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**A STUDY ON THE PREVALENCE AND CLINICAL FEATURES
OF URINARY TRACT INFECTION IN CHILDREN AGED
BETWEEN 0-5 YEARS ADMITTED TO A-BLOCK PAEDIATRIC WING OF THE
UNIVERSITY TEACHING HOSPITAL, LUSAKA, ZAMBIA.**

BY

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A dissertation submitted to the University of Zambia in partial fulfilment of the

requirements of the degree of Master of Medicine in Paediatrics

THE UNIVERSITY OF ZAMBIA

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LIST OF ABBREVIATIONS

DMSA.....	Dimercaptosuccinic Acid
HPF.....	High Power Field
IVU.....	Intravenous Urogram
MCU.....	Micturating Cysto-urethrogram
MSSU.....	Midstream Specimen of Urine
PEM.....	Protein Energy Malnutrition
RBC.....	Red Blood Cells
SPA.....	Suprapubic Aspirate
US.....	Ultrasound
UTI.....	Urinary tract infection
VUR.....	Vesico Ureteric reflux
WBC.....	White blood cells

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DECLARATION

I hereby declare that this dissertation represents my own work and has not been presented either wholly or in part for a degree at the University of Zambia or any other university.

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APPROVAL

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ABSTRACT

Urinary tract infection (UTI) is a common paediatric problem that has not been seriously addressed in Zambia as evidenced by lack of documentation.

UTI causes significant morbidity and mortality in the affected children and their families. UTI has subtle symptoms and signs that are easily overlooked and only a high index of suspicion will allow for a urine sample to be collected from a patient for analysis.

Simple urine analysis and microscopic examination of fresh urine samples can give preliminary results which would be confirmed by the culture of a single organism with a colony count of more than 10^5 /ml.

Pathogens isolated from urine samples and their antibiotic sensitivity pattern differ from area to area. It is important to monitor the prevailing uropathogens and their antibiotic sensitivity pattern on a regular basis.

Due to constraint on resources, the Paediatric wing in the University Teaching Hospital (UTH), does not allow for urine to be cultured routinely. The aims of this cross section study were:

1. To examine whether UTIs are commonly under diagnosed problem in this environment
2. To determine which scening methods best predicts which urine samples should be sent for culture;
3. To identify the prevailing uropathogens and their antibiotic sensitivity pattern in this environment.

From the study results:

1. The prevalence of UTIs was found to be 33%.
2. The infants had a higher prevalence of UTIs as compared to the older children.
3. The prevalence in the females was higher than in the males.
4. Being underweight (as defined by Wellcome classification) per se was not associated with having a UTI.
5. The clinical feature most associated with UTI was fever and gastro-intestinal upsets.
6. The diagnosis commonly associated with UTI were pyrexia without focus of infection and pneumonia.
7. Presence of WBC and nitrites were good predictors of infection.
8. Commonest uropathogens isolated in urine were *Klebsiella* (35.5%) and *E. coli* (29.4%).
9. Most of the organisms isolated are still sensitive to nalidixic acid and nitrofurantoin.

From the study findings, the young child with a fever or gastro-intestinal upsets, should be screened for a UTI with a simple urinalysis and microscopic examination of the urine sample. Those urine samples that have WBC, nitrites or pus cells of more than 1/HPF should be sent for culture. The recommended drugs for treatment of suspected UTI should be nalidixic acid and nitrofurantoin until the culture and sensitivity results are available, when the antibiotic can be changed appropriately.

There should be regular studies to check on the prevailing pathogens and their antibiotic sensitivity pattern.

Studies to show associated abnormalities of urinary tract in children with UTI should be carried out.

A Paediatric Nephrology clinic should be set up with proper guidelines for further management of patients with proven UTI.

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CHAPTER ONE

1.0 INTRODUCTION

The urinary tract is a common site of bacterial infection in infancy and childhood and this has potentially important implications. In Zambia, there is no documentation on infection of the urinary tract. A study done in a suburb health centre in Durban, showed 17% prevalence of urinary tract infections (UTIs), amongst young children (less than five years) who came for treatment of other ailments ⁽¹⁾.

Fever of unknown origin has been commonly associated with UTIs in some studies ^(2,3) and in the Paediatric wing a number of patients are admitted with pyrexia without a focus of infection.

1.1 CONSEQUENCES OF CHILDHOOD UTI

The two major considerations of UTIs are to identify anatomical lesions and vesico-ureteric reflux (VUR) and to prevent recurrent kidney infections and consequent renal dysfunction ⁽⁴⁾.

UTIs cause significant morbidity and suffering for the children as well as inconvenience and anxiety to families ^(5,6,7). Although the majority of children with UTI respond rapidly to treatment, or even clear their infection spontaneously, UTI may recur in a year or two in about 75% of patients ^(6,7,8,9). Some girls have a series of repeated infection ⁽⁶⁾. The recurrence rate in boys is lower, about 15 to 20%. After one year of age, boys have fewer recurrences and it is unusual that boys have repeated infection ⁽¹⁰⁾.

In 10 to 15 % of affected children the inflammation produces irreversible damage of the renal parenchyma especially in those with recurrent UTIs ^(4,5,6). The damaged areas of renal tissue are replaced by fibrous scars, and this can subsequently lead to hypertension and chronic renal dysfunction ^(7,11,12). The kidneys attain their anatomical maturity by the age of seven years and if lesions can be detected early and infections treated early, then chronic pyelonephritis, scarring and consequently hypertension can be minimised ^(4,5). Most data suggests that scarring does not occur after five years of age.

There are no symptoms or physical signs specifically related to the presence of kidney scarring or vesico-ureteric reflux (VUR). Occasionally, loin pain, persisting after infection has been treated, has been attributed to a scarred kidney in the absence of objective evidence. In some patients, particularly young women, the condition may remain undetected throughout childhood and only become apparent during early adult life because of hypertension which may develop when oral contraceptives are used, or during pregnancy ⁽⁵⁾.

Some factors that are associated with renal scarring are: obstruction, vesico-ureteric reflux with dilated urinary tract, young age at onset of UTI, delayed treatment, recurrent pyelonephritis and bacteria of low virulence ^(7,9,10).

1.2 MANAGEMENT

Management should aim at prompt diagnosis, rapid treatment and detecting any underlying feature that might predispose to further infection or lead to long term renal damage before the age of five.

Treatment of the acute infection should be commenced while investigations are being carried out.

Suitable urine sample should be collected before antibiotics are given to the patient.

Urinalysis is done to determine the urine samples that need to be cultured.

The use of simple tools like urinalysis and microscopic examination can help in streamlining the urine samples that are likely to have significant bacteriuria.

The culture and antibiotic sensitivity results will determine what antibiotic should be used.

Two consecutive urine samples should be cultured to increase the sensitivity of the results.

Some authorities advocate that any child with proven UTI should be investigated further by radiological examination ^(4,5,10). Others believe that investigation of UTI are age related such that a neonate with UTI is investigated differently from an older child.

CHAPTER TWO

2.0 JUSTIFICATION AND RATIONALE

There is no baseline data in Zambia, on this relatively common childhood infection whose complications of hypertension and chronic renal failure, leads to a high morbidity and mortality.

There is need to increase awareness amongst health workers on the diagnosis of UTI in infants and children less than five years who may have subtle symptoms and signs. This is the age group in which incidence of UTI is highest and the sequelae of renal damage is reversible as the kidney is still growing and maturing.

Following first diagnosis of UTI, adequate investigation is important to look for any underlying renal tract abnormalities. Those found with abnormalities will require further management as defined below:

- a. Surgery can be recommended for those with posterior urethral valves, stones or grade 4 VUR, for example.
- b. For those with milder grades of VUR, low dose antibiotic prophylaxis can be recommended.

With some baseline data, a good scheme of management of these children can be established for our environment, not only to improve the quality of life, but to prevent long term complications.

CHAPTER THREE

3.0 LITERATURE REVIEW

UTI is an important cause of morbidity at any age, but its recognition and treatment is particularly important in early childhood ^(4,7,12,13). Despite the advent of numerous effective antibacterial agents, the morbidity and mortality of UTI have remained considerable ⁽⁵⁾.

3.1 PREVALENCE

It is difficult to determine the incidence of UTI as some patients may have episodes of UTI without seeking medical attention. In the developed countries, UTI accounts for 20% of all paediatric consultations and chronic pyelonephritis remains one of the major causes of end stage renal failure in childhood ⁽⁵⁾.

The prevalence of UTI is variable, ranging from 1.6% ⁽¹⁴⁾ to 26.9% ⁽¹⁵⁾ depending on the criteria for diagnosis. Although a lot of work has been done to standardise the method of diagnosing UTI, there is still a variation in the criteria used in some regions ^(16,17,18). An audit, conducted in England, of how General Practitioners (GP) managed suspected UTI showed a marked variation in treatment and investigations ^(16,17). Some GP never collected urine and treated blindly and usually referred only the young infants, especially if they were males, with recurrent UTI for imaging.

The study done in Nigeria showed a prevalence of 4% for children less than five years, who were attending the clinic in the urban area and a prevalence of 24% in rural children ⁽¹⁹⁾. The authors attributed this variation to hygiene of the children. Studies done elsewhere, in the developed countries, did not show any significant association between socio-economic status and prevalence of UTI ⁽²⁰⁾.

A study conducted in Harare, Zimbabwe, showed a prevalence of 26.9%, but it should be noted that this was a laboratory based study and the urine samples were from patients, irrespective of age, with suspected UTI ⁽¹⁵⁾.

Of the seven year school entrants in Gotberg, 7.8% of girls and 1.6% of boys had had symptomatic UTI verified by urine culture ⁽¹⁰⁾.

The prevalence of UTI is influenced by sex and age ^(5,6,7,8,9). In infancy, boys tend to have a higher incidence of UTI than girls ^(5,6,7,8,9). This has been attributed to the male infant being more prone to infection generally because they have more congenital abnormalities than the female infant ⁽⁸⁾. After this age group, UTI tends to be more common in females due to the shortness of the urethra, increased susceptibility to trauma and lack of prostatic secretion ⁽⁸⁾.

At a symposium results of autopsies done in infants by Lincoln and Winberg, revealed a predominance of pyelonephritis in the male infants ⁽²⁰⁾. Clarke et al found a high proportion of abnormal images in infant boys and older girls, especially those with recurrent UTI ⁽²¹⁾.

Serum levels of immunoglobulin A (Ig A) are also important in UTI. James-Ellison et al found that in the majority of children, secretory Ig A and Ig A were undetectable at birth. Secretory Ig A and serum Ig A rose significantly during the first year of life and then levelled off throughout childhood ⁽²²⁾. They also found that infants who were breastfed had higher secretory Ig A and serum Ig A than those who were bottlefed. Secretory Ig A is an important component of mucosal immunity ^(5,22,23).

The uncircumcised male child is at a higher risk of developing UTI than the circumcised child ^(5,6,24).

