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URINARY TRACT INFECTIONS AT AGA KHAN UNIVERSITY HOSPITAL NAIROBI - A ONE YEAR EXPERIENCE
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ABSTRACT

***Background*: In developing countries, most of these patients with urinary tract infections (UTI) are normally treated empirically and urine culture is usual ordered for as a last resort in patients refractory to antibiotic treatment.**
***Objective*: To explore the possibility of designing empiric antibiotic therapy for symptomatic UTI in patients at Aga Khan University Hospital by looking at the trends of UTI, common pathogens isolated and their antibiotic susceptibility pattern.**
***Design*: A retrospective clinical-laboratory study.**
***Setting*: Aga Kahn University Hospital- Nairobi.**
***Subjects*: All positive urine cultures between January and December 2008 were included in the study.**
***Results*: A total of 409 urine specimens were retrieved and analysed and 100 cases had negative cultures. Three hundred and nine cases had positive cultures. Sixty eight point seven percent were females while 31.3% were males with a mean age of 31 years. One hundred and thirty five out of 409 patients (33%) had classical signs and symptoms. In 143 (35%) cases *E. coli* was isolated. The other cultures were organisms other than *E. coli*. There was a higher resistance to clotrimazole in *E. coli* (71%) as compared to non-*E. coli* organisms (23%). There was a higher resistance rate to Nalidixic acid in non-*E. Coli* organisms (35%) and higher resistance rate to Augmentin in *E. Coli* 43 versus 18% (c/f non-*E.Coli*). Forty patients in the study had predisposing factors for UTI.**
***Conclusions*: It is sometimes warranted to start the patient on empiric antibiotic treatment before culture results are available. Nitrofurantoin, Cefuroxime, Ciprofloxacin have good sensitively rates and are therefore drugs of first choice for the treatment of uncomplicated urinary tract infection provided that the contraindications and specific precautions are noted.**

INTRODUCTION

Urinary tract infection (UTI) is the most common condition leading to outpatient visits and is also the most common cause of excessive or inappropriate antibiotic usage. Sexually active young women are disproportionately affected, but several other populations, including elderly persons and those undergoing genitourinary instrumentation or catheterisation are also at risk. An estimated 40 percent of women report having had a UTI at some point in their lives (1).

UTIs are the leading cause of gram-negative bacteremia. In the United States, these infections account for approximately seven million office visits and more than one million hospitalisations, for an overall annual cost in excess of United States dollars one billion (1, 2). UTIs also account for at least 40% of all hospital-acquired infections and are in the majority of cases catheter-associated (3-5).

Micro-organisms can reach the urinary tract by haematogenous or lymphatic spread, but there is abundant clinical and experimental evidence to show that the ascent of micro-organisms from the urethra is the most common pathway leading to a UTI, especially organisms of enteric origin (that is, *Escherichia coli* and other *Enterobacteriaceae*). This provides a logical explanation for the greater frequency of UTIs in women than in men and for the increased risk of infection following bladder catheterisation or instrumentation (6). A single insertion of a catheter into the urinary bladder in ambulatory patients results in urinary infection in 1-2% of cases (7).

Haematogenous infection of the urinary tract is restricted to a few relatively uncommon microbes, such as *Staphylococcus aureus*, *Candida* spp., *Salmonella spp.* and *Mycobacterium tuberculosis*, which cause primary infections elsewhere in the

body. *Candida albicans* readily causes a clinical UTI via the haematogenous route, but is also an infrequent cause of an ascending infection if an indwelling catheter is present or following antibiotic therapy.

The concept of bacterial virulence or pathogenicity in the urinary tract infers that not all bacterial species are equally capable of inducing infection. The more compromised the natural defence mechanisms (for example, obstruction, bladder catheterisation), the fewer the virulence requirements of any bacterial strain to induce infection.

In developing countries, most of these patients are normally treated empirically and urine culture is usual ordered for as a last resort in patients refractory to antibiotic treatment (8).

The number of bacteria is considered relevant for the diagnosis of a UTI. In 1960, Kass developed the concept of 'significant' bacteriuria (> 10^5 cfu) in the context of pyelonephritis in pregnancy(9). In a suprapubic bladder puncture specimen, any count of bacteria is relevant.

The aim of this study was to explore the possibility of designing empiric antibiotic therapy for symptomatic UTI in patients at Aga Khan University Hospital by looking at the trends of UTI, common pathogens isolated and their antibiotic susceptibility pattern.

MATERIAL AND METHODS

This was a retrospective clinical-laboratory study comprising of review of laboratory records and their correlation with clinical records. Starting with the microbiology laboratory records, patients were identified. All positive urine cultures between January and December 2008 were included in the study. This was then followed by a file review.

