

## FREQUENCY OF UROLOGICAL CARCINOMAS PRESENTING AS GROSS HAEMATURIA IN PUNJAB PAKISTAN AND RECOMMENDATION FOR ITS EARLY DIAGNOSIS

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### ABSTRACT

**Objective:** To determine the frequency of various causes of gross Haematuria presenting in our hospital and recommend a working protocol to young doctors.

**Study Design:** Prospective descriptive study.

**Place and Duration of Study:** Urology Department, District Headquarter and Teaching Hospital, Sargodha Medical College, from Mar 2012 to Mar 2014.

**Material and Method:** All fresh patients reporting to the hospital with complaints of 'blood in urine' were included in the study, while patients presenting with Microscopic haematuria were excluded. The patients, after being managed by the urology registrar, were given a questionnaire to fill, assisted by a resident, a reference number allotted for follow-up. A request for urine routine examination and urine microscopy/cytology was made to confirm haematuria and exclude malignant cells. Followed by ultrasound, X-Ray KUB, cystoscopy and IVU/CTU scan, as required. The results obtained were recorded and analyzed.

**Results:** A total of 391 patients presented with complaints of 'blood in urine'. Trauma: was the most frequent cause seen in 21.7% (n=85), followed by Urinary tract infections (21.0%, n=82), Urolithiasis (20.2%, n=79) and Urological tumors seen 19.4% (n=76) cases. About two thirds of the patients (56.6%, n=43) with urological tumors were not investigated, at primary health care level, to ascertain the cause and presented with advanced disease.

**Conclusion:** General practitioners should be encouraged to request ultrasound scan for patients presenting with gross haematuria, as urothelial tumours, if detected early, can be managed effectively with better long term outcome.

**Keywords:** Cystoscopy, Hematuria, Neoplasms, Pakistan, Urologic.

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### INTRODUCTION

Haematuria is one of the most alarming symptoms in urological patients and most of them try to consult a medical practitioner immediately. However the young general practitioner, tend to take it lightly by omitting basic investigations to determine the cause and manage empirically on the lines of urinary tract infection or urolithiasis. We were receiving more than half the patients of urological tumors having advance disease, when investigated it was found that the patients were given a course of antibiotics and reassured by general practitioner. Taking natural course, the bleeding stopped in a

few days and the patients were confident that there was nothing wrong. Further, based on this experience, the patients kept on taking the same antibiotics whenever they noticed blood in urine. As the disease advanced and the number of episodes increased which were not controlled with the medication, the patients returned to the doctor, only to be diagnosed as having advanced stage of malignancy.

Considering this typical scenario, we wanted to know the number of patients who had urological tumors and had presented to GP with gross haematuria but missed to avail the opportunity of early diagnosis. Moreover, we also wanted young doctors to be made aware of the importance early diagnosis and to recommend to them a working protocol for detection of these patients amongst those

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presenting with gross haematuria, relevant to our health care setup, so as to make an early diagnosis and initiate appropriate management on acceptable guidelines.

## PATIENTS AND METHODS

This prospective descriptive study was carried out at District Headquarters and Teaching Hospital of Sargodha Medical College. Data of all the new patients, presenting with complaints of Blood in urine i.e. "Gross haematuria", was recorded using questioner and the cause of haematuria was determined. Patients with urological malignancies were further inquired so as to identify the patients who had previous episodes of haematuria and whether they had consulted a medical practitioner. If so, were they investigated? The management at our hospital was also recorded.

Sample size was calculated using online

**Table: Causes of gross haematuria in patients presenting to our hospital.**

Cause	Patients (n)	Percentage (%)
Trauma	85	21.7
UTIs	82	21.0
Urolithiasis	79	20.2
Urinary Tumor	76	19.4
Prostatic Pathologies	66	16.9
Drugs	3	0.8
Exercise	0	0.0

statistical calculator for prevalence survey, available at [www.sampsize.sourceforge.net](http://www.sampsize.sourceforge.net). All fresh patients reporting to the hospital, both in OPD and ER, with complaints of 'blood in urine' were included in the study. While the patients presenting to the OPD following any urological intervention done in our hospital, within 48 hours, being the likely cause of haematuria and patients having Microscopic haematuria, were not included in the study.

