Haematuria: Common manifestation of common and uncommon diseases

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Review Article

Introduction
Haematuria is the presence of blood, specifically red blood cells, in the urine. Abnormal excretion of erythrocyte in urine is called haematuria. Haematuria is a sign that something is causing bleeding in the genitourinary tract: the kidneys, the tubes that carry urine from the kidneys to the bladder (ureters), the prostate gland (in men), the bladder, or the tube that carries urine from the bladder out of the body (urethra). Bleeding may happen once or it may be recurrent. It can indicate different problems in men and women. Causes of this condition range from non-life threatening (e.g., urinary tract infection) to serious (e.g., cancer, kidney disease). Therefore, a physician should be consulted as soon as possible.

Prevalence
Haematuria is one of the common nephrological and urological problems. Prevalence varies 2.5 to 4% among the general population, of them 25% having cystoscopic abnormalities including malignancies. Incidence of haematuria may occurs in up to 10% of the general population. But differences in the age and sex of the populations screened, the amount of follow-up and the number of screening studies per patient account for this range. In older men, who are at a higher risk for significant urologic disease.

Source of erythrocyte
Blood in the urine (haematuria) can originate from any site along the urinary tract whether gross or microscopic.

Screening
The literature agrees that gross haematuria warrants a thorough diagnostic evaluation. By contrast, microscopic haematuria is an incidental finding, and whether physicians should test for haematuria in asymptomatic patients remains at issue. No major organization currently recommends screening for microscopic haematuria in asymptomatic adults, even though bladder cancer may be detected in such patients. Though there is controversy regarding screening for haematuria, because the incidence of serious underlying conditions is relatively low. However, if haematuria is detected, it is very important that patients are thoroughly evaluated, as this is the presenting symptom of many of the urological cancer malignancies, which do not necessarily cause any other symptoms until they are relatively advanced and possibly metastatic (have spread).

Causes of Haematuria

Systemic
- Purpura
- Sickle cell trait
- Bleeding disorders, including anticoagulant drugs

Renal
- Acute glomerulonephritis
  (Primary/Secondary)
- Infarct / papillary necrosis
- Trauma
- Tuberculosis
- Stones
- Renal pelvis ca. and other renal tumours - Wilms' tumour (in children)

Post-Renal
- Ureteric Stones

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-Ureteric neoplasms
-Bladder tumours (transitional cell carcinoma)
-Bladder tuberculosis and bilharziasis
-Radiation cystitis
-Drug-induced cystitis, e.g. cyclophosphamide
-Prostatic enlargement
-Urethral neoplasms
-Bacterial cystitis

Localization
Red cell casts are virtually pathognomonic for glomerular bleeding. Unfortunately, they are a relatively insensitive marker. Therefore, it is useful to examine the character of the red blood cells. Dysmorphic urinary red blood cells show variation in size and shape and usually have an irregular or distorted outline. Such red blood cells are generally glomerular in origin. In contrast, normal doughnut-shaped red blood cells are generally due to lower urinary tract bleeding. Accurate determination of red blood cell morphology may require inverted phase contrast microscopy. The percentage of dysmorphic red blood cells required to classify haematuria as glomerular in origin has not been adequately defined. In general, glomerular bleeding is associated with more than 80 percent dysmorphic red blood cells, and lower urinary tract bleeding is associated with more than 80 percent normal red blood cells. Percentages falling between these ranges are indeterminate and could represent bleeding from either source.

Microscopic haematuria with Proteinuria of 1+ or greater on dipstick urinalysis should prompt a 24-hour urine collection to quantitate the degree of proteinuria. A total protein excretion of >1,000 mg per 24 hours (1 g per day) should prompt a thorough evaluation or nephrology referral and it is likely to be glomerular haematuria. Such an evaluation should also be considered for lower levels of proteinuria (>500 mg per 24 hours [0.5 g per day]), particularly if the protein excretion is increasing or persistent, or if there are other factors suggestive of renal parenchymal disease.

If a careful history suggests a potential "benign" cause for microscopic haematuria, the patient should undergo repeat urinalysis 48 hours after cessation of the activity (i.e., menstruation, vigorous exercise, sexual activity or trauma). No additional evaluation is warranted if the haematuria has resolved. Patients with persistent haematuria require evaluation.

Pattern of haematuria
Gross haematuria: If the blood is visible to the naked eye, it is called gross haematuria. In gross haematuria the urine is pink, red, or dark brown and may contain small blood clots. The amount of blood in the urine does not necessarily indicate the seriousness of the underlying problem. As little as 1 milliliter (0.03 ounces) of blood will turn the urine red.

Microscopic haematuria: If the blood is detected only on a urine test, it is called microscopic haematuria. The recommended definition of microscopic haematuria is three or more red blood cells per high-power field on microscopic evaluation of urinary sediment from two of three properly collected urinalysis specimens. Thus, should be evaluated appropriately. At this time, there is no consensus on when to test for microscopic haematuria in the primary care setting.

Intermittent Haematuria: To account for intermittent positive tests for haematuria the patients with more than three red blood cells per high-power field from two of three properly collected urine specimens. It could be microscopic haematuria or macroscopic haematuria and, thus, should be evaluated appropriately. However, before a decision is made to defer evaluation in-patients with one or two red blood cells per high-power field, risk factors for significant disease should be taken into consideration. High-risk patients should be considered for full urologic and nephrologic evaluation after one properly performed
urinalysis documenting the presence of at least three red blood cells per high-power field.

