Original Research

A STUDY ON ATYPICAL CELLS IN HEMATURIA: CYTOLOGICAL FINDINGS AND CLINICAL IMPLICATIONS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Urine cytology is a simple, rapid, non-invasive, and cost-effective diagnostic tool widely used in the evaluation of urinary tract disorders. It plays an important role in patients presenting with hematuria, aiding in the detection of infections, urolithiasis, and urothelial malignancies. The presence of atypical urothelial cells in urine poses a diagnostic challenge, as it may be associated with both benign and malignant conditions.

Aim: To evaluate the cytological features of atypical cells in urine samples from patients with hematuria and to determine their clinical significance.

Materials and Methods: This descriptive study was conducted in the Department of Pathology at Sree Mookambika Institute of Medical Sciences from June 2025 to February 2026. A total of 4015 freshly voided urine samples were analyzed. Samples were processed by centrifugation at 1500 rpm for 30 minutes, and smears were prepared from the sediment and stained using routine cytological stains. Detailed microscopic examination was performed to identify atypical and malignant cells. In selected cases, three consecutive urine samples were analyzed to improve diagnostic yield. Statistical analysis was carried out using descriptive and inferential methods, with a p-value <0.05 considered significant.

Results: A spectrum of cytological findings was observed, ranging from benign to atypical and malignant lesions. Atypical urothelial cells were identified in a subset of hematuria cases and showed variable association with underlying pathological conditions. Malignant cells were more frequently associated with high-grade urothelial carcinoma. The use of multiple samples improved detection rates.

Conclusion: Urine cytology is an effective adjunctive tool in the evaluation of hematuria, particularly for detecting high-grade malignancies and monitoring recurrence. The presence of atypical cells warrants careful interpretation and further investigation. When combined with clinical and cystoscopic findings, cytology significantly enhances diagnostic accuracy and patient management.

INTRODUCTION

Urine cytology is a simple, cost-effective, rapid, and non-invasive diagnostic tool widely used in the evaluation of urinary tract disorders. It plays an important role in the assessment of patients presenting with hematuria, as well as those with suspected urinary tract infections, urolithiasis, and neoplastic conditions of the urinary system (1).

As an exfoliative cytological technique, urine cytology examines cells that are naturally shed from the lining of the urinary tract, particularly the urothelium, providing valuable insights into underlying pathological processes (2).

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Hematuria is a common clinical presentation and may arise from a wide spectrum of benign and malignant conditions. While infections and urinary tract stones are frequent causes, it is crucial to exclude malignancy, especially urothelial carcinoma, which is one of the most common cancers affecting the urinary system (3). In this context, urine cytology serves as an important initial investigation due to its ease of collection and patient compliance.

Atypical urothelial cells are often encountered in urine cytology specimens. These cells exhibit morphological changes that are not entirely benign but insufficient for a definitive diagnosis of malignancy. Such atypia can be seen in a variety of conditions, including inflammation, calculi, instrumentation, and reactive changes (4). However, the presence of atypical cells raises diagnostic

challenges, as similar cytological features may also be observed in premalignant lesions and malignant tumors, particularly high-grade urothelial carcinoma (5).

The clinical significance of identifying atypical cells lies in their potential association with underlying malignancy. Although urine cytology has high specificity, especially for high-grade tumors, its sensitivity for low-grade lesions is relatively limited (6). Therefore, the detection of atypical urothelial cells often necessitates further evaluation, including cystoscopy, imaging studies, and histopathological examination, to establish a definitive diagnosis.

In addition to its role in initial screening, urine cytology is valuable in the follow-up of patients with known urothelial carcinoma. It is routinely used to monitor for tumor recurrence, particularly in patients who have undergone surgical treatment or intravesical therapy (7). Early detection of recurrent disease through cytological examination can significantly influence patient management and prognosis.

