

*URINARY TRACT INFECTION IN CHILDREN
UNDER FIVE WITH FEVER OF NO OBVIOUS
CAUSE AT KENYATTA NATIONAL HOSPITAL.*

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A DISSERTATION SUBMITTED IN PART FULFILLMENT FOR THE DEGREE
OF MASTER OF MEDICINE IN PAEDIATRICS AT THE UNIVERSITY OF
NAIROBI.

BY


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This thesis is my original work and has not been presented for a degree in any other university.

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DEDICATION.

This book is dedicated to my late father, Shariff Ahmed (Rahimahullahu), my mother Amina Mohamed and my husband Farah Maalim.

ACKNOWLEDGEMENTS.

I wish to extend my appreciation and gratitude to the following who have been of great assistance to me in the course of doing this study without whom it would not have been a reality.

1. My supervisors: Dr. M.J. Luta and Dr. D.A.M. Ngacha for their criticism and guidance all through the stages of this book.
2. My husband Farah Maalim, for his unswerving moral and material support and my daughter Amina, for bearing my absence from her.
3. Mrs Mwaniki, Mr. Chege and Mr. Patrick Nyamora of the Department of Paediatrics for the laboratory work.
4. Miss Janet Musia for the data analysis and her willingness to type the book at the short notice.
5. My relatives Amina Bashir, Abdinaris Idris and Ibrahim Above for their varied supports.
6. All the staff of PFC for their support during my collection of data.
7. The many lecturers and consultants in the department including Prof. Wafula for their advice and support.

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LIST OF ABBREVIATIONS.

UTI	-	Urinary tract infection
KNH	-	Kenyatta National Hospital
CRF	-	Chronic Renal Failure
CNS	-	Central Nervous System
GIT	-	Gastro Intestinal Tract
<i>E. Coli</i>	-	<i>Escherichia Coli</i>
SBU	-	Significant Bacteriuria
WBC's	-	White Blood Cells
hpf	-	High Power Film
CFU/ml	-	Colony per millilitres
°C	-	Degrees centigrade
ESRD	-	End-Stage Renal Disease
RB	-	Risk Benefit
VUR	-	Vesico Ureteric Reflux
P.F.C.	-	Paediatric Filter Clinic
CC	-	Cubic centilitres
CM	-	Centrimetric
MM	-	Millimeters
RBC's	-	Red Blood Cells

SUMMARY.

A descriptive cross-sectional survey was carried out in the out-patient paediatric filter clinic of Kenyatta National Hospital, Nairobi, to determine the prevalence of urinary tract infection among 185 children under 5 years of age who presented with fever of no obvious cause.

The male to female ratio was 1.3:1 and the mean age was 23 months.

Significant bacteriuria (SBU) was found in 41 out of the 185 patients giving a prevalence of 22.2%. The prevalence was higher in males than in females, but the difference was not statistically significant ($P=0.2582$). Clinical symptoms and signs were found to be poor indicators of the presence of urinary tract infection.

Leucocyturia occurred in 40 out of the 41 children with SBU, giving a sensitivity of 97.6%, while presence of nitrites was found to be very specific (94.4%).

Bacteriological studies indicated that *E.coli* was the commonest organism isolated (43.9%) followed by *Staph aureus* (19.5%), *Staph Saprophyticus* (17.1%), *Klebsiella* (9.8%) and *proteus* (7.3%).

Nitrofurantoin, augmentine, nalidixic acid and the

cephalosporins (2nd and 3rd generations) were the drugs most sensitive to the organisms isolated while ampicillin and cotrimoxazole showed high resistant patterns.

The high prevalence rate found in this study emphasizes the need for regular urine checking in children with fever whose cause cannot easily be clinically determined.

INTRODUCTION.

Urinary tract infection is the most common condition in paediatric nephrology (1). It is also the most common bacterial infection found in febrile infants and children who present with fever without an obvious source of infection (2).

At the beginning of the 20th century, febrile infants and small children with UTI could carry an acute mortality of approximately 20% and another 20% developed hypertension and chronic renal failure at a young age (3,4,5). During that period before effective chemotherapeutic agents were available, uncontrolled pyelonephritis was a frequent cause of hypertension and end-stage renal failure in young females (6,7). The advent of widely available health care and of effective antibiotics has made hypertension and CRF from uncontrolled non-obstructive pyelonephritis uncommon in developed countries. However, in developing countries the actual picture is not well established because of lack of sufficient data.

The diagnosis of UTI in young children is challenging due to vague presentation (8). In the neonatal period (birth to 1 month), the symptoms are usually vague, often resembling those of neonatal septicaemia (9). Central nervous System(CNS) symptoms are frequent including irritability, convulsions, irregular respiration, hypotonia and

hypothermia. Cyanosis, ileus, jaundice and an elevated blood urea nitrogen concentration may be present. Failure to thrive was the most common presenting symptom in several large series of studies of infants with UTI during the first month of life. Fever or hypothermia is encountered in about half of the cases.

Beyond the neonatal period and upto 2 years there is a shift from male to female predominance in the occurrence of UTI. By the end of second year of life, the incidence of UTI in girls is probably 10 times that in boys. Some infants presenting with the first episode of UTI present with symptoms of severe acute bacterial infections with systemic manifestations (10). Fever, irritability, meningismus, abdominal distension and vomiting may be present. Other infants are brought in for evaluation because of failure to thrive, GIT symptoms and low grade Fevers. Clinical findings localizing the infection to the urinary tract are usually lacking although parents may note that the urine has a foul odour or has changed in appearance. Intractable diaper rash and perineal erythema appear to be more common in girls with UTI than in those not infected (11).

Many pre-school age girls presenting for the first time with a diagnosis of UTI present with symptoms clearly localized to the urinary tract. Abdominal or suprapubic pain, frequency, urgency and dysuria are common. New or increased enuresis may be present.

However, about half of the girls with symptoms characteristics of infections of the lower urinary tract infection do not have bacterial infections but have bacterial cystitis or the frequency of dysuric syndrome.

A relatively small fraction of pre-school aged children with UTI present with failure to thrive and vague GIT complaints (12).

Although fever and abdominal pain are prominent complaints in pre-school aged children with upper urinary tract infection, the clear cut flank and costo-vertebral angle tenderness encountered in the school-age child with acute pyelonephritis is less frequent.

BACKGROUND AND LITERATURE REVIEW.

Most of the studies done on UTI in children are based on data in the developed countries. There is a paucity of data on urinary tract infection in the developing countries.

In Kenya, Kinuthia, Opondo and Ndinya-Achola retrospectively studied 60 children presenting with their first non-obstructive UTI in Kenyatta National Hospital. Of these 32% had fever, 20% had haematuria, and 20% had dysuria. 60% were aged 0-5 years and *E. coli* was the common causative organisms (13). This shows that fever was the commonest presenting complaint.

Ogola [1990] studied the prevalence of SBU (significant bacteriuria) in a population of Nairobi primary school girls. 17 out of the 639 girls had clinical features of urinary tract infection. 14 had dysuria and only one presented with fever. *E. Coli* was the commonest cause of SBU (62.2%) followed by *Klebsiella* (24.3%) and *strep faecalis* 8.1%. (14). The study found significant leucocyturia in 22.6%, haematuria in 40.5%, nitrites 73.7% and albumin 21.4%.

