Antimicrobial resistance patterns of uropathogens isolated between 2012 and 2017 from a tertiary hospital in Northern Ethiopia

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A R T I C L E   I N F O

A B S T R A C T

Objectives: Urinary tract infections (UTIs) are one of the most common infections in humans. Studies have shown that antibiotics for UTIs are usually prescribed empirically before the results of urine culture are available. The aim of the study was to assess the antimicrobial resistance patterns of bacteria isolated from urine samples over 6 years in Ayder Comprehensive Specialized Hospital (ACSH), in Mekelle, Northern Ethiopia.

Methods: A retrospective study of culture results of UTI samples was conducted in ACSH from January 2012 to December 2017. Data were collected using a structured data sheet format and were analysed using SPSS v.20.0.

Results: Among 1080 urine samples tested during the 6-year period, 308 (28.5%) were positive for bacterial isolates. The majority of participants were female (57.8%). The three most commonly isolated bacteria were *Escherichia coli* (48.1%), *Klebsiella pneumoniae* (16.2%) and *Pseudomonas aeruginosa* (6.5%). *Escherichia coli* was found to be most susceptible to imipenem (100%) and most resistant to ampicillin (94.9%). Similarly, *K. pneumoniae* was sensitive to meropenem (100%) but resistant to penicillin (100%). Multidrug resistance to two or more antimicrobials was observed in 267 isolates (86.7%), with a non-significantly higher prevalence in females ($\chi^2 = 9.65$, $P = 0.29$). The overall pooled bacterial resistance was 57.8%.

Conclusion: This study revealed that most of the urine isolates showed high levels of antimicrobial resistance to commonly prescribed antibiotics although they remained susceptible to imipenem, nitrofurantoin and meropenem. The results call for continuous surveillance of antimicrobial resistance for better management of patients with UTIs.

1. Introduction

Urinary tract infections (UTIs) are one of the most common bacterial infections and account for nearly 7 million office visits and 1 million emergency department visits, resulting in 100 000 hospitalisations, according to the 1997 United States National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey [1]. Globally, approximately 150 million people are diagnosed with UTI each year, costing the global economy in excess of $US6 billion [2]. UTIs include infections of the kidney, ureter, bladder and urethra, usually due to bacteria originating from the digestive tract [3,4]. These bacteria comprise the normal flora of the skin, genital area and anus as well as microbes from exogenous sources through poor sanitary habits and include *Escherichia coli*, *Staphylococcus saprophyticus*, *Citrobacter* spp., *Enterobacter aerogenes*, *Pseudomonas aeruginosa*, *Proteus vulgaris*, *Klebsiella* spp., *Staphylococcus aureus* and *Salmonella* spp. [2].

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UTIs can occur both in male and female patients [5] although they are more frequent in women [1]. It has been reported that 20% of women experience at least a single UTI episode during their lifetime and approximately 3% have more than one episode of UTI per year [2]. This has been attributed to the close proximity of the genital tract and short urethra, pregnancy, catheterisation and sexual intercourse [1,2]. UTIs elevate the risk of pyelonephritis, premature delivery and fetal mortality among pregnant women, and are associated with impaired renal function and end-stage renal disease among paediatric patients [1,6].

Studies have shown that antibiotics are usually prescribed empirically before the results of urine culture are available [7,8]. However, recent reports have shown increasing resistance to commonly used antibiotics [9,10]. Widespread use of antibiotics, together with the length of time over which they have been available, have led to major problems associated with the emergence of antimicrobial-resistant organisms and it is known that antimicrobial resistance can increase complications and costs associated with procedures and treatments [6].

Hence, it is necessary to monitor the rising drug resistance of uropathogens on a regular basis as this will be helpful for the appropriate selection of antimicrobial agents, thereby reducing nosocomial infections due to the emergence of drug-resistant pathogens [2]. Cognisant of this fact, the current study aimed to investigate the antimicrobial resistance patterns of uropathogens at Ayder Comprehensive Specialized Hospital (ACSH), a tertiary hospital in Mekelle, Northern Ethiopia, collected over 6 years.