Information concerning each case was entered in a standard proforma which included:

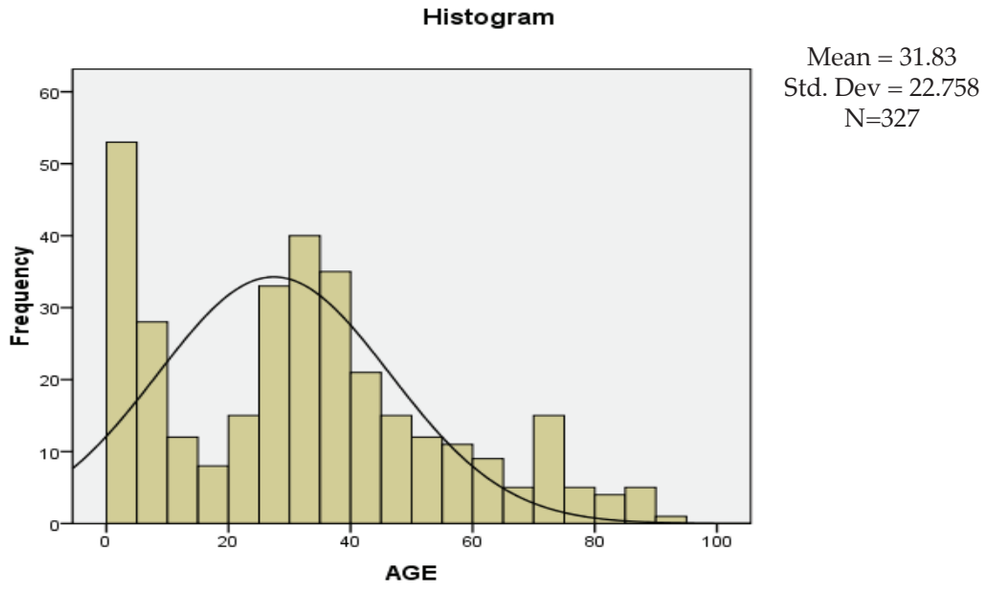
- Patient file number
- Age
- sex
- Presence or absence of pyuria
- Type of organism isolated
- Antibiotic sensitivity pattern of the isolated organism,
- Antibiotic used for treatment of patient,
- Other co morbidities
- HIV status
- Signs and symptoms at presentation

One hundred controls were also included with no growth obtained from urine specimen who had signs and symptoms of urinary tract infection.

RESULTS

A total of 409 urine specimens were retrieved and analysed and 100 cases had negative cultures. Three hundred and nine cases had positive cultures. Sixty eight point seven percent were females while 31.3% were males with a mean age of 31 years. One hundred and four cases were in the pediatric age group. Age distribution is displayed in Figure 1.

Figure 1
Age distribution



The classical signs and symptoms of urinary tract infection include:

- Lower abdominal pain
- Dysuria
- Frequency

One hundred and thirty five out of 409 patients (33%) had classical signs and symptoms.

The complaints of the other 274 patients included non-specific symptoms such as lower abdominal pain (8.6%), chills/fever (10.3%), haematuria (0.2%) and others, and urine microscopy results showed WBC > 5/HPF (pyuria) in 54.3% of the cases.

In 143 (35%) cases *E. coli* was isolated. The other cultures were organisms other than *E.coli* as displayed in Table 1.

Table 1
Spectrum of Organisms isolated

Organism	Frequency	Percentage
E.coli	143	35
ORSA/ORSE/ORSS	11	2.6
Aeromonas hydrophila	4	0.9
Aeromonas iwoffi	1	0.2
C.albicans/Streptococcus spp.	1	0.2
Citrobacter freundii	4	1.0
E.Coli/C.albicans	1	0.2
Enterobacter/C.albicans	1	.2
Entrerobacter	24	5.8
Gram negative bacilli	1	0.2
Klebsiella oxytica	1	0.2
Klebsiella pneumoniae	3	0.7
Klebsiella terrigena	1	0.2
Kluvera	19	4.6
Mycoplasma	1	0.2
No growth	101	24.7
Pseudomonas auregenosa	9	2.1
Proteus Mirabilis	4	1.0
Proteus vulgaris	4	1.0
Providencia	1	0.2
Streptococcus agalactiae	11	2.6
Staphylococcus aureus	15	3.7
Staphylococcus epidermidis	10	2.4
Staphylococcus epidermidis /C.albicans	1	0.2
Staphylococcus saprophyticus	4	1.0
Streptococcus spp.	1	0.2
Total	409	100.0

Key
ORSA –Oxacillin resistant *Staphylococcus aureus*
ORSE -Oxacillin resistant *Staphylococcus epidermidis*
ORSS -Oxacillin resistant *Staphylococcus saprophyticus*

The antibiotic resistance proportions of *E.coli* and non- *E.coli* organisms to the various antibiotics are displayed in Table 2. Upto 70% of the *E.coli* were resistant to Septrin.

