

**A PROSPECTIVE STUDY ON THE CYSTOSCOPIC
FINDINGS IN THE INITIAL EVALUATION OF
GROSS HAEMATURIA AT KENYATTA NATIONAL
HOSPITAL (KNH)**

By

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**A DISSERTATION SUBMITTED IN PART FULFILLMENT
FOR THE DEGREE OF MASTER OF MEDICINE IN
SURGERY OF THE UNIVERSITY OF NAIROBI.**

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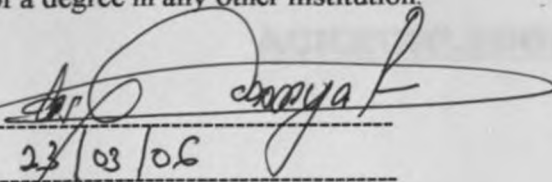


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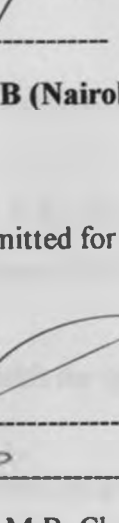
DECLARATION

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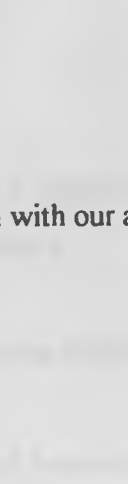
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ACKNOWLEDGMENT

I wish to express my sincere appreciation to:

- i) My supervisors Mr. P.N. Mungai and Mr. F. Owillah for their criticism and guidance in the preparation of this dissertation.
- ii) The Ministry of Health for sponsorship to the M.Med course.
- iii) The Kenyatta National Hospital Ethics and Research Committee for permission to carry out the study.
- iv) My Personal friend Paul Anywayo for his social support.

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STUDY ABSTRACT

- Design:** A prospective observational study over a duration of 6 months.
- Objective:** To document the main cystoscopic findings in the initial evaluation of gross haematuria.
- Setting:** Kenyatta National Hospital, a Teaching and Referral Hospital situated in Nairobi City – the Capital of Kenya.
- Duration:** From 31st May 2005 – 30 November 2005 (Inclusive)
- Study Group:** Patients aged 13 years and above presenting with gross haematuria from whom an informed consent was obtained.
- Method:** Approval was obtained from the Hospitals Ethics and Research committee. Patients underwent evaluation consisting of demographics, basic blood tests, analysis of urine, imaging by ultrasonography. IVU was performed in some cases. The results were entered into a data sheet and statistical analysis was performed using SPSS version 10.
- Results:** Sixty patients were recruited into the study the male to female ratio was 2:1. The mean age was 42.4 years with a range of 18 to 84 years. Cystoscopy was diagnostic in 95% of the cases. Malignancies were detected in 46.6% of the cases with a peak at 60 to 70 years. Most bladder tumours were located on the lateral walls and all primary bladder tumours were transitional cell carcinomas. No malignancy was detected below the age of 35 years.
- Conclusion:** 1) Cystoscopy and ultrasonography are the most useful investigations in the evaluation of gross haematuria and patients above 40 years of age stand a high risk of being diagnosed with a malignancy.
- Recommendations:** All patients presenting with gross haematuria should undergo cystoscopy and ultrasonography.

INTRODUCTION

Haematuria is a serious symptom of urological disease. It often heralds the presence of an underlying malignancy of the urinary tract¹⁻³. Gross haematuria is alarming and obvious to the naked eye; it has a reported community prevalence of 2.5% and is estimated to account for 4 to 20% of all urological visits⁴.

Direct visualization of ureteral orifices and mucosa of the urethra, prostate and bladder is achieved using a cystoscope. The procedure can be extended to obtain biopsy and definitive surgical treatment offered for conditions such as stone in the bladder or distal ureter, superficial bladder cancers, benign prostatic enlargement and urethral strictures. A bladder wash out (Barbotaged) specimen obtained at cystoscopy increases cytologic sensitivity for malignant cells⁵. Flexible cystoscopy can be performed under local anaesthesia in the Doctor's Office with minimal discomfort and morbidity⁶⁻⁹ while providing equivalent or superior diagnostic accuracy¹⁰. Cystoscopy has got a sensitivity of about 90% in the detection of bladder tumours¹¹. There is a general consensus amongst many urologists that cystoscopy can not be safely omitted even in situations where a lesion is detected on imaging of the upper urinary tract¹².

HISTORICAL BACKGROUND

Cystoscopy was first introduced by Phillip Bozzini in 1806; his technique was later improved by Antonin Desormeaus and Joseph Grunfield ¹³. The first cystoscopes had no incorporated irrigation channels; cystoscopy had to be interrupted to introduce a catheter to fill or to empty the bladder. To circumvent this, some endoscopists used air as an examination medium, the endoscopes were simple tubes with no optical system of magnifying lenses.

Air Cystoscopy

The first air cystoscope was designed by Diedrich Rutenberg from Viena in 1876, this was an open speculum closed by a glass window from the examiners end. Light was reflected into the bladder via a concave forehead mirror ¹⁴.

In 1888, Karl Pawlik from Prague improved his endoscope by incorporating a light source at the tip of the instrument and tubes for irrigating the bladder mucosa; he was able to perform several endoscopic procedures such as removal of bladder stones and resection of bladder tumours ¹⁵.

In 1892, Haward Kelly using an instrument of smaller diameter performed cystoscopy under local cocaine anaesthesia. In 1898, he modified his instrument to a length of 15cm and diameter 8mm and performed cystoscopy in males ¹⁶.

In 1909, Leo Burger from New York designed the first cysto urethroscope ¹⁷.

Cystoscopy with Bladder Irrigation

At the turn of the second decade of the twentieth century, the acceptance of air cystoscopy amongst many urologists began to decline. Air proved to be unphysiological for distending the bladder. It irritated the bladder mucosa and therefore painful for the patient. Modern endoscopes using fluids for irrigation were gaining wide acceptance among urologists during the same period.

In 1980s, flexible cystoscopes were introduced ¹⁸. This enabled cystoscopy to be performed under local anaesthesia even in the setting of a Doctor's Office; furthermore, flexible cystoscope has the advantage of enabling cystoscopy to be performed with the patient in supine position.

Modern Aspects of Cystoscopy.

Virtual cystoscopy or CT cystoscopy is the latest development of examining air filled bladder; Thin section Helical CT is used to generate interactive intraluminal views of the bladder mucosa during the detection of bladder masses; This offers information about the bladder surface and not infiltration of tumour into the bladder wall.