2. Materials and methods

2.1. Ethical considerations

Ethical clearance was obtained from the Ethical Review Board of the College of Health Sciences of Mekelle University. Permission for data collection was requested and approved from the Office of Medical Director of ACSH. To ensure confidentiality, the name and other patient identifiers were not used in any of the documents.

2.2. Study inclusion criteria

All patients attending the ACSH Microbiology Laboratory from January 2012 to December 2017 who had not received antimicrobials within the previous 15 days were eligible for urine culture. All bacterial isolates underwent antimicrobial susceptibility testing.

2.3. Antimicrobial susceptibility testing

Antimicrobial susceptibility testing of the isolates was performed by the Kirby–Bauer disk diffusion test on Mueller–Hinton agar [11] for the following antimicrobial agents: tetracycline (30 μg); nitrofurantoin (300 μg); chloramphenicol (30 μg); gentamicin (10 μg); ciprofloxacin (5 μg); doxycycline (30 μg); trimethoprim/sulfamethoxazole (SXT) (25 μg); imipenem (10 μg); ceftriaxone (30 μg); ceftazidime (30 μg); cefepime (30 μg); meropenem (10 μg); ampicillin (10 μg); amoxicillin/clavulanic acid (AMC) (20/10 μg); norfloxacin (10 μg); and penicillin G (10 IU) (Oxoid Ltd., Basingstoke, UK). Resistance data were interpreted according to the National Committee for Clinical and Laboratory Standards (NCCLS) guidelines [12].

2.4. Data analysis

Data analysis was performed using IBM SPSS Statistics v.20.0 (IBM Corp., Armonk, NY). Descriptive statistics such as frequency,

percentage, mean and standard deviation were employed to summarise patient characteristics and other related information. The χ^2 test was used to compare the proportion of bacterial isolates by patient sex and age and for comparison of antimicrobial resistances. A P-value of <0.05 was considered to be statistically significant.

3. Results

3.1. Patient demographic characteristics

Of the total 1080 urine cultures tested during the 6-year period (2012–2017), 308 samples (28.5%) were found to be positive for bacterial isolates. The majority of positive samples were obtained from females (57.8%). The mean patient age was 33.1 years (range 1–87 years). The overall infection rate was highest in the age group 16–35 years (36.0%) (Table 1).

3.2. Proportion of isolated uropathogens

The number of samples cultured in each year tended to increase from 2012 to 2015. The highest percentage of uropathogens (37.0%) was isolated in 2015, followed by 2016 (23.4%). On the other hand, the lowest proportion (3.9%) was recorded during 2012 (Fig. 1).

This study revealed that the internal medicine department presented the highest proportion of uropathogens (39.6%), followed by paediatrics (20.5%) in the 6-year period. A significant proportion of isolates (16.2%) was also found in private clinics in Mekelle city (Fig. 2). The three most commonly isolated bacteria were *E. coli* (48.1%), *Klebsiella pneumoniae* (16.2%) and *P. aeruginosa* (6.5%), whereas *Acinetobacter* spp. (2.3%) was found to be least prevalent (Fig. 3).

3.3. Antimicrobial resistance patterns of uropathogens

This study revealed 100% resistance of uropathogens to ampicillin, tetracycline, doxycycline, ceftriaxone and gentamicin in 2012 and to penicillin in 2012, 2016 and 2017 (Table 2). The mean percentage resistance was also calculated and it was found that ampicillin (93%), penicillin (83%) and tetracycline (78%) had the highest mean percentage resistance, whilst nitrofurantoin (5%) and chloramphenicol (29%) had the lowest mean percent resistance in the 6-year period (Table 2).

In this study, *E. coli* showed significant resistance to all antibiotics to various degrees, except for imipenem and nitrofurantoin. *Escherichia coli* showed high resistance rates (>80%) to ampicillin, AMC and tetracycline. *Klebsiella pneumoniae* was resistant to all antibiotics except meropenem and imipenem. Similarly, *P. aeruginosa* was susceptible only to ceftazidime, imipenem and nitrofurantoin (Fig. 4; Table 3). The overall bacterial resistance was 57.8% (Table 3).

