

A Study on Differential Diagnosis Related to Haematuria in Urological Practice in a Tertiary Hospital

Baki MA¹, Rakib MA², Rashid HO³, Rashid SH⁴, Patwary MHM⁵

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ABSTRACT

Background: Haematuria is the presence of red blood cells in urine, a common clinical finding with multiple differential diagnosis and it can often be a diagnostic dilemma. It serves as a key feature in numerous urological and nephrological disorders. In the differential diagnostics, haematuria is typically classified as painful or painless, and further distinguished as gross haematuria, visible to the naked eye or microhaematuria, detectable only under microscope. The underlying causes are broadly divided into pre-renal (haematological), renal (glomerular) and non-renal (non-glomerular) origins. To avoid missing early indicators of malignant or significant benign conditions, while at the same time avoiding unnecessary investigations, a structured differentiated approach is imperative. This article provides a clear and practical framework to identify patients with clinically significant haematuria and cases those requiring urgent urological intervention.

Methods: This descriptive type of cross sectional study was carried out at Combined Military Hospital, Dhaka with a duration of 12 months from 01 July 2022 to 30 June 2023. A total of 100 respondents were included who presented either with gross or microscopic haematuria in the said duration. Cases were chosen by purposive sampling from patients who reported to urology outpatient department (OPD) or admitted in inpatient ward.

Results: Of the 100 patients, 74% were male and 26% female (ratio 3:1). The highest frequency was observed in the 51-60 years age group (28%). Malignancy accounted for the majority of cases (55%), followed by urolithiasis (21%) and benign prostatic hyperplasia (9%). Among malignancies, transitional cell carcinoma of the urinary bladder (TCC UB) was the predominant type (65.45%).

Conclusion: The occurrence of haematuria should always be given utmost importance in urologic practice. A high index of suspicion regarding all potential aetiologies is needed to deal every single case.

Keywords: Haematuria, Differential diagnosis, Urologic.

1. Major Md Abdul Baki, MCPS (Surgery), FCPS (Urology), BGB Hospital Thakurgaon, 2. Brig Gen Md Abdur Rakib, SGP, MCPS, FCPS (Surgery), FCPS (Urology), FACS, FRCS, CMH Dhaka, 3. Lt Col Harun-Or-Rashid, FCPS (Urology), CMH, Jashore, 4. Lt Col Szal Hafizur Rashid, MCPS (Surgery), FCPS (Surgery), FCPS (Urology) CMH, Cumilla, 5. CGO-1 Md Helal Morshed Patwary, BSc(Hons), MS(Statistics), AFMI

Correspondence: Maj Md Abdul Baki, MCPS (Surgery), FCPS (Urology), BGB Hospital, Thakurgaon, Mobile: 01717-086218, E-mail: baki.sbmc39@gmail.com

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INTRODUCTION

Haematuria is defined as evidence of blood in urine under microscopy and, a common symptom of both benign and malignant surgical or genitourinary conditions. From population screening it was estimated that the prevalence of haematuria, both macroscopic and microscopic, may range from 5% to as high as 20%.¹ It is a complex condition with a multitude of causes and treatment protocol. This article will discuss the differential diagnosis of haematuria from urological perspective in a tertiary care hospital. There is a range of conditions that can cause both visible (VH) and non-visible haematuria (NVH). Gross or macroscopic haematuria is when blood is visible in the urine in naked eye. Whereas, microscopic haematuria is defined as three or more red blood cells per high-powered field under microscopy in a properly collected urine sample. In Australia, microscopic haematuria is defined as more than 10 red blood cells in high field power on microscopic evaluation. This varies from more than 3-10 cells depending on British, European or American definitions. The prevalence of microscopic haematuria is 0.19–21.0%.²⁻³ Macroscopic haematuria is more concerning and warrants thorough investigation, as the prevalence of urinary tract carcinomas among patients with macroscopic haematuria has been reported to be as high as 19%, but usually ranges from 3-6%.²

Visible haematuria is a presenting sign in more than 66% of patients with urological cancer.¹ The sensitivity of visible haematuria in revealing malignancy is significant: 0.83 for urothelial carcinoma of the bladder, 0.66 for ureteric carcinoma, and 0.48 in renal cell carcinomas.⁴ In men aged >60 years, the positive predictive value of visible haematuria for urological malignancy is 22.1%, and in women of the same age it is 8.3%.⁵