3.2 AETIOLOGY AND PATHOGENESIS

3.2.1 Urinary pathogens

These are mainly bacterial with *Escherichia coli* (*E. coli*) being found in 80-90% of first time infection in children ^(7,10,17). Other organisms include *Klebsiella aeruginosa*, *Proteus mirabilis* (especially in boys), *Enterococcus faecalis*, *Pseudomonas* species (particularly after surgery), *Staphylococcus aureus* and *Staphylococcus epidermidis*.

Patients with stones, obstruction and neurogenic bladder disturbances, are more likely to be infected with above organisms other than *E. coli* ⁽¹⁰⁾.

Viral infection of the urinary tract is usually confined to the bladder. Acute haemorrhagic cystitis may occur during an acute febrile illness ^(7,9). The diagnosis is not usually made and the condition is thought to heal spontaneously, but may temporarily increase the bladder susceptibility to bacterial infection ^(7,9). There is no routine check for viral UTI in most health facilities.

Table 1: Common pathogens isolated in urine in the UTH laboratory (1994-1996).

	1994	1995	1996 (first quarter)
Total samples	5236	3662	1178
% Positive	13.5	25.9	17.3
Mixed (contaminants)	1247	784	214

ORGANISM	1994	1995	1996
	No (%)	No (%)	No (%)
E. COLI	330 (45.1)	410 (53.8)	103 (54.0)
KLEBSIELLA	180 (24.6)	158 (20.7)	33 (17.3)
CANDIDA	69 (9.4)	46 (6.0)	23 (12.0)
ENTEROBACTER	40 (5.5)	24 (3.1)	4 (2.1)
STAPH. AUREUS	25 (3.4)	20 (2.6)	6 (3.1)
STR. PYOGENES	20 (2.7)	0 (0)	0 (0)
STR. FAECALIS	17 (2.3)	26 (3.4)	3 (1.6)
P. MIRABILIS	17 (2.3)	31 (4.1)	6 (3.1)
PROTEUS SPP.	13 (1.8)	17 (2.2)	9 (4.7)
CITROBACTER	10 (1.4)	16 (2.1)	1 (0.5)
SALMONELLA	10 (1.4)	15 (2.0)	3 (1.6)
TOTAL	732 (100)	763 (100)	191 (100)

SOURCE: UTH LABORATORY

Table 1 shows that the commonest isolated bacteria in urine, in the UTH laboratory, are *E. coli* and *Klebsiella*. In 1997, *E. coli* accounted for more than 50% of uropathogens. The urine samples are from inpatients and outpatients ⁽²⁵⁾.

In a study done in Ibadan, Nigeria, the predominant bacteria isolated in both inpatients and outpatients was *Klebsiella* species, which accounted for 52.8% of the cases. *E. coli* accounted

for only 25% of isolates ⁽²⁶⁾. This was an unusual finding and it would have been enlightening if further investigations had been carried out on the patients with *Klebsiella* infection.

Studies done elsewhere looking at the uropathogens have commonly isolated *E. coli* ^(1,15). Jeena et al carried out a survey at a primary health care centre in a suburb in Durban, South Africa ⁽¹⁾. *E. coli* accounted for 56% of infection, whilst *Klebsiella pneumoniae* accounted for 19% of UTI in children attending the health facility.

The study done in Harare, Zimbabwe, by Obi et al showed a similar pattern with *E. coli* and *Klebsiella* accounting for 40.5% and 22.1% respectively ⁽¹⁵⁾.

Al Mugerin & Quadri study carried out in Saudi Arabia found *E. coli* to be the most common pathogen accounting for 55.1% whilst *Pseudomonas* accounted for 11.9% ⁽²⁷⁾.

The latter two studies were laboratory based and mode of urine collection was not mentioned.

3.2.2 Pathogenesis

Except in the neonatal period, urinary tract infection results from an imbalance in the normal host-parasite relationship. The parasite is usually a normal bowel commensal and it has been shown that the urinary pathogens correspond closely with the current predominant bowel flora ^(7,9). The bacteria ascend via the urethra to the urinary tract. In the neonatal period, bacteria may reach the urinary tract via the blood stream or the urethra.

The urinary tract is mainly kept free from infection by the washout mechanism affected by regular urine formation and regular emptying of the bladder ^(5,7,9). Urine is kept sterile by the urothelial bacteriocidal activity ⁽²⁸⁾. Therefore, factors that promote urine stasis, like mechanical or functional outflow obstruction, vesico-ureteric reflux (where refluxed urine returns and remains in the bladder), or incomplete emptying of the bladder, may predispose

UTI.

Other conditions which increase susceptibility to infection include: immunosuppression; diabetes mellitus; and chronic granulomatous disease, mainly in boys ^(6,7,9).

Immunological response of the body to UTI is complex and is influenced by several factors, including age of the patient, site of infection, previous exposure to the same organisms and the virulence of the invading organism ⁽⁵⁾. Evidence for the protective role of the immunological response is not clear cut in UTI, and permanent renal damage may be caused by the host inflammatory response than the invading organism itself.

Certain host factors, including production of urethral and cervical Immunoglobulin A (IgA), blood group phenotype P1, influence bacterial adherence to the epithelium of the introitus and the urethra ^(6,9). Individuals with group B blood have a significantly increased risk of developing UTI. The absence of anti-B isohaemagglutination renders an individual more susceptible to infection ⁽⁵⁾.

Some bacteria are able to colonise and invade the urinary tract effectively because of their characteristics. There is evidence that some invading bacteria like *E. coli*, produce endotoxins which inhibit ureteric peristalsis, causing dilatation and stasis of urine ^(5,9).

E. coli is suitably adjusted as it has pili to adhere to P antigen and patients with this blood group may have recurrent UTI ^(5,29,30). In addition, *E. coli* also produces haemolysin and cytotoxin which enhances local inflammation and damage by activating cytokins ⁽³⁰⁾.

In a prospective study analysing the intestinal carriage of P fimbriated *E. coli* as a host susceptibility factor in UTI, the researchers found that patients with P1 blood group and the ones prone to recurrent UTI were more likely to have fimbriated *E. coli* as part of their normal stool flora than the P2 blood group or those who had no UTI ⁽²⁹⁾.

3.3 ASSOCIATED ABNORMALITIES

UTI may be due to an underlying urinary tract abnormality ^(6,7,9). VUR is the most common abnormality associated with UTI, especially recurrent UTI.

In the young infant, the UTI episode may present as a septicaemia and this may be the pointer to a urinary tract abnormality ⁽⁴⁾.

An important abnormality to be considered is VUR, especially in children who come in with recurrent UTI ^(6,7,9). In some studies, reflux has been demonstrated in 30-40% in children with proven UTI ⁽³¹⁾. The reflux may dilate the upper urinary tract in 25-50% of these patients ⁽⁶⁾.

In a study done in Sri Lanka 2/3 of boys with UTI were found to have urinary tract abnormalities, whilst 1/3 of the girls with UTI had congenital abnormalities ⁽³²⁾. This paper though did not state if the UTI was a first occurrence nor did it state the age group studied.

Jaya et al detected VUR in 37% of children with proven UTI ⁽³³⁾.

The difference in prevalence of VUR in children with proven UTI may be due to the variation in the criteria used to select patients. Merrick et al followed up patients for 2-16 years to determine the prognostic value of imaging after UTI with regards to VUR. They concluded that VUR is an important risk factor in boys less than one year and not those more than one year, and in girls VUR is a risk factor at any age ⁽³⁴⁾.

Obstructive malformations were found in some 2% of girls and 10% of boys investigated for UTI ⁽⁶⁾. Posterior urethral valves causes obstruction within the collecting system leading to urine stasis and an increased episodes of UTI.

It is also important to note that significant maturation of kidney function and attainment of the adult level of glomerular filtration rate, takes place in the first two years of life ⁽⁴⁾, although the kidney continues to grow anatomically up to the age of seven years ⁽¹⁷⁾. Recent studies have shown that new scars in the kidneys associated with reflux and infection are rare after the age of five, with most occurring in early childhood ⁽³⁵⁾. Renal scarring or reflux nephropathy identified by urography within one to two years after an acute episode of pyelonephritis, develops in 10-15 % of patients, most probably due to repeated infection ⁽³⁶⁾.

Coulthard et al and Vernon et al on conducting follow-up study of patients with dimercaptosuccinic acid (DMSA) scan that were initially normal concluded that the risk of developing new scars was negligible or very little after four years of age ^(37,38). UTI is more prevalent in the malnourished children and maybe part of the septicaemia associated with malnutrition than underlying urinary tract abnormalities ^(1,39)

There was no difference in prevalence of UTI in underweight children (weight between 60-80% of expected for age with no oedema) as compared to those with normal weight in the study done in Durban ⁽¹⁾.

3.4 CLINICAL PRESENTATION

The symptoms and signs of children with UTI are subtle and a high index of suspicion in a child brought by a mother may clinche the diagnosis ^(6,40). Symptoms of children with UTI depends on the level of infection, as well as the age of the patient.

Infection of the urinary tract may present in the following ways:

Asymptomatic UTI where there are no overt symptoms and bacteriuria may be found during a school entry screening programme for UTIs or during follow-up after treatment of an acute symptomatic UTI.

Non specific symptoms like fever, rigors, vomiting and diarrhoea, failure to thrive or poor weight gain, feeding problems, or febrile convulsions.

Some studies have shown that fever is the single most common clinical feature that is associated with bacterial infection of the UTI ^(2,3).

Classical symptoms associated with the inflammation of the urinary tract; dysuria and frequency, abdominal and suprapubic or loin pain, haematuria, enuresis, cloudy or offensive urine ^(6,7,9).

The clinical picture is also influenced by age.

In the **neonatal period**, the possibility of UTI should be considered in any infant with abnormal weight gain secondary to fluid retention, prolonged jaundice, diarrhoea or vomiting, lethargy or fever ^(6,7,9).

During the **first three years of life** diagnosis of UTI should be considered in any sick child presenting with failure to thrive, feeding problems, vomiting or diarrhoea, sleep disturbance ^(5,6,7,9). Dysuria in this age group is usually due to local irritation rather than a UTI.

In the **older child**, the classical symptoms pointing to the urinary tract become more obvious. UTI has been reported in 50% of patients who are still bed wetting by age five years and in 10% of nocturnal enuretics ⁽⁹⁾.

It is important to consider sexual abuse in children with UTI ⁽⁹⁾.

Some patients may have symptoms and signs compatible with a different diagnosis. As in the case of a study done in Durban, South Africa, they found that 34% of patients with UTI had associated acute respiratory tract (ARI) infection and 23.4% had associated acute diarrhoeal disease (ADD) ⁽¹⁾. There were no differences in clinical features between those with ARI and/or ADD with or without bacteriuria.

3.5 DIAGNOSIS

Diagnosis of UTI in children requires a high index of suspicion and confirmation by finding a single organism with a colony count of 10^5 /ml in fresh urine sample obtained by clean catch or midstream specimen of urine (MSSU) ^(20,41). This is based on Kass's work ⁽⁴²⁾ although it may not be rigidly followed as some studies have shown that 30% of boys with colony count of as low as 10^3 /ml had radiological abnormalities ⁽¹²⁾. Any growth from suprapubic aspirate, ureteric aspirate or renal pelvis is considered to be significant ^(6,12). Mixed growth is usually an indication of contamination of urine ⁽⁴³⁾. The count in such cases does not exceed 10^3 /ml and does not as a general rule, reach 10^5 /ml ⁽⁴³⁾.

