

Renal Data from the Arab World

Microbiological Spectrum and Antibigram of Urinary Tract Infection in a Tertiary Care Center from the Kingdom of Bahrain

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ABSTRACT. Urinary tract infection is the second-most common after respiratory infections. This is a single-center retrospective study conducted in Bahrain Specialist Hospital, Bahrain. Urine culture data from November 2011 until December 2020 was obtained from the hospital database. Out of 28082, 4849 (17.3%) cultures were positive. One hundred and thirty-four (2.8%) showed the growth of multiple organisms. The male-to-female ratio was 3.7. Most of the patients [1872 (39.7%)] were 20–40 years. Men and women were 53.84 ± 25.85 and 43.41 ± 23.89 years, respectively; $P < 0.001$. 4118/4715 (87.3%) were Gram-negative. Five hundred and sixty-four (11.9 %) and 33 (0.7%) were Gram-positive cocci and fungi, respectively. *Escherichia coli* (*E. coli*) was the most common and *Klebsiella* species were second-most common, accounting for 2916 (61.8%) and 586 (12.4%), respectively. 30.2% of all *E. coli* and 130 (22.2%) of all *Klebsiella* species were extended-spectrum beta-lactamase (ESBL) producers. ESBL *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Enterococcus faecalis* were present more in inpatients ($P < 0.001$). *P. aeruginosa* was found more in women ($P < 0.001$). *E. coli* was resistant to cotrimoxazole, ciprofloxacin, and levofloxacin in 28%, 17.3%, and 18.1%, respectively. ESBL *E. coli* and ESBL *K. pneumoniae* were resistant to amoxicillin-clavulanate, cotrimoxazole, ciprofloxacin, and levofloxacin in 73.8%, 62.3%, 62.4%, 58.4% and 68.2%, 62.6%, 55.7%, and 41.8% respectively. There is a high incidence of ESBL *E. coli* and ESBL *K. pneumoniae*. There is alarmingly increased resistance of *P. aeruginosa* to carbapenems. Amoxicillin-clavulanate, cefixime, and cefuroxime are suitable oral antibiotics for empirical treatment. For sick patients, piperacillin-tazobactam, aminoglycosides, and carbapenems should be considered. Antibiotic stewardship is the need of an hour.

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Introduction

Urinary tract infections (UTIs) are among the most commonly encountered community-acquired infections that mandate empirical antimicrobial therapy. This has contributed to the worldwide increase of antibacterial resis-

tance within Enterobacteriaceae, specifically the main uropathogen *Escherichia coli* (*E. coli*).¹ Such spread of antibiotic-resistant uropathogens has limited the use of most of the oral front-line antibiotics as empirical therapeutic options for UTI.²⁻⁴ The rate of multidrug resistance among uropathogenic *E. coli* (UPEC) isolates shows wide variabilities across different geographic regions⁵ and is of particular concern in developing countries where the capacity for regular resistance surveillance is limited and over-the-counter drug purchase (including antibiotics) is rampant in the community.^{6,7} Further, things are made worse by the use of antibiotics in food industry. The study was undertaken to find out the microbiological profile of UTI in the Kingdom of Bahrain and the pattern of antibiotic sensitivity, to guide for the empirical therapy while awaiting culture sensitivity results.

Methods

This is a single-center retrospective study conducted in Bahrain Specialist Hospital, a tertiary care center from the Kingdom of Bahrain. The record of all the urine cultures done from November 2011 until December 2020 was obtained from the hospital database and analyzed. The study was approved by the hospital ethics committee.

Statistical Analysis

Continuous variables are presented as mean $\pm$ standard deviation. The Chi-square test is used to compare categorical variables. Mann-Whitney *U*-test is used to compare non-parametric continuous variables. Statistical analysis was performed using IBM SPSS Statistics for Windows version 25.0 (IBM Corp., Armonk, NY, USA).