One of the most common causes of haematuria is Urinary Tract Infection (UTI), which can be investigated with a urine microscopy, culture and sensitivity. Ureteric and renal stones are another common cause, but these are typically present with pain and microscopic haematuria. In cases where macroscopic haematuria or risk factors are present or if another cause cannot be determined, more extensive investigations to rule out underlying malignancy are recommended. Anticoagulation within the therapeutic range does not increase the prevalence of haematuria. Thus, patients on anticoagulants should undergo the same diagnostic work-up as those not receiving such therapy. Despite extensive investigation, studies have shown that up to 50% of patients with macroscopic haematuria and 70% with microscopic haematuria have no identifiable cause found.⁶ This could also be attributed to transient benign physiological conditions, including vigorous physical exercise, sexual intercourse or menstrual contamination.⁷ Again, haematuria should be differentiated from other conditions which might mimic haematuria such as hemoglobinuria, myoglobinuria, porphyria, bile pigments, and alkaptonuria.⁸

MATERIALS AND METHODS

This descriptive type of cross sectional study was conducted at Combined Military Hospital, Dhaka with a duration of 12 months. A total of 100 adult male and female respondents with age ≥ 18 years, presenting with either gross or microscopic haematuria were included through purposive sampling from the Urology OPD and inpatient wards. Patients those had haematuria due to pre-renal/haematological or glomerular causes, were not selected for this study purpose. Ethical clearance was taken from Institutional Ethical Review Committee of Armed Forces Medical Institute (AFMI) on 29 June 2022 via letter

number 3606/T. Informed written consent was obtained from each case. Patient confidentiality was strictly maintained and no names, contact details were divulged. All the clinical findings and reports were kept confidential. All data were summarized and using descriptive statistics. Mean \pm SD of numerical data were calculated. All data were analyzed using SPSS version 23.

RESULTS

Table 1 illustrates the demographic characteristics of the respondents. A total number of 100 cases were evaluated who fulfilled all the inclusion and exclusion criteria. Patients of both gender were examined. Here, most of the cases were male (74.0%). Highest number of patients were in between ages from 51 to 60 years group (28.0%).

TABLE-I: Socio-demographic characteristics (n=100)

Variables	Frequency	Percentage
Age (in years)		
18-30	10	10.0
31-40	14	14.0
41-50	22	22.0
51-60	28	28.0
61-70	19	19.0
71-80	07	07.0
Mean \pm SD :54.6 \pm 17(19-78)		
Sex		
Male	74	74.0
Female	26	26.0
Occupation		
Service holder	46	46.0
Housewife	19	19.0
Retired personnel	26	26.0
Student	9	8.0
Smoking habit		
Smoker	27	27.0
Non-smoker	73	73.0

Table 2 shows that the leading cause of haematuria was malignancy affecting the urinary tract (55.0%). Amongst malignancy, maximum

cases were TCC UB (36 out of 55, 65.45%). Urolithiasis was the second (21.0%) most prevalent condition. Benign prostatic hyperplasia (BPH) ranked the third (9.0%) largest group.

TABLE -II: Overall distribution of diseases among study population (n=100)

Disease	Number of cases	Percentage of study population
GU Malignancy	55	55.0
a. Renal cell carcinoma (RCC)	15	15.0
b. Bladder TCC	36	36.0
c. Carcinoma Prostate (PCa)	04	4.0
Urolithiasis	21	21.0
a. Renal stone	06	6.0
b. Ureteric stone	14	14.0
c. Vesical stone	01	1.0
BPH	09	9.0
UTI	05	5.0
Trauma/Injury	04	4.0
Genito-urinary Tuberculosis (GUTB)	03	3.0
Schistosomiasis	02	2.0
Gynaecological malignancy	01	1.0
Total	100	100

This doughnut shaped chart visualizes a scenario where 39% of the study population were clinically documented to experience painful haematuria. Of the 100 patients in the study, most of the cases with stone diseases (21%), infection (5%) and injury (4%) were invariably associated with pain. Four cases of urothelial carcinoma and one patient with prostatic adenocarcinoma presented with clot colic due to urinary obstruction. Three respondents with BPH had chronic retention and secondary bacterial infection/cystitis and subsequently experienced pain along with reddish urine. The patient with gynaecological malignancy involving the bladder base reported with painful haematuria possibly due to local nerve entrapment. Rest of the 61% cases were painless.

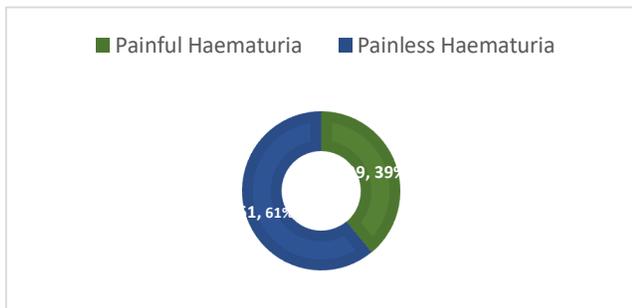


Fig-1: Pie chart demonstrating types of haematuria based on pain sensation.