**Risk Factors for Significant Disease in Patients with Microscopic Haematuria**
- Smoking history
- Occupational exposure to chemicals or dyes (benzenes or aromatic amines)
- Age >40 years - History of urologic disorder or disease
- History of irritative voiding symptoms
- History of urinary tract infection
- Analgesic abuse
- History of pelvic irradiation

**Isolated haematuria**
Patients with microscopic haematuria, a negative initial urologic evaluation and no evidence of glomerular bleeding are considered to have isolated haematuria. Although many such patients may have structural glomerular abnormalities, they appear to have low risk for progressive renal disease. Thus, the role of renal biopsy in this setting has not been defined. Nevertheless, because follow-up data are limited, these patients should be followed for the development of hypertension, renal insufficiency or proteinuria.

**Idiopathic haematuria**
A small number of people experience microscopic haematuria that has no discernible cause. These people normally excrete a higher number of red blood cells. "Joggers haematuria" results from repeated jarring of the bladder during jogging or long-distance running.

**Pseudohaematuria**
Reddish urine that is not caused by blood in the urine is called pseudohaematuria. Excessive consumption of beets, berries, or rhubarb; food coloring; and certain laxatives and pain medications can produce pink or reddish urine.

**What are the symptoms?**
The major symptom is blood in the urine, but it is often invisible to the naked eye. Sometimes there is swelling, high blood pressure, or another symptom of an underlying cause for the haematuria. In many cases, blood in the urine (gross or microscopic) is the only sign of a disorder. In others, a variety of symptoms, such as abdominal pain, decreased urinary force, hesitance, incomplete voiding, fever, frequent urination (polyuria), pain during urination (dysuria), pain in the flank or side, urinary urgency may be present.

**What is significant haematuria?**
Previously we have been taught that haematuria above 10 RBC's per high powered field on MSU was significant and less than 10 were safe. Unfortunately this is not true. The risk of a significant pathology relates to age and various risk factors including smoking, occupational and family history. Several studies have tried to define a safe for haematuria and have concluded that there is no level of haematuria, which is safe to dismiss in any age group.

**How is it diagnosed?**
Haematuria may be diagnosed when blood is observed in the urine or discovered on a urine test. Red urine does not necessarily mean blood in the urine. Beetroot and blackberries can discolour the urine red due to their anthrocyanin pigment, as can various medications, including phenothiazines, prefantacin, and haemoglobinuria and myoglobinuria (filtered breakdown products of blood and muscle). The initial determination of microscopic haematuria should be based on microscopic examination of urinary sediment from a freshly voided, clean-catch, midstream urine specimen. Clues to the underlying cause may be found with a careful history and physical exam and some screening lab tests. If the cause is not apparent, the diagnostic work-up continues step by step until the cause is found. Early tests might include a complete blood count, a urine culture, a 24-hour urine
collection, a blood test renal function, a C3 level (a screening test to look for kidney causes such as inflammation caused by streptococcus or lupus), and an imaging study such as an ultrasound. Both urine dipstick and urine microscopy are sensitive tests to detect haematuria, but only an MSU will differentiate the site of bleeding. Haematuria can be measured quantitatively by any of the following:

1. Determination of the number of red blood cells per milliliter of urine excreted (chamber count),
2. Direct examination of the centrifuged urinary sediment (sediment count) or
3. Indirect examination of the urine by dipstick (the simplest way to detect microscopic haematuria). Given the limited specificity of the dipstick method (65 percent to 99 percent for two to five red blood cells per high-power microscopic field). However, the initial finding of microscopic haematuria by the dipstick method should be confirmed by microscopic evaluation of urinary sediment or chamber count.
4. Up to 3 erythrocyte hpf is considered to be a normal when urinary sediment is examined after centrifugation. Fewer than 4 % people usually excrete more than 3 erythrocyte hpf.
5. Normally adult populations excrete about 107 erythrocyte in 2 litter of urine per day. Normal level of excretion is about 8000 RBCs per ml (when urine is centrifuged) and 13000 (when uncentrifuged urine) are examined.
6. Macroscopic haematuria often causes considerable concern, and just a few mils of blood can turn a whole bladder full of urine quite dark red. Sometimes the site of bleeding can be localised within the urinary tract by determining whether the bleeding is "initial"- i.e. at the beginning of the stream only,"terminal"- i.e. at the end of the stream only, or "complete"- i.e. throughout the entire stream. Initial haematuria generally indicates bleeding from the urethra that is flushed out by the first passage of urine through the urethra. Terminal haematuria can arise from the posterior urethra, bladder neck or trigone (base of the bladder), and is noticed at the end of urination, when the bladder compresses these areas. Total haematuria indicates that the bleeding occurs at the level of the bladder or higher in the urinary tract, so that all of the urine is mixed with the blood, and the entire stream is therefore bloody.
7. Pain that occurs in association with a urinary tract infection or passage of a stone may indicate that the bleeding is from a benign cause.
8. Painless haematuria is generally regarded as secondary to a urinary tract cancer, until proven otherwise. However, all bleeding warrants investigation, to be certain that there is not an associated cancer, besides the more obvious causes for painful bleeding.

How is it treated?
Treatment is aimed at the underlying cause.

How can it be prevented?
Prevention also depends on the underlying cause.

Conclusion
Not all patients need every test, whilst some may need a very thorough evaluation to be confident of detecting cancer. As a rule if patient has had macroscopic haematuria, or is at high risk, tests should continue until a cause is found.

References
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