Table 1
Sociodemographic characteristics of the study participants (*n* = 308).

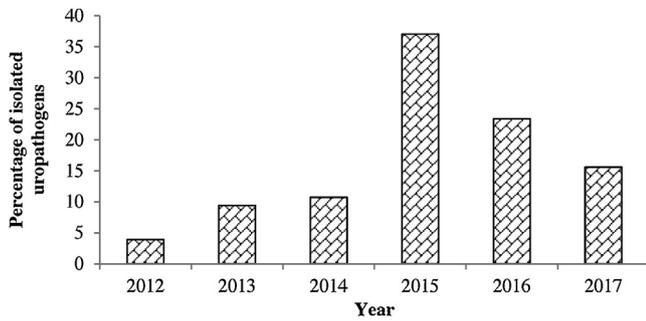| Characteristic	n (%)
Sex	
Female	178 (57.8)
Male	130 (42.2)
Age	
<5 years	51 (16.6)
5–15 years	33 (10.7)
16–35 years	111 (36.0)
36–55 years	28 (9.1)
>55 years	85 (27.6)

Fig. 1. Proportion of uropathogen isolates ($n = 308$) from January 2012 to December 2017 in Ayder Comprehensive Specialized Hospital (Mekelle, Northern Ethiopia).
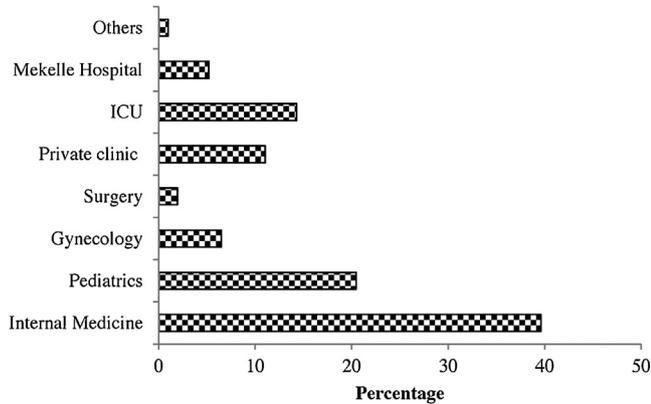

Fig. 2. Proportion of uropathogen isolates ($n = 308$) in different departments of Ayder Comprehensive Specialized Hospital (ACSH) (Mekelle, Northern Ethiopia). Mekelle Hospital is a regional general hospital in Mekelle affiliated with ACSH. ICU, intensive care unit.

In this study, the overall resistance rates to two or more antimicrobials was 86.7% (267/308), and only 3.6% of isolates (11/308) were susceptible to all antimicrobials tested. Resistance rates to two and more antimicrobial agents were 90.5%, 92.0% and 70.0% for *E. coli*, *K. pneumoniae* and *P. aeruginosa*, respectively (Table 4).

4. Discussion

UTIs cause a huge burden on healthcare systems owing to the high prevalence of infections both in community and hospital settings [13]. Effective management of patients with bacterial UTIs commonly relies on identification of the causative organism and selection of an effective antibiotic agent by continuous surveillance of antimicrobial susceptibility patterns of uropathogens in particular regions [14]. We believe that the results of the current study provide some insight into the antimicrobial resistance patterns in Africa where there is a limited amount of antimicrobial resistance surveillance data.

In this study, 308 samples (28.5%) were found to be positive out of the total 1080 urine cultures tested during the 6-year period (January 2012 to December 2017). The majority of positive samples were from females (57.8%), in accordance with other studies [15–17]. Physiological and anatomical differences account for the discrepancy between males and females. This is because of the fact that, compared with females, the drier environment in the urethra of males prevents optimal growth of bacteria. The antimicrobial activity of prostate secretions and the longer distance between the anus and urethra meatus are also among the factors responsible for the differences in prevalence between the two sexes [18].