3.4.1 Urine collection

There are various methods of collecting urine samples for analysis in the laboratory.

3.4.1.i Clean catch urine sample

Infants are particularly prone to pass urine when they are undressed and their diapers are removed. It is a good practice to have a sterile container handy so as to catch the urine being passed. Quality of the urine samples obtained by this method is high, with a relatively low contamination rate, approaching that obtained from a midstream urine sample. Contamination in the uncircumcised infants remains a problem.

3.4.1.ii Midstream urine sample

This method is used in patients who are toilet trained.

The technique enables the first urine which may have "loose" bacteria from the urethra and the peri-urethral region to be omitted. The urethral orifice is uncovered and the patient is asked to pass urine. The first urine is omitted and the mid urine sample is collected in a sterile container.

3.4.1.iii Bag urine sample

After cleansing the perineum of the infant or toddler, a sterile plastic bag is placed around the urethral orifice and remains attached to the child by an adhesive lip. To decrease contamination, the diaper is removed and the child is kept upright. The bag is removed as soon as urine is passed. The urine is removed from a hole made in the bottom of the bag.

3.4.1.iv Suprapubic aspirate urine sample

This is the best technique to obtain an uncontaminated urine specimen. It is a simple procedure in infants since the bladder is an intra-abdominal organ. If ultrasound is used, success rate is 100%. The skin is cleaned with alcohol and a 20ml syringe and sizes 19, 20, 21 gauge needle are used for the procedure. The bladder is punctured 0.5cm above the symphysis pubis with the needle perpendicular to the skin and aspirating as the needle advances until get some urine when aspiration should stop.

3.4.1.v Bladder catheter sample

This is another method of obtaining urine with minimal contamination.

Other methods of collecting urine which are not normally used are from the ureters or renal pelvis.

3.4.2 Multistix examination

Examination of urine using a multistix is useful in detecting proteinuria, haematuria, ph, leucocytes and nitrites which can be associated with UTI ⁽⁷⁾. It is a useful screening method.

Landau et al looked at the association between urinalysis findings and acute pyelonephritis as detected by DMSA scan ⁽³⁾. They concluded that urinalysis done on a freshly voided urine sample may be a sufficient method for the exclusion of acute glomerulonephritis in infants assessed for fever of no obvious origin. The parameters assessed in the urinalysis were presence of leucocytes and nitrite. SPA and catheter urine samples were used. Using a combination of dipstick analysis of leukocyte esterase and nitrite, and microscopy for bacteria

and leukocytes these authors obtained a sensitivity and a specificity of 100% when compared with a positive urine culture for UTI. However, this was a retrospective study of case files ⁽³⁾.

Proteinuria is not a very specific parameter for detection of UTI, as it can occur in any febrile illness, inflammatory disease of other organs, and as a contaminate from the vagina ⁽⁶⁾.

If proteinuria is moderate or severe with nitrites, the sensitivity in detecting UTI is increased ^(5,6).

The multistix strip reacts to granulocyte esterase activity in the urine ⁽⁵⁾. A color change corresponding to a "2+" reaction means roughly 75 and "3+", 500 leucocytes per microlitre ⁽⁶⁾.

Testing for nitrite on a multistix is important, as most uropathogens are able to reduce nitrate to nitrite ^(6,9,16). This reduction is time dependent and a positive test requires a longer bladder time, preferably more than four hours, or significant residual urine ⁽⁶⁾. Sensitivity in infants and small children who void frequently, is reduced to about 40-50% ⁽⁶⁾.

The specificity of a positive test, in girls, is over 99% ^(5,6). It is less reliable in boys since nitrite may accumulate under the prepuce of the normal male, therefore giving a false positive result ^(5,6).

For urine that has not been refrigerated, the nitrite test may be misleading as the growing bacteria produces nitrites ⁽⁶⁾.

Macroscopic haematuria may occur in 20-25% of patients with acute cystitis ⁽⁵⁾.

Optimal growth of bacteria like *E. coli*, occurs between pH 6 - 7. Bacteria growth is inhibited if pH is less than 5 or more than 8. Dilute urine (osmolality less than 250 mosm/kg) lengthens the mean generation time of bacteria. Maximal growth occurs when osmolality is 300 - 1200 mosm/kg.

Glucose in urine does not influence bacterial growth, but enables a higher maximum bacterial count to be achieved.

Iron in urine encourages bacterial multiplication ⁽⁵⁾.

3.4.3 Dipstick examination

Dipstick or dipslide examination of the urine is better than the multistix strip examination, although it does not confirm the diagnosis. A culture of the urine should be done to confirm the diagnosis ⁽⁴⁴⁾. It has proved reliable and practical in paediatric practice ⁽⁵⁾.

The dipslide consists of a plastic slide coated with MacConkey agar on one side and nutrient agar or cysteine lactulose depleted on the other. The slide is attached to the lid of a sterile plastic container. When required for use, the seal is broken and the dipslide removed by unscrewing the lid. The slide may be wetted in a urinary stream or alternatively, a midstream specimen can be collected in a sterile container. The dipslide is dipped in the urine and then replaced in its own container. The slide can then be transported to the laboratory at leisure. If infection is present, the organisms can be subcultured and identified and their sensitivity assessed.

There are two major pitfalls with dipstick examination. There may be confluent growth of colonies of different type although this may be due to contamination. A culture would be needed to differentiate if it is overgrowth or contaminant.

The other pitfall is that some uropathogens do not grow on MacConkey, which is the media used on the dipslide ⁽⁶⁾. Such bacteria will need to be grown on blood agar or other rich culture media.

3.4.4 Microscopy

Urine microscopy using a Fuchs-Rosenthal counting chamber is quick and reliable. The number of red blood cells (rbc) or bacteria per cubic millimeter of urine can be calculated.

Alternatively, a drop of urine can be examined on a microscopic slide covered by a thin glass cover slip. The volume of urine observed in a HPF under these conditions is of the order 1/30000 ml ⁽⁵⁾. Urine microscopy yields immediate results.

A bacteria count in urine of 10^5 /ml will give approximately 3 bacteria per HPF in uncentrifuged urine ⁽⁵⁾. Bacterial count of more than 10^6 /ml will give rise to more than 30 bacteria per HPF and these are easily seen. The number of bacteria seen in the centrifuged deposit depends on the volume of urine centrifuged and the centrifuge speed, since bacteria are not precipitated at low speeds. However, sheets of bacteria will be seen in almost every field when the bacteria count is equal to or more than 10^5 /ml.

Microscopy is useful in detecting pyuria and can sometimes detect motile bacteria on fresh urine.

Pyuria is present in most cases of UTI and a sample without pyuria as an indication of inflammation within the urinary tract speaks against symptomatic UTI ⁽⁹⁾. Pyuria is absent in more than 50% of covert bacteriuria. Pyuria is measured with highest precision by microscopy of unspun urine using a counting chamber; more than five leucocytes per HPF is considered significant.

Red blood cells and casts can be detected on microscopy. In addition, granulocyte casts may be detected.

3.4.5 Culture

Quantitative and semiquantitative methods for the estimation of the bacterial count depend on the assumption that each colony observed on culture medium is derived from a single organism in the inoculum ⁽⁵⁾. Most routine clinical laboratories use semiquantitative methods which include the standard loop method, the filter paper strip method, roller tube culture, and the pipette method.

Interpretation of culture results is dependent on the mode of urine collection.

Samples collected using a bag or by midstream specimen of urine, bacteriuria is considered to be significant if the colony count is more than 10^5 /ml.

Bacteriuria is considered significant for urine samples collected by catheterisation of patient if the colony count is more than 10^3 /ml and any growth from a suprapubic aspirate is considered significant.

It is better to report the actual counts, without interpretation as a low count in a patient who presents with symptoms of UTI, may be significant ^(5,14).

The probability of true bacteriuria in a single culture is not any higher than 70-80% ⁽⁵⁾. It is advisable to repeat the urine culture if it is positive ^(5,6,20).

Media normally used in the UTH laboratory for urine culture are MacConkey and blood agar ⁽²⁵⁾. The urine is incubated for 24 hours before being analysed and bacteriuria is reported as significant if colony count is more than 10^5 / ml of urine. If there is growth of more than one bacteria, it is considered to be contaminated urine sample and a repeat culture on a fresh urine sample is requested for ⁽²⁵⁾.

3.6 ANTIBIOTIC SENSITIVITY PATTERN

Antibiotics used are dependent on the organisms and the changing sensitivity pattern for a particular area ^(4,6,7,9). In the developing countries, organisms are resistant to commonly used antibiotics such as co-trimoxazole and ampicillin. In UTH, like hospitals in other developing countries there is a high rate of resistance to cotrimoxazole and ampicillin ⁽²⁵⁾.

In UTH, the uropathogens antibiotic sensitivity pattern is normally tested with nitrofurantoin and nalidixic acid. This is based on the sensitivity pattern of most common organisms to drugs over the last couple of years. Resistance to nalidixic acid and nitrofurantoin is still very low.

In the Harare study, the most useful drug was ciprofloxacin with the commonest isolate, *E. coli*, being 100% sensitive. Nitrofurantoin and gentamicin were also recommended.

In the Durban study, there was resistance to most of the common antibiotics:

ampicillin (93% resistance), sulfamethoxazole (86% resistance), trimethoprim (79% resistance) and co-trimoxazole (72% resistance). There was 100% sensitivity to gentamicin and nalidixic acid and 96% sensitivity to augmentin and cephalexin.

In Saudi Arabia drugs of choice in the treatment of UTI were nitrofurantoin and cephadrine with gentamicin being added in the very ill children ⁽²⁷⁾.

It is always important to note any history of anti-bacterial treatment as this may affect the bowel flora resistance pattern such that tonsillitis treated with amoxycillin may be followed by UTI with an amoxycillin resistant *Klebsiella* species.

In other areas like Europe co-trimoxazole and trimethoprim are still the drugs of choice in the treatment of UTI ⁽⁶⁾.

3.7 TREATMENT

Single dose or 24 hours treatment maybe used in the older child with an episode of afebrile UTI or in a child whose previous investigation shows no VUR, obstruction or renal parenchyma involvement. This is not recommended in an infant or younger child who presents with a first infection ⁽⁶⁾. Therapy is continued for 5-7 days in uncomplicated cases ^(6,7,41,45).

There is no evidence that treatment of more than 14 days is more effective than the short therapy ⁽⁴⁶⁾.

The urine culture should be negative 36-48 hours in a successfully treated patient

⁽⁷⁾. If culture continues to be positive, an obstructive lesion, VUR or an abscess should be suspected. Recurrent infections may occur in 20-25% of patients, usually within the first few months after the first episode ⁽⁷⁾. This is true especially in those with congenital anomalies of the urinary tract. Follow up urine cultures is therefore a must until the underlying anomaly has been corrected or after seven years when the risk of renal scarring is minimal.