Shah (1976) studied the incidence of urinary tract infection in the infants and children under the age of 6 years. The study also compared pyuria and bacteriuria and assessed the reliability of suprapubic aspiration of urine with the other methods of urine collection. Suprapubic aspiration was done

in 146 cases out of the 400. Clean voided urine was collected in 154 cases and 134 cases collected by bag. The incidence of UTI was found to be 3.5% and suprapubic aspiration of urine was found to be safe, easy and a useful method of obtaining urine for accurate diagnosis of urinary tract infection.

He concluded that there was a possibility that the morbidity and mortality seen in this group may be partly due to unrecognized UTI. In the study there was some correlation of significant pyuria (more than 10 pus cells per Hpf) with positive cultures that indicate UTI (15).

In the developed countries, the prevalence rates of UTIs among the febrile infants and young children ranged from 4.1% to 7.5% (16,17). UTI occurs in 1% of all newborn infants and 30% of infants admitted. There is a marked preponderance of boys and the reason is not known.

UTI affects 2-4% of older infants and children. The prevalence is with girls ten times as often as boys accounting for 0.3-5.8% of admissions to a general paediatric service (18).

Linshaw noted that of the infections that afflict children in the United States, UTIs are second only to those involving respiratory tract. Symptomatic UTIs occur in about 0.14% of infants in the first month, in 1.5%-2% of

children from 1-5 years and has a cumulative risk by eleven years of 1% and 3% for males and females respectively. Approximately 1.2% of children with symptomatic UTI have recurrences. The frequent UTI recurrences cause considerable distress, inability and cost both to the family and the child(19).

Kass in 1956 defined pyuria as at least 5 WBC's per high power field and found it to be present in a third to half of patients with at least 100,000 CFU/ml and only in 2% of those with bacterial counts of less than 100,000 CFU/ml. (20). He concluded that pyuria was of value diagnostically only when it was clearly present and that its absence should not be interpreted as absence of bacteria. Similar findings have been reported by other authors (21,22,23,24). This indicates that culture is a requirement in all children presenting with symptoms because the presence of pyuria alone (on microscopy) has been found to be a poor predictor of positive urine cultures (20).

A recent study by Crain and Creshel of 442 female infants younger than 8 weeks of age who underwent bladder catheterization and a suprapubic aspiration as part of an evaluation for sepsis, reported a low sensitivity (48%) of microscopic urinalysis (either at least 5 WBCs per hpf centrifuged or any bacteria per hpf in uncentrifuged urine) for identifying infants with positive urine cultures (25).

In a study done (1991) on the prevalence of UTI on an unselected population of febrile infants, sensitivity, specificity and predictive value of bacteria and WBC's in the urine for a positive urine culture were determined for 856 catheterized urine specimens. The optimum values for predicting a positive urine culture were determined as five or more WBC's per hpf and any bacteria per hpf. Presence of pyuria alone was found to be relatively poor, nearly half of the UTI's would not have been diagnosed. Presence of bacteriuria alone was more sensitive (86%), but not specific (63%) in identifying infant's UTI accurately (26).

Kramer, Tange and Drummond assessed the relative risks and benefits of 10 potential urine testing strategies (compared with no testing) involving urinalysis and urine culture for children aged 3 to 24 months with fever but no focus on bacteria infection. The results of the decision analysis were expressed as the preventive fraction (the proportion of cases prevented) for end-stage renal disease (ESRD) and hypertension, and as low risk/benefit (RB) ratios. The results showed that a strategy of combined urinalysis and urine culture in febrile children is associated with the most favourable RB profile. It was therefore concluded that upto 50% of the long term sequelae of occult urinary tract infections in young febrile children appear preventable by urine testing, but even the most favourable strategies required testing of thousands of children and unnecessarily treating hundreds for every case (27).

In a discussion of UTI in early childhood by Watson R., it was noted that the infantile kidney was the most vulnerable to damage from vesicoureteral reflux (VUR) combined with UTI. UTI's as well as giving rise to significant morbidity, may provide the clue to an underlying congenital abnormality such as obstructive uropathy (28).

UTI/VUR/RENAL SCARRING.

Since the mid-1970s , management of paediatric patients with UTI's in an unobstructed urinary tract has been based on the theory of a cause-and-effect relationship between UTI's, VUR and the occurrence of renal scarring, i.e. reflux nephropathy. The mechanism of kidney damage has been postulated as the result of urinary tract infection together with a vesicoureteral reflux and intrarenal reflux resulting into a reflux nephropathy.

This concept of the pathogenesis of renal injury with UTI's was supported by retrospective studies such as that of Smellie and colleagues (29). They reported the follow-up evaluation of 570 children with UTI with or without VUR. Two hundred of the children were followed for 10 to 20 years. Renal scarring was found almost exclusively in those with VUR, and fresh scars developed only in those with moderate to severe VUR following infection.

However, Winberg and colleagues described patients with huge VUR, intrarenal reflux and no renal damage and a group of children with slight or no reflux who developed renal scars (30) indicating that other mechanisms may be responsible for renal damage.

The role of virulent P. fimbriated *E. Coli* as a cause of kidney damage in the absence of VUR was demonstrated in an experimental study in monkeys by Roberts and colleagues. Six adult male non-refluxing monkeys were experimentally infected by inoculation of P. fimbriated *E. coli* into the bladder and eight control monkeys were inoculated with a non P. fimbriated *Escherichia coli* strain. Four of the six monkeys inoculated with the P. fimbriated *E. coli* developed acute pyelonephritis, whereas none of the eight inoculated with non-fimbriated *E. coli* bacteria developed pyelonephritis. A large clinical study of the role of P. fimbriated *E. coli* in UTI by Domingue and colleagues gave strong support to the concept that virulent P. fimbriated *E. coli* are the usual pathogens in acute pyelonephritis in immuno-competent patients (31).

Children are thought to be at particular risk for scarring when symptomatic UTIs occur in the first year of life. However, looking at the age at which new scarring in children with UTI was detected, Smellie et al found that new scars were formed at least until age 10, while new scars were less common after age 7, one third of kidneys forming

new scars had been normal at age 5. Older children therefore, are still vulnerable (32).

OBJECTIVES.

GENERAL

To determine the prevalence of urinary tract infection in children under 5 years of age presenting at KNH, Paediatric Filter Clinic with fever of no obvious source.

SPECIFIC

- i. To determine the prevalence of pyuria, bacteriuria and nitrites in the urine of children presenting with fever.
- ii. To determine the pattern of pathogens isolated together with bacteria sensitivity patterns of those children with confirmed urinary tract infection.
- iii. To correlate between microscopic findings of the urine specimen and the urine culture results (i.e. sensitivity, specificity and predictive value).

MATERIALS AND METHODS.

STUDY DESIGN.

Cross-sectional survey (a descriptive study).

SAMPLE SIZE (n)

$$n = \frac{Z^2 \cdot P(1-P)}{d^2}$$

P: estimated prevalence - 4%

α : 5% (in the 95% confidence interval)

Z: the standard deviation (1.96)

d: the absolute precision where difference of the estimated prevalence of no more than 2 was expected.

A sample size of 178 was worked out using the above formular, but 185 children were recruited into the study.