LITERATURE REVIEW

Review of the findings of haematuria evaluation from previous research studies

a) Africa

The earliest studies conducted in Africa showed that infection/infestation with schistosoma haematobium was the main cause of gross haematuria.¹⁹ Studies done later demonstrated a shift from infection/infestation to urological malignancy as the predominant cause of gross haematuria.²⁰ Yeboah and colleagues carried out a study on the causes and management of gross haematuria in Accra Ghana; vesical schistosomiasis was found to be the leading cause of gross haematuria.²⁰ Lesions detected in this study were vesical schistosomiasis (25%), carcinoma of the urinary bladder (11%), urinary tract infection (11%), benign prostatic enlargement (11%) and urolithiasis (7%). Sickle cell gene is a common finding in Negroid race and in this study it was a cause of haematuria in 2% of the patients. Urological malignancies were detected in 16% of the patients. Squamous cell carcinoma constituted 59% of all the urinary bladder neoplasms and in all cases there was an association with vesical schistosomiasis. In this study a diagnosis could not be ascertained in 14% of the patients which is consistent with data available from other centers.^{21,22}

At the Lagos University teaching hospital, Osegbe and co workers conducted a study on the causes of gross haematuria between 1978 – 1981.²³ In this study it was found that infection accounted for 22.6% of all the causes, other lesions identified include urological malignancy 17.4%, schistosomiasis 14.2%, benign prostatic enlargement 7.9% and urolithiasis 7.9%. Haemoglobinopathy accounted for 2% of all cases similar to the finding of a study conducted in Ghana by Yeboah and associates.²⁰ In this study urological malignancy was detected in 17% of the patients which is in keeping with the rate detected by Yeboah and colleagues. Failure to establish a diagnosis in 1.6% of the patients is a great improvement over what is reported in some centers.^{21, 22} the distribution of the lesions by site were as follows renal 23.8%, bladder 40%, ureter 7.6% and prostate 12%. All patients with carcinoma of the urinary bladder presented late and all died within one year after diagnosis; this is a stark contrast to the situation in developed countries where malignancies are detected early.^{24, 25} Delay in presentation in these cases could have been caused by lack of awareness or due to initial empirical treatment for urinary schistosomiasis by general practitioners. Sixty six percent of the lesions identified as causes of haematuria were located in the lower urinary tract, a finding which makes it pertinent to perform cystoscopy on all patients who present with haematuria. Thirty seven percent of cases of vesical schistosomiasis could not have been detected if cystourethroscopy was omitted. In these patients cystoscopy revealed tubercles, ulcers, granulomata and multiple haemorrhagic spots. This study revealed single or multiple bacterial infection in the urine of all patients diagnosed to have carcinoma of the urinary

bladder. Tunner and fellow researchers found out that 39% of patients with urothelial tumours also had infected urine.²⁶ The significance of this is that further investigation should not be abandoned on the presumption that the cause of haematuria is already known; this fact if not recognized may lead to many urothelial malignancies being missed²⁶.

Dawan and fellow researchers carried out a prospective study on macroscopic haematuria between 1985 – 1991 at Ahmed Bello University Teaching Hospital, Nigeria²⁷. In this study urological malignancies were detected in 37% of the patients, this is unlike the two studies previously conducted in West Africa where infective cystitis was the leading cause of gross haematuria.^{20, 23} Lesions identified in this study includes carcinoma of the urinary bladder 31%, benign prostatic enlargement 14%, and urolithiasis 12%. The failed diagnosis rate in this study was 6%; in keeping with the findings in other studies.^{21, 22} Fourteen percent of the patients diagnosed to have carcinoma of the urinary bladder had normal cystoscopic appearance and negative cytology. Cystitis was the commonest pathologic lesion identified in females followed by haemoglobinopathy. In this study, just like other studies conducted in Africa late presentation was noted in most patients with urological malignancies,^{20,23,28-30} this is unlike the situation in Europe where most patients seek treatment at least one week within the onset of symptoms⁵.

Data available from the university of Nigeria teaching hospital (Mbonu and colleagues), identifies benign prostatic enlargement as the commonest cause of

gross haematuria 27%, followed by infection²⁸. Schistosomiasis was an uncommon cause in contrast to the findings of some studies done in West Africa.^{20, 23,27} The cause of haematuria could not be identified in 5% of the patients this corroborates with other research findings in Africa^{20, 23} and Europe.^{21, 22} In this study urological malignancy was less predominant. Recent data from Jos University teaching hospital is in agreement with most West African researchers that more urological malignancies are being detected than was previously the case²⁹.

Sharfi and fellow researchers evaluated 550 patients, presenting with gross haematuria at Soba University Hospital (SUH) in Khartoum between 1982 – 1992.³⁰ Bilharzial uropathy is endemic in Sudan, this study in similarity with others conducted in West Africa, cystoscopy was the most useful investigation in detecting bilharzial lesions of the urinary bladder. The following lesions were detected at cystoscopy carcinoma of the urinary bladder 35.6%, benign prostatic enlargement 23.5%, bilharzial manifestations 22% vesical calculi 12.1% and bacterial cystitis 6.8%. Lesion detected in schistosomal uropathy include sandy patches, interstitial cystitis, bilharzial polyps and bilharzial tubercles. In 29% of the patients diagnosis could not have been attained had the cystoscopic procedure been omitted, a fact stated by other researchers from West Africa.^{23, 27} In 9.3% of the patients a diagnosis could not be established after exhausting all the relevant investigations. This is in agreement with the data available from Europe^{21, 22} and other African countries.^{20,27, 29} In this study 40% of the patients presenting with

gross haematuria had an underlying urological malignancy, this is higher than that reported in the West African countries.^{20,23} Most patients with urological malignancies presented late this could be due to the fact that they relate painless haematuria to vesical schistosomiasis. Squamous cell carcinoma was detected in 42% of the patients with malignancies of the urinary bladder and all were below 40 years of age. This is different from the situation in the western world where transitional cell carcinoma is the commonest histological entity with a peak at 60 years of age.³¹⁻³³ The most common cause of gross haematuria in this study was urolithiasis. Upper urinary tract lesions was a cause of gross haematuria in 56% of the patients. The following causative lesion were detected in the upper urinary tract, calculi 46%, glomerular disease, 6.9% renal tumours 2.4% and benign renal cyst 1.1%. Although sickle cell disease is common in the western part of Sudan, in no patient was haematuria attributable to sickle cell disease.

(b) Europe and North America

Khadra and co workers carried out a prospective study between 1994 – 1997 on patients who attended a haematuria diagnostic service at the Freeman Hospital in U.K; out of 1930 patients evaluated 51% presented with gross haematuria³¹. Urological malignancy was found to be four times more common with gross haematuria than microscopic haematuria, in keeping with the findings of other studies showing a prevalence of 5% and 22% for malignancy in microscopic and macroscopic haematuria respectively³². In 52% of the patients the cause of haematuria could not be determined, this is much higher than the failed diagnosis

rate quoted in most studies ^{21, 22}. Lesions identified in this study include carcinoma of the urinary bladder 19.3%, urinary tract infections 13%, nephrological disease 10%, urolithiasis 3% and renal cell carcinoma 0.9%. There was 24% malignancy rate in association with gross haematuria. Khadra and co-workers found that the likelihood of detecting a urological malignancy was strongly related to the age and sex of the patients. No urological malignancy was detected in female patients below the age of 40 years. A significant finding in this study is that the likelihood of detecting a urological malignancy in anti-coagulated patients was not different from that of the overall group. As pointed out by other researchers patients on anticoagulation therapy will develop symptoms earlier and this should provide the urologist a chance to detect the lesions early enough ²³. A study conducted in Sweden detected a malignancy rate of 24% in association with gross haematuria ³⁴. This is consistent with the finding of a study conducted in the United Kingdom ³². The study conducted in Sweden identified carcinoma of the urinary bladder 15% and prostatic carcinoma 8% as the most common urological malignancies.