Patients with evidence of recurrent UTI are more likely to have an underlying problem, and this must be looked for aggressively. Reflux is the commonest cause of recurrent UTI. Those found to have significant reflux need to be on prophlactic antibiotics ⁽⁷⁾. No serious side effects have been seen with low dose antibiotics ^(3,6).

3.8 FURTHER INVESTIGATION OF PROVEN UTI

Mode of investigating a proven UTI is not universally agreed ^(16,17). Some authorities advocate that every child with documented UTI should have an ultrasound examination of the urinary tract about six weeks after treatment unless the infant fails to respond to antibiotic therapy when radiological examination should be done earlier ^(41,45). The pitfall with the latter is that some of the parenchymal changes are temporal and the parenchyma reverts to normal after the acute infection.

Craig et al argues that micturating cystourethrogram (MCU) need not be deferred for four to six weeks after a UTI ⁽⁴⁷⁾. They carried out a cross-sectional analytical study of preschool children with first symptomatic UTI and found that beyond one week after diagnosis of UTI, the proportion and severity of VUR detected was not associated with the timing of the MCU. Others believe that investigation of a proven UTI are age dependent such that a neonate with UTI is investigated differently from an older child (4,7,9,10).

3.8.1 Infants

Ultrasound examination (US) is advocated and further investigations depends on the US findings. If US is normal, a micturating cysto-urethrogram should be done to detect minor degrees of reflux especially in male infants ^(4,3,12). If unilateral renal or ureteric dilatation is detected, an intravenous urogram (IVU) should be performed. This can detect an obstructed system. On the other hand, if the dilatation is bilateral, in boys, posterior urethral valves should be suspected and confirmed with a MCU.

3.8.2 Young children (less than five years)

A plain abdominal X-ray is advocated after the neonatal period to detect stones. This can be augmented with an US or where available dimercaptosuccinic acid (DMSA) scan. US of the renal tract, can detect a dilated system secondary to vesicoureteric reflux (VUR). VUR is the commonest cause of recurrent UTI with subsequent scarring. Grading of reflux is important as the management depends on the degree of reflux. Using the British classification, grades one and two have minimum reflux with no dilated collecting system such that the risk of scarring is minimal ^(6,7,9). Grade four has the highest risk of reflux and dilatation of the whole collecting system. MCU is the best method of detecting VUR.

The main purpose of an abdominal ultrasound examination is to exclude an obstructed system with dilated collecting duct. Renal imaging can also reveal an inflammatory process in the kidney. Ultrasound is the initial investigation but should be followed by a MCU and/or DMSA as some studies have suggested that it is unreliable in detecting VUR and renal scarring ⁽⁴⁸⁾. MCU and DMSA scan can be used if UTI persists inspite of treatment ⁽⁴⁵⁾. MCU should be done in all neonates to exclude reflux and DMSA, to determine kidney function and extent of scarring. DMSA changes are abnormal in most patients with UTI and a repeat DMSA scan after five months will determine whether the changes are permanent ⁽⁴⁹⁾.

Most studies have shown that currently, DMSA is the most sensitive method of detecting renal scarring and of highlighting the kidney at risk of developing scarring ^(4,6,36). An IVU and DMSA are complimentary investigation and the sensitivity of detecting renal scarring and abnormalities is increased if these two investigative procedures are used ^(50,51).

Merrick et al looked at the prognostic value of imaging after UTI ⁽⁵²⁾. They found that no single investigation at presentation, was able to predict subsequent deterioration, but by

employing combination of imaging investigations, it was possible to detect those patients with high probability of progressive damage.

An IVU is probably still the best single investigation for detecting renal scarring and renal function in our environment where DMSA scanning is not available.

3.9 MONITORING

After a few days it is important to counsel the parents/guardians on the mechanism of UTI and preventive measures with emphasis on regular voiding and bowel habits ^(7,10). Wan et al looked at the toilet habits of children evaluated for UTI and found that those with recurrent UTI had more episodes of constipation than those without UTI. They also passed urine less frequently than their counterparts ⁽⁵³⁾. Oral and/or written instructions should be given.

Check up thereafter depends on the local traditions and resources.

Prophylactic antibiotics should be considered during the period of investigation of a UTI.

Some paediatricians feel that one more check-up with an uneventful cystitis is sufficient, otherwise a six week check up with a repeat urine culture and imaging is recommended ⁽¹⁰⁾.

If all are normal then patient can be followed-up with repeat cultures for a year. If there are recurrent infections or urinary tract abnormalities, the follow-up period is longer and the child may need low dose antibiotic prophylaxis.

Other paediatricians recommend follow-up of at least one year in the very young and ideally until the child is free from infection for two years.

Hypertension and proteinuria are the main markers for serious progressive renal disease. If there is bilateral renal scarring, annual screening for hypertension, proteinuria and renal function are indicated for life.

It is important to emphasize on the need for the child to be brought back for review if symptoms of UTI recur.

Where available dipslide monitoring at home is useful and the guardians can be taught how to do it. This is not available in most developing countries including Zambia.

CHAPTER FOUR

4.0 OBJECTIVES

4.1. GENERAL OBJECTIVE:

To study the prevalence and describe associated clinical features of UTI in children aged 0-5 years admitted to A-Block, the Paediatric wing of UTH.

4.2. SPECIFIC OBJECTIVES:

- 4.2.1. To determine the prevalence of UTI.
- 4.2.2. To determine the commonest clinical features in the 0-5 years age group who are admitted to the Paediatric Wing of UTH.
- 4.2.3. To determine the sensitivity and specificity of multistix as a screening test in the detection of UTI.
- 4.2.4. To determine the sensitivity and specificity of microscopy examination in the detection of UTI.
- 4.2.5. To identify the common organisms isolated in these children.
- 4.2.6. To study the sensitivity pattern of the isolated organism in the urine.

CHAPTER FIVE

5.0 MATERIAL AND METHODS

5.1 STUDY DESIGN

The study was primarily a descriptive cross sectional study with consecutive patient enrolment.

The study was conducted using a questionnaire (Appendix 1) to obtain variables of interest.

5.2 STUDY SITE

The study was conducted in A-block, Paediatric wing of the UTH, Lusaka. The UTH is a tertiary referral hospital although it acts as a secondary as well as a primary health centre.

Most of the patients who come to the hospital are referred from the Lusaka urban district clinics with a few coming from the district hospitals.

Patients are screened in the outpatient department (A01) and those needing admission are sent to the admission ward. In the admission ward, appropriate investigations if available are carried out before the patient is commenced on treatment and admitted into the main wards.

The investigative procedures depend on the availability of facilities and some investigations are not carried out.

5.3 STUDY POPULATION

Children aged between 0-5 years admitted to A-block, Paediatric wing were selected.

5.4 SAMPLING AND SAMPLE SIZE

5.4.1 Criteria for admission into study

Inclusion criteria:

All children aged between 0-5 years admitted to A-block were eligible.

Exclusion Criteria:

Children > 5 years.

Children who had had antibiotics seven days prior to admission.

Children whose condition was very critical (i.e almost dying).

5.4.2 Sampling

This was done by systematic randomisation. Urine samples were taken every other day.

Starting with the first child admitted every fourth child admitted who met the above criteria was included in the study. The next child was chosen if the fourth child did not meet the above criteria.

5.4.3 Sampling bias: Parent bias on collection of urine can not be excluded as most of the urine samples were collected by the guardians. It is a lot easier to collect urine from a boy especially a clean catch. Girls with urine bags are more likely to get contaminants from the peri-anal region.

The culturing of urine in the laboratory did not follow a standard pattern. Therefore some of the urine not cultured may have had significant bacteriuria.

The reliability and quality of the laboratory methods used in this study could not be assessed in this study due to erratic supplies and other factors.

5.4.4 Sample size

This was calculated with an assumption that the prevalence of UTI was between 1-20% using Epi-info statistical calculation of sample size for population studies.

This was based on literature review from the developed countries and within the region.

The sample size was calculated to be 150 patients.

5.5 STUDY PROCEDURE

A verbal consent was obtained for collection of urine from the guardian after explanation of the procedure and the examination of the urine (Appendix 2).

The urine samples were collected Monday through to Friday because of the laboratory logistics. Guardians were asked to collect early morning samples.

5.5.1 Urine collection

5.5.1.i Suprapubic urine sample

This was collected by suprapubic aspirate of urine mostly from neonates.

Dull percussion note of the lower abdomen identified the bladder. The pubis symphysis upper border was identified and the area was then swabbed with normal saline and a spirited swab.

A finger's breath above the pubis symphysis, a G21 needle attached to a 5ml syringe was introduced and directed towards the pelvic region. As the needle was gently pushed in, the plunger on the syringe was withdrawn such that as soon as the needle was introduced into the bladder, urine sample was obtained. This procedure was done with the help of an assistant who held down the infant.

5.5.1.ii Clean catch urine sample

For this procedure the caretaker was given a sterile plain bottle to try and catch the urine during nappy change.

5.5.1.iii Urine bag sample

After cleaning the genital area with water, the researcher applied a sterile urine bag around the urethral orifice and it remained attached to the child by an adhesive lip. The child's diaper was removed and the bag remained in situ until the patient passed urine into the bag. The urine was then placed into a sterile container. Urine was collected by this method in the young children who were not toilet trained.

5.5.1.iv Midstream specimen of urine sample

For the midstream specimen of urine, the caretaker was taught how to clean the genital area with clean water before collecting a mid stream urine sample into a sterile container.

Each urine collected was separated into two. One sample was sent to the laboratory immediately while the other sample was analysed by the researcher using multistix. Variables of interest (namely: ph, specific gravity, leucocytes, nitrites, proteinuria and red blood cells) were noted.

After urine was collected, a questionnaire was filled out by the researcher.

5.5.2 Laboratory examination of the urine

5.5.2.i Microscopic examination

Urine was examined under the microscope. A drop of uncentrifuged urine was examined on a microscope slide covered by a thin glass cover slip. White cells, red cells, epithelial cells, bacteria and casts were looked for in a high power field at a magnification of x400.

5.5.2.ii Culture and sensitivity

Urine in the laboratory was cultured on MacConkey agar and blood agar. Urine was incubated for twenty-four hours before being read.

Urine sample found to have motile bacteria or if culture yields

a colony count of $\geq 10^5/\text{ml}$, was taken to be significant bacteriuria. Any colony count from suprapubic aspirate was considered significant.

5.6 OUTCOME MEASURES

5.6.1 The prevalence of UTI during the study period was determined.

5.6.2 Associations between clinical features and a positive urine culture were determined.

5.6.3 The sensitivity and specificity of multistix variables in predicting a positive urine culture.

5.6.4 The sensitivity and specificity of microscopic variables in predicting a positive urine culture.

5.6.5 Common uropathogens isolated and their antibiotic sensitivity pattern were analysed.

5.7 DATA MANAGEMENT

The questionnaire was stored and analysed using Epi-info statistical software.

The prevalence of UTI during the study period was determined.

Odds ratio with 95% confidence intervals (95% CI) and chi-squared were used to determine the associations.

5.8 ETHICAL CONSIDERATIONS

The research proposal was presented to and approved by the University of Zambia ethical committee.

