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THE ETIOLOGY AND ANTIMICROBIAL SUSCEPTIBILITY PATTERNS OF URINARY TRACT INFECTIONS AT A PRIVATE NIGERIAN TEACHING HOSPITAL IN SOUTH WEST NIGERIA

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ABSTRACT

BACKGROUND: Urinary tract infections (UTI's) are among the commonest bacterial infectious disease in clinical practice with a wide range of etiologic agents. It frequently occurs in both the hospital and the community. AIMS/OBJECTIVES:: To determine the etiology of UTI at BUTH and obtain data on their susceptibility and resistance patterns. METHODS: This was a prospective analysis of data on patients with UTI obtained from in and outpatients over a six month period. Samples had been obtained by clean catch mid-stream urine or suprapubic aspiration. The organisms had been identified by biochemical methods with susceptibility and resistance testing performed. Data analysis was with EPI-INFO version 3.5.1
RESULTS: There were a total of 200 urine samples that had positive growth. Prevalent organisms were *Escherichia coli* (48%) and *Klebsiellaspp* (24%), followed by *Staphylococcus aureus* (10%) and Coagulase Negative *Staphylococci* (6.5%). The risk factors for UTI were female gender (p = 0.00), Diabetes mellitus (p = 0.03) and genitourinary surgery (p = 0.04). Effective antibiotics in-vitro to *Escherichia coli*were Nitrofurantoin and Cefepime at 84.8% and 92.3% respectively; while Cotrimoxazole performed poorly (32.5% susceptibility).
CONCLUSION: Urinary tract infections are an important cause of morbidity in our environment and inaccuracies in diagnosis will prolong morbidity and may lead to costly and unsafe treatments.The prevalent pathogens in our environment are the Gram negative bacilli, *Escherichia coli* and *Klebsiellapneumoneae*. Nitrofurantoin retains efficacy to both urinary pathogens.

KEY WORDS: Urinary Tract Infection, Catheterization, *Escherichia coli*, Risk factors, Nitrofurantoin

ETIOLOGIE ET LES MODELES DE SUSCEPTIBILITE ANTIMICROBIENNE DES INFECTIONS DES VOIESURINAIRES DANS UN HOPITAL PRIVE NIGERIAN D'ENSEIGNEMENT AU SUD OUEST DU NIGERIA

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RESUME
CONTEXTE : Les infections urinaires (UTI) sont parmi les maladies infectieuses bactériennes les plus courantes dans la pratique clinique avec une large gamme d'agents étiologiques. Il se produit fréquemment dans l'hôpital et la communauté. OBJECTIFS : Pour déterminer l'étiologie de UTI à BUTH et obtenir des données sur les modelés de leurs susceptibilités et résistances.
METHODES : Il s'agissait d'une analyse prospective des données sur les patients atteints de UTI obtenue des patients en hospitalisation et externes d'unpériode de six mois. Des échantillons ont été obtenus par prélèvement propre àl'urine moyenne ou par aspiration supra pubienne. Les organismes ont été identifiés par des méthodes biochimiques avec des tests de sensibilité et de résistance effectués. L'analyse des donnéesétait avec EPI – INFO version 3.5.1
RESULTATS : Il y avait un total de 200 échantillons d'urine qui avaient une croissance positive. Les organismes prédominantsétaient*Escherichia coli* (48%) et *Klebsiella spp* (24%), suivi de *Staphylococcus aureus* (10%) et Coagulase négative*Staphylococci* (6,5%). Les facteurs de risque de UTI étaient le sexe féminin (p=0,00), le diabète sucré (p= 0,03) et la

chirurgie génito – urinaire (p= 0,04). Des antibiotiques efficaces in vitro pour Escherichia coli étaient la Nitrofurantoïne et le cefépime à 84,8% et 92,3% respectivement ; tandis que le cotrimoxazole a présenté un mauvais rendement (susceptibilité de 32,5%).
CONCLUSION: Les infections des voies urinaires sont une cause importante de morbidité dans notre environnement et les inexactement dans le diagnostic plongera la morbidité et peut conduire à des traitements coûteux et dangereux. Les pathogènes prédominants dans notre environnement sont les bacilles Gram négatif, *Escherichiacoli* et *Klebsiellapneumoniae*. Le Nitrofurantoïne conserve son efficacité pour les deux pathogènes urinaires.

