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Antibiotic Activity Assessment of Bacterial Strains Isolated from Urine Samples at Butare University Teaching Hospital (Buth) Laboratory.

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Abstract

Urinary tract infections (UTI) are common worldwide and affect all sexes and age groups. An estimated 20% or more of the female population suffers from some form of UTIs in their lifetime. Although antibiotics are the first choice of treatment for many urinary tract infections, antibiotic-resistant strains of bacterial species commonly associated with UTIs, are increasing worldwide. The purpose of this study was to determine the pathogen antimicrobial sensitivity trends of bacterial pathogens associated with UTIs. A retrospective study was carried out on bacteria isolated from the urine of patients at the BUTH laboratory between January 2006 and December 2010. A total of 1611 pathogens have been found. The most commonly isolated bacteria were Escherichia coli (876 strains), Klebsiella Species (190 strains), Coagulase negative Staphylococcus (114 strains), Streptococcus species (97 strains), Proteus species (90 strains) and staphylococcus aureus (86 strains). Most of isolates were resistant to aminopenicillins (ampicillin and amoxicillin) and to trimethoprim- sulfamethoxazole (TMP-SMZ). Strains were rarely resistant to more expensive antibiotics (imipenem and cefotaxime). The most effective antibiotic to almost all isolates was imipenem, which is not commonly used in treatment of UTIs in Rwanda. The rate of amoxicillin and trimethoprim-sulfamethoxazole resistance to Enterobacteriaceae implies that another antibiotic should be used for empirical treatment and that there is a need for new generic drugs in Rwanda. Imipenem could be included as a reasonable alternative for the therapy of UTIs in Rwanda.

Keywords: *Assessment, Antibiotics, Activity, BUTH.*

Introduction

The development of antibiotics completely revolutionized medicine in the second half of the 20th century. Now modern medicine relies on these drugs for treatment and prevention of bacterial infections. The preservation of the activity of antibiotics remains at the present time a condition for the progress of medicine. However, an increasing rate of resistance of bacterial pathogens to antibiotics cause a growing concern worldwide (1, 2).

Urinary tract infections (UTI) are some of the most common human infectious diseases caused by bacteria. These infections affect all age groups of people including men, women and children. Bacteria isolated from urine are becoming resistant to antimicrobials worldwide. It is estimated that 20% or more of the female population suffers from some form of UTIs in their lifetime. In young men, UTIs are rare while in the elderly, they are more common due to enlargement of the prostate gland (prostatic hypertrophy) (3, 4). Studies indicate that a single bladder catheterization carries an infectious risk of 1%, and at least 10% of patients with indwelling catheters become infected (3). UTIs account for more than 7 million of cystitis, 250,000 of pyelonephritis and *E.coli* accounts for more than 90% of the estimated number in the USA (3).

Although antibiotics are the first treatment choice for urinary tract infections, antibiotic-resistant strains of the most common cause of UTIs, are increasing worldwide. In Europe, urinary tract pathogens identification and susceptibility to 12 antimicrobials indicated *Escherichia coli* accounted for 77.0% of isolates. Fourty two of *E.coli* isolates were resistant to one or more of the 12 antimicrobial drugs investigated (5). Resistance was most common to ampicillin (29.8%) and sulfamethoxazole (29.1%), followed by trimethoprim (14.8%), trimethoprim/sulfamethoxazole (14.1%) and nalidixic acid (5.4%) (5, 6).

In many cases, majority of UTIs are treated empirically and antibiotics are given before the final diagnosis results are available. A study done by Mambo *et al*. reported that β -lactams, Trimethoprim/sulfamethoxazole (TMP-SMZ), nitrofurantoin and ciprofloxacin should no longer be used as empirical treatments of

UTI in Rwanda because of their high rate of resistance. A resistance rate ranging from 70 % to 90 % has been reported to TMP-SMZ (2). The purpose of the present study was to determine the causative agents of UTIs and their susceptibility patterns to antibiotics at Butare University Teaching Hospital (BUTH) laboratory. The findings will provide a basis for treatment and management of UTIs, and formulate health policies for importation, supply and use of antimicrobial agents.

Material And Methods

This was a retrospective study carried out on all of the bacterial strains isolated from urine culture of out-patients and inpatients who attended the Butare University Teaching Hospital (BUTH) laboratory with a suspected UTI between January 2006 and December 2010. Bacterial susceptibility testing was performed by disk diffusion method. In this test a standardized suspension of a particular bacterial strain is inoculated onto a solid media to which different antibiotics are applied. After an overnight incubation, the bacterial growth around each disc is observed. If the bacterial strain is susceptible to a particular antibiotic, a clear zone of no growth will be observed around that particular disk. Any zone diameters of inhibition around the disks are measured and the results are reported as indicating susceptibility or resistance of the microorganism to each antimicrobial agent tested. Data were collected from registers of antibiogram of the bacteriology service of BUTH. Microsoft Excel 2007 was used to enter, store and analyze the data.

Results

Table 1 shows that more than 70% of isolates were Enterobacteriaceae. The most frequent isolated species was *E. coli* (54.37%), followed by *Klebsiella* species (11.8%), *coagulase negative Staphylococcus* (7.07%), *Streptococcus* species (6.02%) and then *Staphylococcus aureus* (5.34%).