STUDY SITE: Paediatric filter clinic at Kenyatta National Hospital.

Paediatric filter clinic is part of Casualty Department of KNH. The clinic serves between 120-150 children every day. Approximately 30-50 patients get admitted into the paediatric wards daily. An average of 6-12 patients are seen every day with a diagnosis of fever of no obvious cause.

The filter clinic as is the general role of KNH, serves as a national referral and teaching hospital. Much as it is a

referral entity, the clinic also serves many new patients from Nairobi and its environs.

The age range of patients attended at the clinic is confined to 0-14 years. The personnel in the clinic include a Paediatric Registrar and/or a Medical Officer with two Clinical Officers and five Nurses at any one time. The clinic runs for 24 hours and children below 5 years are attended free.

STUDY POPULATION: All children under 5 years of age in whom the primary clinician at PFC had made an impression of fever of no obvious source.

For the purposes of this study, fever of no obvious source is defined as: a temperature of $\geq 37.5^{\circ}\text{C}$ in an otherwise normal child whose clinical findings are noncontributory, a negative blood slide for malaria parasite and no frank malnutrition or malignancy at initial examination.

INCLUSION CRITERIA.

1. All children under 5 years of age presenting with fever of no obvious source. Fever defined as surface temperature (axillary/thigh of $> 37.5^{\circ}\text{C}$).
2. Free informed verbal consent of parent/guardian/adult companion of the child.

EXCLUSION CRITERIA.

1. Patients with a positive blood slide for malaria parasites.
2. Patients with any obvious cause of the fever e.g.
 - otitis media
 - B pneumonia
 - abscess/wounds
 - tonsillitis
 - meningitis
3. Very sick children and those with severe respiratory distress.

STUDY LIMITATIONS.

1. Collection of urine specimen was confined to Monday - Friday from 8.00a.m. to 4.00p.m.
2. Children who may have been treated elsewhere with antibiotics before presenting in our hospital, hence decreasing yield of bacterial culture.

STUDY PERIOD

Ten weeks (March to June 1998).

STUDY JUSTIFICATION.

Everyday there is a proportion of children who present in our paediatric casualty filter clinic with fever whose source cannot be localised. These children may have urinary tract infections, but the proportion is not clear.

The urinary findings usually go undetected because the working diagnosis of "viral syndrome" or "clinical malaria" may have made laboratory evaluation seem unnecessary. Antibiotics prescribed for these syndromes or for other incompletely evaluated febrile illnesses may modify the course of UTI.

Unfortunately such therapy neither alters the tendency for recurrences of urinary tract infections nor modifies the potential for damage, which may result from a serious obstructive lesion or severe VUR.

This study is aimed at documenting the magnitude of this problem.

ETHICAL CONSIDERATIONS.

1. Informed verbal consent was taken from the parents/guardian/adult companion of all the children who were included the study.
2. Appropriate treatment was administered when necessary.
3. Results and information obtained was kept in confidence.
4. Patients were referred to appropriate experts.

PROCEDURE.

Between the months of March and June 1998 most children below five years of age presenting with fever at the Paediatric Filter Clinic were selected by the nurse doing observations and were referred to the author's desk. Not all the patients were seen by the author as those who were very ill and obviously in respiratory distress were seen elsewhere.

480 febrile children were screened by the author for eligibility for inclusion in the study. Only 185 were included in the study having satisfied the inclusion criteria (41%). The socio-demographic data and a history of presenting illness was taken from the parent/guardian. No direct questions were asked for the presence of symptoms of urinary tract infection. A thorough clinical examination was performed to rule out any obvious cause of fever. Symptoms such as mild cough, diarrhoea or a running nose were not considered as necessarily the cause of the fever. Blood slide for malaria parasites was carried out for all patients to rule out malaria as a possible cause of fever. The details of socio-demographic data, history of clinical examination were entered into a structured proforma. (Appendix I)

METHOD OF URINE COLLECTION.

All urine specimens were collected by the author using suprapubic aspiration or bladder catheterisation or clean catch mid-stream urine. The choice of method of collection depended on the age of the child hence the ability to follow instructions; presence of a full bladder at the time of examination and acceptability of the procedure by the parent/guardian.

Although preference was given to suprapubic aspiration, it was not possible for most patients because most of them presented without palpable bladders and it was also not a procedure most mothers were comfortable with. Second preference was bladder catheterization. This was done in order to avoid high rates of urine contamination. Most cases of spontaneous urination was as a result of passing urine while in preparation for suprapubic aspiration, bladder catheterisation or during abdominal examination.

1. SUPRAPUBIC ASPIRATION.

The procedure was carried out with the patient lying in supine position with the lower extremities held in extension. Eighteen out of the 185 patients (9.7%) underwent this procedure. The suprapubic area was cleaned with methylated spirit. Using a 10cc syringe and gauge 21 needle, aspiration was done in the midline about 2cm above the symphysis pubis with a rapid movement applying suction on syringe as the needle was pushed in. About 5-10cc of

urine was gently aspirated and the needle was withdrawn. There were no complications reported from this procedure in any of the patients.

2. **BLADDER CATHETERISATION.**

All patients who had passed urine just before recruitment or those who had failed suprapubic aspiration, had their urine specimen collected using this method. 106 patients (57.3%) underwent bladder catheterisation under sterile conditions. This comprised the majority of the patients.

After cleaning the hands and putting on sterile gloves, the author made patients lie in semi-lithotomy position while on their mother's lap. In girls, the vulvoperineal region was cleaned (using savlon) after separating the labia to identify the urethra and in boys the glans-penis was cleaned pushing the foreskin backwards. Feeding tubes ranging from size 4-10mm were used depending on the age of the child. The appropriate size tube was gently passed into the bladder and about 5-10cc of urine specimen was collected thereafter the tube gently removed.

3. **"CLEAN-CATCH" MIDSTREAM URINE.**

Urine was obtained from 61 patients (33%) using this procedure. Most of them while examining the abdomen, cleaning the vulvoperineum/glans-penis, or while attempting suprapubic aspiration. Some of the patients above the age

of 2 years were coaxed to pass urine in a wide mouthed sterile bottle. Midstream specimen of urine was collected from all these patients.

All specimens of urine collected were labelled appropriately and taken to the laboratory by the investigator within one hour of collection.

LABORATORY PROCEDURE.

A. **URINE CULTURE.** This was done immediately on receiving the specimen in the Department of Paediatrics, University of Nairobi. Using a platinum wire-loop calibrated to deliver 0.002mls of urine. A specimen of urine was inoculated on Cystein-Lactose-Electrolyte-Deficient (C.L.E.D) agar and incubated at 37°C for 24 hours.

Colony count was done after 24 hours to determine significant bacteriuria. This depended both on method of collection and if the patient was on antibiotics at the time of recruitment.

Significant bacteriuria was considered when:

a. More than 1000 organisms were isolated by bladder catheterisation or if the patient was already on antibiotics irrespective of the method of collection.

b. Any growth obtained from urine specimen collected by suprapubic aspiration.

c. Isolation of organisms more than 100,000

irrespective of collection method.