In this 6-year study, the internal medicine department (39.6%), followed by paediatrics (20.5%) presented the highest proportion
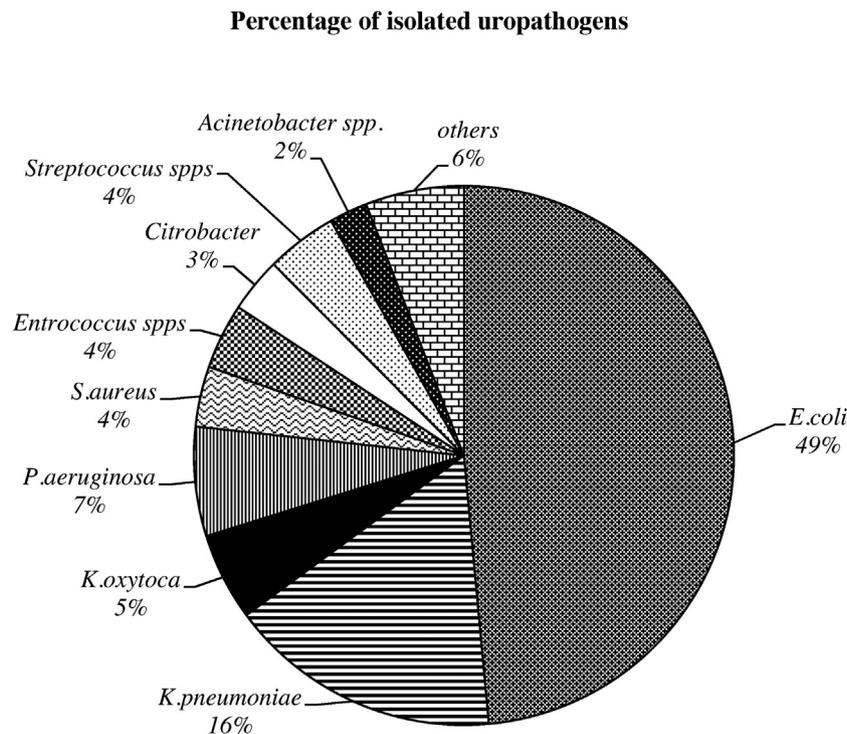
Percentage of isolated uropathogens

Fig. 3. Percentage distribution of different uropathogens isolated from urine sample in Ayder Comprehensive Specialized Hospital (Mekelle, Northern Ethiopia).

Table 2
Percentage resistance to different antimicrobial agents of uropathogens isolated between January 2012 and December 2017 in Ayder Comprehensive Specialized Hospital (Mekelle, Northern Ethiopia).

Antimicrobial	2012		2013		2014		2015		2016		2017		Mean % resistance
	#T	%R	#T	%R	#T	%R	#T	%R	#T	%R	#T	%R	
Ampicillin	11	100	24	96	23	96	90	94	69	91	46	80	93
AMC	3	33	13	85	9	78	49	92	24	83	23	65	73
Cefepime	ND	ND	ND	ND	ND	ND	ND	ND	1	0	19	68	68
Ceftazidime	ND	ND	ND	ND	ND	ND	ND	ND	4	25	19	63	44
Ceftriaxone	1	100	10	30	5	60	11	55	2	0	10	70	53
Chloramphenicol	1	0	15	0	10	50	84	51	27	44	11	27	29
Ciprofloxacin	8	38	17	53	21	48	72	68	53	53	33	48	51
SXT	ND	ND	6	67	10	30	69	87	45	80	22	73	67
Doxycycline	4	100	9	56	11	64	24	71	30	73	2	0	61
Gentamicin	4	100	10	20	15	47	81	47	48	35	13	54	51
Imipenem	ND	ND	ND	ND	ND	ND	32	6	ND	ND	ND	ND	6
Meropenem	1	0	ND	ND	ND	ND	ND	ND	2	0	20	20	10
Nitrofurantoin	9	0	12	0	18	6	77	13	40	3	34	6	5
Norfloxacin	6	33	16	56	7	57	5	60	20	60	ND	ND	53
Penicillin	5	100	5	60	5	60	25	76	4	100	2	100	83
Tetracycline	3	100	5	60	21	76	76	75	62	82	34	76	78