The results in Table 2 shows that isolates of *E.coli* were mostly sensitive to imipenem (98.52%), fluoroquinolones (levofloxacin, 94.28% and ciprofloxacin, 75.8%), cephalosporins (ceftazime, 88.28% and cefotaxime, 89.06%) and nitrofurantoin (78.44%).

High resistance rates were detected with oxacillin (88.88%), trimethoprim-sulfamethoxazole (81.13%), sulfamethoxazole (81.25%), erythromycin (81.58%) and trimethoprim (80%).

Table 1. : Bacteria species isolated and identified from urine culture

Table 2. : Antibiotic susceptibility patterns of *E. coli*

	YEAR						
BACTERIA	***2006***	***2007***	***2008***	***2009***	***2010***	***Total***	***%***
E.coli	38	95	230	264	249	**876**	**54.37**
Klebsiella spp	6	30	50	64	40	**190**	**11.8**
Coagulase negative Staphylococcus	4	0	46	25	39	**114**	**7.07**
Streptococcus spp	0	3	19	34	41	**97**	**6.02**
Proteus spp	1	14	31	34	10	**90**	**5.58**
Staphylococcus aureus	2	14	14	31	25	**86**	**5.34**
Enterococcus	0	4	12	20	10	**46**	**2.85**
Neisseria gonorrhoea	0	1	4	9	24	**38**	**2.35**
Enterobacter spp	0	1	11	9	8	**29**	**1.8**
Acinetobacter	0	0	1	6	10	**17**	**1.05**
Citrobacter spp	1	0	8	3	0	**12**	**0.74**
Pseudomonas spp	2	0	2	2	2	**8**	**0.49**
Shigella	0	0	1	0	1	**2**	**0.12**
Providencia	0	0	0	0	2	**2**	**0.12**
Salmonella typhi	0	0	1	0	1	**2**	**0.12**
Serratia	0	0	0	0	1	**1**	**0.062**
Eduardsiella	0	0	0	0	1	**1**	**0.062**
Total	54	162	430	501	464	1611	100

ANTIBIOTICS	***Isolates (n)***	***Sensitive n (%)***	***Resistant n (%)***	***Intermediate n (%)***
Chloramphenicol	689	369(53.55)	305(44.26)	15(2.17)
Tetracycline	385	92(23.89)	284(73.76)	9(2.33)
TMP-SMZ	583	106(18.18)	473(81.13)	4(0.68)
Ampicilline	389	63(16.19)	315(80.97)	11(2.82)
Amoxicillin	244	42(17.21)	194(79.5)	8(3.27)

Cefotaxime	686	611(89.06)	71(10.35)	4(0.58)
Ciprofloxacin	690	524(75.8)	163(23.62)	4(0.58)
Penicilline	16	6(37.75)	10(62.5)	0(0)
Nitrofurantoin	667	524(78.44)	76(11.4)	67(10.04)
Naldixic acid	805	524(65.1)	275(34.16)	6(0.74)
Oxacillin	36	4(11.11)	32(88.88)	0(0)
Gentamicin	592	228(38.62)	257(43.4)	107(18.07)
Erythromycin	38	5(13.16)	31(81.58)	2(5.26)
Lincomycine	46	11(29.91)	32(69.56)	3(6.52)
Amikacin	305	136(44.59)	106(34.75)	63(20.65)
Kanamycine	309	117(37.86)	146(47.25)	46(14.88)
Cephalothin	175	41(23.43)	112(64)	22(12.57)
Bacitracine	5	1(20)	4(80)	0(0)
Vancomycine	20	3(15)	16(80)	1(5)
Ceftazidine	111	98(88.28)	11(9.91)	2(1.8)
Sulfamethoxazole	96	14(14.58)	78(81.25)	4(4.16)
Trimethoprim	70	14(20)	56(80)	0(0)
Amoxicillin-Clavulanic acid	130	51(39.23)	60(44.12)	19(14.61)
Imipenem	68	67(98.52)	1(1.147)	0(0)
Novobiocine	8	1(12.5)	6(75)	1(12.5)
Levofloxacin	35	33(94.28)	1(2.86)	1(2.86)

The results of sensitivity and resistance of isolated *Klebsiella* strains to different antibiotics are shown in Table 3. The most effective antibiotics were imipenem (100%), ciprofloxacin (67.76%) and cefotaxime (65.75). Increased resistance of *Klebsiella* isolates to other antibiotics was observed but high resistance rates were detected with vancomycin (100%), aminopenicillins (ampicillin, 97.59% and amoxicillin, 86.3%) and erythromycin (87.5%).