MOTS – CLÉS: L'infection des voies urinaires, Cathétérisme, *Escherichia coli*, Les facteurs de risque, Nitrofurantoïne.

INTRODUCTION

Urinary tract infections (UTI's) are among the commonest bacterial infectious disease in clinical practice with a high rate of morbidity. They are described as bacteriuria associated with or without urinary symptoms and are exceeded in frequency among ambulatory patients only by respiratory and gastrointestinal infections. It is the second most common infectious presentation in community practice and over 150 million people are diagnosed with UTI each year, with economic implications [1, 2, 3, 4].

The urinary tract is usually sterile, but bacteria may rise from the peri anal region, possibly leading to UTI in what is typically described as an ascending infection. Pathogens in the bladder may stay silent or can cause irritating symptoms like urinary frequency and urgency. UTI's are associated with sequelae such as renal scarring, pyelonephritis, renal and failure and as such need to be accurately diagnosed. In the light of antimicrobial resistance it is also vital that susceptibility results are reliable and accurate for the use of the clinician in the management of the patient.

Females bear the higher burden of UTI than males and are more likely to experience UTI than men. Nearly one in three women will have had at least an episode of UTI requiring antimicrobial therapy by the age of 24 years. In addition about fifty percent of all women will experience one UTI during their lifetime. Those at increased risk of UTI include infants, pregnant women, the elderly, patients with spinal cord injuries and/or those catheterized, patients with diabetes mellitus, patients who are immune-deficient, and patients with underlying urologic abnormalities[5].

Among women 18–30 years old, the incidence of acute uncomplicated urinary tract infections (UTIs) is estimated to exceed 0.5 episodes per annum. These infections are a major source of morbidity and health care costs in this population. Identified risk factors for such infections include sexual activity, spermicide-based contraception, and a history of previous UTIs[6].

The etiology of UTI is also affected byother underlying host factors that complicate UTI, such as age (the extremes of life), diabetes mellitus, spinal cord injury, or catheterization. Consequently, complicated UTI has a more diverse etiology than uncomplicated UTI, and organisms that often do not cause disease in healthy patients can cause significant disease in hosts with anatomic anomalies, metabolic derangements or immunologic compromise. The pathogens associated with UTI are changing the way they present in infections due to antimicrobial resistance [7].

There is the need to know the pattern of presentation of UTI's in our local practice as this would aid clinicians in the management of such patients. In addition few studies have been conducted in our local environment to understand the risk factors for the acquisition of UTI's as well as the picture as it pertains to resistance with first-line agents among patients with acute uncomplicated UTI.

The diagnosis may not always be straightforward as it may mimic other clinical conditions including an acute abdomen. Physicians therefore need accurate laboratory support in order to distinguish it from other diseases that have a similar clinical presentation as some UTIs are asymptomatic or present with atypical signs and symptoms.

AIM: To obtain data on etiology of UTI and their susceptibility patterns as well as the risk factors.

OBJECTIVES: To assess the in-vitro efficacy of antibiotics towards the pathogens responsible for UTI in BUTH and to determine the microbial pathogens causing UTI's at the Babcock University Teaching Hospital

MATERIALS AND METHODS

Study site/design/population: the study site was the Medical Microbiology Department of the Babcock University teaching Hospital, a 140 bed facility located in Ilisan South West Nigeria.; This is a retrospective study of data focusing on the frequency of uro-pathogens and their antibiotic susceptibility in different gender and age groups of patients and data from December 2015 – April 2016 were analyzed. The study population consisted of patients from ages One to Ninety Nine years, with suspected UTI being treated in the inpatient department or an outpatient clinic of a tertiary center in South West Nigeria. All

were referred because of urinary symptoms such as dysuria or unexplained acute febrile illness. Demographic data, epidemiological factors, and antibiotic susceptibility of pathogens were obtained from patient records.

Sample Collection: urine specimens had been previously obtained from adult patients via the clean-catch midstream technique.UTI was defined as the growth of a single pathogen of $>10^5$ colony forming units/ml by properly collected urine specimen (suprapubic aspiration, catheterization, or midstream specimen) in patients with urinary symptoms.

Sample Size: The average isolation rate of organisms from urine is approximately 15%, using the Kish formula this gives a sample size of 200 patients.

Antimicrobial Susceptibility Testing: This was done on Mueller- Hinton agar (Oxoid UK) using disk diffusion (Kirby Bauer's) technique. This method was done according to Clinical and Laboratory Standards Institute (CLSI) guidelines to determine susceptibility of UTIs agents [8].