In Belfast city Johnston and Kaane identified transitional cell carcinoma of the urinary bladder as the commonest urological malignancy. ³⁵ This was detected in 14% of the patients and no malignancy was detected in patients below 50 years of age. The malignancy rate in this study and the relative proportion of transitional cell carcinoma tallies with the research findings in other parts of Europe. ^{35, 37} Chahal et al detected a malignancy rate of 19.2% in association with gross

haematuria the commonest malignancy being transitional cell carcinoma of the urinary bladder accounting for 17% of all urological malignancies and 85% of all neoplasms of the urinary bladder.³⁶ A three-year prospective study (2001 – 2003) conducted at Queen Elizabeth Hospital U.K detected a malignancy rate of 17.64%.³⁷

Alisahi and associates (1993 – 1997) studied 1046 patients with haematuria who were referred to the Dundee Royal infirmary.³⁸ Thirty seven percent of these presented with gross haematuria. The commonest urological malignancy identified was transitional cell carcinoma of the urinary bladder accounting for 20% of all cases and 80% of all urological malignancies. This is similar to the findings of studies done in other parts of Europe^{35, 37} but differ to a great extent with data available from bilharzial endemic zones of Africa where squamous, cell carcinoma of the urinary bladder is the commonest histological entity identified,³⁰ There was 24.5% association of gross haematuria with urological malignancy similar to research findings from Sweden and Freeman Hospital U.K, which yielded rates of 24% and 24.2% respectively.^{32, 33} In this study it was found that males below 70 years of age were more likely to harbour urological malignancies than females. This higher risk was not observed in males of 70 years of age. Alisahi and associates found that in patients presenting with gross haematuria the percentage found to have transitional cell carcinoma increases steadily with age from 11% at 40 years of age to 30% at 90 years of age. The sensitivity of cystoscopy for tumours of the urinary bladder was superior to cytology. In this

study it was found that the cytologic sensitivity was less for well-differentiated tumours, in keeping with the finding in other studies. This emphasizes the need to perform cystoscopy in all patients with haematuria.

A study carried out of the Wellington Hospital in U.K detected malignancies in 6.1% of the patients with haematuria⁴⁰. In this study 46.1% of the cystoscopies yielded positive findings. Lesion, identified cystoscopically in this study were bladder tumours 12.5%, urethral strictures 7.5%, meatal stenosis 3%, bladder neck stenosis, 2% and calculi 1%.

In Boston (U.S.A) Fielding et al detected significant lesions in 60% of the patients with gross haematuria on convectional cystoscopy⁴¹. In the same study it was found that 40% of the biopsies were positive for transitional cell carcinoma and 45% of the biopsies were negative for malignancy.

A study conducted at the Royal Marsden Hospital by Turner and associates detected urological malignancy in 12.5% of the patients with gross haematuria⁴². Most malignancies identified were superficial bladder cancers. The following lesions were identified cystoscopically in this study, cystitis 38%, prostatitis 10% and benign prostatic enlargement 11%. Cytology gave disappointing results with 83% false negative rate; this stresses the need to perform routine cystoscopy in all patients. In 5% of the patients the diagnosis could not be established after performing all the relevant investigation.

Cuttino et al carried out cystoscopic evaluation of anticoagulated patients in the medical school of North Carolina; they detected significant lesions in 46% of the patients.⁴³ This finding gets support from many research studies.^{44, 45} The following lesions were identified cystoscopically by Cuttino et al as the cause of bleeding, tumours of the urinary bladder 13%, haemorrhagic cystitis 13% and benign prostatic enlargement 40%. Antoloak and Mellinger noted that 13% of the patients on Warfarin sodium with gross haematuria had significant lesions.⁴⁴ This is supported by the findings of Lewis et al that noted significant lesions in 58.6% of the patients, 13.9% of these being urological malignancies.⁴⁵ The significance of these findings is that anticoagulated patients with gross haematuria should not be denied cystoscopy based on false premise that the cause of haematuria is already known.

Cartel and Rous in a study conducted at the Medical University of South Carolina found that inflammatory cystitis was the leading cause of haematuria 27%, followed by benign prostatic enlargement 18% and urolithiasis 14%. Twenty three percent of the patients had associated urological malignancy consistent with studies done in Europe.³¹⁻³⁴ There was 9% failure to make a diagnosis in this study which is in agreement with the finding in many centres.^{20, 21, 22, 27, 28}

Mariani and associates evaluated 1000 consecutive haematuria patients of the Kaiser Medical Centre – U.S.A, between 1976 – 1996.⁴⁷ A causative lesion was located in the urethra in 59.2% of the cases. Lesions identified on cystourethroscopy include benign prostatic enlargement 16.5%, transitional cell

carcinoma of the urinary bladder 6.5%, cystitis 4.3%, bladder neck varicosities 3.3% and cystitis cystica 3.0%. Squamous cell carcinoma of the urinary bladder was a rare finding in this study. By site the lesions were distributed as follows urethral 59.2%, bladder 19.7%, renal 47%, renal pelvis 4% and ureteral 0.9%. Urological malignancy was detected in 7% of the patients, which is lower than the rate detected in Europe³¹⁻³³ and some parts of Africa.²⁷⁻³⁰ In 11.7% of the patients the diagnosis could not be reached after performing all the available relevant investigations.

c) South East Asia

Between 1994 – 1997 Sidney and co researchers carried out a prospective study of 312 patients presenting with gross haematuria at the Queen Mary Hospital University of Hong Kong.⁴⁸ Carcinoma of the urinary bladder was the commonest urological malignancy 27%, this is similar to findings from Europe,³¹⁻³⁴ America⁴⁶ and some parts of Africa.^{28,30} Other malignancies identified in this study were renal cell carcinoma 5%, Carcinoma of the renal pelvis 2.5%. The following benign lesions were identified in the lower urinary tract benign prostatic enlargement 11% and cystitis 4%. In 45% of the patients the cause of haematuria could not be explained, this is higher than the failed diagnosis rate in most parts of Europe.^{21,22}

Data available from Tan Tock Seng hospital in Singapore indicates that urolithiasis 27% was the predominant cystoscopic finding in patients with gross

haematuria⁴⁹. Other lesions, identified in this study were urological malignancy 14.2%, urethral stricture 2.7%, cystitis 1.8% and benign prostatic enlargement 0.9%. The prevalence of BPE in this study is lower than that found in some parts of Africa^{28, 30} and North America.^{46, 47} The malignancy rate of 14% in this study is consistent with the findings in some parts of Europe⁴² and the early studies conducted in Africa.²⁰ Most urological malignancies were detected in patients over 50 years of age, this is in agreement with studies done in Europe.^{31, 38} In 22% of the patients the diagnosis could have been missed if cystoscopy was not performed.

Goonerwardena and associates in Sri Lanka detected a malignancy rate of 31.5% in association with gross haematuria,³⁰ which is in agreement with data available from some parts of Africa, Asia, Europe and North America.^{27, 46, 48} It was found in this study that carcinoma of the urinary bladder was the commonest malignancy detected in patients over 40 years of age; below this age urolithiasis was the predominant cause.