Table 3. : Antibiotic susceptibility patterns of *Klebsiella* species

ANTIBIOTICS	*Isolates (n)*	*Sensitive n (%)*	*Resistant n (%)*	*Intermediate n (%)*
Chloramphenicol	149	61(40.94)	88 (59.06)	0 (0)
Tetracycline	92	34 (36.96)	56 (60.87)	2 (2.17)
TMP-SMZ	113	31(27.43)	81 (71.68)	1 (0.88)
Ampicillin	83	2 (2.41)	81 (97.59)	0 (0)
Amoxicillin	73	8 (10.96)	63 (86.3)	2 (2.74)
Cefotaxime	146	96(65.75)	46 (31.5)	4 (2.74)
Ciprofloxacin	152	103 (67.76)	46 (30.26)	3 (1.97)
Penicillin	5	0 (0)	5 (100)	0 (0)
Nitrofurantoin	147	70 (47.62)	69 (46.94)	8 (5.44)
Naldixic acid	174	113 (64.94)	61 (35.06)	0 (0)
Oxacillin	6	0 (0)	5 (83.33)	1 (16.67)
Gentamicin	112	40 (35.71)	61 (54.46)	11 (9.82)
Erythromycin	8	1 (12.5)	7 (87.5)	0 (0)
Lincomycine	7	1 (14.28)	5 (71.43)	1 (14.28)
Amikacin	83	46 (55.42)	24 (28.91)	13 (15.66)
Kanamycine	72	29 (40.27)	33 (45.83)	10 (13.89)
Cephalothin	41	8 (19.51)	32 (78.05)	1 (2.44)
Vancomycine	4	0 (0)	4 (100)	0 (0)
Levofloxacin	5	2 (40)	3 (80)	0 (0)
Ceftazidine	28	18 (64.28)	9 (32.14)	1 (3.57)
Sulfamethoxazole	28	8 (28.57)	20 (71.43)	0 (0)
Trimethoprim	21	7 (33.33)	14 (66.67)	0 (0)
Amoxicillin-clavulanic acid	29	16 (55.17)	12 (41.38)	1 (3.45)
Imipenem	15	15 (100)	0 (0)	0 (0)
Novobiocine	4	1 (25)	3 (75)	0 (0)

Among gram positive, *coagulase negative Staphylococcus* were the most isolated (See Table 1). They were mostly sensitive to imipenem (100%), levofloxacin (100%), cephalothin (87.5%), amikacin (88.63%), kanamycin (74.4%) and ciprofloxacin (76.25%). High resistance rates were detected with trimethoprim (100%) and nalidixic acid (85.15%) as shown in Table 4.

Table 4. : Antibiotic susceptibily patterns of coagulase negative *Staphylococcus*

ANTIBIOTICS	*Isolates (n)*	*Sensitive n (%)*	*Resistant n (%)*	*Intermediate n %)*
Chloramphenicol	87	50 (57.47)	37 (42.53)	0 (0)
Tetracycline	38	19 (50)	19 (50)	0 (0)
TMP-SMZ	80	32 (40)	47 (58.75)	1 (1.25)
Ampicillin	30	16 (57.14)	11 (39.28)	1 (3.57)
Amoxicillin	29	22 (75.86)	7 (24.14)	0 (0)
Cefotaxime	87	63 (72.4)	21 (24.14)	3 (3.45)
Ciprofloxacin	83	64 (77.1)	18 (21.7)	1 (1.2)
Penicillin	92	51 (55.43)	38 (41.3)	3 (3.26)
Nitrofurantoin	68	57 (83.82)	10 (14.7)	1 (1.47)
Naldixic acid	101	12 (11.88)	86 (85.15)	3 (2.97)
Oxacillin	89	27 (30.34)	58 (65.17)	4(4.5)
Gentamicin	76	56 (73.68)	19 (25)	1 (1.32)
Erythromycin	81	52 (64.2)	29 (35.8)	0 (0)
Lincomycine	65	48 (73.8)	14 (21.53)	3 (4.6)
Amikacin	45	40 (88.9)	4 (8.9)	1 (2.22)
Kanamycine	43	32 (74.4)	10 (23.25)	1 (2.32)
Cephalothin	24	21 (87.5)	3 (12.5)	0 (0)
Vancomycine	26	16 (61.54)	11 (42.31)	0 (0)
Ceftazidine	18	8 (44.44)	7 (38.9)	3 (16.67)
Sulfamethoxazole	6	4 (66.67)	2 (33.33)	0 (0)
Trimethoprim	5	0 (0)	5 (100)	0 (0)
Amoxicillin-clavulanic acid	12	9 (75)	3 (25)	0 (0)
Imipenem	6	6 (100)	0 (0)	0 (0)
Novobiocine	24	17 (70.83)	7 (29.17)	0 (0)
Levofloxacin	9	9 (100)	0 (0)	0 (0)

Other gram positive bacteria which were isolated were *Streptococcus* species. They were sensitive to amoxicillin-clavulanic acid (100%), imipenem (100%) and cefotaxime (84.93%). High resistance rates were detected with sulfamethoxazole (100%), nalidixic acid (92.16%), trimethoprim (80%), TMP-SMZ (82.08%), and aminoglycosides (amikacin, 79.17% and gentamicin, 75.95%) as shown in table 5.

