Dijlah Journal of Medical Sciences (DJMS) Vol. 3, No. 2, May, 2026, pp. 218-224
P-ISSN: 3078-3178, E-ISSN: 3078-8625, paper ID: 24

REVIEW ARTICLE

Hematuria: Urological Investigations: A Review

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Article Info

Article history:

Received February, 03, 2026
Revised February, 15, 2026
Accepted February, 27, 2026

Keywords:

Hematuria,
CT,
Cystoscopy,
Urinary Tract

ABSTRACT

Hematuria is a common clinical manifestation with a wide range of causes, from benign, transient diseases to serious malignancies of the urinary system. Hematuria can be gross or microscopic, each with different diagnostic significance and risk assessment implications. While many causes are benign, including infection, urinary tract stones, and benign prostatic hyperplasia, hematuria can also be the earliest sign of urothelial carcinoma or kidney malignancies. Studies have shown that tumor detection rates are significantly higher in patients with gross hematuria than in those with microscopic hematuria. Therefore, a comprehensive clinical evaluation is crucial, including medical history, physical examination, laboratory tests, imaging studies, and cystoscopy. Urinalysis and urine culture help differentiate between glomerular and non-glomerular causes, while urine cytology can serve as an adjunct in high-risk cases. Imaging techniques such as ultrasound and CT urography play a central role in assessing upper urinary tract diseases. Cystoscopy remains the gold standard for examining the lower urinary tract. Existing guidelines, including those from the American Urological Association and the European Association of Urology, recommend a risk-adaptive diagnostic approach to optimize cancer screening and minimize unnecessary invasive procedures. This article reviews the etiology, classification, and evidence-based urological diagnosis of hematuria in clinical practice.

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1- INTRODUCTION

Hematuria (a bloody urine), whether microscopical or macroscopical, is widespread presentation in clinical practice. It is common in 2.5-20% of people. Urine discoloration consequent to other causes other than the blood can simulate gross hematuria e.g. dehydration, hemoglobinuria, myoglobinuria, bile pigments, beetroot ingestion, coffee consumption and drugs like methyl dopa, phenazopyridine, rifampicine and laxatives [1, 2]. A wide range of hematuria causes is present, the most common include urinary tract infections (UTI), bladder tumor, renal cancer, urolithiasis, benign prostatic hyperplasia (BPH) and prostate cancer, other less common include injury, radiation cystitis, bilharziasis and medical causes include glomerulonephritis e.g. post-infectious glomerulonephritis, thin basement membrane nephropathy, IgA nephropathy and hemolytic uraemic syndrome [3, 4], (Table 1). Many of these causes of hematuria are benign, however it may be the representative of early feature of malignancy in urinary tract specially bladder tumor which is recognized in 25% of patients with obvious hematuria [5, 6]. A round 14% of patients exhibiting frank hematuria and 3% of patients displaying non visible hematuria are discovered to have

tumors, however this is less in patients with ages under 45 years. In current multicentre study of 10,896 patients, patients with frank hematuria had tumor incidence of 26% versus 6.38% in microscopic hematuria patients [7]. Thus thorough investigations are recommended to detect critical pathology.

Table (1): Etiology of hematuria

Etiology	Causes
Temporary	Exercise Injury Coitus Pelvic organ prolapse
Malignant	Renal cell carcinoma Urothelial tumors Prostate cancer
Infectious/inflammatory	Pyelonephritis Lower urinary tract infection Radiation cystitis Foreign body
Renal medical disease	Thin basement membrane nephropathy Immunoglobulin A nephropathy
Obstructive	BPH Urolethiasis

Urology guidelines emphasize risk-appropriate diagnosis, particularly for patients with persistent or asymptomatic microscopic hematuria and known risk factors such as advanced age or smoking. Because delayed assessment can lead to missed diagnoses of malignancies or other serious underlying conditions, structured diagnostic processes help optimize patient outcomes and guide treatment. Studies and guideline updates continuously refine the indications and sequence of urological examinations to achieve a balance between early detection and minimizing unnecessary invasive procedures [8]. This study aims to outline the etiologies of hematuria and the methods of urological examination and assessment in clinical practice.

Hematuria Classification

It is categorized into gross (visible) or microscopic (non-visible). Gross hematuria is linked with a great hazard of significant malignancy which necessitates full urological assessment [9]. Microscopic hematuria is more prevalent and frequently benign particularly in young patients [10].

Gross hematuria usually has a clear cause, consistent with the patient's medical history, clinical signs and symptoms (e.g., passing of kidney stones, acute hemorrhagic cystitis, or sickle cell crisis). However, many other conditions can also cause gross hematuria (Figure 1). Therefore, the assessment of gross hematuria should be based on the patient's symptoms and accompanying clinical and laboratory findings. In adults over 40 years of age (some sources suggest an upper age limit of 35 years), unexplained gross hematuria may suggest bladder cancer or upper urinary tract cancer. Therefore, most specialists recommend referral to a urologist for imaging and cystoscopy to rule out cancer [11].