Isolates with intermediate resistance were grouped with resistant isolates in the analysis. The antibiotic disks (Oxoid UK) comprised of ampicillin (10µg), ciprofloxacin (5µg), nitofurantoin (300µg), ceftriaxone (30µg), cefotaxime (10µg) and gentamicin (10µg), cefepimeand trimethoprim-sulfamethoxazole (25µg), cefepime (30µg), cefuroxime (30µg), cefpodoxime (30µg), ceftazidime (30µg), meropenem (30µg), ampicillin-sulbacatam (30µg), cefoxitin(30µg), co-amoxiclav (25µg).

Antimicrobial resistance for extended spectrum beta lactamases was determined by the double disk diffusion method where a Co-Amoxiclav disc was placed 20 mm centre to centre in between a Ceftazidime and Ceftriaxone disc. A dumb bell appearance or distortion on the side facing the Co-Amoxiclav was a phenotypic indicator of ESBL expression. MRSA – Methicillin Resistant *Staphylococcus aureus* were detected by using a Cefoxitin30µg disc as a surrogate marker, a zone size less than 20 mm was indicative of Methicillin resistance.

Data Analysis: EPI INFO version 3.5.1 was used to detect significant differences between the age groups and the prescribed treatment, the bacteriological culture results and the antimicrobial susceptibility of the isolates. A P value of <0.05 was considered statistically significant.Statistical analysis was performed with Pearson's χ^2 test as well as Fisher's exact test and odds ratio for categorical variables.Informed Consent: consent is implied to have been given during the course of specimen analysis. Ethical Issues: ethical approval was sought and obtained from the Babcock University Human Research Ethics Committee – BUHREC.

RESULTS

In all, there were 200 patients records recruited into the study. The mean age of the participants in the study was 38.2 years (Standard deviation 20.86) with the patients ranging from ages 1 – 99. The male to female ratio was 0.27:1. In the study 20% (n = 32) of the 158 females were pregnant. Also 17% (n=33) were catheterized, 35% of patients were hospitalized (n=70) (Table 1).

TABLE 1: SUMMARY STATISTICS

Variable		Frequency (N)	Percentage (%)
Gender	**Male**	**42**	**21**
	Female	**158**	**79**
Pregnant	**Yes**	**32**	**20**
	No	**126**	**80**
Pediatric	**Yes**	**21**	**10.5**
	No	**179**	**89.5**
Elderly	**Yes**	**33**	**16.5**
	No	**167**	**83.5**
Catheterized	**Yes**	**34**	**17**
	No	**166**	**84**
Admission Status	**Inpatient**	**70**	**35**
	Outpatient	**130**	**65**
Asymptomatic Bacteriuria	**Present**	**32**	**16**
	Absent	**168**	**84**

Variable		Frequency (N)	Percentage (%)
Post-operative patients	**Yes**	**10**	**5**
	No	**190**	**95**
Benign Prostatic Hypertrophy	**Yes**	**10**	**5**
	No	**190**	**95**
	No	**198**	**99**
ESBL production	**Positive**	**8**	**4**
	Negative	**192**	**96**
MRSA production	**Positive**	**4**	**2**
	Negative	**196**	**98**
Type of UTI	**Complicated**	**98**	**49**
	Uncomplicated	**102**	**51**
Pyelonephritis	**Present**	**6**	**3**
	Absent	**194**	**97**
Diabetes Mellitus	**Positive**	**7**	**3.5**
	Negative	**193**	**96.5**
Recurrent UTI	**Yes**	**5**	**2.5**
	No	**195**	**97.5**

ESBL = Extended Spectrum Beta Lactamases, UTI – Urinary Tract Infection Mean age = 38.32 years, Range 1 - 99 years, S.D = 20.86

Asymptomatic bacteriuria was seen in 16% (n=32). Post-operative patients accounted for 5% of patients (n=10), the same percentage of patients had Benign Prostatic hypertrophy with 2 male patients presenting with testicular swellings. About 4% of patients (n=8) had an ESBL elaborating organism and 2% (n =4) harbored an MRSA strain in their urine. In addition 49% (n=98) had a complicated UTI, while Pyelonephritis was recorded in 6% of patients (n=3). Diabetes mellitus was seen in 7 patients while 5 had a history of recurrent UTI, only one patient among the females presented with threatened abortion.