Table 5. : Antibiotic susceptibility patterns of *Streptococcus* species

ANTIBIOTICS	*Isolates (n)*	*Sensitive n (%)*	*Resistant n (%)*	*Intermediate n (%)*
Chloramphenicol	86	64(74.41)	22(25.59	0(0)
Tetracycline	32	19(59.37)	13(40.62)	0(0)
TMP-SMZ	68	12(17.65)	56(82.35)	0(0)
Ampicillin	23	18(78.26)	3(13.04)	2(8.7)
Amoxicillin	20	13(65)	7(35)	0(0)
Cefotaxime	75	64(85.33)	11(14.67)	0(0)
Ciprofloxacin	82	49(59.76)	33(40.24)	0(0)
Penicillin	83	61(73.5)	21(25.3)	1(1.2)
Nitrofurantoin	36	23(63.9)	13(36.1)	0(0)
Naldixic acid	51	4(7.84)	47(92.16)	0(0)
Oxacillin	81	19(23.46)	59(72.84)	3(3.7)
Gentamicin	78	17(21.8)	60(76.9)	1(1.28)
Erythromycin	79	53(67.1)	25(31.6)	1(1.26)
Lincomycine	51	30(58.82)	21(41.18)	0(0)
Amikacin	25	4(16)	20(80)	1(4)
Kanamycine	25	7(28)	17(68)	1(4)
Cephalothin	19	14(73.68)	4(21.05)	1(5.26)
Bacitracine	19	4(21.05)	15(78.95)	0(0)
Vancomycine	41	31(75.61)	10(24.39)	0(0)
Ceftazidine	5	4(80)	1(20)	0(0)
Sulfamethoxazole	12	0(0)	12(100)	0(0)
Trimethoprim	6	1(16.67)	5(83.33)	0(0)
Amoxicillin-clavulanic acid	12	12(100)	0(0)	0(0)
Imipenem	9	9(100)	0(0)	0(0)
Novobiocine	35	20(57.14)	15(42.86)	0(0)

Table 6 indicates susceptibilily results of *Proteus* species to antibiotics. The most effective antibiotics for treatment of *Proteus* species were imipenem (94.12%), ciprofloxacin (75%), and ceftazidime (77.78%). High resistance rates were detected with levofloxacin (100%), sulfamethoxazole (88.24%), trimethoprim (90%), ampicillin (86.67%), chloramphenicol (85.07%), tetracycline (84.32%), and TMP-SMZ (81.58%).

Table 6. : Antibiotic susceptibility patterns of *Proteus* species

ANTIBIOTICS	*Isolates (n)*	*Sensitive n (%)*	*Resistant n (%)*	*Intermediate n (%)*
Chloramphenicol	67	9 (13.43)	57 (85.07)	1 (1.5)
Tetracycline	51	8 (15.68)	43 (84.32)	0 (0)
TMP-SMZ	38	7 (18.42)	31 (81.58)	0 (0)
Ampicillin	45	6 (13.33)	39 (86.67)	0 (0)
Amoxicillin	36	6 (16.67)	30 (83.33)	0 (0)
Cefotaxime	69	48 (69.56)	21 (30.44)	0 (0)
Ciprofloxacin	72	54 (75)	17 (23.61)	1 (1.39)
Nitrofurantoin	79	22 (27.85)	54 (68.35)	3 (3.8)
Naldixic acid	85	47 (55.29)	37 (43.53)	1 (1.18)
Oxacillin	4	0 (0)	4 (100)	0 (0)
Gentamicin	53	19 (35.85)	29 (54.72)	5 (9.43)
Amikacin	37	17 (45.95)	17 (45.95)	3 (8.1)
Kanamycine	37	7 (18.92)	25 (67.56)	5 (13.51)
Cephalothin	32	8 (25)	22 (68.75)	2 (6.25)
Levofloxacin	2	0 (0)	2 (100)	0 (0)
Ceftazidine	18	14 (77.78)	4 (22.22)	0 (0)
Sulfamethoxazole	17	2 (11.76)	15 (88.24)	0 (0)
Trimethoprim	10	1 (10)	9 (90)	0 (0)
Amoxicillin-Clavulanic acid	14	5 (35.71)	9 (64.29)	0 (0)
Imipenem	17	16 (94.12)	1 (5.88)	0 (0)

Staphylococcus aureus was sensitive to levofloxacin (100%), imipenem (91.67%), cefotaxime (87.69%), amikacin (88), kanamycin (81.5%), and ciprofloxacin (80.08%). High resistance rates of *Staphylococcus aureus* were detected with nalidixic acid (84.31%), penicillin (80.9%), oxacillin (70.6%), TMP-SMZ (68.63%), and trimethoprim (66.67%) as shown in Table 7.

Table 7 : Antibiotics susceptibility patterns of *Staphylococcus aureus*

ANTIBIOTICS	*Isolates (n)*	*Sensitive n (%)*	*Resistant n (%)*	*Intermediate n (%)*
Chloramphenicol	66	45 (68.2)	21 (31.8)	0 (0)
Tetracycline	45	26 (57.78)	18 (40)	1 (2.22)
TMP-SMZ	51	16 (31.37)	35 (68.63)	0 (0)