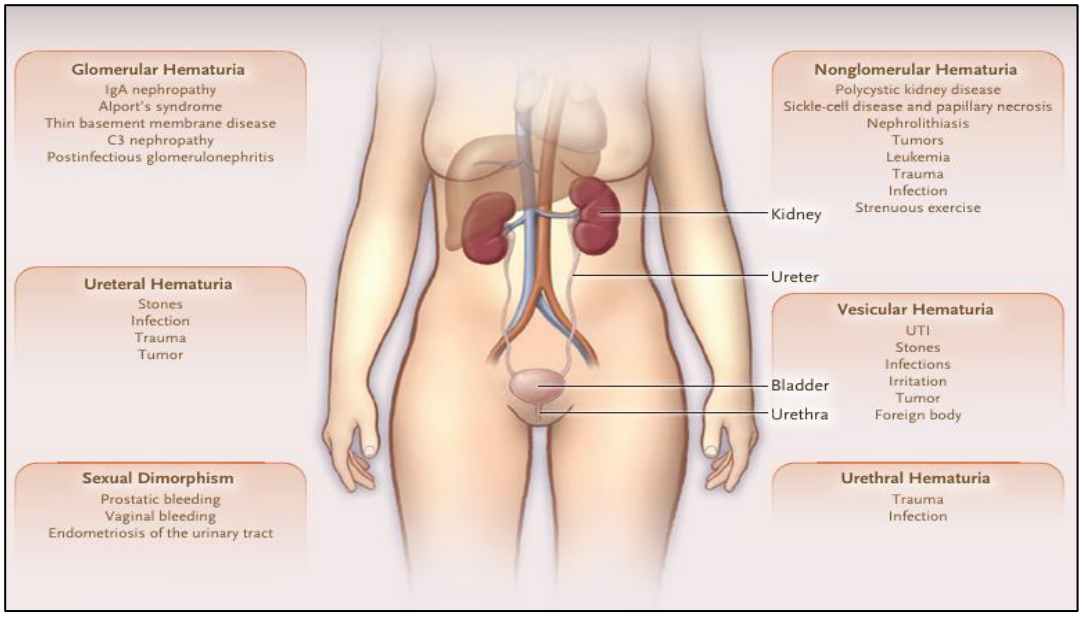

Fig (1): Hematuria classified by location. Hematuria is classified according to its location in the urinary tract [11]

Clinical Assessment

Initially a detailed history should be taken focusing on age of the patient, history of smoking, occupational exposure, use of medication especially anticoagulants and accompanying symptoms as pain, lower urinary tract infection (UTI) symptoms, as in Table 2.

Physical examination may add evidences like flank masses and systemic disease signs [12].

Table (2): History related hematuria

Scope	Assessment	Clinical relation
Hematuria types	Gross or microscopic Timing whether initial, terminal or total	Gross & total types are correlated with malignancy. Timing indicates bleeding site
Onset & interval	Sudden or gradual Temporary or persistent	Persistent recommends comprehensive evaluation
Pain	Loin pain Ureteric colic	Suggests calculi or UTI, painless hematuria suspects tumors
LUTS (lower urinary tract symptoms) **Irritative/obstructive**	Frequency, dysuria, urgency, nocturia, weak stream, hesitancy, intermittency, terminal dribbling, sense of incomplete emptying	Indicates UTI, BPH or bladder pathology
Risk points for cancers	Age > 40 years, long term smoking, occupational exposure to chemicals, pelvic irradiation	Powerful suspension of urothelial tumors
Drugs	Anticoagulants, NSAID (non-steroidal anti-inflammatory drugs)	May disclose pathology
Past surgical history	Injury, calculi, malignancy	Raise the probability of recurrent disease
Past medical history	Coagulaopathy, kidney disease	Indicates glomerular etiology
Family history	Renal, bladder tumors or inherited renal pathology	Suspects familial or hereditary diseases
Gynecological history	Menstrual or vaginal bleeding	May eliminate non-urological cause of bleeding

A local study included 1,560 randomized urine samples collected over a three-year period from patients with hematuria (gross or microscopic hematuria). All samples underwent clinical and microscopic (cytological) examination. The study found atypical cells in 23.7% (370 cases) of hematuria. Of these, 48.7% (180 cases) were confirmed to be malignant by cystoscopy and histopathology. The remaining atypical cell cases were reactive, caused by surgery or foreign bodies. No atypical cells were found in 1,190 cases (76.3%). Urine cytology can differentiate urothelial changes from high-grade bladder tumors and is therefore a valuable tool, especially when clinicians and cytopathologists work closely together. Urine cytology can be used as an adjunct to the evaluation of patients with hematuria [13].

Laboratory Investigations

Urinalysis is necessary to assure hematuria and differentiate between glomerular and non-glomerular etiology. Urine culture is essential to confirm the presence of infection. Renal function tests give clue to the condition of kidneys. Urine cytology may help in patients with suspected urothelial tumors [14] as shown in table 3.