The patients after being appropriately managed, were given a questionnaire to fill, assisted by a resident.

Request for urine routine examination (to confirm haematuria and exclude glomerular disease) and urine microscopy/cytology (to exclude malignant cells), was made. It was

followed by ultrasound, x-Ray KUB, cystoscopy and IVU / CTU scan, as required.

The data was recorded and analyzed using SPSS version 21. Frequency of different causes, male to female ratio and average age etc. was calculated and data was presented in graphic form.

## RESULTS

A total of 391 patients presented with complaints of 'blood in urine' (i.e. gross Haematuria) from March 2012 to March 2014. There were 295 (75.45%) male and 96 (24.55%) female patients male to female ration of 3:1, and average age was 44.94 years (range 12 to 89 years). Following causes of haematuria were observed (table, fig-1).

Trauma was the most frequent cause in our study with 21.7% (n=85) of cases. The injuries

responsible were blunt trauma of the abdomen, penetrating injuries and pelvic fracture. Quite a few Iatrogenic injuries were also seen.

Urinary tract infections were found in 21.0% (n=82) of the patients with predominance of females.

Urolithiasis emerged as the third most frequent cause with 20.2% (n=79) in our study. Patients gave history of pain and previous episodes, while few had history of passage of stones as well.

Urethral and prostatic causes were observed in 16.9% (n=66) cases. More frequently seen in patients from rural areas. Chronic urinary retention, Urethral stricture dilatation and failed/traumatic catheterization were the noted causes.

We had only 0.8% (n=3) patients with haematuria caused by drugs as consulted by the oncology unit. However no such patient presented in OPD or ER.

No cases related to heavy physical activity were seen.

Urological tumors were seen in 19.4 % (n=76) cases. Of these 14 (18.4%) patients, who were from urban areas, had first episode and came directly to our hospital, while 62 (81.6%) patients, from rural areas, had history of similar episode in the past. Of these n=19 (30.6%) had one previous episode while 43 (69.4%) had two or more episodes (fig-2), for which they had consulted a GP. Of these 62 patients only 23 (37.1%) were investigated while 39 (62.9%) were given treatment by the primary treating doctor/quack at the time of first episode (fig-3). Therefore only 43.4% (n=33) patients presented early, while 56.6% (n=43) reported with advance disease.

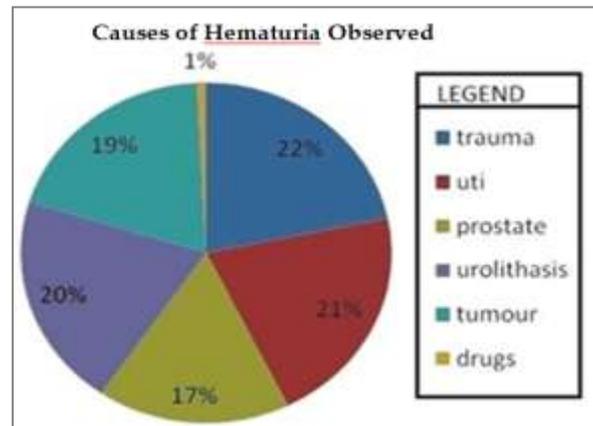
**DISCUSSION**

Haematuria is an alarming urological symptom, seen in many pathologies related to urological system, causing the patient to consult a doctor. On one end of the spectrum it may be due to some relatively inconsequential cause while at the other, it may be an ominous symptom of a life threatening disease. It was observed that haematuria is infrequently given the due importance by the general practitioners, who usually treatment it empirically as urinary tract infection or urolithiasis and the patient is lost to follow up until it is too late.