Ampicillin	17	6 (35.3)	11 (64.7)	0 (0)
Amoxicillin	13	9 (69.23)	4 (30.77)	0 (0)
Cefotaxime	65	57 (87.69)	7 (10.77)	1 (1.54)
Ciprofloxacin	74	60 (80.08)	12 (16.2)	2 (2.7)
Penicillin	68	12 (17.65)	55 (80.9)	1 (1.47)
Nitrofurantoin	47	34 (72.34)	12 (25.53)	1 (2.13)
Naldixic acid	51	8 (15.69)	43 (84.31)	0 (0)
Oxacillin	68	15 (22.06)	48 (70.6)	5 (7.35)
Gentamicin	60	43 (71.67)	12 (20)	5 (8.33)
Erythromycin	69	42 (60.9)	25 (36.23)	2 (2.9)
Lincomycine	42	29 (69.04)	10 (23.81)	3 (7.14)
Amikacin	25	22 (88)	2 (8)	1 (4)
Kanamycine	27	22 (81.5)	2 (7.4)	3 (11.11)
Cephalothin	17	13 (76.47)	2 (11.76)	2 (11.76)
Vancomycine	28	15 (53.57)	11 (39.3)	2 (7.14)
Ceftazidine	10	6 (60)	3 (30)	0 (0)
Sulfamethoxazole	12	4 (33.33)	8 (66.67)	0 (0)
Trimethoprim	5	2 (40)	3 (60)	0 (0)
Amoxicillin-Clavulanic acid	10	8 (80)	2 (20)	0 (0)
Imipenem	12	11 (91.67)	1 (8.33)	0 (0)
Novobiocine	18	14 (77.78	3 (16.67)	1 (5.55)
Levofloxacin	4	4 (100)	0 (0)	0 (0)

Other Gram positive bacteria encountered during the study were *Enterococcus species*. They were sensitive to amoxicillin-clavulanic acid (83.33%), cefotaxime (70.27%), and imipenem (62.5%). High resistance rates were observed against novobiocine (100%), trimethoprim (100%), sulfamethoxazole (100%), bacitracin (100%), nalidixic acid (81.48%) and oxacillin (81.82%) as shown in Table 8.

Table 8. : Antibiotic susceptibility patterns of *Enterococcus* species

ANTIBIOTICS	*Isolates (n)*	*Sensitive n (%)*	*Resistant n (%)*	*Intermediate n (%)*
Chloramphenicol	39	23 (58.97)	15 (38.46)	1 (2.56)
Tetracycline	19	8 (42.1)	9 (47.37)	2 (10.53)
TMP-SMZ	24	5 (20.83)	19 (79.17)	0 (0)
Ampicillin	14	7 (50)	7 (50)	0 (0)
Amoxicillin	18	9 (50)	9 (50)	0 (0)
Cefotaxime	37	26 (70.27)	10 (27.03)	1 (2.7)
Ciprofloxacin	36	15 (41.67)	19 (52.77)	2 (5.56)
Penicillin	39	19 (48.72)	20 (51.28)	0 (0)
Nitrofurantoin	22	9 (40.91)	12 (54.54)	1 (4.54)
Nalidixic acid	27	4 (14.81)	22 (81.48)	1 (3.7)
Oxacillin	33	6 (18.18)	27 (81.82)	0 (0)
Gentamicin	33	10 (30.3)	21 (63.63)	2 (6.06)
Erythromycin	34	18 (52.94)	14 (41.17)	2 (5.88)
Lincomycine	23	8 (34.78)	15 (65.22)	0 (0)
Amikacin	17	4 (23.53)	12 (70.58)	1 (5.88)
Kanamycine	17	6 (35.29)	10 (58.82)	1 (5.88)
Cephalothin	9	4 (44.44)	5 (55.56)	0 (0)
Bacitracine	2	0 (0)	2 (100)	0 (0)
Vancomycine	9	3 (33.33)	6 (66.67)	0 (0)
Ceftazidine	5	2 (40)	2 (40)	1 (20)
Sulfamethoxazole	8	0 (0)	8 (100)	0 (0)
Trimethoprim	7	0 (0)	7 (100)	0 (0)
Amoxicillin-Clavulanic acid	6	5 (83.33)	1 (16.67)	0 (0)
Imipenem	8	5 (62.5)	3 (37.5)	0 (0)
Novobiocine	6	0 (0)	6 (100)	0 (0)

The sensitivity and resistance of *Neisseria gonorrhoeae* to various antibiotics are shown in Table 9. The most effective antibiotics to *Neisseria gonorrhoeae* were ceftazidime (100%) and cefotaxime (96.55%). High resistance rates were detected with amoxicillin-clavulanic acid (100%), trimethoprim (100%), sulfamethoxazole (100%), TMP-SMZ (92.59%), nalidixic acid (88.46%) and oxacillin (87.87%).

Table 9 : Antibiotic susceptibility patterns of *Neisseria gonorrheae*

ANTIBIOTICS	*Isolates (n)*	*Sensitive n (%)*	*Resistant n (%)*	*Intermediate n (%)*
Chloramphenicol	35	27 (77.14)	7 (20)	1 (2.86)
Tetracycline	11	4 (36.36)	7 (63.64)	0 (0)
TMP-SMZ	27	1 (3.7)	25 (92.59)	1 (3.7)
Ampicillin	6	3 (50)	3 (50)	0 (0)
Amoxicillin	3	1 (33.33)	2 (66.67)	0 (0)
Cefotaxime	29	28 (96.55)	1 (3.45)	0 (0)
Ciprofloxacin	32	19 (59.37)	9 (28.13)	4 (12.5)
Penicillin	37	18 (48.64)	19 (51.35)	0 (0)
Nitrofurantoin	14	10 (71.43)	4 (28.57)	0 (0)
Nalidixic acid	26	2 (7.69)	23 (88.46)	1 (3.85)
Oxacillin	33	3 (9.91)	29 (87.87)	1 (3.03)
Gentamicin	29	9 (31.03)	16 (55.17)	4 (13.79)
Erythromycin	36	22 (61.11)	13 (36.11)	1 (2.78)
Lincomycine	24	9 (37.5)	14 (58.33)	1 (4.17)
Amikacin	5	2 (40)	3 (60)	0 (0)
Kanamycine	6	2 (33.33)	4 (66.67)	0 (0)
Cephalothin	5	3 (60)	2 (40)	0 (0)
Vancomycine	10	3 (30)	7 (70)	0 (0)
Ceftazidine	3	3 (100)	0 (0)	0 (0)
Sulfamethoxazole	3	0 (0)	3 (100)	0 (0)
Trimethoprim	2	0 (0)	2 (100)	0 (0)
Amoxicillin-Clavulanic acid	6	0 (0)	6 (100)	0 (0)
Imipenem	4	1 (25)	3 (75)	0 (0)
Novobiocine	12	2 (16.67)	8 (66.67)	2 (16.67)