#T, number of isolates tested against each antimicrobial agent; %R, percentage of isolates resistant to the antimicrobial agent; AMC, amoxicillin/clavulanic acid; SXT, trimethoprim/sulfamethoxazole; ND, not done.
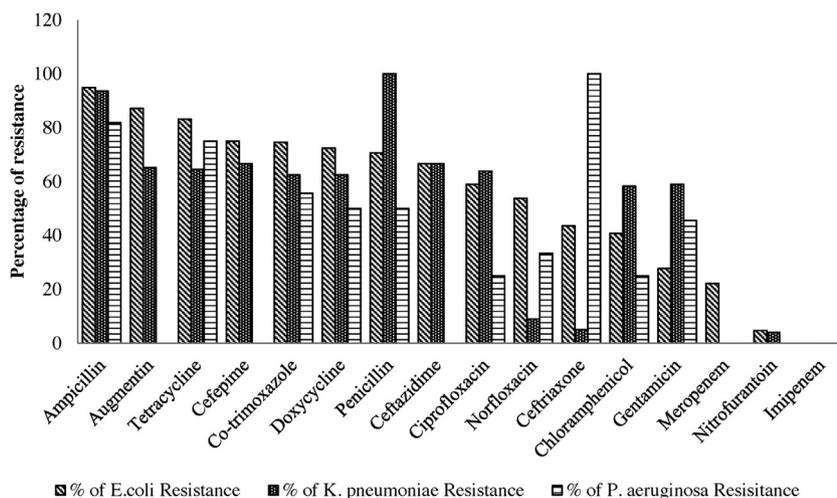

Fig. 4. Percentage resistance pattern of the three most prevalent isolated uropathogens in Ayder Comprehensive Specialized Hospital (Mekelle, Northern Ethiopia).

of uropathogens. This differs from a study by Sarasu and Rani in 2017 where the paediatrics department presented the highest proportion [19].

It was also found that the three most common pathogens isolated from positive urine cultures were *E. coli* (48.1%), *K. pneumoniae* (16.2%) and *P. aeruginosa* (6.5%). Other studies also showed that the most common uropathogens were *E. coli* and *K. pneumoniae* [2,18]. This could possibly be due to the fact that Gram-negative bacteria are abundantly present in the urinary tract. Also, uropathogenic strains of *E. coli* are believed to display a variety of virulence properties that help them to colonise the host mucosal surfaces and circumvent host defences to allow invasion of the normally sterile urinary tract [20].

The current study showed that *E. coli* was susceptible to imipenem, nitrofurantoin and meropenem. Susceptibility of *E. coli* to nitrofurantoin was 89.7%, comparable with a study in London, UK (94%) [21]. Nitrofurantoin is effective against many Gram-positive and Gram-negative uropathogens and the activity of this antimicrobial is greatly enhanced at pH ≤ 5.5. Most enterococcal

isolates are susceptible to nitrofurantoin and can be used prophylactically for recurrent UTIs. *Klebsiella pneumoniae* was susceptible to meropenem (100%) and nitrofurantoin (83.3%) but was resistant to penicillin (100%) and ampicillin (93.6%) and intermediate to gentamicin (18.5%) and AMC (17.4%). *Pseudomonas aeruginosa* was susceptible to nitrofurantoin (85.7%) but resistant to ampicillin (81.8%), similar to a study conducted in Pakistan [22].

Most isolates of Gram-negative bacteria were resistant to two or more drugs (multidrug-resistant) compared with Gram-positive isolates. Similar results were reported from a study conducted in other parts of the country [23]. This indicates that multidrug resistance is increasingly becoming a major problem in the management of uropathogens in Ethiopia. This raises alarms to implement nationwide antimicrobial surveillance and susceptibility testing with proper culture-based diagnosis of UTIs and with strict adherence to antibiotic policy to inhibit the spread of drug-resistant micro-organisms in the country.

Given the increased incidence of antimicrobial resistance in UTIs, bacterial culture remains an important test in the diagnosis of

Table 3
Pooled antimicrobial resistance patterns of uropathogens isolated in Ayder Comprehensive Specialized Hospital (Mekelle, Northern Ethiopia).