Various population based studies have demonstrated that asymptomatic haematuria is prevalent in general population from 1 to 16 percent depending up on the risk according to the age group, with older age having a higher prevalence rate<sup>1</sup>.

Haematuria can be classified as being glomerular, diagnosed by the presence of proteinuria and/or the presence of RBC casts in the urine (It is beyond the scope of this study).

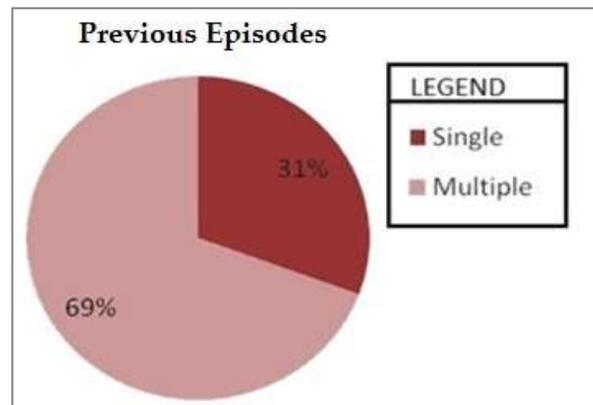
The other variety is non-glomerular haematuria, subdivided into upper and lower tract causes including stones, tumors, infections, prostatic, iatrogenic and exercise.



**Figure-1: Causes of gross haematuria observed in patients presenting to our hospital.**

Haematuria can be clinically classified, on the basis of the amount of blood in urine.

Microscopic haematuria as defined by The American Urological Association (AUA) is clinically significant if three or more red blood cells present per high-power field on microscopic



**Figure-2: Percentage of patients presenting with single or multiple previous episodes of hematuria to GPs.**

evaluation of urinary sediment from two out of three properly collected urinalysis specimens<sup>2,3</sup>.

Significant haematuria in young active adults (below 40 years) may be present in up to 38.7% but only 0.1% is related to urolgical neoplasia and does not warrant any further

urological investigations<sup>4</sup>. However IVU and USG may be used in these patients to limit radiation dose and cost<sup>5</sup>. Furthermore urinary cytology is not considered cost effective in this group, as demonstrated by Andrew H. Feifer et al, who studied 200 low risk patients with microscopic haematuria and found no positive urinary cytology<sup>6</sup>.

Gross haematuria is defined as blood or blood clot in urine visible by naked eye. Here it is worth mentioning that only 1 ml of blood in one liter of urine can impart red color to the urine<sup>1</sup>. It is responsible for up to 4-20% visits to urological hospitals<sup>7</sup>.

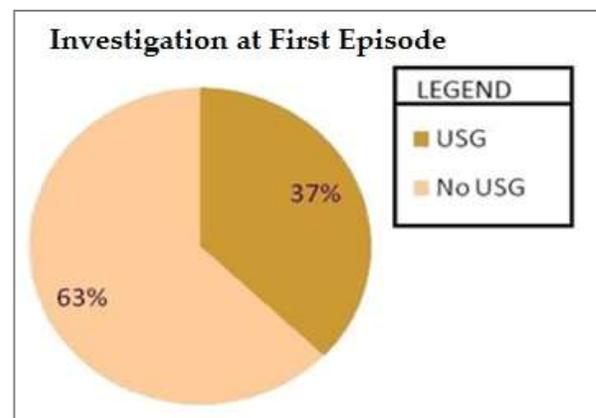
We studied 391 patients who presented with complaints of 'blood in urine' i.e. "gross Haematuria" from March 2012 to March 2014. Trauma was the most frequent cause of gross haematuria observed. Most of the cases were secondary to road traffic accidents with blunt trauma of the abdomen and flank causing renal injuries and pelvic fracture causing bladder and urethral injuries. Penetrating injuries like stab and gunshot involving lumbar and hypogastric regions also presented with gross haematuria. Gross haematuria is seen in approximately 14% of children presenting with trauma, as depicted by Taylor et al<sup>8</sup>. While a significant number of adult patients also present with gross haematuria to A&E department.