B. URINALYSIS. This was performed using Comburl0 test reagent strips manufactured by Boeringer Mannheim. Using the manufacturer's instructions, a dipstix test for leucocytes, proteins, red blood cells and nitrites was done using well mixed uncentrifuged fresh urine specimen. Visual reading of the results was done comparing colour changes of the impregnated areas on the strip. Reading was done after 60 seconds for proteins, R.B.Cs and nitrites and after 120 seconds for leucocytes as recommended by the manufacturers.

C. MICROSCOPY. For this procedure, urine was spun in a centrifuge tube at low speed for 3 minutes. The deposit was put on a slide, covered with a coverslip and examined under a microscope (power x 10 and x 40) for pus cells, R.B.Cs, casts, yeast cells and bacteria.

D. DATA ANALYSIS

All raw data was entered on an IBM computer utilising SPSS/PC+ system. Frequency distribution was done and statistical differences obtained using Chi Square test. EPI INFO was used to calculate P values using Fishers Exact tests where numbers were too small. Otherwise SPSS programme was used for Chi Square test. P value was of statistical significance when P was ≤ 0.05 .

RESULTS.

A. DESCRIPTION OF THE POPULATION STUDIED.

Between the months of March and June 1998, one hundred and eighty five (185) febrile children with no localising signs from the Paediatric Filter Clinic (K.N.H.) were recruited into the study. Out of these, 41 (22.2%) had significant bacteriuria. 163 (90%) were treated as out-patients and 22 (10%) as in-patients.

Age range	-	0-60 months
Mean age	-	23 months
Male:female ratio	-	1.3:1.

TABLE 1 AGE DISTRIBUTION OF STUDY POPULATION

Age (months)	Number	Percentage
0 - 6	25	13.5
>6 - 12	48	25.9
>12 - 24	44	23.8
>24 - 36	25	13.5
>36 - 48	21	11.4
>48 - 60	22	11.9
Total	185	100

Most children seen were below 24 months of age (63.2%). This only reflects the age distribution of population seen in PFC at KNH.

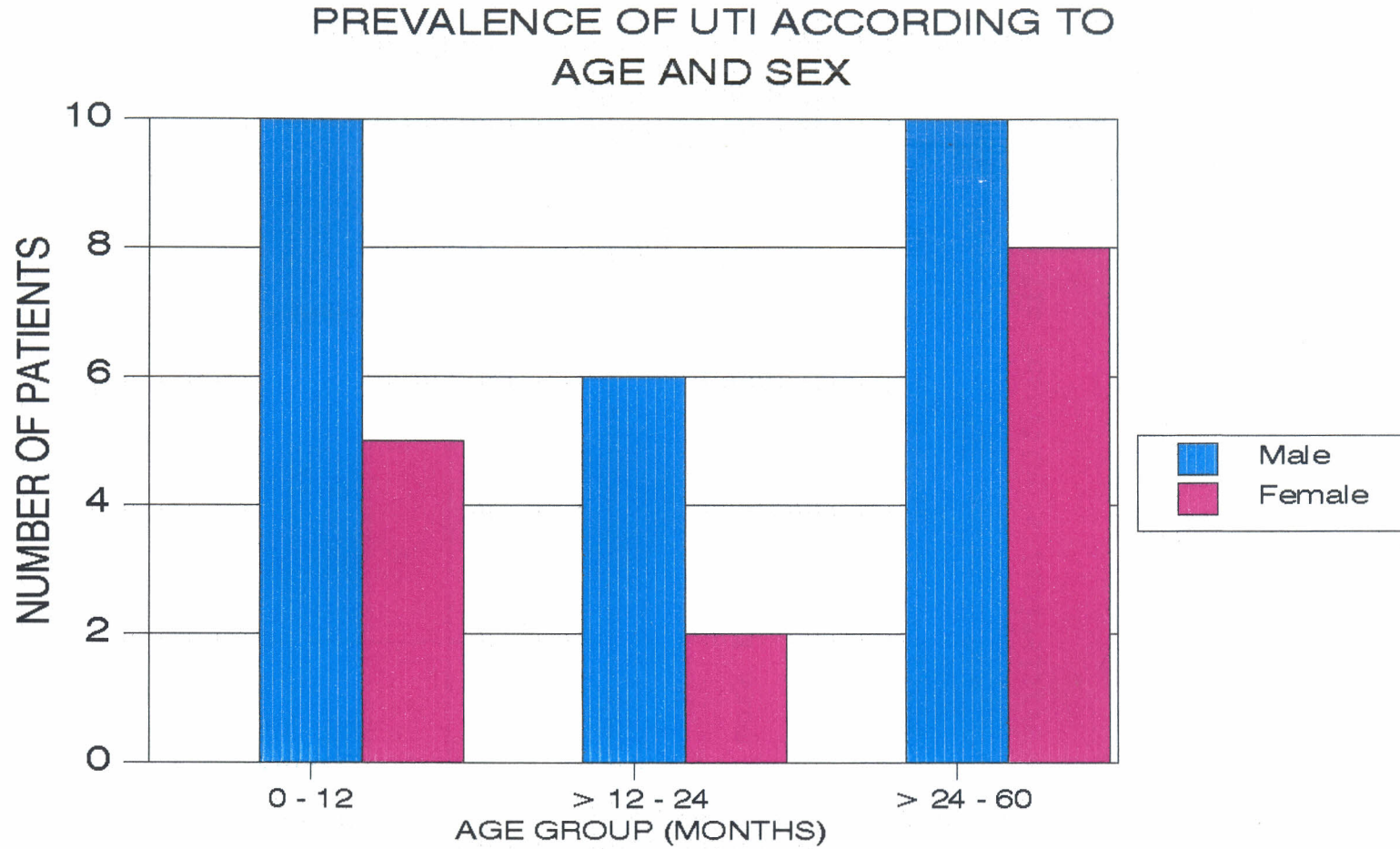


FIGURE 1.

In all age groups, more males were seen compared to females, a pattern different from most previous studies.

TABLE 2. DISTRIBUTION OF URINARY TRACT INFECTION BY AGE AND SEX.

Prevalence of U.T.I. was calculated and found to be 22.2%, i.e. 41 out of 185 patients.

Age (years)	Male		Female		P value
	no.	%	no.	%	
0 - 1	10	(24)	5	(16)	0.4221
> 1 - 2	6	(23)	2	(11)	0.3116
> 2 - 5	10	(29)	8	(24)	0.6859
Total	26	(25)	15	(18)	

There were more boys who had UTI (25%) compared to girls (18%) in all age groups (0-5 years). More than half the children who had UTI were below 2 years of age. There was no significant statistical difference in the occurrence of UTI between males and females. (P value more than 0.05 means there is no statistical significant difference).