The predominant pathogen in the urine of our patients was *Escherichia coli*accounting for 48% (n=96) cases (Figure 1). This was followed by *Klebsiellaspp* with 24% (n=48) and *Staphylococcus aureus* 10.5% (n=21). Others isolated were *Staphylococcus epidermidis* 6.5%, (n=13), *Proteus spp* 4.5% (n=9), *Pseudomonas spp* 3.5% (n=7), *Staphylococcus saprophyticus* 2% (n=4) and *Salmonella spp* 1% (n=2).

Three risk factors were identified and these were: gender as females were 0.4 times more likely to have an organism isolated from their urine in our center [O.R=0.4, 95% CI=0.2-0.8, χ^2 = 6.64, p=0.00], diabetic patients who were 6.6 times more likely to have a UTI [O.R=6.6, 95% CI=0.8-55.7, χ^2 = 3.9, p=0.03] and Postoperative patients [O.R=4..44, 95% CI= 1.0-21.5, χ^2 = 4.05, p=0.04] (Table 2).

FIGURE 1: ORGANISMS ISOLATED FROM URINE

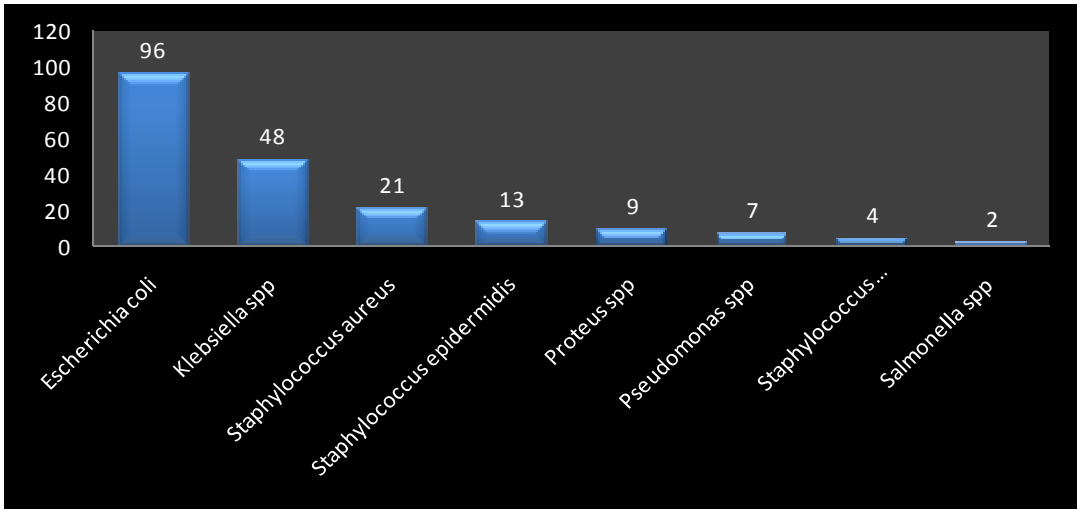

TABLE 2 RISK FACTORS FOR ACQUISITION OF *ESCHERICHIA COLI* UTI

Variable		*Escherichia coli*		Odds ratio	Confidence Interval	Chi Square	P value
		Positive	Negative				
Adults	Yes	68	77	0.74	0.4 – 1.4	0.9	0.33
	No	30	25				
Asymptomatic Bacteriuria	Positive	17	15	1.22	0.6 – 2.6	0.26	0.61
	Negative	81	87				
Gender	Female	70	88	0.4	0.2-0.8	6.64	0.00
	Male	28	14				
Type of UTI	Complicated	53	45	1.5	0.9-2.6	1.99	0.16
	Uncomplicated	45	57				
Diabetes Mellitus	Present	6	1	6.6	0.8 – 55.7	3.9	0.03*
	Absent	92	101				
Elderly	Yes	21	12	2.05	0.95 – 4.43	3.39	0.06
	No	77	99				
Admission status	In-patient	38	32	1.39	0.77 – 2.48	1.20	0.27
	Outpatient	60	70				
Postoperative	Yes	8	2	4.44	1.0 – 21.5	4.05	0.04*
	No	90	100				
Pregnant	Yes	11	21	0.49	0.22 – 1.07	3.26	0.07
	No	87	81				

* Fishers exact test

The rates of susceptibility by Escherichia was seen with Nitrofurantoin and Cefepime 84.8% and 92.3% highest respectively followed by Genticin, Ceftriaxone, Cefpdoxime and Co-Amoxiclav, 71.8%, 70,8%, 70.6% and 68.4% respectively. Ampicillin/Sulbactam and Cotrimoxazole displayed the lowest rates of susceptibility – 23.9% and 20.7% each (Table 3).