Studies conducted in Japan yielded inconsistent findings. Nashikiko and colleagues detected urological malignancy in 22% of the patients with gross haematuria,⁵¹ while Hinyokiko Kiyoo and co workers detected a malignancy rate of 7%.⁵² The following lesions were identified by Hinyokiko and co researchers, urinary tract infection 53%, urinary tract calculi 1.5% and carcinoma of the urinary bladder 20%.

STUDY OBJECTIVES

(a) Main Objective

To determine the main cystoscopic findings in the initial evaluation of gross haematuria.

(b) Specific Objectives

- 1) To determine how often cystoscopic evaluation results in the diagnosis of a urological malignancy.
- 2) To determine the site of the lesions cystoscopically.
- 3) To determine the histological findings after cystoscopic biopsy.
- 4) To determine the surgical treatment offered
- 5) To determine the age and sex distribution of patients undergoing cystoscopic evaluation for gross haematuria.

JUSTIFICATION OF STUDY

Gross haematuria demands a complete investigative approach as there may be an underlying urological malignancy in upto 23% of the cases.³² Cystoscopy is valuable endoscopic procedure in the initial evaluation of gross haematuria; this enables direct visualization of the bladder cavity and biopsies can forthwith be obtained from suspicious bladder lesions. Cystoscopy is mentioned in a few studies previously done at Kenyatta National Hospital in relation to cancer of the urinary bladder.^{53,54,55} My study is different in the sense that the study population comprises patients presenting with gross haematuria regardless of the cause as opposed to the previous studies where the study population was obtained from patients with a presumed clinical diagnosis of cancer of the urinary bladder. This study aims to establish the main cystoscopic findings in patients who present with gross haematuria.

PATIENTS AND METHODS

Study Design

This was a six months prospective observational study of patients presenting with gross haematuria who underwent cystoscopic evaluation between 31/05/05 to 30/11/05 (inclusive).

Study Area

The study was conducted at Kenyatta National Hospital which is a National referral and teaching hospital situated in the city of Nairobi, the Capital of Kenya. This hospital is the largest in East and Central Africa.

Study Population

All new patients who presented to the urology clinics and surgical wards with a complaint of gross haematuria.

Study Group

This was obtained from the study population that met the eligibility criteria within the study period.

Eligibility Criteria

- a) **Inclusion** – Patients aged 13 years and above who then underwent cystoscopic evaluation for gross haematuria.
- b) **Exclusion Criteria**
 - i) Patients presenting with microscopic haematuria.
 - ii) Those who did not consent for enrollment into the study
 - iii) Where gross haematuria was an immediate consequence of a traumatic event.

Sampling

Since the number of patients who normally undergo cystoscopic evaluation for gross haematuria annually is small (approximately 90) as evidenced by K.N.H theatre statistics, sampling was not done but rather all patients who met the eligibility criteria within the study period were recruited in the study.

Method and Data Handling

Patients who met the eligibility criteria underwent evaluation consisting of demographics, blood tests, urine culture and urine cytology for malignant cells. All patients underwent trans abdominal sonography of the kidneys, ureter and bladder. Intravenous urography was performed in some cases. The intra-operative cystoscopic findings were recorded together with any surgical treatment offered.

Patients were then followed up in the clinics to establish the histological findings after biopsy. Data collected was entered into computer software statistical package for social sciences (SPSS) for statistical analysis.

Ethical Issues

The study protocol was reviewed and approved by K.N.H Ethics and Research Committee prior to commencement of the study. Informed consent was obtained prior to recruitment of patients into the study. Information obtained from the patients and patients notes was handled with strict confidentiality and was used strictly and solely for achieving the objective of the study.

Study Limitations

The study was limited by the following factors:-

1. Loss of patients to follow-up.
2. Patients not being able to afford the cost of some investigations, especially intravenous urogram.
3. Un available records during subsequent follow-ups.

Sample size

The minimum sample size was estimated to be 51. This was calculated from the computer estimation of sample size for descriptive study. In the year 2004, 797 new patients were attended to at the urology clinics in KNH. Gross haematuria accounts for 5 to 20% of new attendance to urology clinics from studies done elsewhere⁴.

Population size	797
Expected frequency	10%
Worst acceptable frequency	18%

Confidence level	Sample Size
80%	22
90%	36
95%	51
99%	84
99.9%	128
99.99%	168

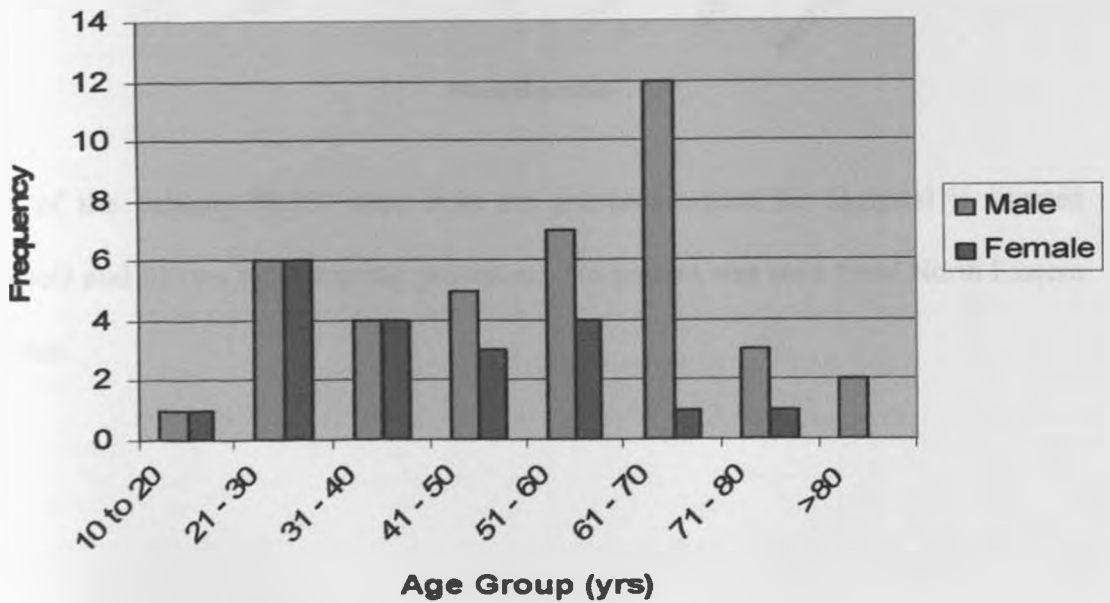
RESULTS

60 patients were enrolled into the study. There were 40 males and 20 females with a male to female ratio of 2:1.