Results

A total of 28,082 urine samples were analyzed during the study period. Four thousand and eight hundred forty-nine (17.3%)

samples showed the growth of organisms. One hundred and thirty-four out of 4849 (2.8%) showed growth of multiple organisms, concerning for contamination and were excluded from the analysis. Women and men accounted for 3821 (81%) and 894 (19%) (Ratio-3.7:1) cases, respectively. Most of the patients were in the age group of 20–40 years, accounting for 1872 (39.7%) of all cases. The mean age for men and women was 53.84 ± 25.85 and 43.41 ± 23.89 years respectively ($P < 0.001$). Most involved men were in the age group of 60–80 years and women in the age group of 20–40 years. Gram-negative bacilli accounted for 4118/4715 (87.3%) of all infections. Gram-positive cocci and fungi accounted for 564 (11.9 %) and 33 (0.7%) of all cases, respectively. In men and women, Gram-negative infections accounted for 81.8% (724) and 89.3% (3393), respectively. *E. coli* was the most common organism grown, accounting for 2916 (61.8%) of all cases. Extended-spectrum beta-lactamase (ESBL) *E. coli* accounted for 30.2% of all *E. coli*. *Klebsiella* species were the second most common Gram-negative bacilli grown, accounting for 586 (12.4%) of all cases. ESBL *Klebsiella pneumoniae* accounted for 130 (22.2%) of all *Klebsiella* species grown. Overall, ESBL organisms accounted for 974 (20.6% of all cases). *Pseudomonas* species and *Acinetobacter baumannii* were the most common Gram-negative bacilli grown from the nonfermenters group accounting for 77.2% and 17.9% of the nonfermenters group and 173 (3.7%) and 40 (0.8%) of all cases, respectively. *Enterococcus faecalis* followed by Group B streptococcus, and *Staphylococcus saprophyticus* were the most common Gram-positive cocci cultured, accounting for 323 (57.3%), 74 (13.1%), and 36 (6.4%) of all Gram-positive cocci cultured, respectively. Gram-positive infections were significantly higher in men ($P < 0.001$). ESBL *K. pneumoniae*, *Pseudomonas aeruginosa*, and *E. faecalis* was present in 4.8%, 9.7%, and 10.5% of inpatients as against 2.5%, 2.4%, and 6.0%, respectively of outpatients ($P < 0.001$). *P. aeruginosa* was found in 8.2% and 2.6% of

females and males, respectively; ($P < 0.001$). *E. coli* was resistant to cotrimoxazole, ciprofloxacin, and levofloxacin in 28%, 17.3%, and 18.1%, respectively. ESBL *E. coli* was resistant to amoxicillin-clavulanate, cotrimoxazole, ciprofloxacin, and levofloxacin 73.8%, 62.3%, 62.4%, and 58.4%, respectively. *K. pneumoniae* was sensitive to amoxicillin-clavulanate, cefixime, cefuroxime, septran, ceftriaxone, ceftazidime, piperacillin-tazobactam, ciprofloxacin, levofloxacin, amikacin, meropenem and imipenem in 87.8%, 94.6%, 92.3%, 88%, 95.9%, 95.9%, 96.8%, 92%, 90.6%, 98.2%, 98%, and 99.5% respectively. ESBL *K. pneumoniae* was resistant to amoxicillin-clavulanate, cotrimoxazole, ciprofloxacin, and levofloxacin in 68.2%, 62.6%, 55.7%, and 41.8%, respectively. Enterococcus was sensitive to penicillin, ampicillin, amoxicillin-clavulanate, vancomycin, and imipenem in 91.4%, 90.1%, 96.3%, 99.4%, and 96.7%, respectively. Results are summarized in Tables 1-3 and Figures 1-4.

Discussion

UTI is one of the leading causes of infection in the community. In our study, out of 28,082

samples, 4849 (17.3%) samples showed the growth of pathogenic organisms. Similar results were reported by Mohammed et al in a study from Libya.⁸ Women constituted 81% of all cases, consistent with several other studies,^{9,10} which demonstrated a higher incidence of UTI in women. This is attributed to the short urethra that allows easy access to bacteria from the perianal region. UTI was most common in the 20–40 years of age group. This is consistent with a study from Yadav et al, which showed the highest risk of UTI in the sexually active group.¹¹ The mean age of UTI for men was significantly higher, with men involved predominantly in the age group of 60–80 years. This is attributed to benign prostatic hypertrophy, which resulting voiding difficulties and urine stasis. Gram-negative organisms accounted for 87.3% of all cases. *E. coli* was the most common organism cultured in (61.8%) of all cases. *E. coli* was the most common organism in both men and women and outpatients and inpatients. The prevalence of *E. coli* in other studies ranges from 48% to 65%.¹² *Klebsiella* species were the second-most common Gram-negative bacilli grown, accounting for 586 (12.4%) of all cases and this is similar to other reports (8%–26%).¹³ ESBL *E. coli* accounted for 30.2% of all

Table 1. Microbiological spectrum of urinary tract infection.