TABLE 3 ANTIMICROBIAL SUSCEPTIBILITY PATTERN OF *ESCHERICHIA COLI*

Antibiotic	Susceptible (%)	Resistant (%)	P value
Augmentin	**68.4**	**31.6**	**0.00**
Cefepime	**92.3**	**7.7**	**0.16**
Cefpodoxime	**70.6**	**29.4**	**0.79**
Ceftazidime	**69.5**	**30.5**	**0.78**
Ceftriaxone	**70.8**	**29.2**	**0.83**
Cefuroxime	**57**	**43**	**0.82**
Ciprofloxacin	**39.5**	**60.5**	**0.00**
Cotrimoxazole	**20.7**	**79.3**	**0.94**
Genticin	**71.8**	**28.2**	**0.40**
Nitrofurantoin	**84.8**	**15.2**	**0.00**
Ampicillin/Sulbactam	**23.9**	**76.1**	**0.23**
Piperacilin/Tazobactam	**52.0**	**48.0**	**0.20**

Linear regression analysis showed that with decreasing age there was a higher likelihood of isolating the following organisms *Klebsiellaspp. p*=0.01, *Proteus spp. p*=0.03, *Staphylococcus aureusp*=0.00 and *Staphylococcus saprophyticus.*Whereas with increasing age the following was likely to be isolated, *Pseudomonas sppp*=0.00 and *Escherichia colip*=0.04 (Table 4).

TABLE 4: LINEAR REGRESSION ANALYSIS OF AGE VERSUS ORGANISMS

Organism	Coefficient	Std Error	F-test	P-Value
Klebsiellaspp	**-8.53**	**3.43**	**6.20**	**0.01**
Proteus spp	**-15.05**	**6.76**	**4.96**	**0.03**
Pseudomonas spp	**21.85**	**7.59**	**8.29**	**0.00**
Salmonella spp	**-19.22**	**13.85**	**1.93**	**0.17**
Staphylococcus aureus	**-15.43**	**4.67**	**10.92**	**0.00**
Staphylococcus epidermidis	**-8.72**	**5.94**	**2.16**	**0.14**
Staphylococcus saprophyticus	**-16.47**	**9.89**	**2.77**	**0.01**
Escherichia coli	**8.40**	**2.89**	**8.40**	**0.04**

DISCUSSION

Urinary tract infections are prevalent in clinical practice both in in-patients and out patients. In our facility urine samples for microscopy culture and susceptibility are among the most frequently requested tests. Most physicians will attend to cases of UTI often in their routine health care practice. They are also one of the most frequent clinical bacterial infections in women, accounting for nearly 25% of all infections. Around 50–60% of women will experience an episode in their lifetime [9].

We report a rate of asymptomatic bacteriuria in 10% of our patients similar to those of some studies that reported 8% of patients having asymptomatic bacteriuria.We also report a higher frequency of UTI's in females,which is the norm in literature due to the anatomic differences of male and female genito-urinary tracts. Prior studies showed that one in three females will have at least one symptomatic UTI necessitating antibiotic treatment by the age of twenty four [10]. One of the possible reasons for repeated episodes in females could be due to errors in processing urine samples, thereby reporting commensals as pathogens. In addition urine samples may not be collected properly as a result of patients

not being educated on specimen collection by the physician. The young and sexually active tend to come down with it often, but it is also seen in elderly, postmenopausal women. The likelihood of recurrence is also high in patients who have had a previous episode of a UTI[11].

We found the following to be significant risk factors for UTI – female gender, the presence of diabetes mellitus and post-operative states. Clinicians in concert with the laboratory therefore need to have a heightened sense of awareness when dealing with urine samples from these patients.