Following chart summarizes that total 77% of patients presented with gross haematuria, whereas only 18% of patients were found to have asymptomatic microscopic haematuria, rest of the 5% of patients initially had microscopic haematuria that turned out to be visible or symptomatic later on.

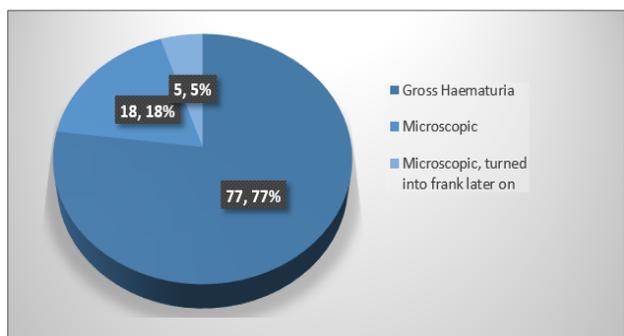


Fig-2: Pie chart showing types of haematuria based on presentation.

DISCUSSION

Our data of 100 respondents shows that minimum recorded age was 19, whereas maximum was 78 and mean age was being 54.6 years. Again, highest 28 (28%) respondents were in the age group of 51-60 years followed by 22% cases were in the age range of 41-50 years. A clear male predominance was observed (74%), with a male-to-female ratio of 3:1. Female patients are significantly less in number due to social and religious bindings, and shyness to attend the male doctors. Therefore, they also present with

comparatively longer history of symptoms and more complicated cases than their counterpart and interestingly more than half of them had UTI along with the main disease. This similar observation was also noted in Ingelfinger et al.⁸ where they stated that evaluation in women is often delayed, which may contribute to worse outcomes among female patients. A female respondent was admitted to urology ward with gross haematuria but after having all the relevant investigations she was diagnosed as a case of cervical carcinoma invading the bladder wall.

In our cohort, cancerous conditions of the genitourinary system (55%) were the leading cause of haematuria. Within this category, bladder TCC was the most prevalent (36 out of 55) malignant lesion, comprising 65.4% of all cancer cases. RCC was the second most common malignancy accounting for 15.0% of all and 27.3% of malignant cases. Prostate cancer was reported in 7.3% (4 out of 55) of the cancer patients. These findings are not familiar with some studies done elsewhere. Yeoh et al.⁷ found the prevalence of urinary tract carcinomas among patients with macroscopic haematuria to be only 19%. Current study implies that malignancy consists of more than half of all cases as the study was conducted in a tertiary level hospital and most of the cases were referred from different peripherally placed military hospital. Gross haematuria should always be taken cautiously and is considered as ‘red flag’ for genitourinary malignancy. In this current study, total 9% of patients with microscopic haematuria and up to 46% of patients with gross haematuria were confirmed as malignant case. Almost same result was found by Avellino et al.⁹ in which they found that roughly 4% of patients with microscopic haematuria and up to 40% of patients with gross haematuria could harboring a malignancy.

This study, analyzing the clinical presentation of haematuria in 100 patients, found that 39% presented with painful haematuria, while for the majority (61%), it was painless (Chart-1). This mix of experiences reminds us that while pain is a powerful clue, it doesn't tell the whole story, a perspective echoed in more recent medical research. The most common pathologies associated with painful hematuria in our cohort were stone disease (21%), infection (5%), and trauma (4%). The pain here acts like a clear alarm bell for sudden blockage or inflammation in the urinary system. This fits perfectly with what experts have been saying, like in a 2015 review which stressed that pain often guides us toward these acute, urgent issues.¹⁰ Our findings strongly support this classic view. Here, most of the cases with microhaematuria was associated with pain or dysuria. Again, in our study, painful haematuria was linked to urinary stone disease instead of UTI. In our study, urolithiasis was second most common issue related to haematuria, affecting 21% of the study population. Ureteric stones were of notable concern, making 67% (14 out of 21 cases) of all stone diseases. This observation implies that urolithiasis is more common (21%) in young military personnel due to vigorous exercises or excessive exertional duty pattern.