METHOD OF URINE COLLECTION

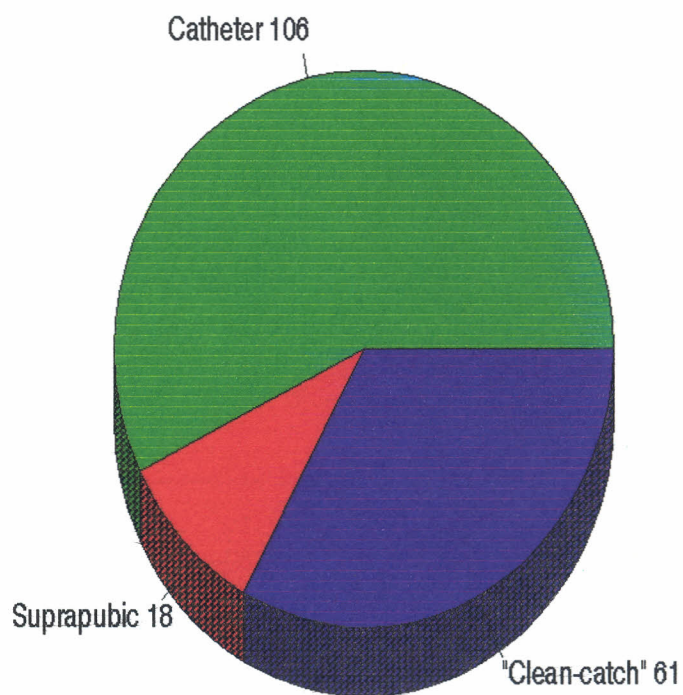


FIGURE 2 .

TABLE 3. YIELD RATE ACCORDING TO METHOD OF URINE COLLECTION.

Method	Without UTI		With UTI		Total	
	n	(%)	n	(%)	n	(%)
1. Suprapubic	17	(11.8)	1	(2.4)	18	(10)
2. Catheterization	83	(57.6)	23	(56.1)	106	(57)
3. Spontaneous (voiding)	44	(30.6)	17	(41.5)	61	(33)
Total	144	(100)	41	(100)	185	(100)

P. value 0.06145 using EPINFO programme to calculate Chi-square (χ^2).

Even though 3 different methods of collecting urine specimens were used, and the proportions appeared higher with the catheterization method, there was no significant statistical difference seen in using the different methods.

TABLE 4. TYPES OF ORGANISMS ISOLATED

Organism	Number	Percentage
<i>E. Coli</i>	18	43.9
<i>Staph. aureus</i>	8	19.5
<i>Staph. saprophyticus</i>	7	17.1
<i>Klebsiella</i>	4	9.8
<i>Proteus</i>	3	7.3
<i>Kleb + E.Coli</i>	1	2.4
Total	41	100

There was only one case of a mixed growth. *E. coli* was the commonest isolate.

TABLE 5 UTI YIELD RATES IN CHILDREN PREVIOUSLY EXPOSED TO ANTIBIOTICS.

Exposure to antibiotics	With UTI		Without UTI	
	N	(%)	N	(%)
No exposure	16	(39)	56	(39)
Exposed	16	(39)	72	(50)
No idea	9	(22)	16	(11)

P value = 0.3738

The yield rates were exactly the same in the groups of children who were exposed to antibiotics and the ones not exposed to antibiotics prior to their presentation to the PFC and subsequent recruitment into the study.

There were a few children whose parents/guardian had no idea of any prior antibiotic use. Statistically there was no significant difference in the yield rates (p value >> 0.05).

TABLE 6 COMMON PRESENTING COMPLAINTS.

Presenting complaints of the febrile children under study comparing those with and without urinary tract infection.

Symptom	With UTI		Without UTI		P value
	n	%	n	%	
Loss of appetite	30	73	113	78	0.4746
Vomiting	30	73	94	65	0.3429
Diarrhea	13	32	48	33	0.84509
Cough	13	32	45	31	0.95559
Abdominal pains	12	29	34	24	0.4597
Failure to thrive	10	24	26	18	0.3660
Convulsions	4	10	15	10	0.5546
Dysuria	3	7	8	6	0.8656
Painful defaecation/ constipation	3	7	6	4	0.3405
Body swelling	2	5	3	2	0.33026
Others (n=12)	2	5	10	7	0.6223

Others:

- (4) sneezing/nasal blockage
- (1) photophobia
- (2) foul smelling urine
- (1) scratching vulva
- (2) headaches/joint pains
- (1) body itch
- (1) swelling around the neck

There was no significant statistical difference between febrile children with and those without UTI for the common presenting complaints. However, symptoms like vomiting, failure to thrive, painful defaecation (constipation) and body swelling occurred more commonly in children with UTI compared to those without UTI.

CLINICAL PRESENTING COMPLAINTS

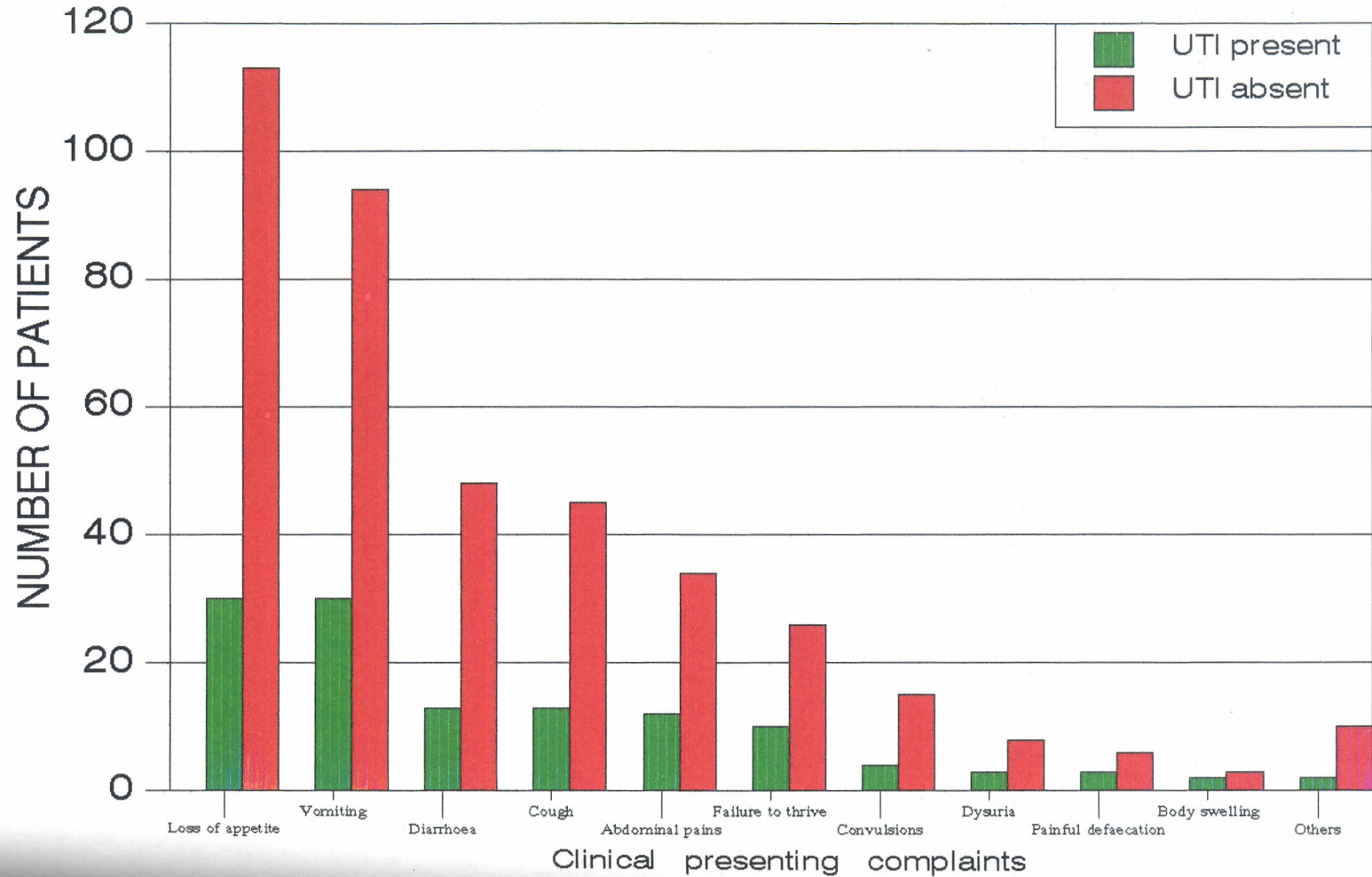


TABLE 7 DEGREE OF TEMPERATURE IN RELATION TO UTI

Temperature (°C)	With UTI n (%)	Without UTI n (%)
<38.4	25 (61)	67 (47)
>=38.4	16 (39)	77 (53)
Total	41 (100)	144 (100)