Antimicrobial	*Escherichia coli*		*Klebsiella pneumoniae*		*Klebsiella oxytoca*		*Pseudomonas aeruginosa*		*Staphylococcus aureus*		*Enterococcus* spp.		*Citrobacter* spp.		*Streptococcus* spp.		*Acinetobacter* spp.	
	Tt	R n (%)	Tt	R n (%)	Tt	R n (%)	Tt	R n (%)	Tt	R n (%)	Tt	R n (%)	Tt	R n (%)	Tt	R n (%)	Tt	R n (%)
Ampicillin	136	129 (94.9)	47	44 (93.6)	15	13 (86.7)	11	9 (81.8)	5	3 (60.0)	8	5 (62.5)	10	10 (100.0)	9	9 (100.0)	6	5 (83.3)
AMC	70	61 (87.1)	23	15 (65.2)	3	3 (100.0)	ND	ND	2	1 (50.0)	ND	ND	ND	ND	3	3 (100.0)	2	2 (100.0)
Cefepime	8	4 (50.0)	3	2 (66.7)	3	1 (33.3)	ND	ND	ND	ND	2	1 (50.0)	ND	ND	2	0	1	1 (100.0)
Ceftazidime	6	4 (66.7)	6	4 (66.7)	4	2 (50.0)	1	0	1	1 (100.0)	ND	ND	2	1 (50.0)	2	1 (50.0)	ND	ND
Ceftriaxone	23	10 (43.5)	2	1 (50.0)	ND	ND	4	4 (100.0)	ND	ND	ND	ND	ND	ND	2	1 (50.0)	ND	ND
Chloramphenicol	76	31 (40.8)	24	14 (58.3)	4	0	4	1 (25.0)	9	0	8	3 (37.5)	2	1 (50.0)	5	1 (20.0)	5	1 (20.0)
Ciprofloxacin	100	59 (59.0)	36	23 (63.9)	10	4 (40.0)	12	3 (25.0)	6	3 (50.0)	9	6 (66.7)	7	4 (57.14)	7	5 (71.5)	5	3 (60.0)
SXT	75	56 (74.7)	8	5 (62.5)	9	6 (66.7)	9	5 (55.6)	4	4 (100.0)	5	5 (100.0)	5	2 (40.0)	5	4 (80.0)	2	2 (100.0)
Doxycycline	40	29 (72.5)	16	10 (62.5)	3	0	4	2 (50.0)	3	2 (66.7)	3	3 (100.0)	ND	ND	4	2 (50.0)	2	1 (50.0)
Gentamicin	87	24 (27.6)	27	16 (59.3)	8	4 (50.0)	11	5 (45.5)	7	3 (42.9)	2	2 (100.0)	5	1 (20.0)	6	0	5	1 (20.0)
Imipenem	13	0	8	0	1	0	1	0	1	1 (100.0)	3	1 (33.3)	1	0	ND	ND	ND	ND
Meropenem	9	2 (22.2)	4	0	3	1 (33.3)	ND	ND	1	0	2	1 (50.0)	ND	ND	1	0	1	1 (100.0)
Nitrofurantoin	107	5 (4.7)	24	1 (4.2)	9	2 (22.2)	7	0	3	0	9	1 (11.1)	2	1 (50.0)	8	0	2	0
Norfloxacin	26	14 (53.8)	10	9 (90.0)	3	1 (33.3)	6	2 (33.3)	1	0	ND	ND	3	2 (66.7)	1	1 (100.0)	1	0
Penicillin	17	12 (70.6)	3	3 (100.0)	ND	ND	4	2 (50.0)	5	5 (100.0)	ND	ND	1	1 (100.0)	5	4 (80.0)	1	1 (100.0)
Tetracycline	95	79 (83.2)	31	20 (64.5)	13	9 (69.2)	8	6 (75.0)	6	5 (83.3)	8	5 (62.5)	7	6 (85.7)	10	7 (70.0)	5	5 (100.0)
Overall antimicrobial resistance of individual bacterium	888	519 (58.4)	272	167 (61.4)	88	46 (52.3)	82	39 (47.6)	54	28 (51.9)	59	33 (55.9)	45	29 (64.4)	70	38 (54.3)	38	23 (60.5)
Overall antimicrobial resistance of all isolated and tested bacteria							Total tested, 1596				*n* (%) resistant, 922 (57.7%)							

Tt, total number of tested bacterial strains; R n (%), number (%) resistant; AMC, amoxicillin/clavulanic acid; ND, not done; SXT, trimethoprim/sulfamethoxazole.