Table (3): laboratory investigations in hematuria

Investigation	**Aim**
Urinalysis	Assure hematuria Glomerular vs non-glomerular
Urine culture	Detect infection
Renal function tests	Basic renal condition
Urine cytology	Detect high risk malignancy

Cytologic Analysis

Urinalysis has long been recommended as an adjunct to cystoscopy to help detect small cancerous lesions that may be missed during the procedure. In a study by Mishriki et al., 2278 patients underwent urinalysis, and only 2 were diagnosed with cancer based on cytological findings. A study by Hofland et al. showed that cancer was detected in 4 out of 1000 urine samples, with 2 of those cancers being detected solely through cytological examination. Currently, cytological analysis is only used for cases of gross hematuria or symptomatic hematuria [15].

Imaging

For adults diagnosed with microscopic hematuria, imaging studies should be performed. As with gross hematuria, ultrasound combined with cystoscopy has proven to be the most cost-effective method. Halpern et al. used decision analysis to study the simulated cancer detection rate and associated costs (expressed as the additional cost of cancer detection) in patients with asymptomatic microscopic hematuria. They analyzed four imaging modalities: CT urography alone, cystoscopy alone, CT urography combined with cystoscopy, and ultrasound combined with cystoscopy. Ultrasound combined with cystoscopy detected the most cancers per unit of cancer detection cost. If ultrasound was used instead of CT urography, only one additional case of cancer was detected [16].

Cystoscopy

For patients with gross hematuria of unknown cause, cystoscopy is usually recommended to rule out cancer, most commonly bladder cancer. The 2012 AUA guidelines recommended cystoscopy for all patients over 35 years of age with microscopic hematuria, while the 2020 AUA guidelines introduced risk stratification and recommended immediate cystoscopy only for high-risk patients [17].

Upper Urinary Tract Imaging

Imaging is essential element in the evaluation of hematuria. Ultrasound is considered a first line investigation of hematuria in young or low risk patients [18], while in high-risk patients CT urography is regarded as the gold standard for diagnosis of urothelial cancers and renal masses [19, 20]. MRI urography may be useful in cases of CT contraindications, as in table 4.

Table (4): Imaging studies in hematuria

Imaging	Advantage
Ultrasound	Safe, cheap
CT urography	High reliability
MRI	No radiation

Evaluation of Lower Urinary Tract

Cystoscopy persists to be the backbone for assessment of lower U. T. It is advised for all patients with gross hematuria, those aged over 40 years with microhematuria and those who are smokers [9, 21].

Follow-Up

For patients with hematuria, follow-up is a crucial component of clinical management, especially in those with persistent or recurrent hematuria and those with known risk factors for urinary tract malignancies. Appropriate monitoring ensures early detection of missed or emerging lesions and avoids unnecessary invasive procedures. For patients with gross hematuria who have undergone comprehensive examinations, including cystoscopy and upper urinary tract imaging, and whose results are negative, re-evaluation is necessary if hematuria recurs. Recurrent gross hematuria requires repeated cystoscopy and imaging because it is closely associated with urothelial carcinoma, especially in patients over 40 years of age or smokers, as emphasized in the guidelines of the American Urological Association and the European Association of Urology. For microscopic hematuria, follow-up is typically based on risk stratification:

1. Low-risk patients (age <40 years, non-smokers, no history of occupational exposure, no irritating urinary tract symptoms): Repeat urine examination after 6–12 months. If hematuria disappears, no further investigation is necessary; if hematuria persists, re-examination may be required.

2. Intermediate-risk patients: Regular urinalysis and clinical monitoring are recommended. If hematuria persists for more than 12 months, repeat imaging or cystoscopy should be considered.

3. High-risk patients (age > 40 years, history of smoking, exposure to chemicals, previous pelvic radiotherapy, or history of urothelial carcinoma): Close monitoring is necessary, with repeat cystoscopy and imaging within one year, even if the initial results are normal. In some cases, urine cytology may be used as an adjunct.

For hematuria caused by benign causes (e.g., urinary tract infection, urinary tract stones, or benign prostatic hyperplasia) follow-up aims to confirm whether the hematuria has disappeared after treatment. If bleeding persists after adequate treatment, further investigation is needed to rule out malignancy. For patients receiving anticoagulation therapy who develop hematuria, symptoms should not be solely attributed to the medication. Routine urological examinations and follow-up are still necessary, as anticoagulation therapy may reveal an underlying cause that is not the causative factor. Positive urine cultures were more common in females with blood group O, and it was found a significant correlation between asymptomatic bacteriuria and the early age group of toilet training [22]. If the hematuria is glomerular, referral to a nephrologist is recommended. Follow-up includes monitoring renal function, proteinuria, and blood pressure. Re-examination is recommended if recurrent or persistent hematuria occurs, especially in the presence of risk factors [10, 23].

4- CONCLUSION

Hematuria should not be ignored as it may indicate serious urinary tract disease, particularly malignancy. A structured risk stratification diagnostic strategy is crucial for accurate diagnosis and timely intervention. According to current guidelines, ultrasound, CT urography, and cystoscopy remain the most important diagnostic procedures. Urine cytology plays a selective complementary role in high-risk or gross hematuria. Early referral and appropriate follow-up can improve treatment outcomes and reduce misdiagnosis. Strict adherence to evidence-based medicine recommendations ensures balanced, safe, and cost-effective management of patients with hematuria.

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