Notably, our study highlights that pain is not exclusive to benign conditions. We documented four cases of urothelial carcinoma and one of prostatic adenocarcinoma presenting with "clot colic" due to urinary tract obstruction. This complicates the traditional teaching that painless hematuria is the hallmark of malignancy. A 2018 retrospective analysis by Chen and Colleagues found that 15-20% of bladder cancer patients reported discomfort or pain at presentation, often related to clot retention or bulky disease.¹¹ Furthermore, we observed three patients with Benign Prostatic Hyperplasia (BPH) whose

painful hematuria was linked to chronic retention and secondary infection from urinary stasis. This pathophysiology is consistent with findings from the 2016 EPIC study, which identified urinary stasis as a significant risk factor for recurrent urinary tract infections and complicated hematuria in elderly males with bladder outlet obstruction.¹² This reinforces the importance of assessing bladder drainage and function in patients with hematuria, particularly in older male populations.

The single case of painful hematuria from a gynecological malignancy involving the bladder base, attributed to potential local nerve entrapment, illustrates a less common but critical mechanism. This aligns with multidisciplinary perspectives emerging in the 2010s, as highlighted in a 2019 gynecologic oncology review by Sharma et al., which detailed how locally advanced pelvic malignancies can cause hematuria with pain through direct invasion and perineural involvement, blurring urological and gynecological symptom boundaries¹³. Conversely, our finding that 61% of cases were painless is consistent with the dominant clinical teaching. Large cohort studies from the early 2010s, such as the analysis by Edwards et al.¹⁴, continued to report painless hematuria as the most common presenting symptom for bladder cancer, driving screening and referral guidelines. However, our juxtaposition of a significant painful minority (39%) against this majority suggests a spectrum of presentation. This calls for a refined clinical approach where the absence of pain should not lower the index of suspicion for serious disease, and the presence of pain should not automatically rule out malignancy, particularly when obstructive symptoms are present. These results were also supported by Khadra et al.⁶ and Yafi et al.¹⁵

In the current study, gross haematuria was the presenting symptom in 77% of patients, while 18% had asymptomatic microscopic haematuria. In 5% of patients, initial microscopic haematuria later progressed to gross haematuria (Chart-2). It was noticed that many patients with gross haematuria reported to surgical OPD first and then to urology OPD as referral cases. Whereas, many of the cases of microhaematuria were referred from nephrology OPD after being confirmed that the disease was non-glomerular in origin. This result is supported by Bolenz et al.¹⁶ where the reported prevalence of microhaematuria ranged between 1.7% and 31.1%.

Here, three cases of genitourinary tuberculosis (GUTB) were identified in the current study. This finding aligns with the known endemicity of tuberculosis in the Indian subcontinent, of which Bangladesh is a part. The prevalence of extrapulmonary TB, including GUTB, remains disproportionately high in this region compared to global averages, a persistent public health challenge documented in contemporary literature.¹⁷ Furthermore, two cases of schistosomiasis (bilharziasis) were diagnosed. Given that schistosomiasis is not endemic to Bangladesh, these cases are highly suggestive of travel-related or deployment-acquired infection. This is a significant consideration, as one plausible epidemiological link is the history of military or peacekeeping deployments to endemic regions in the Middle East or Africa by members of the armed forces, a recognized risk factor for imported parasitic diseases.¹⁸

CONCLUSION

Haematuria signifies a wide spectrum of urological or nephrological pathology, or sometimes may bear no significance at all. The

key challenge for clinicians is to get the correct patients assessed reasonably so that serious or potentially life-threatening conditions are not overlooked. Again, haematuria can be a sign of grievous underlying genitourinary disease. Thoughtful and systematic evaluation of the full genitourinary system should be initiated in the primary care setting and urologic consultation should be obtained, based on suspected aetiology of haematuria. A standard methodical assessment of the genitourinary system is of paramount importance for the early accurate detection and prompt successful management of the underlying urologic disease.

RECOMMENDATIONS

While malignancy and stones were predominant, the study acknowledges a broad differential including pre-renal and renal causes. We recommend establishing a formal referral and collaboration pathway between urology, nephrology and haematology departments. This is crucial to efficiently diagnose and manage glomerulonephritis, coagulopathies, or other systemic conditions presenting with haematuria, ensuring comprehensive patient care. Given the high prevalence of malignancy (55%), particularly among older adults, in this cohort, we recommend adopting a formal, risk-stratified clinical pathway for all patients presenting with haematuria. Since haematuria is a critical early sign of serious conditions like bladder cancer, we recommend initiating awareness campaigns targeting the public and primary healthcare providers. The message should emphasize that any episode of visible blood in the urine, even if painless and transient, requires immediate urological consultation. This is vital for early detection and improved outcomes.

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