Haematuria – A Sinister Sign with a Wide Spectrum of Diagnosis

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ABSTRACT
Objective: To assess the extent of presentation of different causes of gross haematuria in our hospital.
Study Design: Prospective descriptive study.
Place and Duration of Study: GMC Jammu, from Mar 2013 to Mar 2019
Material and Method: All new patients who reported 'blood in urine' symptoms to the hospital were included in the analysis, while patients with Microscopic Haematuria were omitted. The patients were given a questionnaire to fill out, helped by a resident, after being managed by the urology registrar, with a reference number assigned for follow-up. To validate haematuria and remove malignant cells, a request for urine routine analysis and urine microscopy/cytology was made, as needed, followed by ultrasound, X-Ray KUB, cystoscopy and IVU/CTU scan. The findings were recorded, reported and analysed.
Results: A total of 586 patients experienced 'blood in urine' complaints. Trauma: 21.7 percent (n=127) was the most common cause observed, followed by urinary tract infections (21.0 percent, n=123), urolithiasis (20.2 percent, n=119) and 19.4 percent (n=114) of urological tumours. Around two-thirds of patients (57.1 percent, n=65) with urological tumours were not tested at the primary health care stage to assess the cause of haematuria and eventually ended up being diagnosed with progressive disease.

Keywords: haematuria, bladder haematuria tract infections, urolithiasis.

INTRODUCTION
Haematuria in urological patients is one of the most troubling signs and most of the afflicted patients immediately seek a medical consultation¹. Bladder cancer in India accounts for 3.9 percent of all cancer cases, according to the Indian cancer registry data for men². The young general practitioner, however, appears to take it lightly by omitting basic research to identify the cause and treat the patients on the lines of urinary tract infection or urolithiasis empirically. When investigated further by urologists, it was found that more than half of the patients presenting with haematuria were given a course of antibiotics and reassured by a general practitioner ended up with malignancy and advanced disease. The bleeding used to stop after a few days, taking a normal path, and the patients were assured that nothing was wrong. In addition, on the basis of this practice, patients decided to take the same antibiotics if they saw blood in their urine. As the disease progressed and the number of episodes that were not managed by the drug increased, the patients returned to the doctor only to be diagnosed with an advanced malignancy stage.

In view of situations like these, we studied the number of patients who had urological tumours and had gross haematuria presented to GP but missed the opportunity for early diagnosis. In addition, we also
wanted to make young doctors aware of the importance of early diagnosis and inculcate in them a working procedure for the identification of these patients among those suffering from gross haematuria, applicable to our health care system.

PATIENTS AND METHODS

These prospective descriptive studies were conducted at GMC Jammu. Data was recorded using the questionnaires for all new patients who reported urinary blood complaints, i.e., "Gross Haematuria," and the cause of Haematuria was established. Patients with urological malignancies were also asked if they had contacted a general practitioner for the treatment of haematuria. If so, had they been examined? The management at our hospital was also registered.

The sample size was estimated using the online prevalence calculator on www.sampsize.sourceforge.net.

Inclusion Criteria:

All patients in the OPD and ER reporting of 'blood in urine' issues were included in the analysis. Exclusion criteria:

1. Patients who presented to the OPD after urological operation within 48 hours in our hospital were not included in the study.
2. Patients with microscopic haematuria.

After being adequately treated, the patients were given a questionnaire to complete, helped by a resident.

Urinary routine screening (haematuria validation and glomerular disease exclusion) and urinary microscopy/cytology (to rule out malignant cells) was requested. Ultrasound, x-ray KUB, cystoscopy and IVU/CET scan were followed, as required.

The data were documented in SPSS version 21 and analysed. It was measured and the data was displayed in graphical form, in terms of incidence of various triggers, male to female ratio and averages etc.

Results

From March 2012 to March 2019, a total of 586 patients reported 'blood in urine' (i.e., gross Haematuria) complaints. There was a 3:1 male to female ratio of 443 (75.5 percent) male and 143(24.55 percent) female patients, and the mean age was 44.94 years (range 12 to 89 years). Causes of haematuria have been observed as follows.

In our study, trauma was the most common cause, with 21.6 percent (n=127) of cases. Blunt trauma to the abdomen, penetrating trauma and pelvic fracture were the injuries responsible. And a few Iatrogenic wounds have also been seen.

Urine tract infections were detected in 20.9% (n=123) of the female-predominant patients.

With 20.3 percent (n=119) in our study, Urolithiasis emerged as the third most frequent cause. Patients

<table>
<thead>
<tr>
<th>Causes of gross haematuria</th>
<th>Patients (n)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trauma</td>
<td>127</td>
<td>21.6%</td>
</tr>
<tr>
<td>UTI</td>
<td>123</td>
<td>20.9%</td>
</tr>
<tr>
<td>Urolithiasis</td>
<td>119</td>
<td>20.3%</td>
</tr>
<tr>
<td>Urothelial Tumours</td>
<td>114</td>
<td>19.4%</td>
</tr>
<tr>
<td>Prostatic / Urethral Pathology</td>
<td>99</td>
<td>16.9%</td>
</tr>
<tr>
<td>Drug induced</td>
<td>5</td>
<td>0.86%</td>
</tr>
<tr>
<td>Exercise</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>
had a history of discomfort and prior episodes, although few have a history of stone movement.