CHAPTER SIX

6.0 RESULTS

Data was collected over a four month period.

A total of 185 bottles of sterile urine containers were distributed. 160 questionnaires were filled out. Only 102 (63.8%) of these questionnaires were available for analysis. 15 containers were not traced, 7 samples were not recorded as having arrived in the laboratory, 21 had missing culture reports (although the microscopy had been done), 25 had mixed growth which were taken to be contaminants, 3 samples were said to have disintegrated cells and were not examined and there was 1 container said to be unsterile.

From the questionnaires analysed the following results were obtained:

6.1 DEMOGRAPHIC DATA

6.1.1 Sex distribution

Overall there were 55 male and 47 female patients giving a sex ratio of M:F 1.2:1.

Of the 55 males and 47 females there were 16 males (29%) and 18 females (38.8%) who had significant bacteriuria fulfilling the diagnosis of UTI.

6.1.2 Age distribution

The youngest patient was four days old and the oldest was sixty months. There were four neonates.

The mean age for the study group was 32.1 months with the median being 31 months.

Figure 1: Age distribution of the study population

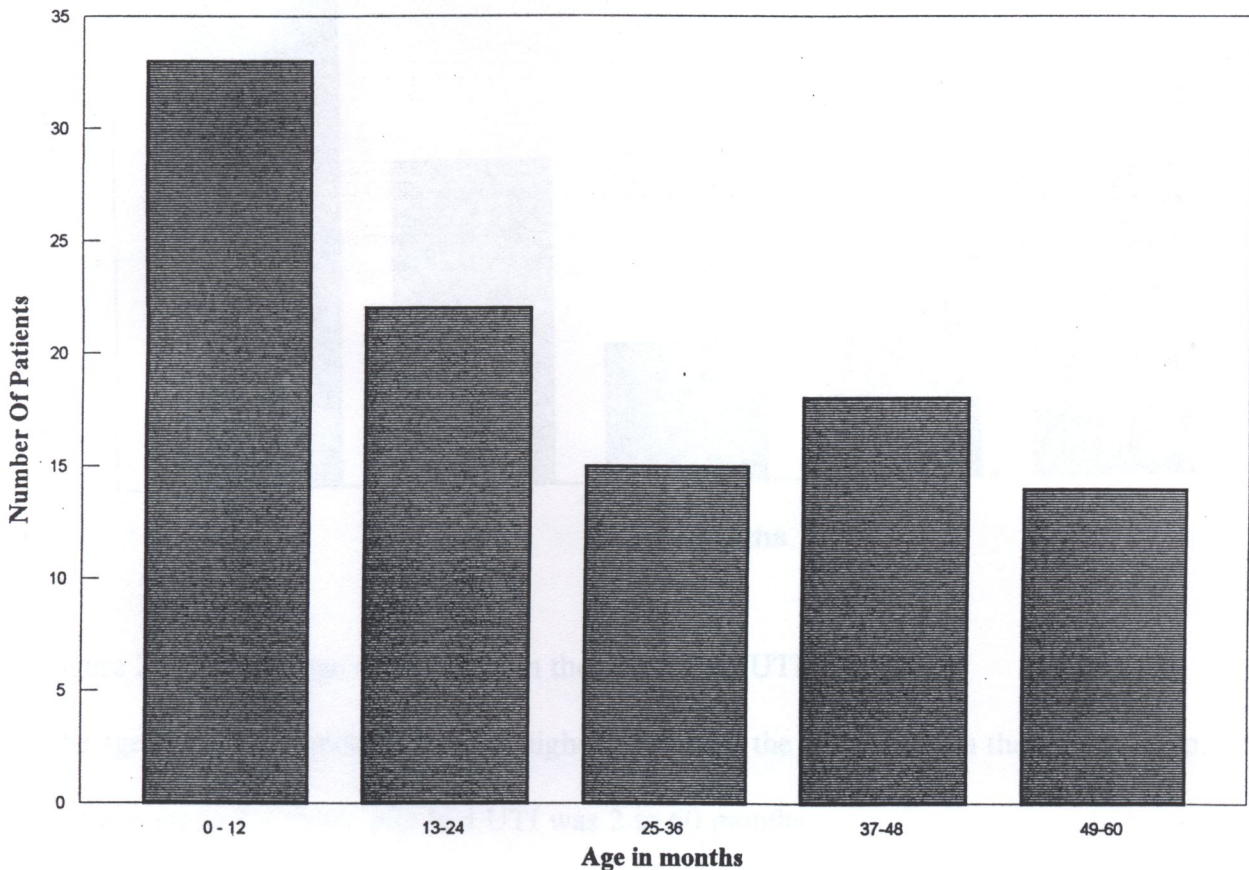


Figure 1 shows the age distribution of the study population.

There was a high proportion of infants admitted to the study which was a reflection of overall admissions during the study period.

Figure 2: Age distribution of study subjects with UTI

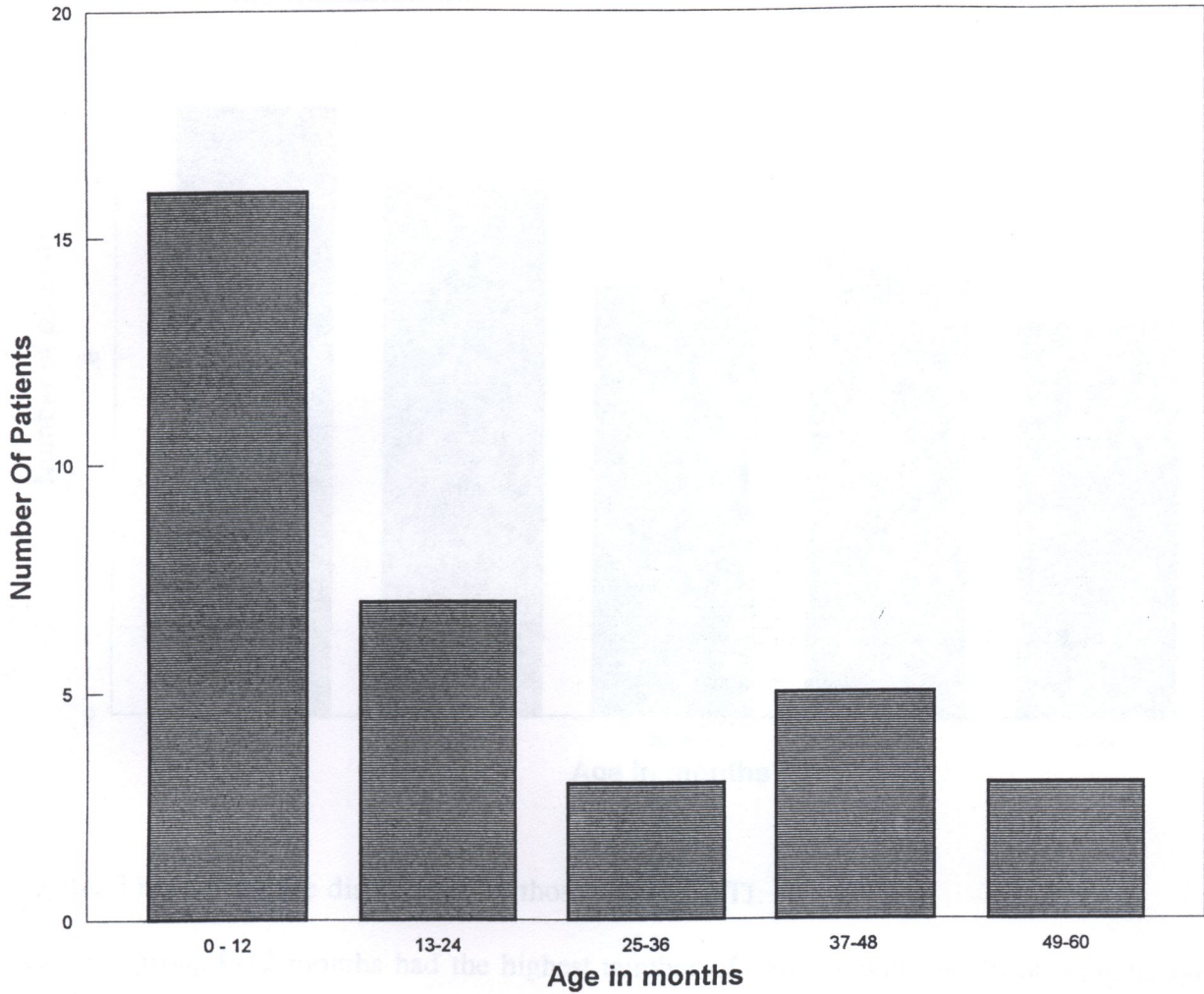


Figure 2 shows the age distribution in those who had UTI.

The age group 0-12 months had the highest UTI with the least being in the oldest group.

The age range for those who had UTI was 2 to 60 months.

The mean and the median age for those with UTI was 27.8 and 25 months respectively.

Figure 3: Age distribution in study subjects without UTI

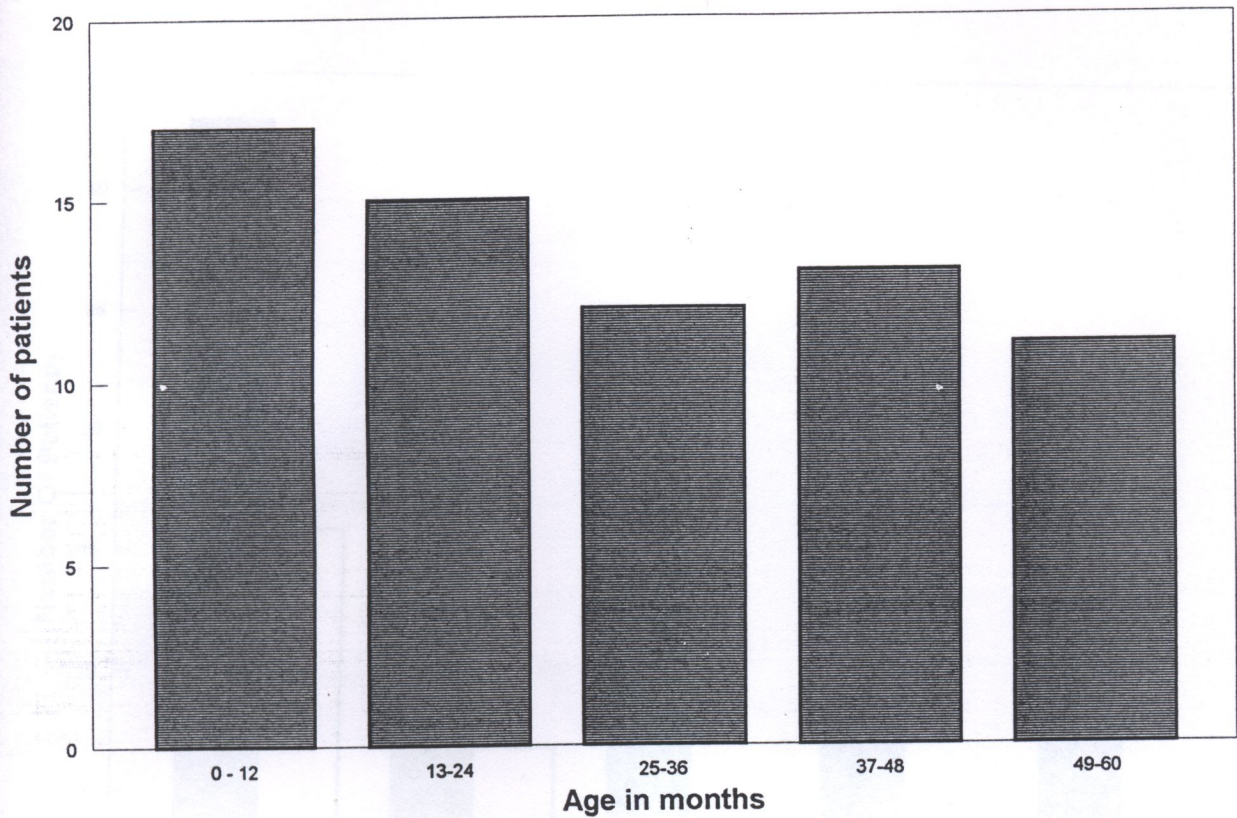


Figure 3 shows the age distribution in those without UTI.