Acinetobacter species were susceptible to imipenem (100%), aminoglycosides (amikacin, 100% and kanamycin, 100%) and ciprofloxacin (87.5%) (Table 10). High resistance rates were observed with amoxicillin-clavulanic acid (100%), cephalothin (100%), ampicillin (100%), and nitrofurantoin (75%).

Table 10. : Antibiotic susceptibility patterns of *Acinetobacter*

ANTIBIOTICS	*Isolates (n)*	*Sensitive n (%)*	*Resistant n (%)*	*Intermediate n (%)*
Chloramphenicol	13	5 (38.46)	8 (61.54)	0 (0)
Tetracycline	5	4 (80)	1 (20)	0 (0)
TMP-SMZ	11	5 (45.45)	6 (54.55)	0 (0)
Ampicillin	4	0 (0)	4 (100)	0 (0)
Amoxicillin	4	3 (75)	1 (25)	0 (0)
Cefotaxime	12	7 (58.33)	5 (41.67)	0 (0)
Ciprofloxacin	16	14 (87.5)	2 (12.5)	0 (0)
Nitrofurantoin	8	1 (12.5)	6 (75)	1 (12.5)
Naldixic acid	13	8 (61.54)	4 (30.77)	1 (7.69)
Gentamicin	13	8 (61.54)	4 (30.77)	1 (7.69)
Amikacin	4	4 (100)	0 (0)	0 (0)
Kanamycine	3	3 (100)	0 (0)	0 (0)
Cephalothin	2	0 (0)	2 (100)	0 (0)
Ceftazidine	3	1 (33.33)	2 (66.67)	0 (0)
Sulfamethoxazole	2	1 (50)	1 (50)	0 (0)
Trimethoprim	2	1 (50)	1 (50)	0 (0)
Amoxicillin-Clavulanic acid	2	0 (0)	2 (100)	0 (0)
Imipenem	1	1 (100)	0 (0)	0 (0)

Citrobacter isolates were more sensitive to ciprofloxacin (90%), cefotaxime (81.81%), and nitrofurantoin (70%) (Table 11). High resistance rates were recorded with aminopenicillins (ampicillin, 100%, and amoxicillin, 100%), penicillin (100%), oxacillin (100%) and erythromycin (100%).

Table 11 : Antibiotic susceptibility patterns of *Citrobacter* species

ANTIBIOTICS	*Isolates (n)*	*Sensitive n (%)*	*Resistant n (%)*	*Intermediate n (%)*
Chloramphenicol	8	5 (62.5)	3 (37.5)	0 (0)
Tetracycline	5	2 (40)	2 (40)	1 (20)
TMP-SMZ	7	2 (28.57)	5 (71.43)	0 (0)
Ampicillin	6	0 (0)	6 (100)	0 (0)
Amoxicillin	6	1 (16.67)	5 (83.33)	0 (0)
Cefotaxime	11	9 (81.81)	2 (18.19)	0 (0)
Ciprofloxacin	10	9 (90)	1 (10)	0 (0)
Penicillin	3	0 (0)	3 (100)	0 (0)
Nitrofurantoin	10	7 (70)	2 (20)	1 (10)

Naldixic acid	12	7 (58.33)	5 (41.67)	0 (0)
Oxacillin	4	0 (0)	4 (100)	0 (0)
Gentamicin	6	2 (33.33)	2 (33.33)	2 (33.33)
Erythromycin	1	0 (0)	1 (100)	0 (0)
Lincomycine	3	2 (66.67)	1 (33.33)	0 (0)
Amikacin	6	4 (66.67)	1 (16.67)	1 (16.67)
Kanamycine	4	2 (50)	1 (25)	1 (25)
Cephalothin	5	1 (20)	4 (80)	0 (0)
Ceftazidine	4	2 (50)	2 (50)	0 (0)
Sulfamethoxazole	2	0 (0)	1 (50)	1 (50)

The most effective antibiotics for treatment to *Pseudomonas species* were ciprofloxacin tested to only three isolates which were 100% sensitive, aminoglycosides (gentamicin, 80% and amikacin, 66.67%) (Table 12). High resistance rates were observed with trimethoprim (100%), TMP-SMZ (83.33%), aminopenicillins (amoxicillin, 100% and ampicillin, 100%), kanamycin (100%), cephalothin (100%) and tetracycline (100%).