Relating to Pyuria, 59.7% of the females had pyuria as compared to 40.8% of males. Patients were arbitrarily divided into three age groups; <10, 11-50, 51-90. Pyuria was observed mainly in patients <10 years and age followed by patients in the age group 31-40 years as further displayed in Table 3. The list of antibiotics used for therapy and the frequency of their usage is displayed in Table 4.

Table 2
Antibiotic Resistance patterns

Antibiotics Tested	Resistant *E.coli* %	Resistant Non- *E.coli* organisms %
Septrin	101(71)	60(23)
Augmentin	62(43)	47(18)
Nalidixic acid	45(31)	94(35)
Ciprofloxacin	37(26)	55(21)
Gentamycin	25(17)	28(11)
Cefuroxime	20(14)	32(12)
Cefotaxime	20(14)	33(12)
Ceftriaxone	11(8)	14(5)
Nitrofurantoin	8(0.05)	26(0.09)

Table 3
Age category and pyuria

Age Category	Pyuria Yes	Pyuria No	Total
<10	40	47	87
11-20	8	9	17
21-30	23	30	53
31-40	45	27	72
41-50	18	18	36
51-60	9	9	18
61-70	10	10	20
>70	18	6	24
Total	171	156	327

Table 4
Antibiotics used for therapy

Antibiotic used for treatment	Frequency	Percentage
Cefuroxime	57	32.2
Augmentin	42	23.7
Quinolones	29	16.4
Amoxil	6	3.4
Ceftriaxone	15	8.5
Antifungals	12	6.8
Nitrofurantoin	7	4.0
Septrin	2	1.1
Cefzil	2	1.1
Macrolides	2	1.1
Vancomycin	1	0.6
Paramomycin	1	0.6
Doxycycline	1	0.6
Total	177	100

Forty one patients in the study had predisposing factors for UTI. Ten patients were pregnant, one had a history of recent catheterisation and one had a Foley Catheter *in situ*. Four patients had diabetes mellitus while nine had hypertension. Six had chronic obstructive airway disease while nine were positive for the human immunodeficiency virus. Three patients had a history of recurrent urinary tract infection. The rest of the data is displayed in Table 5.

Table 5
Co-morbidities

Co-morbid	Frequency	Percent
Depression	1	2.4
Diabetes mellitus	4	9.8
Hypertension	9	22.0
Urinary catheter	10	24.4
Cancer	3	7.3
Pregnancy	10	24.4
Ischaemic heart disease	1	2.4
Trauma	1	2.4
Sickle cell disease	1	2.4
Urinary tract malformation	1	2.4
Chronic obstructive Airway disease	6	14.6
Recurrent UTI	3	7.3
Tuberculosis	1	2.4
HIV	9	2.2
Total	51	100.0

DISCUSSION

Normal urine is sterile. An infection occurs when gastrointestinal commensals colonise the urethra and begin to multiply. Majority of infections are due to *E. coli*. The urinary system is structured in a way that prevents entry of infection. The ureters and bladder normally prevent urine from backing up toward the kidneys, and the flow of urine from the bladder help wash bacteria out of the body(10, 11).The highest incidence of urinary tract infection in our study was in females aged 20-40. Female patients have more UTI than male patients. Women are more prone to UTIs because their urethra is much shorter and closer to the anal opening than in males, and they lack the bacteriostatic properties of prostatic secretions. Among the elderly, UTI frequency in both sexes is roughly in equal proportions (11).

In our study urinary tract infections in males was frequently observed in older men> 50years. This is due, in part, to an enlarged prostate in older men. Urinary tract infections most commonly occur in older men with prostatic disease, outlet obstruction or urinary tract instrumentation. These infections occasionally occur in young men who participate in anal sex (exposure to *E. coli* in the rectum), who are not circumcised (increased *E. coli* colonisation of the glans and prepuce) or whose sexual partner is colonised with uropathogens (8, 12). In men (unlike in women), a urine culture growing more than 1,000 CFU of a pathogen per mL of urine is the best sign of a urinary tract infection, with a sensitivity and specificity of 97 percent(13).