Enterobacteriaceae	Number of cultures	Nonfermenters	Number of cultures
<i>E. coli</i>	2036	<i>Pseudomonas aeruginosa</i>	171
ESBL <i>E. coli</i>	880	<i>Pseudomonas putida</i>	2
<i>Klebsiella pneumoniae</i>	446	<i>Acinetobacter baumannii</i>	40
ESBL <i>Klebsiella pneumoniae</i>	130	<i>Burkholderia cepacia</i>	4
<i>Klebsiella oxytoca</i>	10	<i>Stenotrophomonas maltophilia</i>	7
<i>Proteus mirabilis</i>	161	Total	224 (4.7%)
<i>Proteus vulgaris</i>	3	Other Gram-negative bacilli	
<i>Enterobacter aerogenes</i>	87	<i>Pasturella multocida</i>	1
<i>Enterobacter cloacae</i>	40	<i>Providentia stuarti</i>	1
<i>Citrobacter koseri</i>	42	<i>Pantoea agglomerans</i>	3
<i>Citrobacter freundii</i>	8	<i>Chryseobacterium indologenes</i>	2
<i>Citrobacter youngae</i>	1	Total	7
<i>Morganella morganii</i>	22	Fungus	
<i>Serratia marcescens</i>	9	<i>Candida albicans</i>	12
<i>Serratia fonticola</i>	4	Non-candida albicans	20
Salmonella group	8	Total	32 (0.7%)
Total	3887 (82.4%)		

E. coli: *Escherichia coli*, ESBL: Extended spectrum beta-lactamase.

Table 2. Distribution of infective organisms with gender.

Organism	Male (%)	Female (%)	P
<i>E. coli</i>	267 (31.3)	1769 (46.1)	<0.001
ESBL <i>E. coli</i>	167 (19.6)	713 (18.6)	ns
<i>Klebsiella pneumoniae</i>	63 (7.4)	383 (10)	0.02
<i>Enterococcus faecalis</i>	96 (11.2)	227 (5.9)	<0.001
<i>Pseudomonas aeruginosa</i>	70 (8.2)	101 (2.6)	<0.001
<i>Proteus mirabilis</i>	42 (4.9)	119 (3.1)	0.009
<i>Klebsiella pneumoniae</i> ESBL	26 (3.0)	104 (2.7)	ns
<i>Enterobacter aerogenes</i>	20 (2.5)	67 (1.7)	ns
<i>Staphylococcus saprophyticus</i>	3 (0.4)	42 (1.1)	
<i>Citrobacter koseri</i>	19 (2.2)	23 (0.6)	<0.001
Group B Streptococcus	12 (1.4)	62 (1.6)	ns
<i>Enterobacter cloacae</i>	6 (6.7)	34 (0.9)	ns
<i>Acinetobacter baumannii</i>	2 (0.7)	38 (1.0)	
MRSE	25 (2.9)	11 (0.3)	<0.001
<i>Staphylococcus aureus</i>	5 (0.6)	31 (0.8)	ns

E. coli: *Escherichia coli*, ESBL: Extended-spectrum beta-lactamase, MRSE: *Methicillin-resistant staphylococcus epidermidis*.

E. coli. This is similar to 27.4% in another study from Bahrain.¹⁴ ESBL *K. pneumoniae* accounted for 130 (22.2%) of all *Klebsiella*. The Kingdom of Saudi Arabia reported a rate of 27%–33% of ESBL production among their community-onset UPEC,^{15,16} while in Qatar, Khan et al¹⁷ reported the occurrence of ESBL-resistant isolates among 34% of *E. coli*. Such variability of ESBL production rate among UPEC was mostly explained by the difference in the practice of antimicrobial use among

human as well as animal sectors.¹⁸ The emergence of drug-resistant *E. coli* is becoming a global concern, and infections caused by these organisms represent a major challenge to clinicians when treating community-onset UTI.¹⁹ ESBL *K. pneumoniae*, *P. aeruginosa*, and *E. faecalis* were present in 4.8%, 9.7%, and 10.5% of inpatients as against 2.5%, 2.4%, and 6.0%, respectively in outpatients. The difference was statistically significant. This suggests severe clinical

Table 3. Distribution of infecting organisms based on outpatient or inpatient status.