Table 12 : Antibiotic susceptibility patterns of *Peudomonas* species

ANTIBIOTICS	*Isolates (n)*	*Sensitive n (%)*	*Resistant n (%)*	*Intermediate n (%)*
Chloramphenicol	6	0 (0)	5 (83.33)	1 (16.67)
Tetracycline	3	0 (0)	3 (100)	0 (0)
TMP-SMZ	6	1 (16.67)	5 (83.33)	0 (0)
Ampicillin	3	0 (0)	3 (100)	0 (0)
Amoxicillin	1	0 (0)	1 (100)	0 (0)
Cefotaxime	5	1 (20)	1 (20)	3 (80)
Ciprofloxacin	3	3 (100)	0 (0)	0 (0)
Nitrofurantoin	5	1 (20)	4 (80)	0 (0)
Naldixic acid	7	2 (28.57)	5 (71.43)	0 (0)
Gentamicin	5	4 (80)	1 (20)	0 (0)
Amikacin	3	2 (66.67)	1 (33.33)	0 (0)
Kanamycine	1	0 (0)	1 (100)	0 (0)
Cephalothin	1	0 (0)	1 (100)	0 (0)
Sulfamethoxazole	1	0 (0)	0 (0)	1 (100)
Trimethoprim	1	0 (0)	1 (100)	0 (0)
Amoxicillin-Clavulanic acid	1	0 (0)	0 (0)	1 (100)
Imipenem	2	1 (50)	0 (0)	1 (50)

Discussion and Conclusion

This was a retrospective study carried out on all of the bacterial spicies isolated from urine culture of out-patients and inpatients who attended the Butare University Teaching Hospital (BUTH) laboratory with a suspected UTI between January 2006 and December 2010.

Escherichia coli was the most prevalent pathogen isolated (54.37%) as it was found in previous studies (2, 7, 8, 9). However, cases of *E. coli* are slowly declining in Rwanda compared to that in some other countries. A related study in Madagascar found that *E.coli* comprised 67.2% of total isolates (8) while in another study done in Poland, *E.coli* comprised 83.7% of all isolates (9).

Escherichia coli was susceptible to drugs like imipenem and fluoroquinolones (levofloxacin and ciprofloxacin), cephalosporins (ceftazidine, cefotaxime) and nitrofurantoin. Even though isolates of *E.coli* were susceptible to these mentioned drugs, their susceptibility is known to be decreasing. In a similar study done in the same laboratory, nitrofurantoin was 96% active compared to 78.44% in the present study and ciprofloxacin was 98.69% active compared to 75.8% in the present study (10). The activity of aminoglycosides to *E.coli* was extremely decreased; comparing present findings with earlier studies obtained in the same laboratory, gentamicin (38.62% vs. 92%), and amikacin (44.59% vs. 94.5%). Reduced activity of ciprofloxacin and nitrofurantoin might be due to the misuse of these drugs by the population. These drugs can be bought over the counter without prescription at low prices compared to cephalosporins and carbapenems which were highly active. Another contributing factor to the reduced activity of these drugs is that in many situations they are dispensed by non-professionals with inadequate or no knowledge of dosage regimens, indications or contraindications. Aminoglycosides are supposed to be administered intravenously under prescription only in hospitals to reduce cases of misuse.

In the present study, a higher proportion of strains of *E .coli* were resistant to oxacillin (88.88 %), trimethoprim-sulfamethoxazole (81.13 %) and amoxicillin (79.5 %). The phenomenon of increased resistance to TMP-SMZ and amoxicillin is similar to that observed in Madagascar (8). These antibiotics are commonly used in Rwanda

because they are cheap and easily available. Their extensive use explains the high selection pressure towards drugs and subsequent emergence of resistant bacteria strains. Conversely, many bacterial strains are rarely resistant to more expensive drugs (2).

Bacterial species in the family of Enterobacteriaceae (See Table 2, 3, 6 and 10) were sensitive to imipenem, fluoroquinolones (ciprofloxacin or levofloxacin) and cephalosporins (cefotaxime or ceftazidime). The high susceptibility to imipenem reported in the study was an indication that carbapenems resistance is yet to be fully established in species of the family of Enterobacteriaceae in Rwanda. Cefotaxime and ceftazidime are usually available in hospitals which makes the drugs not easily accessible to the general public.

Even though ciprofloxacin was among the most effective drug against members of Enterobacteriaceae family, the activity of this drug was reduced compared to its previous activity (10). Our findings compared to previous reported activity of Enterobacteriaceae to ciprofloxacin were *Klebsiella* species (67.76% vs. 100%), *Proteus* species (75% vs. 100%), *Acinetobacter* (87.5% vs. 97.84%) and *Citrobacter* (90% vs. 100%). The decline in activity of ciprofloxacin activity could be due to the misuse of the drug, to the low price and availability of this drug. Another possible contributing factor could be the use of suboptimal doses of drug, inability to complete prescribed doses, and manufacture and distribution of substandard counterfeit drugs. If not adequately addressed there is indication that bacterial resistance to ciprofloxacin is likely to increase in the near future and pose major challenge to UTIs treatment.

