastic
HGUC (36)	35	1
SHGUC (16)	14	2
AUC (6)	5	1
LGUC (2)	1	1
NHGUC (18)	1	17
Total	56	22

Table 4. Statistical analysis of BWC vs Histopathology

BWC Result	Histopathology Positive	Histopathology Negative	Total
positive	55	2	57
Negative	1	20	21
Total	56	22	78

Parameter	Value
Sensitivity	98.2%
Specificity	90.9%
Positive Predictive Value (PPV)	96.5%
Negative Predictive Value (NPV)	95.2%
Diagnostic Accuracy	96.1%
Fisher's Exact Test p-value	<0.0001
Chi-square with Yates correction	59.31
ROC-AUC	0.946

On comparing the cytological diagnosis of BWC on cytospin method with histopathology findings, the sensitivity of BWC was 98.2%, specificity was 90.9% and Positive Predictive Value was 96.5% and Negative Predictive Value was 95.2 (Table.4) and overall diagnostic accuracy

was 96.1%. Fisher's exact test demonstrated a statistically significant association between bladder wash cytology and histopathological diagnosis ($p < 0.0001$). ROC analysis demonstrated excellent diagnostic performance with an Area Under the Curve (AUC) of 0.946. (Fig-8)

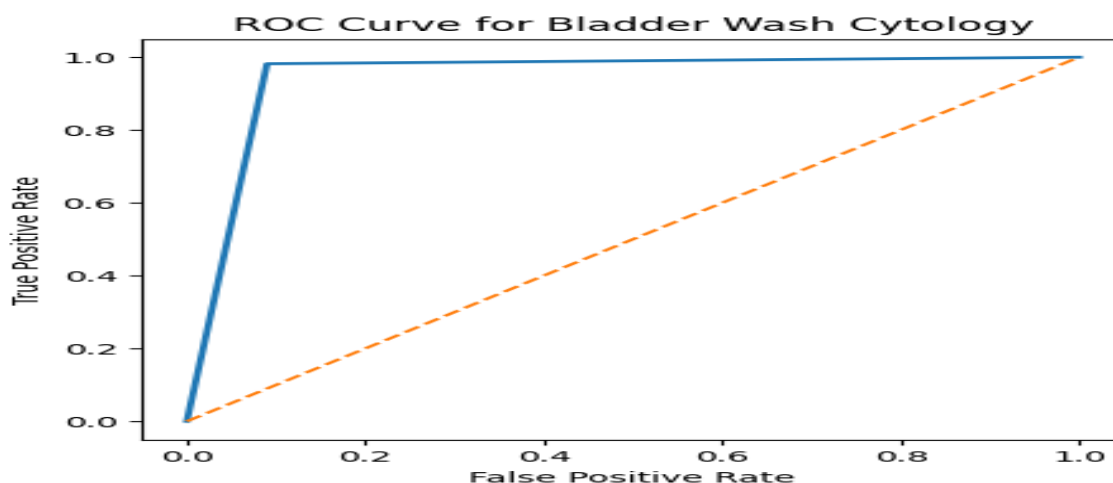


Fig-8: Receiver Operating Characteristic (ROC) curve demonstrating excellent diagnostic performance of bladder wash cytology with an AUC of 0.946.

DISCUSSION

Urinary bladder cancer is 9th most commonly diagnosed cancer worldwide with increasing incidence and mortality rate. The latest Globocan 2022 data has estimated 614,298 new cases of bladder cancer across the world, making 7.1% increase from the data reported in 2020 and 220,596 deaths annually [7,8]. Diagnosis of urinary bladder cancer is based on clinical-imaging features, cystoscopic findings, histopathological examination and urine cytology. Majority of the cases present as non-muscle invasive tumor, initially diagnosed after endoscopic resection and strict surveillance is required even after intravesical treatment to detect recurrence. As there is high recurrence rate of superficial bladder tumor, so current standard follow-up protocol is maintained by cystoscopy [9]. But cystoscopy procedure is costly and uncomfortable to patient and also creates great burden for a tertiary care Hospital for regular follow-up. Sometimes cystoscopy may miss the tiny tumors. Therefore, some non-invasive procedures like urine cytology had been introduced to reduce the

cystoscopic examination with high accuracy. Since 2022 based on urine cytology, The Paris system has been introduced as standardised diagnostic and screening technique for detection of urinary bladder tumors. There are different methods of cytology sample collection from urinary tract, most common sample is spontaneous voided urine, the others are Bladder Wash samples before or during cystoscopy, catheterized urine sample and rarely direct brushing. The sensitivity of diagnosing HGUC on bladder wash sample is quite high ranging from 90% to 94% as shown by Flezar MS and Alhamar M in their previous studies [10,11]. The current study had assessed bladder washing cytology as interpreted by The Paris System (TPS) and compared the results with histopathology. The findings support the clinical usefulness of TPS by showing high diagnostic accuracy, especially for high-grade urothelial carcinoma (HGUC).