E.coli was the most common organism (35%) associated with urinary tract infection in our study and this is similar to other studies(20). *Escherichia coli* is the most common cause of uncomplicated UTI and accounts for approximately 75 to 95 percent of all infections (14-17). A longitudinal study of 235 women with UTIs found that *E. coli* was the only causative agent in 69.3 percent of cases and was a contributing agent in an additional 2.4 percent of cases (18). *Staphylococcus saprophyticus* is a distant second, accounting for only 5 to 20 percent of infections. Other Enterobacteriaceae, such as *Klebsiella* and *Proteus*, occasionally cause UTI. Although *S. saprophyticus* is less common than *E. coli*, it is more aggressive. Approximately one half of patients infected with *S. saprophyticus* present with upper urinary tract involvement, and these patients are more likely to have recurrent infection (14).

There was a higher resistance to clotrimazole (septrin) in *E.coli* as compared to non-*E.coli* organisms in our study which were more resistant to Nalidixic acid. This is most likely due to the fact that most Gram positive organisms are relatively resistant to Nalidixic acid and it is routinely used as a selective medium to suppress Gram positive organisms and allow Gram negative isolation. For the above reasons clotrimazole and Nalidixic acid are not good choices in the empirical treatment of urinary tract infection.

There was a higher resistance rate to Augmentin in *E. coli* (c/f non-*E.coli*) in our study. This is possibly due to hyper production of Beta-lactamases. In other studies up to one third of uropathogens are resistant to ampicillin and sulfonamides, but the majority are susceptible to trimethoprim-sulfamethoxazole (85 to 95 percent) and fluoroquinolones (95 percent)(15).

This was hardly the case in our study as most of our isolates were resistant to trimethoprim-sulfamethoxazole (septrin) and this may possible be due to the increased usage of this drug in HIV infected patients as prophylaxis against Pneumocystis infection.

Table 6 compares our results with the Australian Outpatients Study (19), Chan's study(20) and H.K. Chan study. It was found that the resistance to nitrofurantoin was universally low. Resistance to Nalidixic acid was low in the Australian Outpatients study and H.K. Chan study (21), but higher in Chan's study and our study. On the other hand, resistance to ampicillin is high both in H.K. Chan study and in Chan's study, but lower in the Australian Outpatients study and our study. Resistance to Cotrimoxazole varied significantly, namely 24, 70 , 41 and 52% (Table 6).

Table 6

Comparison of Antibiotic Resistance (%) amongst Three Different UTI Studies

Antibiotic	Australian outpatients	S.P. Chan study	H.K. Chan study	Our study
Ampicillin	45	69	61	35
Septrin	24	70	41	52
Nitrofurantoin	0	2	0	11
Nalidixic acid	2	28	2	44

Pyuria was most common seen in females 59.7% as compared to males 40.8% and it was also observed in younger patients < 10 years of age and in young adults too (31-40 years). UTI occurs nearly 50 times more often in women than men under the age of 50 and increases in both men and women over age 50, with the female-to-male ratio decreasing as prostate disease becomes more prevalent among older men (22). This would explain why the incidences of pyuria were higher in the females in our study.

Between ten and twenty percent of patients who are hospitalised receive an indwelling Foley catheter. Once this catheter is in place, the risk of bacteriuria is approximately five percent per day. With long-term catheterisation, bacteriuria is inevitable. Catheter-associated urinary tract infections account for 40 percent of all nosocomial infections and are the most common source of gram-negative bacteremia in hospitalised patients (23). In our study 24% of the patients had catheter associated urinary tract infections (24).

In our study ten had urinary tract infection in pregnancy. Symptomatic urinary tract infections complicate one to two percent of pregnancies, usually in women with persistent bacteriuria (25-27). Most pregnant women with pyelonephritis should be hospitalised. Initially, these patients should receive intravenous antibiotic therapy. They should complete a 14-day course of acute antibiotic therapy followed by nightly suppressive therapy until delivery.

In conclusion, one should obtain a mid-stream urine from patients suspected to have UTI, for culture and sensitivity tests if possible since it is a very important guide to treatment. It is sometimes warranted to start the patient on empiric antibiotic treatment before culture results are available.

Ampicillin and Cotrimoxazole (Septrin) should not be the first line of empirical treatment since resistance was found to be pretty high 35-52%.

Resistance to Nalidixic acid was also found to be pretty high in non-*E. Coli* organisms in our study and in *E. coli* in Chan's study and should therefore not be used either as empiric treatment.

Nitrofurantoin, Cefuroxime, Cefaclor, Ofloxacin and Ciprofloxacin have good sensitively rates and will therefore be effective first line treatment for uncomplicated urinary tract infection provided that the contraindications and specific precautions are noted. Since the resistance to ampicillin is very high, Cephalosporins should be used for the empirical treatment of urinary tract infection in pregnancy, since they are very effective and relatively safe.

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