Iatrogenic injuries following traumatic catheterization, urethral dilatation, endoscopic procedures etc. are also a common cause of gross haematuria, as there are few trained urologists and most of the patients are handled by the GPs or quacks with limited expertise in the field.

Keeping in view that Sargodha is located in the stone forming belt<sup>9</sup>, the number of patients presenting with urolithiasis is significant, thus quite a few patients present with gross haematuria. They have a significant history of irritative urological symptoms, colicky pain and previous similar episodes, with occasional history of passage of stones. Bladder and urethral calculus were common along with a few ureteric

calculi. Microscopic haematuria is much more common and can be seen in up to 85% of cases while gross haematuria is relatively rare<sup>10</sup>.

We diagnosed urinary tract infections in around twenty one percent of the cases who had presented with haematuria. It is in comparable with other studies, as observed by Gösta Wallmark et al. Who also noted that the infections associated with *Staphylococcus* were more commonly associated with haematuria<sup>11</sup>, and more common in the females. However the response to the antibiotics was appreciable. This group also included patients suffering from chronic infections like tuberculosis. It is worth



**Figure-3: Percentage of patients investigated at first episode of haematuria by GP.**

mentioning that tuberculosis is prevalent in Pakistan, especially amongst the low socioeconomic group. As depicted by United Nations Development Program (UNDP), Human Development report 2016, 45.6% of the Pakistani population is living below multidimensional poverty line<sup>12</sup>. Furthermore, due to lack of awareness and misconception that tuberculosis is incurable, the patients have a tendency to hide their disease till it becomes advanced and symptoms like haematuria appear.

Sargodha is surrounded by many small agricultural villages with little or no medical facilities, a situation where quackery flourishes, these quacks try to do minor procedures including catheterization and urethral dilations with disastrous complications. Ignored symptoms of enlarged prostate lead to Urinary

retention and may at times present as haematuria. In our study it was more frequently seen in patients from rural areas, who consider it as normal aging process or take treatment from the quacks and present only after repeated episodes of haematuria. A few also gave the history of failed/traumatic catheterization which became the reason for referral. Ramyil et al. observed that thirty seven percent of the patients with BPH or prostatic carcinoma presented with haematuria<sup>13</sup>. While we had about seventeen percent patients in this category.

Various drugs are known to be responsible for haematuria like cytotoxic drugs while others may only change the color of urine being confused with haematuria. We didn't find any patient, in ER or OPD, with haematuria caused by drugs, however, we did have consultations from oncology unit for complaints of haematuria. Patients on anti Tuberculosis treatment (Rifampicin and INH) seen in OPD were questioned about the discoloration of urine. They knew it to be the side effect of anti-tuberculosis therapy. Some of the other agents causing urinary discoloration are Myoglobin, haemoglobin, porphyrins from endogenous sources whereas Rhubarb, black, berries, beet root, artificial food colors and medicines like Rifampin, desferoxamine, Phenolphthalein, Phenazopyridine etc. are a few notable exogenous causes<sup>3</sup>.

Heavy exercise and marathon runners are documented to have micro-haematuria<sup>14</sup>. They may occasionally have gross haematuria but in our study we did not detect any such case.

Urological tumors are an important cause of gross haematuria. About twenty percent of the patients of carcinoma of bladder present with gross haematuria<sup>15</sup>. We were receiving a significant number of patients with advanced bladder carcinomas, who gave history of previous similar episodes, which compelled us to carry out this study.