The age group 0-12 months had the highest number of patients with the 49-60 months age group having the least number.

The age ranged from 4 days to 60 months.

The mean and median age was 34.3 and 36 months respectively.

Figure 4: Proportion of patients who had a UTI in each age group

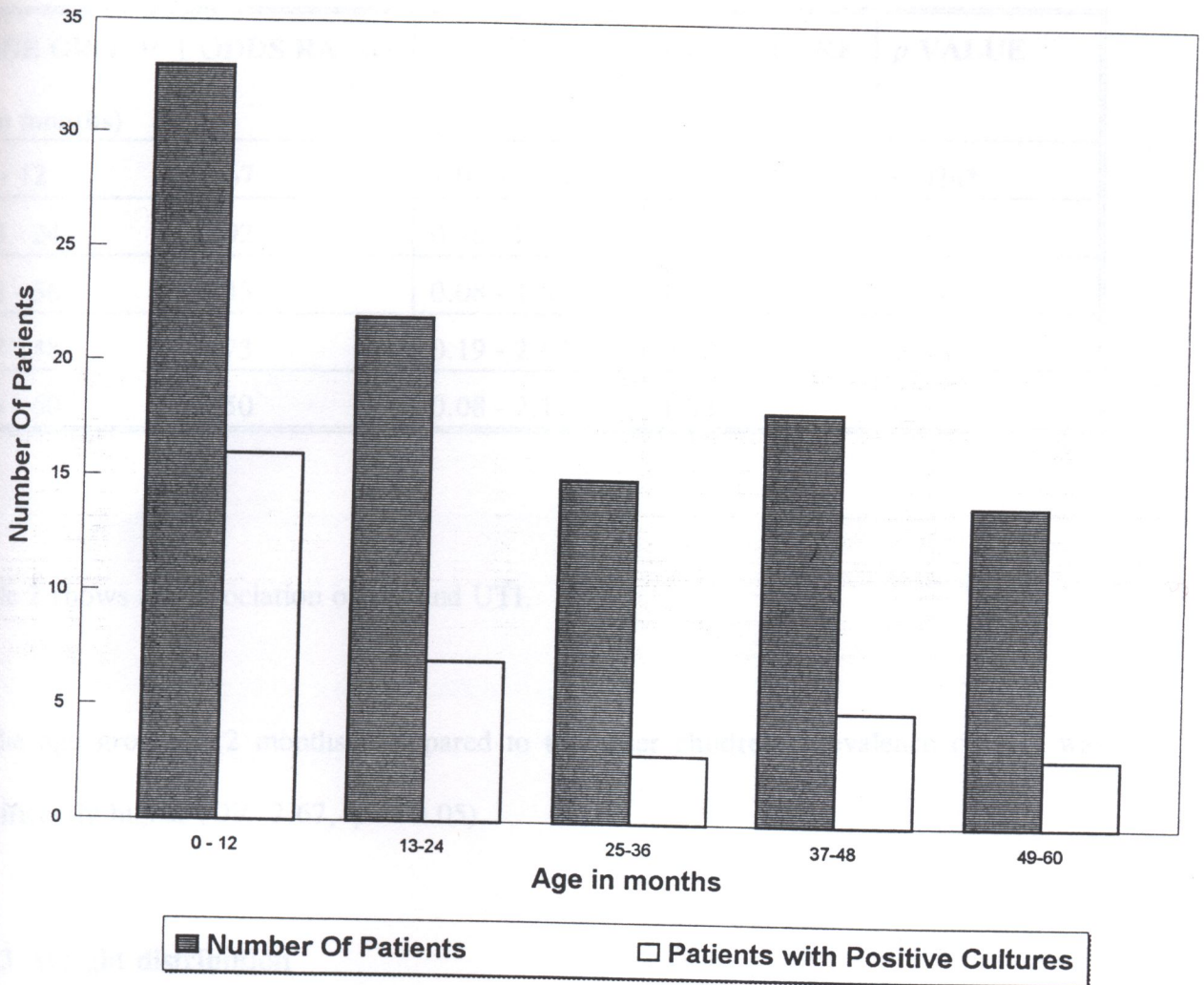


Figure 4 shows the proportion of patients who had UTI in each age group.

The infants had a higher proportion of UTI when compared with the older children. The age group 48-60 months had the lowest proportion of patients with UTI.

Of the 8 male infants recruited, 4 (50%) had UTI, whereas 5 (55%) of the 9 female infants had UTI. There was no significant association between this age group and sex (OR 0.8, p 0.6).

Table 2: Association between age and UTI

AGE GROUP (in months)	ODDS RATIO	95% CI	CHI SQUARE	p VALUE
0 - 12	2.67	1.02 - 6.93	5.04	0.024*
13 - 24	0.92	0.28 - 2.75		0.8
25 - 36	0.45	0.08 - 1.87	1.41	0.24
37 - 48	0.73	0.19 - 2.47	0.30	0.58
49 - 60	0.50	0.08 - 2.11	1.02	0.30

Table 2 shows the association of age and UTI.

In the age group 0-12 months, compared to the older children, prevalence of UTI was significantly higher (OR 2.67, $p < 0.05$).

6.1.3 Weight distribution

Being underweight for age using the Wellcome classification, did not show any significant association with a positive urine culture (OR 0.5, p value 0.13).

6.1.4 Mode of urine collection of samples analysed

Table 3: Mode of urine collection of samples analysed

n = 102

METHOD	NUMBER OF PATIENTS	POSITIVE CULTURE	PROPORTION (%)
SPA	11	3	27.3
CLEAN CATCH	14	7	50
URINE BAG	17	9	52.7
MSSU	60	15	25

Table 3 shows the method of urine collection of the samples analysed. The majority of patients gave midstream urine specimen.

About half of the urines collected by clean catch and urine bags were positive, 50% and 52.7% respectively.

6.2 PREVALENCE

Out of 102 urine samples, there were 34 positive cultures giving a prevalence of 33%.

6.3 CLINICAL FEATURES

Table 4: Association between clinical features and UTI

n = 102

CLINICAL FEATURE	ODDS RATIO	95% CI	CHI SQUARE	<i>p</i> VALUE
FEVER	1.55	0.59 - 4.25	0.95	0.3
DIARRHOEA	1.32	0.31 - 5.05	0.2	0.65
VOMITING	0.42	0.04 - 2.21	1.23	0.23
REFUSING FEEDS	2.2	0.74 - 7.43	2.36	0.12
DYSURIA	7.22	1.17 - 75.84	6.94	0.01*

Table 4 shows the associations of the various clinical features evaluated with UTI.

The commonest features associated with UTI were dysuria, refusing to feed, fever and diarrhoea. Dysuria was the strongest predictor of UTI (OR 7.22, *p* < 0.05)

6.4 ADMISSION CLINICAL DIAGNOSIS

Figure 5: Distribution of clinical admission diagnosis in the study subjects

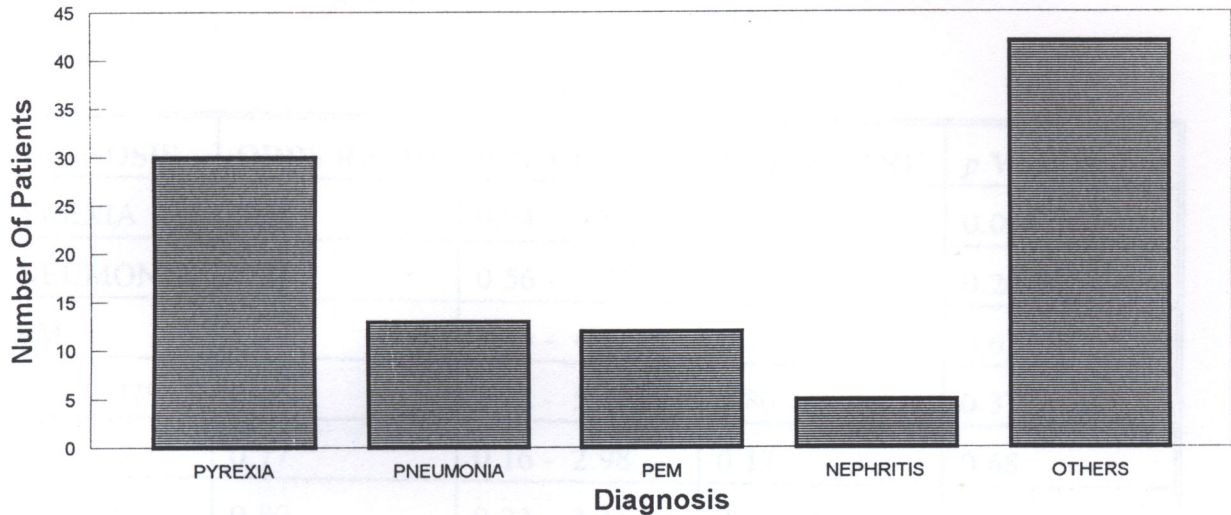


Figure 5 shows the common clinical diagnosis made amongst the study subjects.

The most common clinical diagnosis amongst the patients recruited to the study was pyrexia, pneumonia and PEM.