Thus, cytological evaluation of hematuria samples, particularly the identification and interpretation of atypical urothelial cells, remains a critical component in clinical practice. Understanding the spectrum of cytological changes and their clinical implications is essential for accurate diagnosis and appropriate patient management.

Aim: To evaluate the cytological features of atypical cells in urine samples from patients presenting with hematuria and to determine their clinical significance.

Objectives

To study the cytomorphological characteristics of atypical urothelial cells in urine samples.

To categorize urine cytology findings in hematuria cases based on established reporting systems.

MATERIALS AND METHODS

This was a descriptive observational study conducted in the Department of Pathology at Sree Mookambika Institute of Medical Sciences. The study was carried out over a period of nine months, from June 2025 to February 2026.A total of 4015 freshly voided urine samples were received and analyzed during the study period. Samples were collected from patients presenting with hematuria and other urinary tract-related complaints. Relevant clinical details, including history of urinary tract infection, urolithiasis, malignancy, and family history, were obtained wherever available.

For cytological examination, approximately 5–10 mL of freshly voided urine was collected in sterile containers. First early morning samples were avoided, as prolonged bladder storage may lead to cellular degeneration and compromise cytological interpretation. In selected cases, especially those with high clinical suspicion, three consecutive urine samples collected over three days were analyzed to improve diagnostic yield.

Each urine sample was processed by centrifugation at 1500 rpm for 30 minutes. The supernatant was discarded, and the sediment was used to prepare 3–6 smears on clean glass slides. The smears were then fixed and stained using routine cytological stains such as Hematoxylin and Eosin (H&E) and/or Papanicolaou stain.

Microscopic examination was performed in detail to assess cellular morphology, with particular emphasis on identifying atypical and malignant urothelial cells. Cytological features such as nuclear enlargement, hyperchromasia, irregular nuclear borders, increased nuclear-cytoplasmic ratio, and presence of abnormal cell clusters were carefully evaluated. Special attention was given to samples from patients with hematuria, suspicious clinical findings, or a positive family history of malignancy. The cytological findings were categorized into benign, atypical, suspicious, and malignant groups based on established cytological criteria.

Statistical Analysis

Data obtained from the study were entered into Microsoft Excel and analyzed using appropriate statistical software (such as SPSS). Descriptive statistics were used to summarize the data, including frequencies, percentages, and proportions. The association between cytological findings and clinical parameters was assessed using the Chi-square test or Fisher's exact test where applicable. A p-value of less than 0.05 was considered statistically significant.

RESULT

Out of 4015 urine samples, 182 samples are from cases of hematuria (4.5%) It includes both gross and microscopic hematuria. Out of 182 samples only 40 samples showed atypical cells. Of which 6 cases are proved to be malignant and other 16 cases are due to reactive changes. In urine cytology cancer cells can be obscured by RBCs and autolysis artefacts. Microscopic hematuria may be intermittent in bladder carcinoma. hence a negative result does not exclude the diagnosis. Atypical cells are seen in inflammatory conditions, uro lithiasis, systemic and intra vesical therapy, and may also occur in urothelial tumors of all grades.

The atypical cells are small hyperchromatic with nuclear enlargement and altered nucleo cytoplasmic ratio. Mitotic figures may be seen. In low grade papillomas there is no significant diagnostic finding and it is difficult to diagnose such tumors. Occasional erythrocytes and atypical cells such as elongated cells, without any inflammation and necrosis in a clean background. Cytologic finding of highly pleomorphic tumor cells is important because extensive search for the primary is warranted in

such cases. Grade 2 and grade 3 tumors are recognized easily by the presence of markedly atypical urothelial cells and recognizable cancer cells, occurring singly or in loosely structured clusters. Smaller cancer cells were of a higher grade than tumors with larger cells.