Figure 1: Distribution by Sex

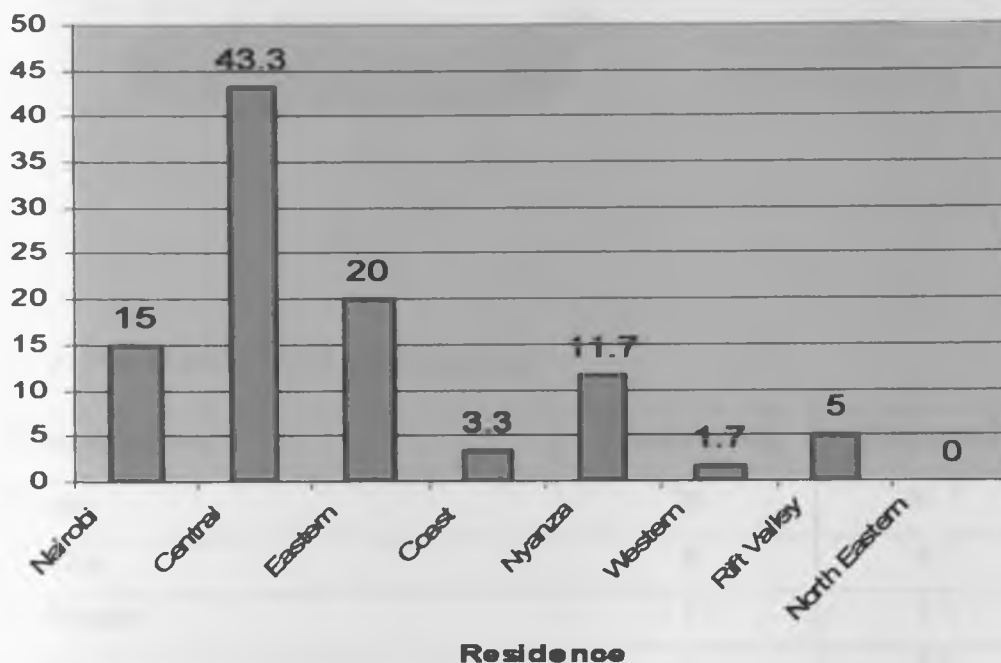


Figure 2: Distribution of the Age Groups



The mean age was 43.4 years with a range of 18 to 84 years. The median age and mode were 51 and 61 years respectively. Below the age of 40 years equal numbers of both sexes were seen above that age there was predominance of males.

Figure 3: Distribution According to the Area of Residence



Most of the patients 78.3% were from the province where the Hospital is situated (Nairobi) and its two neighbouring provinces. No patient was seen from North Eastern province.

Figure 4: Distribution Based on Smoking as a Risk Factor



Table 1: Distribution Based on Occupation

Occupation	Frequency	Percent
Farmer	28	46.7
Teacher	4	6.7
Policeman	1	1.7
Clerk	5	8.3
Student	5	8.3
Artisan	3	5
Shopkeeper	1	1.7
Driver	4	6.7
Tailor	3	5
Watchman	2	3.3
Fisherman	4	6.7
Total	60	100

Figure 5: Urine Cytology for Malignant Cells (Overall)

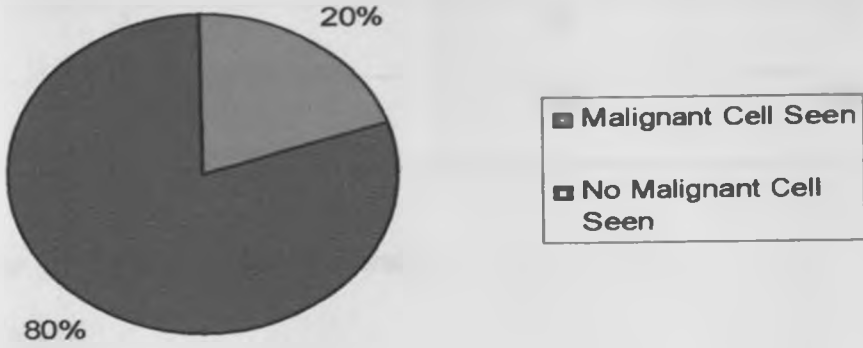


Figure 6 : Urine Microscopy for Ova of S.hematobium

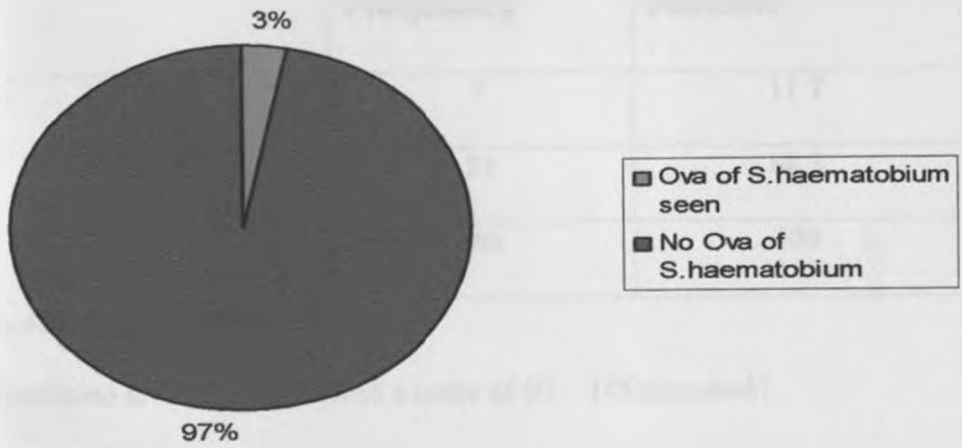


Table 2: Haemoglobin Level in g/dl

	Frequency	Percent
Normal	15	25
Low	45	75
Total	60	100

Ref-range for K.N.H Haematology Laboratory

Male 14 – 18 g/dl

Female 12 – 16 g/dl

The mean haemoglobin level was 11 g/dl with a range of 3.5 – 18 g/dl.

Table 3: Creatinine Level in micromol/litre

	Frequency	Percent
Elevated	7	11.7
Normal	53	88.3
Total	100	100

K.N.H assay (60 – 120)micromol/l

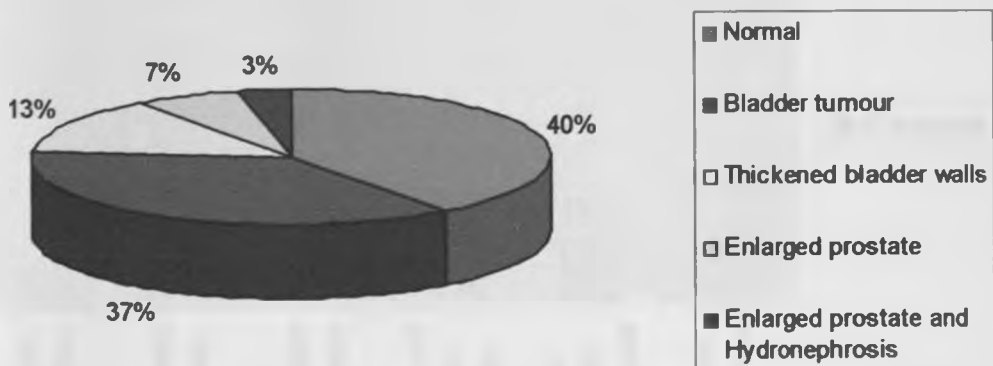
The mean creatinine level was 91.34 with a range of 60 – 145micromol/l.