Figure 6: Proportion of patients with UTI in the common clinical diagnosis

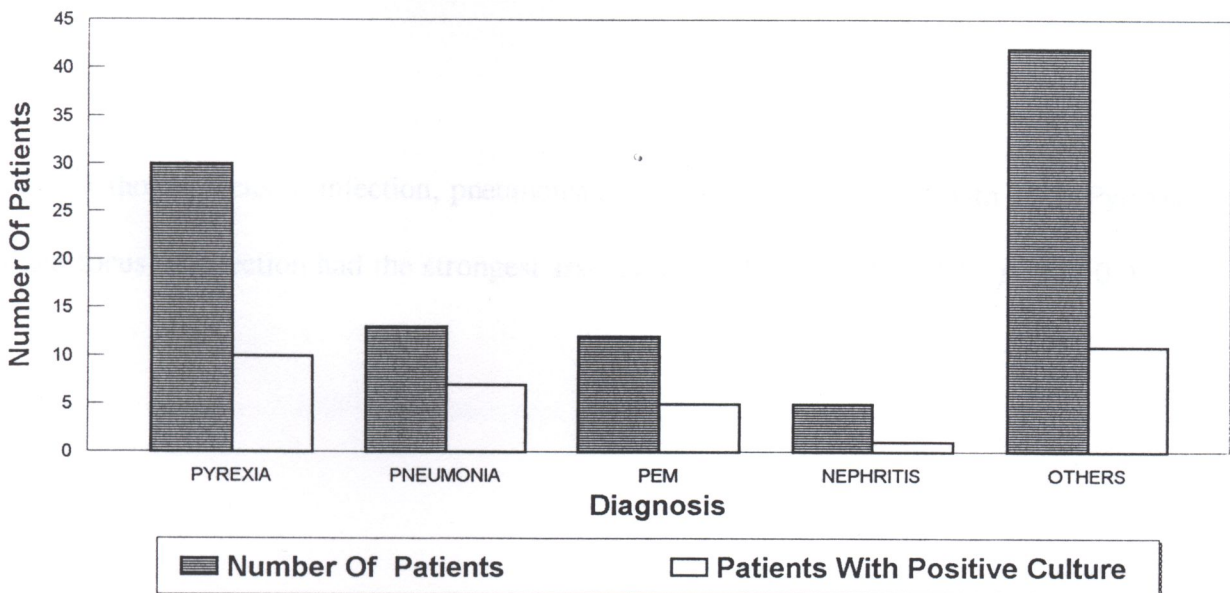


Figure 6 shows the proportion of patients with UTI in the common clinical diagnosis.

Study subjects who had clinical diagnosis of pyrexia ? cause, had the highest proportion of positive cultures

Table 5: Association between the admission diagnosis and UTI*n* = 102

DIAGNOSIS	ODDS RATIO	95% CI	CHI SQUARE	<i>p</i> VALUE
PYREXIA	4.64	0.94 - 30	4.64	0.02*
PNEUMONIA	1.94	0.56 - 6.72	1.41	0.20
PEM	1.29	0.33 - 4.9	0.18	0.67
NEPHRITIS	0.48	0.02 - 5.19	0.80	0.37
RTI	0.77	0.16 - 2.98	0.17	0.68
MALARIA	0.80	0.22 - 3.41	0.14	0.71
OTHERS	-	-	-	-

Table 5 shows the associations between the various clinical diagnosis of the study subject and UTI.

Pyrexia without a focus of infection, pneumonia and PEM were associated with UTI. Pyrexia without focus of infection had the strongest association with UTI (OR 4.64, *p* < 0.05).

6.5 URINALYSIS

Table 6: Sensitivity and specificity of multistix examination in detecting UTI

n = 92

	SENSITIVITY (%)	SPECIFICITY (%)
PROTEIN	86*	29.5
RBC	31	70*
WBC	17	95*
NITRITE	3.4	98.4*
pH 5	10.3	13
pH 6	44.5	37.7
pH 6.5	20.6	8.2
pH 7	20.6	36.1
pH 7.5	3.4	4.9
SG 1.010	17	26
SG 1.020	20.6	21
SG 1.025	17	34
SG 1.035	44.8	18

Table 6 shows the sensitivity and specificity of multistix variables evaluated.

Proteinuria had the highest sensitivity followed by SG 1.035 and pH 6, whereas nitrites had the highest specificity followed by leucocytes and haematuria.

6.6 MICROSCOPY

Table 7: Sensitivity and specificity of microscopic examination in detecting UTI

$n = 92$

	SENSITIVITY (%)	SPECIFICITY (%)
PUS CELLS	100	0
EPITH. CELLS	100	4.8
RBC	20.7	85.7
WBC	6.9	100
CASTS	3.4	96.8
PUS CELLS > 1/HPF	59	63

Table 7 shows the sensitivity and specificity of microscopy variables that were evaluated. pus cells had the highest specificity, followed by WBC, cast cells and RBC whereas epithelial cells, and pus cells had the highest sensitivity.

6.7 PATHOGENS ISOLATED

Klebsiella and *E. coli* were the main urine pathogens accounting for 35.5% and 29.4% respectively, followed by *Enterobacter* (14.7%), *Candida* (8.8%), *Pseudomonas*, *Proteus* and *Staphylococcus* - 11.8%.

6.8 ANTIBIOTIC SENSITIVITY PATTERN

Table 8: Antibiotic sensitivity pattern

n = 30

DRUG	NUMBER OF URINE SAMPLES	SENSITIVITY (%)
NALIDIXIC ACID	30	90
NITROFURANTOIN	30	90
GENTAMICIN	4	100
CHLORAMPHENICOL	1	100
NORFLOXACIN	2	100
CIPROFLOXACIN	1	100

Nalidixic acid and nitrofurantoin were the most commonly used drugs in determining sensitivity of uropathogens to antibiotics.

CHAPTER SEVEN

7.0 DISCUSSION

7.1 PREVALENCE

The prevalence of UTI in this study was relatively high (33%). Other studies done within the region show a prevalence range from 17% ⁽¹⁾ to 26.9% ⁽¹⁵⁾. The study done in Zimbabwe was laboratory based and urine samples were taken from patients suspected to have UTI irrespective of the age.

Kala and Jacobs found a prevalence of 35% in malnourished children ⁽³⁹⁾.

In the South Africa study, samples of urine were taken from children attending a periurban clinic for different ailments ⁽¹⁾.

The true prevalence in the community could be lower than that found in this study as the majority of our patients were referred from the clinics and were ill enough to be admitted into the hospital. Blood cultures to correlate the urinary tract findings would have been useful in determining whether the positive urine culture was part of a septicaemic episode or true bacteriuria.

Repeat urine cultures for those with significant bacteriuria could have also helped in increasing the sensitivity of culture results.

There were more male respondents than females (M:F 1.2:1). This could be due to the fact that there were more males admitted to the ward than females, (M:F 1.1:1) during the study period. Another explanation could be that the guardians may have found it easier to collect urine samples from boys than girls, especially in those who were not toilet trained.

7.1.1 Sex distribution

The prevalence was higher in the females (38.3%) than in the males (29%). This is similar to other studies ^(5,6,7,8,9) in which the female child has a higher prevalence than their male counterparts except in infancy.

7.1.2 Age distribution

The prevalence was also affected by age.

The infant child was 2.5 times more likely to have UTI than the older child. Many studies have shown that the incidence of UTI is highest in the younger child, especially in infancy ^(5,6,7,9). As the child increases in age, the risk of developing UTI seems to decrease. In this study, association of UTI with age was minimal in the 49-60 months age group (OR 0.5, *p* 0.3)

In this study, the male infant did not have a higher chance of having UTI as compared with the female infant (OR 0.8, *p* 0.6). Studies have shown that the prevalence of UTI in boys is highest during infancy and decreases as they grow up, whereas in girls it increases with age ^(5,6,7). Some authors believe that the incidence of UTI in the first 6 months of life is equal in both sexes and thereafter the incidence in the females starts to increase ⁽⁹⁾.

7.1.3 Weight

In this study, being underweight (as defined by the Wellcome classification) *per se* was not a risk factor for having UTI (OR 0.5, *p* 0.13)

A study done in South Africa showed that being underweight *per se*, did not make a child more susceptible to UTI ⁽¹⁾. Patients with severe malnutrition, though, are more prone to UTI which is thought to be part of the septicaemic picture ⁽³⁹⁾. The authors also attributed the high prevalence to the fact that most of these patients come in with gastroenteritis and faecal contamination of the peri-urethral area may promote colonization of the area.

7.1.4 Mode of urine collection

Most of the urine sample was collected by the midstream method. No catheter urine was collected due to non availability of catheters. Quality of urine collected by this method is said to be high ⁽⁵⁾ with relatively low contamination rate. Contamination in uncircumcised infants remains a problem ⁽²⁴⁾. This was a factor that was not looked for in this study although the population looked at were from areas where circumcision is not carried out at a young age.

In the study subjects there was a high proportion of patients with UTI who had urine collected by clean catch method or urine bag (table 3). The possibility of contamination cannot be ruled out.

Of the 127 urine samples that were cultured 25 (20%) had mixed growth and were not analysed as they were taken to be contaminants. The mode of urine collection for these patients were analysed and they showed that of the 25 contaminated urine 13 (52%) were collected by

MSSU, 8 (32%) by clean catch, 3 (12%) by urine bag and 1 (4%) by SPA.

These cultures should ideally have been repeated to determine those who may have had UTI.

7.2 CLINICAL FEATURES

Few of the patients with UTI had symptoms specific to the urinary tract.

Dysuria had the most significant association with a positive urine culture although the Confidence Intervals were wide. This is a specific symptom for UTI, that should be sought in any child who is able to communicate.

Other clinical features which were associated with UTI were fever and refusal to breast feed or anorexia. This association is stronger if the symptoms are found in the same patient. The above symptoms are not specific for infections of the urinary tract, but are useful pointers towards making a diagnosis of UTI. A suitable urine sample should be collected in a patient presenting with such symptoms.

Many studies have shown that presentation of UTI especially in younger children is subtle and often overlooked as a possible diagnosis ^(5,7,9).

Hoberman looked at the prevalence of UTI in febrile infants ⁽²⁾. He concluded that UTI is the single most common bacterial infection in febrile infants in that environment.

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7.3 ADMISSION DIAGNOSIS

Only two patients had an initial diagnosis of chronic UTI. The most common diagnosis as shown by Figure 5 was fever without a focus of infection, followed by pneumonia and protein energy malnutrition (PEM). During the study period, the commonest reason for admission was pneumonia, followed by protein energy malnutrition and malaria (Table 9). An initial diagnosis of UTI was made in less than 1% (16 patients out of the 5150) of children less than or equal to 60 months that were admitted during the study period. This could be that there are more obvious infections that are easily picked up by the clinicians or UTI is not usually considered as a possible diagnosis.

Jadresic et al conducted a one year prospective survey of urine specimens submitted for bacteriological investigations ⁽¹⁶⁾. They concluded that UTI in children is usually underdiagnosed and not managed well because of the varying management schedule of suspected UTI by the General Practitioners.

In the study done in Durban, South Africa, they found that patients who came in with Acute Diarrhoeal Disease (ADD) and Acute Respiratory Tract Infection (ARI), as defined by WHO, had a significant association with a positive urine culture. Therefore patients coming to health centres with symptoms and signs of ARI or ADD should have a urine culture.

Table 9: Admission diagnosis (November 1997 to February 1998)*n* = 5150

DIAGNOSIS	PROPORTION OF TOTAL ADMISSIONS (%)
PNEUMONIA	16.1
PEM	13.6
MALARIA	13.2
ADD	10.2
SEPTICAEMIA	4.8
FTT	4.2
RTI	3.7
CHRONIC COUGH (TB)	2.5
URTI	2.4
ANAEMIA	2.4
MENINGITIS	2.3
CEREBRAL MALARIA	2.2
CHRONIC DIARRHOEA	2.0
OTHERS	20.4

SOURCE: UTH A-BLOCK ADMISSION WARD

Table 9 shows the common admission diagnosis in the 0 - 5 years in admission ward during the study period ⁽⁵⁴⁾.