Table 4
Multiple antimicrobial resistance patterns of uropathogens in Ayder Comprehensive Specialized Hospital (Mekelle, Northern Ethiopia).

Isolate	Antibiogram [*n* (%) resistant][a]								
	R0	R1	R2	R3	R4	R5	R6	R7	R8
Escherichia coli (*n* = 148)	2 (1.4)	12 (8.1)	25 (16.9)	28 (18.9)	42 (28.4)	23 (15.5)	11 (7.4)	5 (3.4)	0
Klebsiella pneumoniae (*n* = 50)	1 (2.0)	3 (6.0)	10 (20.0)	7 (14.0)	11 (22.0)	10 (20.0)	5 (10.0)	2 (4.0)	1 (2.0)
Klebsiella oxytoca (*n* = 16)	1 (6.3)	4 (25.0)	1 (6.3)	0	3 (18.8)	5 (31.3)	2 (12.5)	0	0
Pseudomonas aeruginosa (*n* = 20)	3 (15.0)	3 (15.0)	8 (40.0)	3 (15.0)	1 (5.0)	1 (5.0)	1 (5.0)	0	0
Staphylococcus aureus (*n* = 11)	0	2 (18.2)	3 (27.3)	3 (27.3)	2 (18.2)	0	1 (9.1)	0	0
Enterococcus spp. (*n* = 12)	2 (16.7)	1 (8.3)	1 (8.3)	1 (8.3)	3 (25.0)	3 (25.0)	1 (8.3)	0	0
Citrobacter spp. (*n* = 10)	0	0	2 (20.0)	2 (20.0)	6 (60.0)	0	0	0	0
Streptococcus spp. (*n* = 13)	1 (7.7)	1 (7.7)	3 (23.1)	3 (23.1)	2 (15.4)	2 (15.4)	1 (7.7)	0	0
Acinetobacter spp. (*n* = 7)	0	0	1 (14.3)	3 (42.9)	3 (42.9)	0	0	0	0
Other (*n* = 21)	1 (4.8)	4 (19.0)	4 (19.0)	1 (4.8)	4 (19.0)	3 (14.3)	2 (9.5)	2 (9.5)	0
Total (*n* = 308)	11 (3.6)	30 (9.7)	58 (18.8)	51 (16.6)	77 (25.0)	47 (15.3)	24 (7.8)	9 (2.9)	1 (0.3)

[a] R0, susceptible to all antimicrobials tested; R1–R8, resistant to one to eight antimicrobials, respectively.

UTIs. This method is necessary for determination of the identity of the infecting micro-organism(s) for antimicrobial susceptibility testing. Moreover, it helps to document infection and allows an estimate of the level of bacteriuria [24,25].

5. Conclusion

The predominant bacterial isolates in the present study were *E. coli*, *K. pneumoniae* and *P. aeruginosa*. Most of the isolates showed high levels of antimicrobial resistance to commonly prescribed drugs such as ampicillin, norfloxacin and SXT. Hence, alternative antibiotics should be used for the treatment of UTIs instead of the drugs that were found to have the highest resistance. Some of the factors that need to be considered when changing therapy include cost and safety of the antibiotic in the target population. There is no guarantee, however, that the new standard of care will not lead to the emergence of new resistant strains unless strict policy on the appropriate use of these 'precious' antibiotics is implemented at all levels of the health system. In addition, we call for continuous surveillance of antimicrobial resistance for better management of patients with UTI. Finally, we recommend using culture-based diagnosis for UTI.

Competing interests

None declared.

Ethical approval

Ethical clearance was obtained from the Ethical Review Board of the College of Health Sciences, Mekelle University [ref. no. ERC 1255/2018]. Permission for data collection was requested and approved from the Office of Medical Director of ACSH. To ensure confidentiality, the name and other patient identifiers were not used in any of the documents.

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