Table 4: Urine Culture

	Frequency	Percent
No growth	21	35
Escherichia coli	19	31.7
Proteus spp	5	8.3
Klebsiella	5	8.3
Pseudomonas	2	3.3
Staph aureus	4	6.7
Staph epidemidis	1	1.7
Enterococcus spp	1	1.7
Citrobacter	2	3.3
Total	60	100

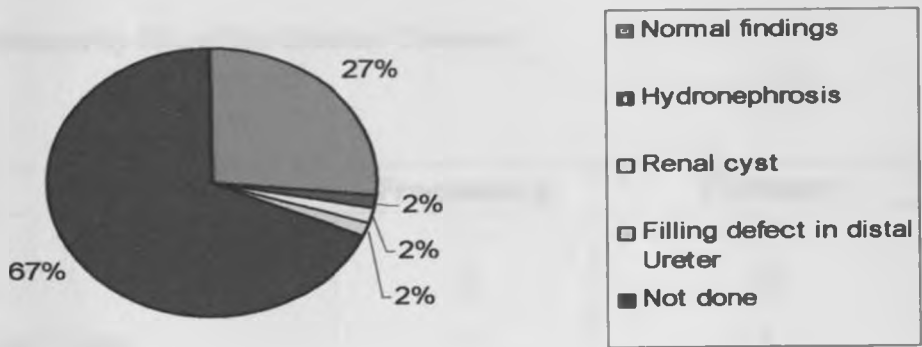
There was 65% infection rate in association with gross haematuria. The commonest organism was Eschenchia colli, this was isolated in 31.7% of the patients and accounted for 48.7% of the organisms isolated.

Figure 7: Ultrasound Findings



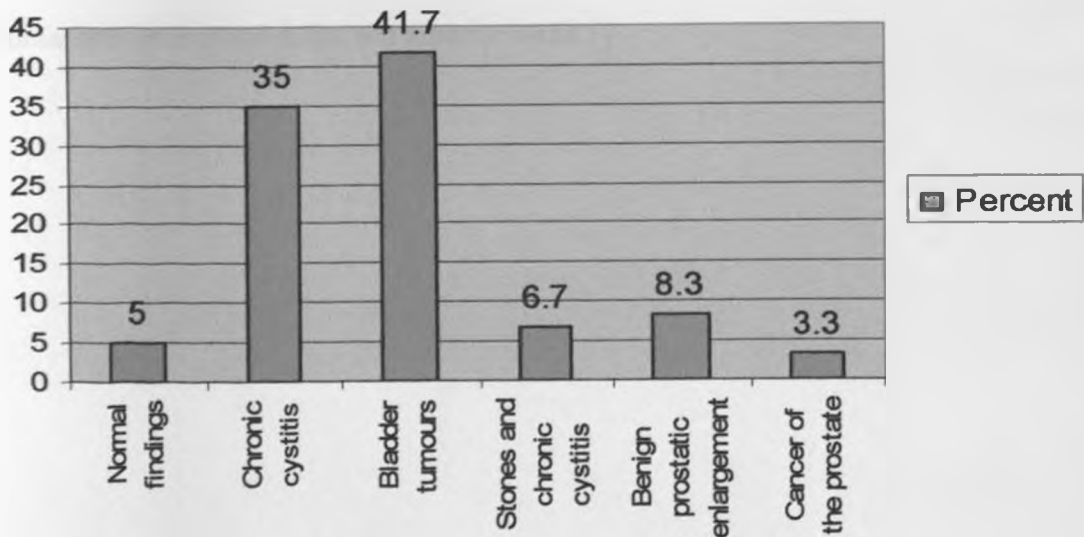
Ultrasound examination was performed in all patients and was diagnostic in 60% of the cases. Bladder tumours were detected in 36.7% of the cases.

Figure 8: Imaging of the Upper Urinary Tract by Intravenous Urography (IVU)



IVU was performed in 19% of the patients and normal upper urinary tract was seen in 26.7% of all cases.

Figure 9: Cystoscopic Features



Bladder tumours were the commonest lesions identified 41.7% followed by features of chronic cystitis. In 5% of the patients there was normal cystoscopic appearance of the urethra and bladder. Cystoscopic evaluation was diagnostic in 95% of the patients. Three tumours missed on sonography were detected by cystoscopic evaluation.

Table 5: Distribution by Site of the Bladder Tumours

	Frequency	Percent
Trigone	7	28
Lateral walls	10	40
Lateral wall and trigone	2	8
Posterior wall	2	8
Multifocal	3	12
Posterior wall and Trigone	1	4
Total	25	100

Most of the tumours were located on the lateral wall, (40%) and the trigone 28% No tumour was seen in the dome and anterior walls.

Figure 10. Histological Findings

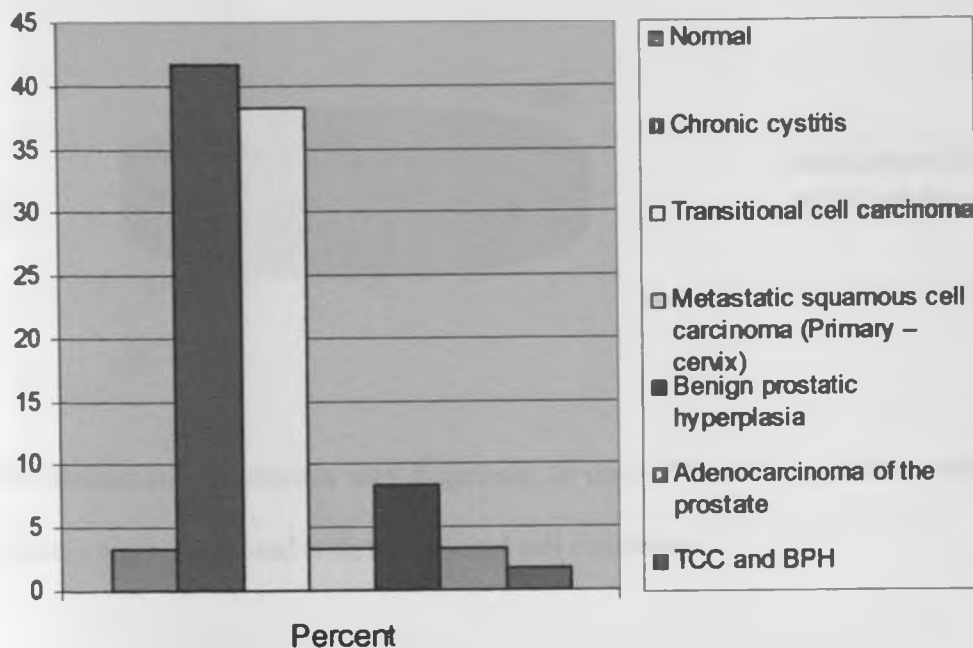
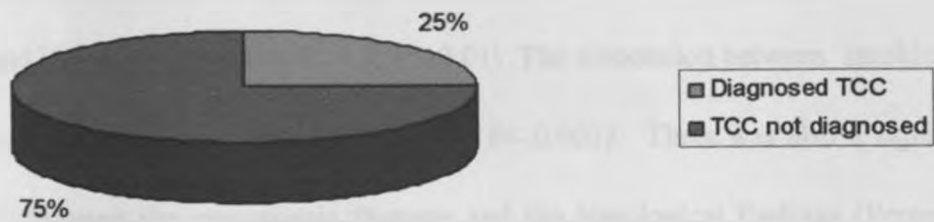


Figure 11: Smokers diagnosed with transitional cell carcinoma (TCC)



Figure 12: Non smokers with transitional cell carcinoma



Transitional cell carcinoma was diagnosed in only 25% of non smokers while 65% of smokers were diagnosed with transitional cell carcinoma.