P. value = 0.1455

The study compared the prevalence of UTI among children with a temperature $>$ or $= 38.4^{\circ}\text{C}$ to those with a lower temperature.

Median temperature = 38.4°C .

Although the frequency of UTI was greater in children with temperature lower than 38.4°C , the difference was not statistically significant. (P value was > 0.05)

TABLE 8 (a) CORRELATION BETWEEN BIOCHEMICAL (DIPSTIX) FINDINGS AND URINE CULTURE.

Test	With UTI no (%)	Without UTI no (%)	P value
Leucocytes +	21 (51)	42 (29)	0.0000
Leucocytes ++	12 (29)	7 (5)	0.0000
Leucocytes +++	7 (17)	1 (1)	0.0000
Leucocytes Nil	1 (2)	94 (65)	--
Proteins +	17 (42)	61 (42)	0.81218
Proteins ++	3 (7)	12 (8)	0.77592
Proteins +++	0 (0)	2 (1)	0.43679
Proteins Nil	21 (51)	69 (48)	--
Nitrites +ve	22 (54)	8 (6)	0.0000
Nitrites -ve	19 (46)	136 (94)	--
Blood +	9 (22)	30 (21)	0.53789
Blood ++	8 (30)	8 (6)	0.00428
Blood +++	0 (0)	1 (1)	0.63288
Blood Nil	24 (59)	105 (73)	--

Key:

Leucocytes + 10-25 leuco/ μ l
 ++ 75 leuco/ μ l
 +++ 500 leuco/ μ l

Blood + 5-10 erythro/ μ l
 ++ 50 erythro/ μ l
 +++ 250 erythro/ μ l

Protein + 30 mg/dl
 ++ 100 mg/dl
 +++ 500 mg/dl

The appearance of leucocytes of whatever degree was found to correlate better with SBU. Same goes with nitrites and blood (50 erythro/ μ l).

Appearance of protein on dipstix was not different between the 2 groups.

TABLE 8 (b) CORRELATION BETWEEN MICROSCOPIC FINDINGS AND URINE CULTURE.

Test	With UTI no (%)	Without UTI no %	P value
Pus cells +	22 (54)	72 (77)	0.0000
Pus cells ++	15 (37)	4 (21)	0.0000
Pus cells +++	4 (10)	0 (0)	0.0000
Pus cells Nil	0 --	68 (100)	-
RBCs +	13 (32)	22 (63)	0.1246
RBCs ++	2 (5)	0 (0)	0.0032
RBCs +++	0 (0)	2 (100)	0.5109
RBCs Nil	26 (63)	120 (82)	-
Bacteria +	16 (39)	7 30	0.0000
Bacteria ++	3 (7)	0 0	0.0000
Bacteria Nil	22 (54)	137 82	-

Key:

Pus cells + (0-5)
 ++ (5-10)
 +++ (above 10)

Bacteria + (scanty)
 ++ (moderate)

Presence of bacteria and pus cells (of all degrees) were found to be statistically significant. The correlation was higher in those children with SBU as opposed to the ones without UTI. Mild to moderate degrees of RBC's was also significant.

TABLE 8(c)

CORRELATION BETWEEN BIOCHEMICAL (DIPSTICK) FINDINGS OF URINE SPECIMEN AND URINE CULTURE RESULTS (I.E. SENSITIVITY, SPECIFICITY AND PREDICTIVE VALUE).

Test	Sensitivity	Specificity	Predictive value	
			+ve(%)	-ve(%)
Leucocytes	97.6	65.3	44.4	98.9
Nitrites	53.7	94.4	73.3	87.7
Proteins	48.8	47.9	21.1	76.7
Blood	41.5	72.9	30.4	81.4

Leucocytes on dipstick was found to be most sensitive criteria for identifying children with UTI while the presence of nitrites was the most specific for SBU.

TABLE 8 (d) COMBINING DETECTION OF LEUCOCYTES AND
 NITRITES

Test	With UTI n (%)	Sensitivity	Specificity
Leucocytes	90 (49)	97.6	65.3
Nitrites	30 (16)	53.7	94.4
Leucocytes + Nitrites	22 (54)	53.6	95.1

When combining detection of leucocytes and nitrites, the sensitivity is still low, however, the test becomes more specific. Therefore combining leucocytes and nitrites as a diagnostic tool has no advantage over isolated detection of either nitrites or leucocytes.

TABLE 8 (e)

CORRELATION BETWEEN MICROSCOPIC FINDINGS OF URINE SPECIMEN AND URINE CULTURE RESULTS (I.E. SENSITIVITY, SPECIFICITY AND PREDICTIVE VALUE) .

Test	Sensitivity	Specificity	Predictive value	
			+ve (%)	-ve (%)
Pus cells	100	47.2	35	100.0
Bacteria	46.3	95	73.1	86.1
RBCs	36.6	83.3	38.5	82.2

Pus cells on microscopy were 100% sensitive while presence of bacteria on microscopy was most specific for SBU.

TABLE 9 BACTERIAL PATHOGEN ISOLATED WITH THEIR SENSITIVITY PATTERNS

Drug tested	E.coli (n=18)		Proteus (n=3)		S.Saproph (n=7)		S.aureus (n=8)		Klebsiella (n=4)		Klebsiella+ E.coli(n=1)	
	n	%	n	%	n	%	n	%	n	%	n	%
Ampicillin	1	5.6	0	0.0	2	28.6	0	0.0	1	25.0	0	0.0
Augmentine	18	100	3	100.0	7	100.0	8	100.0	4	100.0	1	100.0
Cotrimoxazole	1	5.6	0	0.0	2	28.6	0	0.0	1	25.0	0	0.0
Cefaclor	16	88.9	0	0.0	7	100.0	6	75.0	4	100.0	1	100.0
Ceftazidine/Ceftriaxone	18	100	3	100.0	7	100.0	8	100.0	4	100.0	1	100.0
Suprapen	17	94.4	3	100.0	7	100.0	8	100.0	4	100.0	1	100.0
Gentamicin	*12 13 tested	92.3	*2 2 tested	100.0	*6 6 tested	100.0	*6 7 tested		*3 4 tested	75.0 all	*0	0.0
Nalidixic acid	17	94.4	3	100.0	2	28.6	3	37.5	4	100.0	0	0.0
Nitrofurantoin	17	94.4	3	100.0	7	100.0	8	100.0	4	100.0	0	0.0
Cefuroxime	18	100	3	100.0	7	100.0	8	100.0	4	100.0	0	0.0

For gentamicin sensitivity patterns, not all specimens were tested. This was a laboratory error (omission).:
 E.coli only 13 specimens tested, Proteus only 2 out of 3 specimens
 S.Saproph 4 out of 7 specimens, S. aureus 7 out of 8 specimens
 Klebsiella all tested against gentamicin.