In 19.4 percent (n=114) occurrences, urological tumours were seen. In these 21 (18.4 percent) urban patients, the first episode happened and came immediately to our hospital, while 93 (81.6 percent) rural patients have a history of a related episode in the past. Of these, n=29 (31.1%) had a previous episode, while 64 (68.8%) had two or more episodes on which a GP had been contacted. Just 34 (36.6%) of these 93 patients were examined, while 59 (63.4%) were seen by the main prescribing doctor/quack at the time of the first episode (fig-3).

Consequently, only 42.9 percent (n=49) of patients reported early on, while 57.1 percent (n=65) reported with advanced disease which was not followed up at the initial place of presentation.

In 16.9 percent (n=99) cases, urethral and prostatic causes were found, more commonly seen with rural-area patients. The noted factors included chronic urinary retention, Urethral stricture dilatation and failed/traumatic catheterization.

When consulted by the oncology team, we only had 0.8 percent (n=5) patients with haematuria caused by medications. There were no such patients in OPD or ER.

No cases were found linked to intense physical exercise.

Discussion

Haematuria is a distressing symptom that can be found in many urology related pathologies, prompting the patient to visit a doctor. It can be attributed to some relatively inconsequential causes at one end of the spectrum, while it can be an ominous symptom of a life-threatening illness at the other. It has been found that haematuria is seldom given due importance by general practitioners, who typically treat it empirically as an inflammation of the urinary tract or urolithiasis and lose the patient before it is too late to follow up.

Haematuria can be categorized as glomerular, diagnosed with proteinuria and/or the presence of RBC casts in the urine (which is outside the scope of this study). The other type is non-glomerular haematuria, subdivided into causes of the upper and lower tract, including stones, cancers, cancers, prostatic, iatrogenic, and exercise.

Various population-based studies have been carried out and found that asymptomatic haematuria is widespread from 1% to 16% in the general population, depending on the risk according to the age group, with a higher incidence rate for older age groups.
The American Urological Association (AUA) describes microscopic haematuria as clinically significant if three or more red blood cells per high power field are present from two out of three properly obtained urinalysis specimens on microscopic examination of urinary sediments.\textsuperscript{4,5} Severe haematuria may occur in up to 38.7 percent of young active adults (under 40 years), but only 0.1 percent is associated with urological neoplasia and does not require further urological study.\textsuperscript{6} However, to reduce the radiation exposure and cost, IVU and USG may be used in these patients.\textsuperscript{7} In addition, urinary cytology in this population is not considered cost-effective, as seen by Andrew H. Feifer et al, who analysed 200 patients with microscopic haematuria at low risk and found no positive urinary cytology.\textsuperscript{8}

Gross haematuria is characterized as blood that is noticeable by the naked-eye or blood clot in the urine. It should be noted here that only 1 ml of blood in one litre of urine will give the urine a red colour. Up to 4-20 percent of urological hospital admissions are accounted for haematuria.\textsuperscript{7,9}

From March 2014 to March 2019, we observed 586 patients who reported 'blood in urine' symptoms, i.e., 'gross Haematuria.' The most prominent cause of gross haematuria observed was trauma. Many of the incidents were secondary to road traffic accidents with blunt abdominal and flank trauma causing renal injury and bladder, and urethral injuries caused by pelvic fracture. Gross haematuria was also presented in patients with penetrated wounds such as stab and gunshot affecting lumbar and hypogastric areas. In approximately 14 per cent of children with injuries, gross haematuria was seen, as shown by Taylor et al.\textsuperscript{10} Although a large number of adult patients still present to A&E with gross haematuria.

The reasons for gross haematuria were also frequent iatrogenic accidents following catheterization, urethral dilation, endoscopic treatments etc.

Since urinary stones are very common, the number of patients with urolithiasis presenting with haematuria is also to be taken into account. These patients have a long history of irritative urological signs, colicky pain and past related episodes, including sporadic history of stone passage. Bladder and urethral calculi were popular, along with a few urethral calculi. Microscopic haematuria was much more common and was found in up to 85 percent of cases, whereas gross haematuria was relatively rare.\textsuperscript{11}

In about 21\% of the patients that had presented with haematuria, we diagnosed urinary tract infections. As observed by Gösta Wallmark et al, it is similar to other research, who also found that Staphylococcus-related infections were more often associated with haematuria\textsuperscript{12} and were more prominent in females. The reaction to the antibiotics was, however, noticeable. Patients suffering from chronic infections like tuberculosis were also included in this group. It should be noted that tuberculosis is very common in India, especially among the low socio-economic population.