DISCUSSION

Urine cytology remains an essential adjunct in the evaluation of patients with hematuria, particularly for the detection of urothelial malignancies. The identification of malignant cells in urinary sediment or bladder washings necessitates thorough clinical evaluation, even in the absence of cystoscopic or radiological abnormalities, as emphasized in classical cytopathology literature (7). This highlights the high specificity of cytology in diagnosing significant urothelial lesions, especially high-grade tumors and carcinoma in situ (CIS).

Carcinoma in situ of the bladder is a flat, high-grade lesion that may not always produce visible abnormalities on cystoscopy. In such cases, cytology plays a crucial diagnostic role, as atypical or frankly malignant cells may be shed into the urine. Bladder barbotage has been recommended as a useful technique to obtain representative samples of bladder epithelium with minimal contamination from the upper urinary tract, thereby improving diagnostic accuracy (8). Furthermore, in cases with persistent atypia, bladder biopsy is warranted even when cystoscopic findings are unremarkable.

Urothelial carcinoma demonstrates a variety of histological variants, each with distinct clinical and cytological features. Squamous cell carcinoma (SCC) of the bladder, for instance, is commonly associated with chronic irritation and infection, particularly in regions endemic for Schistosoma haematobium infection (9). SCC often arises from areas of squamous metaplasia or leukoplakia and is characterized cytologically by keratinized cells with dense eosinophilic cytoplasm, pyknotic nuclei, and the presence of “ghost cells” due to extensive keratinization. Adenocarcinoma of the bladder, although less common, is associated with risk factors such as intestinal metaplasia, exstrophy of the bladder, villous adenoma, cystitis glandularis, and nephrogenic adenoma (10).

The diagnostic accuracy of urine cytology has been well documented. According to Koss, carcinoma of the bladder of grade II or higher can be identified with an accuracy of approximately 78%, which increases to about 91% for high-grade tumors (7). However, the sensitivity of cytology is limited in detecting low-grade papillary tumors, which often require cystoscopic evaluation for definitive diagnosis.

Follow-up of patients with urothelial carcinoma presents additional challenges, particularly in those undergoing radiotherapy. Radiation-induced cellular changes can mimic malignancy, complicating cytological interpretation (11). Despite these limitations, urine cytology remains a valuable tool in monitoring disease recurrence. It is recommended that follow-up evaluation includes examination of three consecutive urine samples to enhance detection rates.

Although cystoscopy remains the gold standard for diagnosis and surveillance, cytological analysis offers a non-invasive, cost-effective complementary approach. It is particularly useful in detecting high-grade lesions and recurrence following treatment, including in patients who have undergone radical cystectomy with urinary diversion (12). Thus, the integration of cytology with clinical and cystoscopic findings significantly improves the overall diagnostic and prognostic assessment of urothelial tumors.

CONCLUSION

Urine cytology is a valuable, non-invasive, and cost-effective diagnostic tool in the evaluation of patients presenting with hematuria. It plays a significant role in the detection of urothelial malignancies, particularly high-grade tumors and carcinoma in situ, where cytological features are more distinct and reliable. The identification of atypical urothelial cells, although not always diagnostic of malignancy, warrants careful interpretation and further clinical evaluation due to their potential association with premalignant and malignant conditions.

In this study, cytological examination of urine samples proved to be useful in differentiating benign from suspicious and malignant lesions when correlated with clinical findings. While its sensitivity for low-grade tumors remains limited, its high specificity makes it an important adjunct to cystoscopy. The use of multiple consecutive samples enhances diagnostic accuracy and reduces false-negative results.

Furthermore, urine cytology is an essential tool in the follow-up of patients with known urothelial carcinoma, aiding in the early detection of recurrence or progression. Despite certain limitations, such as interpretative challenges in reactive atypia and post-radiotherapy changes, it continues to be an indispensable component of urological evaluation.

Overall, cytological assessment of hematuria samples, particularly the evaluation of atypical cells, contributes significantly to early diagnosis, appropriate management, and improved prognosis of urinary tract malignancies.

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