7.4 URINALYSIS AND URINE CULTURE

All urines had multistix examination done except for ten.

The variables that had a high specificity were WBC and nitrites (95 and 98.4% respectively). These two variables had low sensitivity and as such there would be high rate of false negativity. In this study they would not be good screening tools. Proteinuria had a sensitivity of 86% and specificity of 30%. There would be too many false negatives and would not be too useful as a screening tool. The variables would be good predictors of infection.

A retrospective study done to look for the best predictors of UTI in urinalysis found that presence of white cells and nitrite were good indicators. The latter was sensitive but not very specific ⁽⁵⁵⁾.

7.5 MICROSCOPY EXAMINATION AND URINE CULTURE

There were ten urine samples whose microscopy results were not recorded although the culture was done. Two of these were said to be old specimen unsuitable for microscopy but suitable for culture.

Pus cells more than 1/HPF was the best predictor of UTI. It had a specificity of 63% and a sensitivity of 59%. There would be less false positive and false negative result with this variable than the other variables studied. Presence of pus cells is a good indicator of inflammation within the urinary tract and urine samples found to have pus cells should be cultured.

All the urine samples had occasional or more pus cells and 94 of the samples were reported to have occasional or more epithelial cells.

Most studies have shown that microscopic examination of urine is useful and can be used to screen urine that should be cultured ^(1,5,6,7).

No bacteria were reported to have been seen by microscopic examination in this study. It is possible that bacteria may have been detected but not reported on the request form. Microscopy can detect bacteria in a high power field especially if the density of bacteria is high ($> 10^5$ /ml) or if there are motile bacteria ⁽⁵⁾.

Red blood cells are an important finding and may signify a cystitis or infection higher up in the renal tract especially if casts are present. In this study RBC, WBC and casts were found to have a high specificity and low sensitivity and would not be useful as screening tools.

7.6 UROPATHOGENS ISOLATED

In this study, *Klebsiella* was the most common bacteria isolated. This is an unusual finding as most studies isolate *E. coli* predominantly ^(5,7,27,41). The study done in Nigeria is the only one that seemed to have had a higher prevalence of *Klebsiella* ⁽²⁶⁾.

Klebsiella is the second most common uropathogen in most studies ^(5,10,27,56). *Klebsiella* is sometimes associated with patients who have indwelling urine catheters or those who are debilitated ⁽⁵⁾.

The urine samples analysed in the laboratory over the last four years have isolated mostly *E. coli*, followed by *Klebsiella* (refer to table 1) ⁽²⁵⁾

7.7 ANTIBIOTIC SENSITIVITY PATTERN

It is difficult to make any meaningful comments on the current sensitivity pattern as the antibiotics tested varied depending on the organism isolated. Nitrofurantoin and nalidixic acid were examined in all cases (30/34) except where *Candida* and *Staphylococcus* were isolated. Resistance to these two antibiotics was found in 10% of the cases. This compares well with studies done in the region where the sensitivity to these drugs ranges from 80 to 100% (1,15). They are recommended as the first line of treatment for any suspected UTI. In the developed countries cotrimoxazole and trimethoprim are still used as first line treatment except in infants where cefotaxime may be used initially.

E. coli sensitivity to nalidixic acid and nitrofurantoin in the UTH laboratory has remained high with less than 1% resistance being recorded in the first half of 1998 (25).

Table 10: Resistance pattern of *E. coli* in the UTH laboratory between 1994 and 1996

ANTIBIOTIC	1994 (%)	1995 (%)	1996 (%)
TETRACYCLINE	81	78	73
AMPICILLIN	82	85	48.9
COTRIMOXAZOL	81	60	54.6
CHLORAMPHENI	54	51	48.9
GENTAMICIN	8	14	15.6
CEFOTAXIME	0.4	2	5
NALIDIXIC	4	3	0
CIPROFLOXACI	not tested	0	1.4

SOURCE: UTH LABORATORY

Table 10 shows the resistance trends of *E. coli* between 1994 and 1996 in the UTH laboratory.

The resistance of *E. coli* to most of the drugs seems to be decreasing over the years especially against ampicillin where it has decreased by almost 40%. Unfortunately, the figures for 1997 are not available.

Table 11: Resistance pattern of *Klebsiella* in UTH laboratory between 1994 and 1996

ANTIBIOTIC	1994 (%)	1995 (%)	1996 (%)
TETRACYCLINE	78	71	64.6
AMPICILLIN	90	82	50.8
COTRIMOXAZOL	80	76	61.5
CHLORAMPHENI	64	60	46.1
GENTAMICIN	55	51	41.5
CEFOTAXIME	2	9	1.5
NALIDIXIC	6	16	1.5
CIPROFLOX	not tested	0	3.1

SOURCE: UTH LABORATORY

Table 11 shows the resistance trends of *Klebsiella* between 1994 and 1996 in the UTH laboratory.

There is an apparent decrease in resistance of *Klebsiella* to the antibiotics tested. There is 40% decrease in the resistance of *Klebsiella* to ampicillin. Unfortunately, the figures of 1997 resistance pattern are not available.

The apparent decrease in resistance may be a reflection of the laboratory's use of antibiotic

discs. The antibiotics are not used uniformly as testing antibiotic discs are not consistently available. The results may be skewed to the antibiotic most frequently used.

Lack of funds has also made it necessary for the laboratory to test only certain antibiotics for particular specimens. Urine samples are more likely to be tested using nitrofurantoin and nalidixic acid discs than blood samples.

Another explanation could be that there has been a decrease in the use of these antibiotics and thus the uropathogens sensitivity to these drugs has increased.

CHAPTER EIGHT

8.0 CONCLUSION

The prevalence of UTI in this study was 33% though most of the patients found to have UTI did not have symptoms.

Patients who come in with pyrexia, loss of appetite vomiting and diarrhoea, should be looked upon with high index of suspicion, especially if they are less than two years, as the prevalence of UTI is higher in this age group.

A simple urinalysis to detect moderate to heavy proteinuria, nitrites and the specific gravity can help to select urine samples which should be sent to the laboratory for culture.

In this study, microscopy was not very useful as all the patients had epithelial cells and pus cells. Only if the pus cells were reported to be more than 1cell/HPF association significant.

Klebsiella and *E. coli* were the most common pathogens isolated.

Antibiotics of choice for UTI in our environment should be nitrofurantoin and nalidixic acid.

A study involving a larger number of sample urines tested with a wider variety of antibiotics, would be more conclusive.

The changing pattern of organisms and drug resistance should always be looked for.

CHAPTER NINE

9.0 RECOMMENDATIONS

- 9.1 Urinalysis should be done on all infants and pyrexia children with no focus of infection coming into admission ward.
- 9.2 Culture of urine samples for those with proteinuria of more than 2+, nitrites leucocytes especially if there is more than one of these factors present.
- 9.3 Standardise the hospital laboratory management of urine samples. If urinalysis is positive for protein, nitrites and leucocytes, the urine should be cultured inspite of the microscopy findings.
- 9.4 A Paediatric nephrology clinic should be established for proper and regular follow up of these patients. It can also pave way for these patients to have further standardised investigations.
- 9.5 Standardise management of UTIs in children in UTH.
- 9.6 Further studies to include imaging as determined by availability of resources to detect prevalence of scarring and renal abnormalities that may be associated with UTI in our environment.
- 9.7 Regular studies to detect the changing patterns of uropathogens and antibiotics sensitivity.

CHAPTER TEN

10.0 LIMITATION OF STUDY

10.1 Selection bias

Systematic randomization was used. A number of the patients were not suitable as they had been on antibiotics prior to admission.

Another source of bias would have been from patients who were passing urine infrequently. The guardians may not have felt so motivated to collect the urine and these patients may actually have had a UTI. This could have been avoided if all the patients had been catheterised so that catheter samples were collected or if all had urine bags attached correctly.

10.2 Sampling bias

Studies involving guardians usually have this problem. In this study, it may have been easier to collect urine from a boy than a girl especially those who are not toilet trained. This can be minimised if the researcher or an assistant collect the urine themselves.

Increasing the sample size can also minimise sampling bias.

10.3 Validity of results

During the study the researcher should have checked the reliability of the laboratory results by having the same urine sample cultured twice. In this way the standard of the laboratory can be determined.

The validity of the results could also have been increased by repeating the urine cultures on another urine specimen from patients with positive cultures.

Sending urine samples to another laboratory could have helped in increasing the validity of the results.

Unfortunately, time and finances could not allow for this.

APPENDIX 1.**QUESTIONNAIRE**

HOSPITAL NO.

STUDY NO.

NAME.....

SEX..... M/F..... WEIGHT ON ADMISSION:.....

DATE OF BIRTH.....GESTATION:

PLACE OF BIRTH: HOSPITAL/CLINIC/DOMICILE

RESIDENTIAL ADDRESS OF GUARDIAN:

DATE OF URINE COLLECTION:

HOW URINE WAS COLLECTED: SPA/ CLEAN CATCH/ URINE BAG

DATE OF ANALYSIS IN LAB:

HISTORY AND PHYSICAL EXAMINATION**PAST MEDICAL HISTORY OF UTI**

FEVER : YES/NO VOMITING : YES/NO

DIARRHOEA : YES/NO IRRITABILITY : YES/NO

FEEDING WELL : YES/NO NOT PASSING URINE : YES/NO

DYSURIA/DIFFICULTIES/CRYING PASSING URINE : YES/NO

WEAK URINE STREAM : YES/NO

BALANITIS : YES/NO PALPABLE KIDNEYS : YES/NO

ABDOMINAL PAINS : YES/NO

OTHER SYMPTOMS :

ADMISSION DIAGNOSIS:

RESULTS:

1. MULTISTIX

PROTEIN...

RBC...

WBC...

NITRITE...

2. MICROSCOPY

RBC YES/NO

WBC YES/NO

CASTS YES/NO

OTHERS.....

3. CULTURE RESULTS POSITIVE/NEGATIVE

4. SENSITIVITY

APPENDIX 2

CONSENT FORM

Introduction by researcher and a brief explanation about the study and the importance of the study. The different procedures were then explained.

Urine sample will be collected from your child using the following methods:

MSSU: When the child wants to pass urine, you will clean the genitalia with some water and then ask the child to void. Let the first urine pass and then collect the mid urine sample into this sterile container.

Clean catch: During a nappie change try and catch the urine as the child voids.

Urine bag: A urine bag will be attached around the urethral opening. As soon as your child voids urine tell the nurse on duty to put it in the sterile container given you.

Suprapubic aspirate: Urine sample will be collected from the bladder by the abdominal route. A needle attached to a syringe will be introduced into the distended bladder to collect urine.

It was also explained that refusal to participate in the study would in no way interfere with the normal management of the patient.

The guardians were also invited to come and collect the results of the urine culture in the children's clinic.

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