The most sensitive drugs were augmentine, cephalosporins and nitrofurantoin. Ampicillin and cotrimoxazole show high resistant patterns.

DISCUSSION.

Of the 185 patients recruited into the study at the paediatric filter clinic, 41 (22.2%) had urinary tract infection. This is a higher prevalence than that reported in the general population both locally and elsewhere (14,15,16,17).

Shah in 1976 at KNH reported a prevalence of 3.5% whereas Ogola reported a prevalence of 5.8%.

The figures in previous studies cannot be compared with figures in this study because the study groups are different and "fever" which is the entry point of this study population is a frequent presenting symptom/sign of urinary tract infections. Hence the high prevalence rates. Most of the previous studies have reported lower prevalences even when the groups under study were high risk for urinary tract infection. Munyi (1991) reported a prevalence of 8.1% among 86 children with lymphopoeitic malignancies. This low figure may have been influenced by the method of urine collection used where most low colony counts were considered as contaminants (33). Mwaura (1976) on the other hand reported relatively higher prevalence of 17% amongst children with malnutrition.

Hellestein reported prevalence rates of UTI among febrile infants and young children to range from 4.1% to 7.5% (22). The findings of this study cannot be compared with the other studies because no similar study of fever and UTI has been done in this region. Therefore it is possible that we have not been aware of the magnitude of UTI in these patients who present with fever of no obvious source. This is supported by a retrospective study done by Kinuthia, Opondo and Achola where they found that almost a third of the children presenting with their first non-obstructive urinary tract infection at KNH had fever.

Chabar C et al also noted that UTI's account for a significant number of cases of unexplained febrile illness in children under 3 years of age (35).

In this study a preponderance of males was noted in age groups ranging from birth to 5 years. Of the children with UTI in age group 0-1 year, 58% were boys and 42% girls. A similar pattern was observed in children of ages above 1 year and 5 years. In the latter case the distribution was 55% boys and 45% girls. The age trends in this study are clearly different from most previous studies.

Epidemiological investigations have shown that males are more commonly infected during the first three to six months of life and after this age, there is a change in gender related predominance. In older children UTI's are significantly more common in girls than in boys (35). Other studies have shown that during the neonatal period, there is a striking male predominance in the occurrence of all infections, including those of the urinary tract. Female preponderance for urinary tract infections becomes evident after the first 6 months of life and is increasingly apparent throughout the first year and subsequently (36,37,38).

Contrary to the observations of this study, Winbery and Brumfitt et al reported in different studies that in the neonatal period, UTI is quite common equally in boys and girls and in both sexes the majority of the infections occur during the first year of life. After this time infections are rare in boys but continue to be fairly common in girls (38,39). Similar trends to this study were reported both by Kunin (40) and Munyi (33), where SBU did not appear to be influenced by age as the proportions of patients with SBU in various age groups were very similar. The pattern of age and sex distribution in this study can be explained by the fact that in all age groups there were more males recruited

in the study as compared to females (ratio 103:82).

On methods used for urine collection in this study, the investigator made sure that all the procedures were done under strict sterile conditions and all specimens were collected by the investigator in order to avoid contamination. Though all the three methods of urine collection were used, emphasis was laid on suprapubic and the catheter methods to eliminate the possibility of contamination. About 67% of the urine specimens were collected using either suprapubic aspiration or bladder catheterization. The application of a method of urine collection that is not likely to invite contamination has been an approach used by many investigators to distinguish true bacteriuria from contamination (41,42,43).

The study compared the rates of bacterial isolates with the methods of urine collection. The commonest organism isolated was *E.coli* comprising 44% of the isolates followed by *Staph aureus* (19.5%), *staph saprophyticus* (17%), *klebsiella* (10%), *proteus* (7%) and 2.4% was a mixed growth of *klebsiella* and *E.coli*. There was a heavy mixed bacterial isolate in a child with malnutrition. The high frequency was previously observed in other studies involving older children (13,14,15). Davies et al (44) studied nosocomial

infections in a pediatric hospital and found *E.coli* to be the commonest organism isolated (26%) followed by *Enterococcus Sp.* (15%), *pseudomonas sp* (13%), *Klebsiella Sp.* (10%) and coagulase - negative *staphylococcus* (9%). The usual urinary pathogens in the infants or children with a first UTI is *E. coli* but *klebsiella sp. proteus, pseudomonas sp, enterobacter sp* and *enterococci* can also be the cause of infection with first diagnosed UTI. Organism other than *E. coli* are encountered with increased frequency amongst children with recurrent urinary tract infections (45). The concept of recurrent UTIs was not dealt with in this study. Other references have reported *E.coli* to cause more than 75% of UTI in all paediatric age groups, the remaining being due to other gram-negative enterobacteria especially *klebsiella, proteus mirabilis* and *pseudomonas aeruginosa*. *Enterococci* and coagulase negative *staphylococci* (e.g *staphylococcus saprophyticus*) are the most frequently implicated gram-positive organism in this study probably because the target group are mostly out-patients. *Pseudomonas sp* are mainly hospital acquired infections.

Apart from *staph aureus*, none of the other isolates are known to be normal commensals of the urinary tract. *Staphylococcus saprophyticus* a coagulase negative *staphylococcus* (which comprised 17% of the isolates in this

study) has been recognised as a common cause of UTI in adolescent girls and young women and is now being encountered with some frequency as a urinary pathogen in children (45).

The study has also looked at the clinical presentation of these children with fever of unknown source. The commonest presenting symptoms were loss of appetite (73%), vomiting (73%) and diarrhoea (32%). However, there was no significant statistical difference between those with UTI and those without. It was observed in this study that symptoms like vomiting, convulsions, dysuria, painful defaecation / constipation and UTI occurred more frequently in the group with UTI compared to the group without. However there was no significant statistical differences in all of them as demonstrated in table 5. It would have been more interesting and more informative to classify the symptoms in the different age groups (from neonatal period through infancy to the older child). However, this would require a much larger study group and would form the basis of future investigations. The above findings are not surprising. Symptoms of UTI in children have always been known to be vague, hence the need to investigate and follow up any fever of no obvious source. It is important to note at this point that GIT manifestation are common in children with UTI as

was demonstrated in this study.

On correlating between dipstix findings and urine culture, presence of leucocytes of whatever degree (+, ++, +++) correlated very well with significant bacteriuria. The difference was statistically significant and similar to nitrites and the presence of blood (50 eryth/ul) in the urine. There are many variables related to the quantification of leucocytes in urine that urine microscopy yields only a quantitative appraisal. The reasons for this are that leucocytes in the urine can originate from outside the urinary tract especially in the vagina and it is often difficult to distinguish renal tubular epithelial cells from polymorphonuclear cells when examining unstained urinary sediments.