Jammu is surrounded by several small farming villages with little to no medical services, a condition where quackery flourishes, such quacks attempt to perform minor operations with catastrophic complications, including catheterization and urethral dilatations. Ignored signs of an enlarged prostate contribute to urinary retention which can manifest as haematuria at times. In our research, it was seen more often in patients from rural areas who found it to be a natural ageing phase or who were seeking care from quacks and diagnosed with haematuria only after prolonged episodes. The history of failed/traumatic catheterization, was also provided by a few. Ramyil et al. found that haematuria was present in 37 percent of patients with BPH or prostatic carcinoma\textsuperscript{13}. We had about seventeen percent of this category’s patients.

Various drugs, such as cytotoxic drugs, are considered to be responsible for haematuria, while some can simply affect the colour of the haematuria-confused urine. We did not see any patients with haematuria caused by prescriptions in ER or OPD, but we had oncology unit appointments for haematuria problems. Anti-tuberculosis treatment patients (Rifampicin and INH) seen in OPD were asked about urinary discoloration. They knew it was a side effect of treatment for antituberculosis. Myoglobin, haemoglobin, porphyrins from endogenous origins are some of the other substances that induce discoloration of urine, while rhubarb, black, fruit, beet root, artificial food colours and drugs such as rifampin, desferoxamine, phenolphthalein, phenazopyridine, etc. are a few prominent exogenous triggers.
It is known that intense activity and marathon runners have micro-haematuria\(^\text{14}\). They may have gross haematuria rarely, but we did not detect any such case in our research.

A significant cause of gross haematuria is urological tumours. Gross haematuria is present in around twenty percent of patients with bladder carcinoma\(^\text{15}\). A large number of patients with advanced bladder carcinoma who have had a history of previous related episodes have been treated, enabling us to perform this research.

We found that 19.4% of the patients who registered gross haematuria symptoms to our hospital suffered from urological neoplasm. William C. Carter, Stephen N. Rous, who found that 23% of patients who had gross haematuria had urothelial carcinoma as the cause of their haematuria, also made similar observations\(^\text{15}\). Old age, male gender, tobacco smoking, chemical contamination (cyclophosphamide, benzene, aromatic amines), pelvic radiation, schistosomiasis, etc.\(^\text{16}\) are some of the major risk factors that place the patient in the high-risk category for these urological malignancies. The unfortunate part of our patients' tale is that they had referred to a doctor earlier in the history of the illness but were not adequately treated, thereby failing to take advantage of the early detection advantages.

Some important considerations to be kept in mind when treating a patient with haematuria at the level of a general practitioner are that approximately 60 to 70 percent of patients can be properly detected by history and relevant physical exam and basic investigations,\(^\text{17}\) and incorporating urinary cytology and cystoscopy offers diagnosis in up to 95 percent of cases\(^\text{18}\).

If the patient had normal to strenuous physical exercise, any viral illness, sexual activity, DRE or instrumentation, and menstruation in women within a few days prior to examination or had minor injuries, the findings would likely be null because of the likelihood of temporary haematuria induction.\(^\text{19}\)

New testing approaches such as Multidetector Computerized Tomography Urography (MCTU) are more prone to the diagnosis of upper tract TCC\(^\text{20,21}\), but they are pricey and not readily available in our healthcare system, so they cannot be openly used.

AUA suggests that all patients over 40 years of age and those younger but with symptoms indicating urothelial carcinoma and haematuria\(^\text{4}\) or pathological urinary cytology can undergo cystoscopy\(^\text{22}\) in order to complete the evaluation, but only urethra and bladder lesions can be identified and in-situ lesions cannot be detected consistently\(^\text{23}\).

In comparison, a survey performed by Messing et al. for haematuria diagnosis and screening showed that 21.1% of the general population over 50 years of age had haematuria episodes, but only 1.1% had urological cancers as the cause. Showing that while home screening could be feasible for patients over 50 years,\(^\text{24}\) it was not cost-effective for a hospital or community-based screening program, as haematuria prevalence is about 1.38 percent,\(^\text{25}\) so it is worthwhile to thoroughly examine patients with gross haematuria.

A prompt assessment is useful for the early diagnosis of treatable urothelial carcinomas\(^\text{26}\). Microscopic haematuria should also be tested immediately for renal function and should be consulted by a nephrologist if proteinuria, elevated serum creatinine or red cell casts are observed. If physical activity, trauma, menstruation, etc. are suspected, imaging and urinary cytology may be re-evaluated after treating the cause. And where there is gross haematuria, with or without clots, at least an ultrasound should be performed, and if the findings are positive, urological consultation should be prescribed.

**Conclusion:** -

General practitioners should be advised to order an ultrasound scan for patients with gross haematuria, since urothelial tumours can be easily treated for a greater long-term result if diagnosed early.

**References:** -