In our study, the highest incidence of bladder carcinoma was seen in 61-70 years age group (31.7%) with a mean age of 57.03 years. The

study's mean age distribution and male preponderance (4:1) are in good agreement with other international studies and global epidemiological patterns reported in GLOBOCAN as well as Pierconti F et al. and Mikou P et al. studies [12,13]. According to Antoni S et al, bladder cancer primarily affects older men and becomes much more common after the age of 50 [14]. These patterns are also reflected in our results, confirming the cohort's validity. The increased incidence of urinary bladder cancer among male population may be due to excess tobacco smoking, alcohol consumption and excess exposure to environmental pollutant than female population -which is well explained by Misra V in their review study [15].

Cellular preservation and high yield are necessary for urine cytology interpretation, so advance technology for concentration techniques are available now a days like cytospin method, liquid based cytology in addition of conventional method. Previous studies on TPS for diagnosis of HGUC in bladder wash cytology by cytospin technique showed acceptable sensitivity of 49.2 % by previous studies of Raab S, 51% by Yafi FA et al and 81.5% by Chhabra S et al. [16,17,27]. On the other hand, Liquid based cytology was accepted as better technique with increased and preserved cellular details in a clear background shown by a comparative study of Kim JY and found sensitivity of LBC and cytospin method was 60.9% and 59.9% and specificity was 94.7% and 95.2% [18] respectively. As LBC is costly and sophisticated technique, so we adopt cytospin method that implementing TPS on bladder wash cytology for diagnosing urothelial carcinoma in this study, that might be contributed for better preservation of nuclear- cytoplasmic details. In our study, the highest cases were diagnosed as HGUC by cytospin method (43.9%). TPS-based studies, which highlighted the effectiveness of cytology in identifying high-grade disease, are consistent with the high percentage of HGUC (43.9%) and SHGUC (19.5%) in bladder washings.

According to review of Chen F, TPS improves urine cytology by lowering the overdiagnosis of atypical cells and strengthening the standards for HGUC diagnosis [19]. Our AUC rate (7.3%) is comparable to other published series like Pöyry E study and falls within the suggested TPS limit (<10–15%) [20].

In comparison with recent research work on high-risk groups by A. Gupta et al., in this study high grade urothelial carcinoma was the most frequent histological diagnosis (62.8%) included HGUC and SHGUC diagnosed on cytology. This study's high diagnostic sensitivity (98.2%) is also in same line with the A. Gupta et al.' sensitivity range of 92.86% [21]. By reducing equivocal interpretations, Chen F. showed that TPS increases specificity for high-grade lesions [19]. Our study's strong correlation lends credence to these conclusions. These were linked to reactive atypia when inflammation was present, pitfalls that have been extensively reported in the literature on urine cytology, including by Hashim MA. [22]. Scanty cellularity, a known problem, particularly in low-grade tumours, was the cause of less reporting in BWC. Because there is less exfoliation, urine cytology is less sensitive for LGUC, according to Bansal S et al study [23]. These results highlight the fact that although TPS significantly increases diagnostic precision, urothelial cytology still has some inherent limitations. [19]

Similar diagnostic parameters, with sensitivity ranging from 84.8% to 94% for HGUC using TPS with bladder wash cytology, have been reported in Indian studies by Sahoo SR and Aradhana Saikia [19,24]. Due to a higher percentage of high-grade cases and the efficient use of TPS criteria, our sensitivity (98.2%) is marginally higher. Though the bladder washings provide better preservation of urothelium, less contaminated background, more detailing of nucleus and cytoplasm over urine cytology but the cells of LGUC do not attract the pathologist's eye for less cytological atypia. Hence BWC is the diagnostic modality for detection of HGUC with high sensitivity and

specificity as there is marked cellular atypia, pleomorphism and necrosis.

The sensitivity (98.2%) and specificity (77.2%) of the bladder wash cytology is quite acceptable in this study and comparable to the Chhabra S et al and Bieri U et al reported studies [25, 26], especially in the high-grade urothelial carcinoma cases. The low frequency of AUC diagnoses in this study is an indication of strict TPS compliance and the reason why diagnostic transparency will be enhanced.

The reason behind the false positive cases was mostly reactive atypia in the background of inflammation whereas the single false negative case was probably because of scant cellularity. These are the limitations that are commonly known in urinary cytology.

On the whole, the results of this study justify the fact that bladder wash cytology should be used as a supplement to histopathology, especially in the detection and follow-up of high-grade and recurrent tumours of the urinary bladder.

CONCLUSION

When evaluated with the Paris system, bladder wash cytology is proved to have high diagnostic value in high-grade urothelial carcinoma. BWC should be adopted as a crucial part of follow-up in adjunct to histopathology in the procedure of diagnosis and surveillance of neoplasia of the urinary bladder. Despite the fact that low-grade lesions are difficult to diagnose, the standardized reporting enhances clinical usefulness and diagnostic reliability.

Declaration by Authors

Ethical Approval: Approved

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