We found that 19.4 percent of the patients who reported to our hospital with complaints

of gross haematuria were suffering from urological neoplasm. Similar observations were also made by William C. Carter, Stephen N. Rous, who observed that 23 per cent of the patients who presented with gross haematuria had genitourinary carcinoma as the cause of their haematuria<sup>16</sup>. Some of the important risk factors which put the patient in high risk group for these urological malignancies are old age, male gender, cigarette smoking, chemical exposure (cyclophosphamide, benzenes, aromatic amines), pelvic radiation, schistosomiasis etc<sup>15</sup>. The sad aspect of the story of our patients is that they had reported to a doctor earlier on in the course of the disease but were not properly evaluated, thus failed to avail the benefits of early diagnosis.

Certain important points to be kept in mind while managing a patient of haematuria at general practitioner level are that history and basic investigations can acceptably diagnose about 60 to 70 percent of the patients<sup>17</sup> and combining Urine cytology and cystoscopy provides diagnosis in up to 95% of the cases<sup>18</sup>.

If the patient has undergone moderate to strenuous physical activity within a couple of days prior to testing or had mild trauma, any viral infection, sexual activity, DRE or instrumentation, and menstruation in females, the results would probably be invalid due to possibility of induction of transient haematuria<sup>19</sup>.

The newer investigation modalities like Multidetector Computerized Tomography Urography (MCTU) are more sensitive in diagnosing of upper tract TCC<sup>20,21</sup> but are expensive and not widely available in our healthcare setup thus cannot be freely utilized.

AUA recommends that all patients above 40 years and those younger but with complaints suggestive of urothelial carcinoma and haematuria<sup>2</sup>, or abnormal urinary cytology should undergo cystoscopy<sup>22</sup> so as to complete the evaluation even though it can only detect lesions in the urethra and bladder, and it cannot reliably detect in-situ lesions<sup>23</sup>.

Moreover a study carried out by Messing et al. for detection and screening of haematuria revealed that 21.1% of the general population above 50 years of age, had episodes of haematuria but only 1.1% had urological cancers as its cause. Showing that although home screening for the patients above 50 years may be feasible<sup>24</sup>, but it was not cost effective for a hospital or community based screening program, as prevalence of haematuria is around 1.38%<sup>25</sup>, but fully investigating patients who present with gross haematuria is worthwhile.

Timely evaluation is beneficial in early detection of treatable urothelial carcinomas<sup>26</sup>. Therefore microscopic haematuria should prompt evaluation of renal functions and if proteinuria, raised serum creatinine or red cell casts are found nephrologist should be consulted. If vigorous exercise, trauma, menstruation etc are suspected, re-evaluation, after managing the cause, should be done by imaging and urinary cytology<sup>17</sup>. And if gross haematuria is present, with or without clots, at least an Ultrasound should be done and Urological consultation recommended if results are positive.

## CONCLUSION

General practitioners should be encouraged to request ultrasound scan for patients presenting with gross haematuria, as urothelial tumours, if detected early, can be managed effectively with better long term outcome.

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## CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