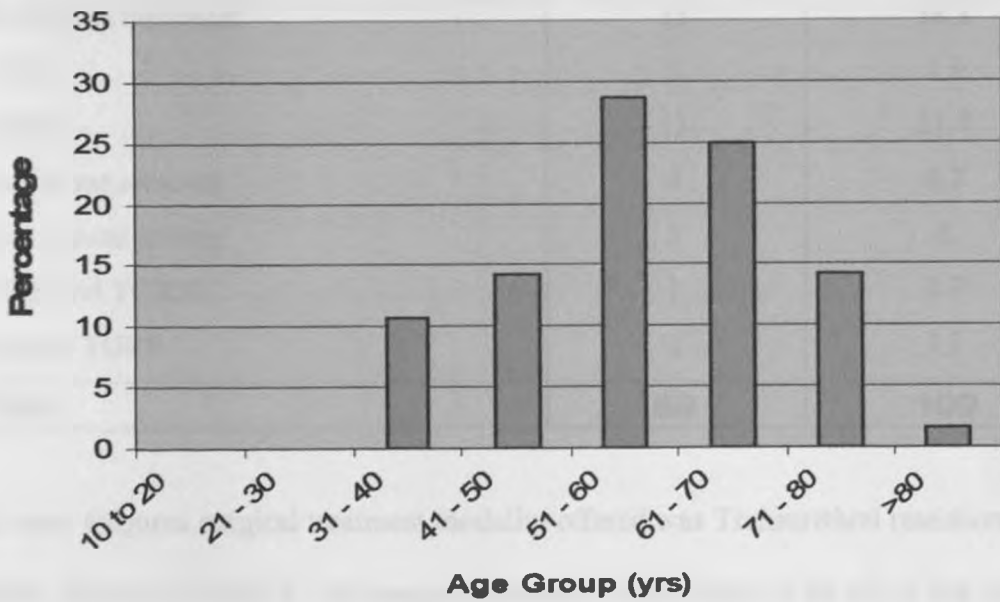
Table 6: Co-relation between histological diagnosis and the findings of cytological analysis of urine

Malignant condition	Diagnosed Histologically		Malignant cells seen on cytology	
	Frequency	Percent	Frequency	Percent
TCC	24	85.7	11	40.8
Adenocarcinoma of the prostate	2	7.15	0	0
Metastatic squamous cell carcinoma of the cervix	2	7.15	1	1.9
Total	28	100	12	42.9

Chronic cystitis was the most frequent histological finding 41.7% followed by transitional cell carcinoma 38.3%. The histological findings were reported as normal in

3.3% of the cases. The overall malignancy rate was 46.6%. There was no case of false positive or false negative cytology, this gives a sensitivity of 42.9% and a specificity of 100%. There is however a significant co-relation between malignancy detection by cytology and histology. (Pearsons χ^2 8.1, $P < 0.01$). The association between smoking and malignancy was significant. (Pearsons χ^2 17.7, $P < 0.001$). There was also a significant co-relation between the cystoscopic features and the histological findings (Pearsons χ^2 18.8, $P < 0.001$).

Figure 13: Distribution of Diagnosed Malignant Condition by Age Group



Most malignancies were detected above this age of 40 with a peak at 51 – 60 Age group.

No malignancy was detected below the age of 31 years.

Figure 14: Histological Grading of the Transitional Cell Carcinoma



Table 7: Surgical Treatment Offered

6.

	Frequency	Percent
No surgical treatment	35	58.3
TURP	2	3.3
TURBT	13	21.7
Open stone removal	4	6.7
Open prostatectomy	3	5
TURP and TURBT	1	1.7
Channel TURP	2	3.3
Total	60	100

The most frequent surgical treatment modality offered was Transurethral resection of the bladder tumour (TURBT). No surgical treatment was offered to 58.3% of the patients. One patient had both superficial bladder tumour and BPE and he underwent TURBT and TURP.

Table 8: Non surgical treatment offered

Treatment	Frequency	Percent
Radiotherapy	10	25
Convectional antibiotics	25	62.6
Anti tuberculous drugs	2	5
Anti schistosomal drugs	2	5
Hormonal	1	2.5

All patients with unresectable bladder tumours were offered radiotherapy. Two patients had features of chronic cystitis suggestive of tuberculous infection and were put on anti tuberculous drugs. Anti schistosomal drugs were offered to two patients. The rest of the patients with chronic cystitis (25) were put on conventional antibiotics. One patient with cancer of the prostate declined orchidectomy and was put on hormonal treatment.

DISCUSSION

The male to female ratio in this study was 2:1 in keeping with the findings of other studies^{23,31,38}. Male to female ratio of 3:1 is mentioned in several studies^{27,48,54}. The mean age at presentation was 43.4 years with a range of 18 – 83 years which reflects the figure quoted in other studies done in some parts of Africa²⁷⁻³⁰. The mean age at presentation is however lower than that quoted in the European series (50 – 60)^{21,35,38,47}.

Inflammatory cystitis due to schistosoma haematobium was diagnosed in only 3.3% of the patients, higher figures are quoted in studies done in Sudan and West Africa²⁷⁻³⁰. The overall urine infection rate in this study was 65%, *Escherichia coli* being the most prevalent organism isolated. Dawan and associates reported 66% infection rate in association with gross haematuria²⁷ while Turner and colleagues found 55% infection rate in association with gross haematuria and a 39% rate in association with malignancy.²⁶

Several researchers have strongly contested the role of urine cytology in the detection of genitourinary malignancy.^{31,36,38} There is also lack of uniform consistency between studies with regards to the sensitivity of cytological analysis of urine samples in the detection of genitourinary malignancy^{31,36,38}. Several researchers have reported sensitivity rates of 70% and above. Aziz and Ndaguatha found a rate of 93.1%⁵³ while Mbonu, Turner and Colleagues found rates varying between 70- 90%^{26,28}. On the contrary, some researchers have reported very low sensitivity rates.^{31,36,38}

Researchers at the Dundee Royal infirmary reported cytologic sensitivity of 25%,³⁸ investigators in Freeman Hospital (U.K) quoted 26% sensitivity rate³¹, while Chahol and Colleagues found 42% sensitivity rate.³⁶ In this study urine cytology was positive in 12 out of 28 patients diagnosed with malignancy. There were no false negative or false positive findings, this gives a cytologic sensitivity of 42.7%.

There are possible explanations for the variation in sensitivity of urine cytology between different studies.

- i) Cytologic sensitivity is generally poor for low grade tumours⁵.
- ii) Factors related to experience of the cytologist.
- iii) Method of specimen collection – barbotaged urine samples obtained at cystoscopy have high cytologic sensitivity⁵.

In this study however there was a significant correlation between malignancy detection by cytology and histological analysis (Pearsons χ^2 8.1 $p = 0.01$).