Appearance of protein on dipstix had no correlation with significant bacteriuria.

Leucocytes on dipstix was found to be a more sensitive criteria (sensitivity 97.6%) for identifying children with UTI while the presence of nitrites on dipstix was more specific (specificity 94.4%) for SBU (see table 6(a) & (c)).

The value of dipstix in the diagnosis of UTIs remains

controversial. It is a sensitive screening procedure but it cannot be used as a diagnostic test. The dipstix used in this study included both detection of leucocytes and Nitrites. When both reagents are positive the predictive value is about 99% for leucocytes and 87.7% for nitrites.

Microscopic examination of the urine was found to be useful though not definitive. The results of this study indicated that 100% of those with UTI had pyuria (75 WBC's/high-power field). Pyuria was also found in 44% of those without UTI proven by culture. The urine gram-stain (microscopy) was found to be a sensitive procedure for identifying UTI. The presence of bacteria in urine correlated very well with the presence of SBU on culture.

This study has re-emphasized the importance of urine testing to prevent long-term sequelae of occult urinary tract infections in young febrile children. Similar results were shown by a study by Kramer et al where a risk-benefit analysis was done for urine testing in young febrile children. Kramer's study (1994) was done to assess the relative risks and benefits of ten potential urine testing strategies compared with no testing. The tests included urinalysis and urine culture for children aged 3 to 24 months with fever but no focus of bacterial infection. In

Kramer's study a strategy of a combination of urinalysis and urine culture in children with temperatures $\geq 39^{\circ}\text{C}$ was associated with the most favourable Relative Risk and Benefit (RB) profile. The conclusion was that up to 50% of long-term sequelae of occult urinary tract infections in young febrile children can be prevented through urine testing.

As far as antibiotic sensitivity is concerned the highest sensitivity was registered with augmentin, third generation cephalosporins (ceftazidime and ceftriaxone) and cefuroxime. With none of the specimen being resistant in vitro. The mentioned drugs had a sensitivity of 100% followed by nitrofurantoin, suprapen, cefaclor and gentamicin. Nalidixic acid was found to be less sensitive to gram-positive organisms (*staph saprophyticus* and *staph aureus* with sensitivity of 28.6% and 37.5% respectively). Very low sensitivity patterns were registered with ampicillin and cotrimoxazole which was below 28%. Similar pattern was registered in previous local studies (16,17), however, resistance to ampicillin and cotrimoxazole is much higher in this study.

CONCLUSIONS.

1. Prevalence of UTI in febrile children, which is 22% in our set up, is comparatively higher than figures registered in previous studies. This prevalence is probably due to our entry point, which is 'fever', a condition not applied in previous studies.
2. Clinical presentation of UTI in children remains vague. A high index of suspicion of UTI in children presenting with fever of no obvious cause is necessary so as to evaluate them appropriately.
3. Though cotrimoxazole and ampicillin are currently recommended as first line treatments for UTI, this needs to be re-evaluated in the light of the sensitivity pattern that has emerged from this study.
4. Dipstick examination especially when combined with microscopy is a reliable screening method for urinary tract infection and may be used in compromised circumstances to document UTI.

RECOMMENDATIONS.

1. The findings of this study places more emphasis on the need to carry out urinalysis routinely on all children who present with fever of no obvious cause.
2. Nitrofurantoin and augmentine should be used as first line drugs for empirical treatment of urinary tract infection.
3. Given the current socio-economic conditions of our country, there is need for a study to be undertaken to evaluate a reliable and cost-effective method of urine testing (dipstick or microscopy or culture or a combination of any two).

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APPENDIX I.

PROFORMA: PREVALENCE OF URINARY TRACT INFECTION.

Name:.....

Date of birth..... Sex.....

Residence.....

Study no.....

PRESENTING COMPLAINTS (Volunteered information - no direct questions)

Nausea/loss appetite Yes/No.

Hematuria Yes/No.

Dysuria Yes/No.

Failure to thrive Yes/No.

Vomiting Yes/No.

Abdominal pains Yes/No.

Others (specify).....

SIGNIFICANT PAST HISTORY

H/O Hospitalization Yes/No.

H/O out patient management Yes/No

If yes, specify.....

DRUG HISTORY

H/O recent antibiotic use for the presenting
complaint Yes/No/No idea

If yes, specify.....

GENERAL EXAMINATION:

Pallor..... LN enlargement.....
 Oedema..... Jaundice.....
 Dehydration..... Cyanosis.....
 Obvious septic lesions..... Wt..... Ht.....

VITAL SIGNS.

Pulse..... Resp. rate..... Temp.....
 Ears.....
 Throat.....
 Nose.....

INVESTIGATIONS.

1. B/S for MPS POSITIVE/NEGATIVE
2. Urinalysis i. Suprapubic/catheterization
 ii. Microscopy -
 Nitrites/pyuria/bacteriuria/etc
 iii. Organisms - isolated

LABORATORY FINDINGS STUDY NO.....

A. BIOCHEMISTRY

PH.....
 Leucocytes.....
 Nitrites.....
 Proteins.....
 Blood.....

B. MICROSCOPY/DEPOSIT

- Pus cells.....
- Yeast cells.....
- RBC's.....
- Bacteria.....
- Others(specify).....

C. CULTURE Growth (G)

- (i) Specify kind of growth.....
- (ii) Strength of growth..... (light, moderate, heavy)

No growth (NG).

D. SENSITIVITY Resistant=R Sensitive=S.

Ampicillin	[]	Nalidixic	[]
Augmentine	[]	Nitrofurantoin	[]
Chloramphenicol	[]	Suprapen	[]
Cotrimoxazole	[]	Rocephin	[]
Cefaclor	[]	Zinnat	[]
Ceftrazidine (fortum)	[]	Gentamicin	[]
Cephalexine	[]	Streptomycin	[]

Paediatrician's sign.....
 Date.....

tel: 726300/726450/726550
fax: 725272
teleggrams: "MEDSUP", Nairobi



KENYATTA NATIONAL HOSPITAL
P.O. Box 20723, Nairobi

Ref. KNH/ERC/01/565.....

Date...7th December, 1998

Dr. Khadija A. Abdalla,
Department of Paediatrics,
Faculty of Medicine,
University of Nairobi.

Dear Dr. Abdalla,

RE: REVISED RESEARCH PROPOSAL "PREVALENCE OF URINARY TRACT INFECTION IN CHILDREN UNDER 5 YEARS OF AGE PRESENTING WITH FEVER AT THE PAEDIATRIC FILTER CLINIC IN KENYATTA NATIONAL HOSPITAL" (P657/2/98)

This is to inform you that the Kenyatta National Hospital Ethical and Research Committee has reviewed and approved the revised version of your above cited research proposal.

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 data base that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Thank you.

Yours faithfully,

PROF. A.N. GUANTAI
SECRETARY, KNH-ERC

c.c. Prof. K.M. Bhatt,
Chairman, KNH-ERC,
Dept. of Medicine, UON.

Deputy Director (CS),
Kenyatta N. Hospital.

Supervisors: Dr. M.J. Luta)
Dr. D.A.M. Ngacha) Dept. of Paediatrics, UON.

Dean, Faculty of Medicine, UON.

Chairman, Department of Paediatrics, UON.