## REFERENCES

- Gary D, Grossfeld, Carroll PR. Evaluation of asymptomatic microscopic hematuria. *Urol Clin North Am* 1998; 25(4): 661-76.
- Grossfeld GD, Wolf JS, Litwan MS, Hricak H, Shuler CL, Agerter DC, et al. Asymptomatic microscopic hematuria in adults: Summary of the AUA best practice policy recommendations. *Am Fam Physician* 2001; 63(6): 1145-54.
- Sokolosky MC. Hematuria. *Emerg Med Clin North Am* 2001; 19(3): 621-32.
- Froom P, Ribak J, Benbassat J. Significance of microhaematuria in young adults. *Br Med J (Clin Res Ed)* 1984; 288: 20.
- Kevin N, O'Regan MB, Owen J, O'Connor, Patrick McLoughlin, Michael M. Maher. The role of imaging in the investigation of painless hematuria in adults. *Seminars in Ultrasound, CT and MRI (Renal Imaging)*. *Semin Ultrasound CT MR* 2009; 30(4): 258-70.
- Feifer AH, Steinberg J, Tanguay S, Armen G, Brimo AF, Kassouf W. Utility of urine cytology in the workup of asymptomatic microscopic hematuria in low-risk patients. *Urology* 2010; 75(6): 1278-82.
- Vasdev N, Kumar A, Veeratterapillay R, Andrew C. Thorpe. Hematuria secondary to benign prostatic hyperplasia: Retrospective analysis of 166 men identified in a single one stop hematuria clinic. *Curr Urol* 2013; 6(3): 146-9.
- Taylor GA, Eichelberger MR, Potter BM. Hematuria. A marker of abdominal injury in children after blunt trauma. *Ann Surg* 1988; 208(6): 688-93.
- Hussain M, Lal M, Ahmed S, Zafar N, Naqvi SA, Abid-ul-Hassan, et al. Management of urinary calculi associated with renal failure. *J Pak Med Assoc* 1995; 45(8): 205-8.
- Tanagho EA, McAninch JW. *Smith's general urology*, 16th ed. New York, NY: McGraw-Hill; 2003.
- Gösta Wallmark Ingrid Arremark Barbro Telander. *Staphylococcus saprophyticus: A frequent cause of acute urinary tract infection among female outpatients*. *J Infect Dis* 1978; 138(6): 791-97.
- Human Development report 2016, Multidimensional Poverty Index. p219; UNDP 2016.
- Ramyil VM, Dakum NK, Liman HU, Udeh EI. The management of prostatic haematuria. *Niger J Med* 2008; 17(4): 439-42.
- P Lu-thje, I Nurmi. Recurrent macroscopic haematuria due to bladder blood vessels after exercise induced haematuria. *Br J Sports Med* 2004; 38(3): e4.
- Sharma S, Ksheersagar P, Sharma P. Diagnosis and treatment of bladder cancer. *Am Fam Physician* 2009; 80(7): 717-23.
- Carter WC, Rous SN. Gross hematuria in 110 adult urologic hospital patients. *Urology* 1981; 18(4): 342-44.
- Restrepo NC, Carey PO, Milton S. Evaluating hematuria in adults. *Am Fam Physician* 1989; 40(2): 149-56.
- Gofrit ON, Katz R, Shapiro A, Yutkin V, Pizov G, Zorn KC et al. Gross Hematuria in Patients with Prostate Cancer: Etiology and Management. *ISRN Surgery* 2013; 685327.
- James M. Sutton MD. Evaluation of hematuria in adults. *JAMA* 1990; 263(18): 2475-80.
- Wang LJ, Wong YC, Huang CC, Wu CH, Hung SC, Chen HW. Multidetector computerized tomography urography is more accurate than excretory urography for diagnosing transitional cell carcinoma of the upper urinary tract in adults with hematuria. *J Urol* 2010; 183(1): 48-55.
- Wang HL, Wong YC, Chuang CK, Huang CC. Diagnostic accuracy of transitional cell carcinoma on multidetector computerized tomography urography in patients with gross. *J Urol* 2009; 181(2): 524-31.
- Cohen RA, Brown RS. Clinical practice Microscopic hematuria. *N Engl J Med* 2003; 348(23): 2330-8.
- Mary M. McDonald, daniel swagerty, louis wetzel. Assessment of microscopic hematuria in adults. *Am Fam Physician* May 2006; 73(10): 1748-54.
- Messing EM, Young TB, Hunt VB, Roecker EB, Vaillancourt AM, Hisgen WJ, et al. Home screening for hematuria: Results of a multiclinic study. *J Urol* 1992; 148(2 Pt 1): 289-92.
- Paik SK, Kim TK. Prevalence and evaluation of asymptomatic microscopic hematuria in adults. *Korean J Urol* 1993; 34(4): 642-47.
- Nieder AM, Lotan Y, Nuss GR, Langston JP, Vyas S, Manoharan M, et al. Soloway Are patients with hematuria appropriately referred to Urology? A multi-institutional questionnaire based survey. *Urol Oncol. Seminars and Original Investigations* 2010; 28(5): 500-503.