The role of transabdominal sonography in the detection of bladder tumours is well established.¹² The sensitivity of transabdominal sonography in the detection of bladder tumours ranges from 60 to 80%.¹² As pointed by other investigators the main drawback of sonography is the fact that it is subject to inter observer variability.^{12,32,48} In this study sonography was performed in all patients and bladder tumours were detected 36.7% of the cases. Sonography missed 12% of the tumours which were subsequently picked up on cystoscopy, overall sonography was diagnostic in 60% of the patients.

Intravenous urography was performed in only 31.79% of the patients due to financial constraints on the part of the subjects. Some investigators have argued that it is not necessary to perform intravenous urography in all patients presenting with gross haematuria since ultrasonography can give equivalent or superior diagnostic information.¹² Transitional cell carcinoma is a pan urothelial tumour and therefore it appears logical to perform intravenous urography whenever bladder cancer is suspected so as to rule out synchronous upper urinary tract tumours.

Cystoscopic evaluation was diagnostic in 95% of the patients. Some researchers have reported diagnostic sensitivity of cystoscopy to be greater than 90% in the detection of bladder tumours.¹¹ Cystoscopy picked 12% of the bladder tumours which were missed on ultrasonography. Five percent of the patients had normal cystoscopic appearance one of which was reported on histologic examination to have features of carcinoma insitu. The most frequent cystoscopic feature was tumour of the urinary bladder 41.7%, followed by chronic cystitis (35%). Researchers in Khartoum detected bladder tumours in 45% of the patients.³⁰ Investigators at the Ahmed Bello University Teaching Hospital in Nigeria detected bladder tumours in 31% of the patients followed by cystitis 22% and benign prostatic hypertrophy 14%.²⁷ Most studies have shown that prostatic carcinoma is not a frequent cause of gross haematuria,^{23,27-30} in this study cystoscopic evaluation yielded bleeding from prostatic carcinoma in 3.3% of the patients.

Most of the bladder tumours were located on the lateral walls (40%) and Trigone (28%). A previous study conducted locally had shown most tumours to be located in the trigone

(51%).⁵⁴ All primary malignancies of the urinary bladder in this study were of the transitional cell type. In Europe and North America transitional cell carcinoma is the most frequent type of bladder malignancy accounting for over 95% and this is confirmed by consistent unity between different studies.^{31,34,37,38,46,47} In the bilharzial endemic zones of Egypt, Sudan and West Africa, squamous cell carcinoma accounts for between 20 to 50% of urinary bladder malignancies^{23,27-30}. Two patients had normal cystoscopic appearance and histological features this gives a failed diagnosis rate of 3.3%. The failed diagnosis rate 3.3% is similar to the finding of other studies done in Africa.^{20,23} Cystoscopic evaluation yielded the diagnosis of a malignancy in 46.6% of the patients. The malignancy rate of 46.6% is higher than the rate of 23% mentioned in most studies.^{31,46} A possible explanation for the high malignancy rate could be due to the fact that most patients with gross haematuria due to Benign prostatic hypertrophy do not routinely undergo cystoscopic evaluation in KNH. Two patients (3.3%) were known to have squamous cell carcinoma of the cervix and had developed metastasis to the bladder at the time they presented with gross haematuria. This study showed that there was a significant co-relation between the cystoscopic impression and the eventual histological diagnosis (Pearsons χ^2 18.8, $p = 0.001$). No malignant condition was diagnosed below the age of 35 years. Most malignancies (53.6%) were detected between the age of 50 – 60 years. This is similar to the findings of studies done in Asia⁴⁸⁻⁵⁰, UK^{31,37,39} and other parts of Africa.²⁷⁻³⁰ Alisahi and associates detected 90% of bladder malignancies in those aged above 60 years.³⁸

In this study there was a strong association between smoking and malignancy (Pearsons χ^2 17.7, $p = 0.001$). Several studies have confirmed reduced risk of detecting urological malignancy in those below 40 years of age.^{31,38,47} In this study 55% of the males who presented with gross haematuria were eventually diagnosed with a malignancy, a lower rate of 30% was seen in females. Most bladder malignancies were of histological grade I and II in keeping with findings in other studies.^{38,54}

In general only 41.7% of the patients who presented with gross haematuria were offered surgical treatment. Transurethral resection of the bladder tumour was the most frequent surgical treatment modality offered.

CONCLUSION

1. Cystoscopy and Trans abdominal ultrasound of the kidney ureter and bladder are the most valuable investigations in the evaluation of gross haematuria.
2. Urine cytology for malignant cells has got a supportive role in the evaluation of gross haematuria.
3. Gross haematuria in patient aged above 40 years should be regarded with suspicion as the chances of detecting a malignancy are high.
4. Transitional cell carcinoma is the most frequent type of urological malignancy associated with gross haematuria.
5. There is a high malignancy rate in association with gross haematuria.

RECOMMENDATIONS

1. Cystoscopy and Abdominal Ultrasound should be mandatory in all patients presenting with gross haematuria.
2. A wide scale study should be carried out in the bilharzial endemic zones of coastal region and shores of Lake Victoria to see if histological pattern of bladder tumours is changing.
3. A large multicentre study similar to this would be a valuable scientific resource to be compared against studies done in other parts of the world.

Appendix i

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Appendix ii

DATA COLLECTION FORM

Cystoscopic Findings In The Initial Evaluation Of Gross Haematuria.

Study Code

In patient number

A) PERSONAL AND DEMOGRAPHIC DATA

Name :

Age in years :

District of usual Residence :

Occupation :

Smoking Yes No

If yes to the above state duration and average cigarettes smoked per day

.....

B) PRE-OPERATIVE DATA

Laboratory Investigations

i) Urine based tests

Urinalysis

Urine cytology.....

Microscopy culture and sensitivity.....

ii) Heamatological

Hb

Platelets

PTI

iii) Biochemical

Serum Creatinine

iv) Others (Specify)

.....

Imaging

1) KUB X-Ray

2) KUB ULTRA SOUND

3) I.V.U.

4) C.T. Scan

5) Others (Specify)

C) INTRA-OPERATIVE DATA

1) Type of cystoscopy

2) Cystoscopy findings.....

.....

3) Cystoscopic impression.....

4) Surgical treatment offered.....

5) Other treatment modalities.....

Post Operative Data

1) Histology report.....



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Date: 31st May 2005

Dr. Otieno Simba Raymond
Dept. of Surgery
Faculty of Medicine
University of Nairobi

Dear Dr. Otieno

**RESEARCH PROPOSAL: "A PROSPECTIVE STUDY ON THE
CYSTOSCOPIC FINDINGS IN THE INITIAL EVALUATION OF
GROSS HAEMATURIA AT KENYATTA N. HOSPITAL" (P45/03/2005)**

This is to inform you that Kenyatta National Hospital Ethics and Research Committee has reviewed and **approved** revised version your above cited research proposal for the period 31st May 2005 to 30th May 2006. You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given.

On behalf of the Committee, I wish you fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of database that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely,

Prof. A. N. GUANTAI
SECRETARY – KNH-ERC

Cc: Prof. K. M Bhatt, Chairperson, and KNH-ERC
The Deputy Director (C/S), KNH
The Dean, Faculty of Medicine, UON
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