The pathogens causing UTI are consistent across the globe. We report a preponderance of *Escherichia coli*, followed by *Klebsiellaspp* and *Staphylococcus aureus*. These findings also mirror those of other studies showing that the microbial ecology of urinary pathogens has largely remained the same. [12]

Enteric bacteria (in particular, *Escherichia coli*) have been and remain the most frequent cause of UTI, although there is some evidence in certain reports that the percentage of UTIs caused by *E. coli* is decreasing this does not appear to be the scenario in our hospital. A different study from ours showed the percentage of UTIs caused by *E. coli, Proteus* species, and *Pseudomonas species* decreasing, whereas the percentage of UTIs caused by yeasts, group B streptococci, and *Klebsiella pneumoneae* increased [13].

A retrospective analysis of UTI at Jos in Nigeria by Jombo et al, revealed that the commonest pathogens in outpatients was *Escherichia coli*, while in in-patients it was *Klebsiella spp*, with the Quinolones and Cefuroxime the most effective antibiotics in-vitro[14].

Other pathogens such as *Pseudomonas spp* and *Proteus spp* are often recovered from patients who are catheterized. *Pseudomonas aeruginosa* is an opportunistic human pathogen that is especially adept at forming surface-associated biofilms. It causes catheter-associated urinary tract infections (CAUTIs) through biofilm formation on the surface of indwelling catheters and it has high rates of therapeutic failure[15].

Catheter-associated UTI is the most common nosocomial infection, accounting for over a million cases in hospitals. The catheterization rate from our study was 34% which happens to be less than that reported by similar centers which report figures as high as 54%. The risk of UTI increases with increasing duration of catheterization. In non-institutionalized elderly populations, UTIs are the second most common form of infection, accounting for nearly 25% of all infections [5, 16].

Catheter associated UTI also extends hospital stay and adds to the direct cost of acute care hospitalization. It is associated with increased mortality. A Study on Catheterization rates suggested that nosocomial CAUTI are associated with substantially increased mortality rates. It is therefore important to accurately define the local epidemiology of CA-UTI [17].

Complications may arise from UTI's especiallyif bacteria enter the blood stream, they could cause severe complications, including septicemia, shock and, rarely, death. Conversely there may also be hematogenous spread of bacteria from the bloodstream into the kidney causing UTI's in patients who are hospitalized, catheterized or who have undergone genitourinary surgery[8, 18, 19]. In uncomplicated cases the infection is easily treated with a short course of an antibiotic, but in recent times there is increased resistance to many of these antibiotics resulting in treatment failure. Uncomplicated UTI should be distinguished from complicated UTI, which has a risk of severe illness and attendant effects such as renal scarring [20].

For the treatment of UTI's the Physician should be guided by the results of diagnostic tests and recent antimicrobial susceptibility of urinary pathogens also because the microbiologic characteristics of acute, uncomplicated UTI are highly predictable in women, antimicrobial therapy is usually empiric. As a result of this a short-course (3-day) therapy is commonly used, however practices may vary with fluoroquinolones in non-pregnant females preferred by[21]. The Infectious Diseases Society of America (IDSA) advocates trimethoprim-sulfamethoxazole (SXT) as initial therapy for females with acute uncomplicated bacterial cystitis in settings where the prevalence of SXT resistance does not exceed 10 to 20%.Our figure is 79.3% which is quite high. This guideline may not be suitable for Nigeria. Reports from elsewhere show that the resistance rates to SXT is unacceptably high and organisms such as *Enterococcus spp* are intrinsically resistant to it [22].

Other alternatives for short term therapy of UTI's include the use of Trimethoprim or Nitrofurantoin which were successful in over 80% of the cases. Nitrofurantoin appears to still retain high success rates even in this era of increasing antimicrobial resistance as evidenced from the high rates of susceptibility by pathogens. Cotrimoxazole on the other hand has disappointingly low rates of susceptibility and in some centers. Cotrimoxazole is not considered a first-choice drug for UTI [22].

Patients with frequent urinary tract infection ought to be placed on prophylactic antibiotics, which can be

patient-initiated, post-coital, or long-term low-dose therapy. Females with recurrent urinary tract infection in pregnancy should be considered for long-term antibiotic prophylaxis. In addition long term suppression of infection may include fiveday courses of β-lactams such as Co-Amoxiclav or Nitrofurantoin depending largely on local susceptibility patterns[22, 23].

CONCLUSION

Urinary tract infections are important causes of morbidity in our environment; and care needs to be placed on the diagnosis and management of such infections. The prevalent pathogens in our environment are the Gram negative bacilli: *Escherichia coli* and *Klebsiella pneumoneae*. Nitrofurantoin however still retains efficacy to both Gram negative and positive organisms.

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