Gram-positive cocci were susceptible to the major drugs used on these species except *Enterococci* germs which were resistant to many antibiotics. *Coagulase negative staphylococci* were mostly sensitive to imipenem (100 %) and levofloxacin (100 %). High resistance rates were detected with trimethoprim (100 %), nalidixic acid (85.15 %) and oxacillin (65.17 %). *Staphylococcus aureus* were mostly sensitive to levofloxacin (100 %), imipenem (91.67 %), cefotaxime (87.69 %), amikacin (88 %), kanamycin (81.5 %), and ciprofloxacin (80.08 %). High resistance rates of *Staphylococcus aureus* germs

were detected with nalidixic acid (84.31 %), penicillin (80.9 %), oxacillin (70.6 %) and TMP-SMZ (68.63 %). The resistance of *Staphylococcus aureus* was reported by previous researchers (11).

The high susceptibility to imipenem recorded is an indication that carbapenems resistance is not fully established in *Staphylococci* issociated with UTI in Rwanda. The high susceptibility (See Table 2, 3, 6 and 10) of imipenem to gram negative bacteria can be explained by the infrequent use of the antibiotic in the developing world because of its cost and limited availability (2).

Streptococci were sensitive to amoxicillin-clavulanic acid (100 %), imipenem (100 %) and cefotaxime (85.33 %). High resistance rates were detected to sulfamethoxazole (100 %), nalidixic acid (92.16 %), trimethoprim (83.33 %), TMP-SMZ (82.35 %), and aminoglycosides (amikacin and gentamicin with 80 % and 76.9 % respectively). Based on the literature, the agents of choice in treatment of *streptococcus* infections were penicillin G and V although a decreased activity to these agents was observed. Alternative options are oral cephalosporins or macrolide antibiotics (12), although resistance to the latter is expected (for example for erythromycin 32.89% of resistance was observed).

Enterococci were mostly sensitive to amoxicillin-clavulanic acid (83.33 %), cefotaxime (70.27 %), and imipenem (62.5 %). High resistance rates were observed to other antibiotics, more particularly to novobiocine (100 %), trimethoprim (100 %), sulfamethoxazole (100 %), bacitracin (100 %), nalidixic acid (81.48 %) and oxacillin (81.82 %). *Enterococci* frequently develop resistance to antibiotics (12).

Neisseria gonorrhoeae and *Pseudomonas* species were other gram negative isolated in BUTH laboratory. The most effective antibiotics to *Neisseria gonorrhoeae* were ceftazidine (100 %) and cefotaxime (96.55 %). High resistance rates were detected with other tested antibiotics, particularly to amoxicillin-clavulanic acid (100 %), trimethoprim (100 %), sulfamethoxazole (100 %), TMP-SMZ (92.59 %), nalidixic acid (88.46 %) and oxacillin (87.87 %). A previous study found that *N. gonorrhoeae* is sensitive to many antibiotics, including penicillin and ciprofloxacin. However, resistance to these

agents is spreading worldwide and penicillinase-producing *N. gonorrhoeae* is fairly common (13). Fluoroquinolones were typically effective against *N. gonorrhoeae*, although resistance to these drugs is also spreading based on findings of the present study (nalidixic acid, 88.46% and ciprofloxacin, 28.13% of resistance).

In conclusion, the study findings indicated commonly used antibiotics for the treatment of UTI in Rwanda were not very full efficacious. Nitrofurantoin, amoxicillin, TMP-SMZ, and naldixic acid should no longer be used as first-line treatment of uncomplicated UTIs in Rwanda. Ciprofloxacin and some of cephalosporins (cephalothin and ceftazidime) should no longer be relied upon as first-line treatment of complicated UTIs in Rwanda. We suggest that antimicrobial agent such as imipenem could be alternative therapy for uncomplicated UTI, and should be introduced in the national guidelines for UTI treatment. Imipenem should be used in empirical treatment and as first-line drug in treatment of UTIs in Rwanda.

Cefotaxime and ciprofloxacin were effective to some of gram negative species (*E.coli*, *Klebsiella*, *N. gonorrhoeae*, *Enterobacter*, *Citrobacter*) and to most of Gram positive (*Staphylococcus aureus*, Coagulase negative *Staphylococcus* and *Streptococcus* species). For this reason these drugs should be used as second line in treatment of UTIs in Rwanda. Even though ciprofloxacin was effective to many isolates, resistance to the drug is increasing in Rwanda. The study highlights the need for the research and development of new antimicrobial agent.

The efficacy of aminoglycosides used in hospitals in case of serious UTIs, is on the decline especially for gentamicin, amikacin and kanamycin. These use of these drugs should be reduced and withdraw as first-line and in empirical treatment of UTIs in Rwanda. It is suggested that these drugs should be used only when antibiogram results indicate sensitivity of isolated germs to the drug.

Nitrofurantoin, one of the drugs of choice in treatment of UTIs was effective to some of germs isolated including *E.coli* and *Citrobacter* species. Although the activity of this drug decreased in the past decade, it is still effective to *E. coli* (10). Nitrofurantoin can be

included in second-line drugs treating uncomplicated UTIs in Rwanda. The drug is applicable in pregnancy and is tolerated by the body compared to other drugs such as aminoglycosides and TMP-SMZ which may have serious adverse drug reactions. Another reason is that this drug is not expensive.

We recommend that the findings form a basis for a more detailed multicentric study on antimicrobial resistance in Rwanda. National policies for antimicrobial drugs sourcing, supply and rational use should be formulated with regard to current emerging antimicrobial resistance trends. There is urgent need to formulate public health education for patients and general public on inappropriate use and importance of compliance with instructions on medical use of antimicrobials.

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