Organism	Outpatient (%)	Inpatient (%)	P
<i>E. coli</i>	1859 (45.4)	172 (22.9)	<0.001
ESBL <i>E. coli</i>	720 (17.6)	160 (7.5)	0.016
<i>Klebsiella pneumoniae</i>	390 (6.0)	56 (7.5)	ns
<i>Enterococcus faecalis</i>	244 (6.0)	79 (10.5)	<0.001
<i>Pseudomonas aeruginosa</i>	98 (2.4)	73 (9.7)	<0.001
<i>Proteus mirabilis</i>	145 (3.5)	18 (2.4)	ns
<i>Klebsiella pneumoniae</i> ESBL	94 (2.5)	36 (4.8)	<0.001
<i>Enterobacter aerogenes</i>	79 (1.9)	8 (1.1)	ns
<i>Staphylococcus saprophyticus</i>	44 (1.1)	1 (0.1)	
<i>Citrobacter koseri</i>	35 (0.9)	7 (0.9)	ns
Group B Streptococcus	66 (1.6)	8 (1.1)	ns
<i>Enterobacter cloacae</i>	31 (0.8)	9 (1.2)	ns
<i>Acinetobacter baumannii</i>	31 (0.8)	9 (1.2)	ns
MRSE	25 (0.6)	11 (1.5)	0.012
<i>Staphylococcus aureus</i>	36 (0.9)	0	

E. coli: *Escherichia coli*, ESBL: Extended spectrum beta-lactamase, MRSE: *Methicillin resistant staphylococcus epidermidis*.

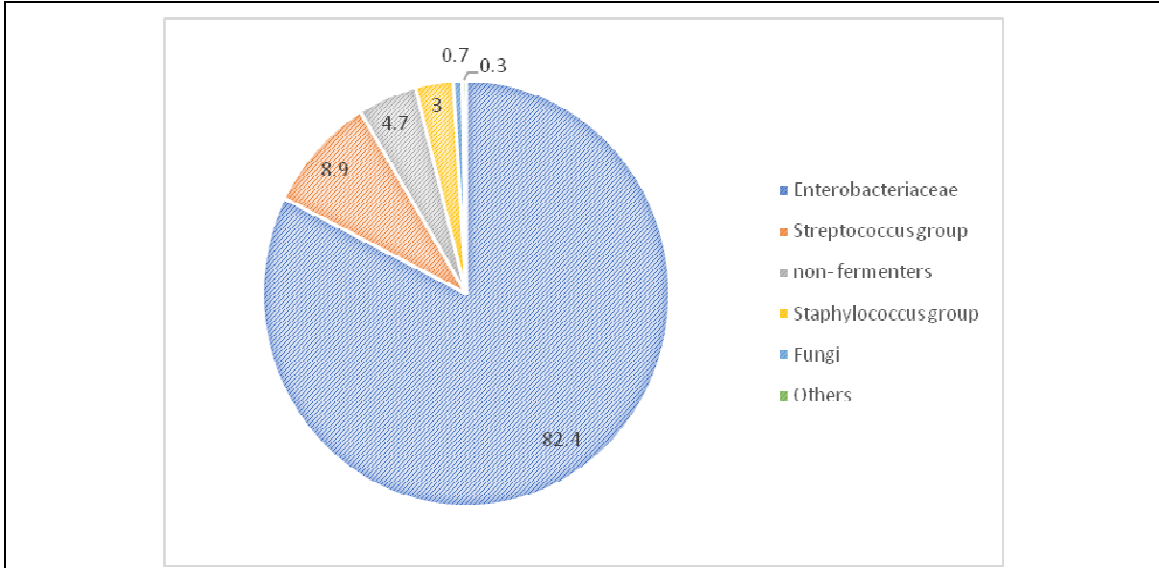


Figure 1. Percentage of organisms contributing to the microbiological spectrum.

manifestations mandating admission in patients with these infections. *P. aeruginosa* was significantly found to be higher in females as compared to men. There was no difference in the incidence of ESBL *E. coli* and ESBL *K. pneumoniae* across the gender.

There was a significant difference in the incidence of ESBL *E. coli* between inpatients and outpatients, with more cases in outpatient

than inpatient setting. This suggests a high incidence of ESBL *E. coli* in the community. An antibiogram of non-ESBL Gram-negative bacteria revealed 28% and 23.9% resistance of *E. coli* and proteus to cotrimaxole, making it unsuitable for empirical treatment of UTI. Non-ESBL *E. coli* and *P. aeruginosa* were resistant to ciprofloxacin in 17.3% and 19.2% respectively. Resistance to levofloxacin was

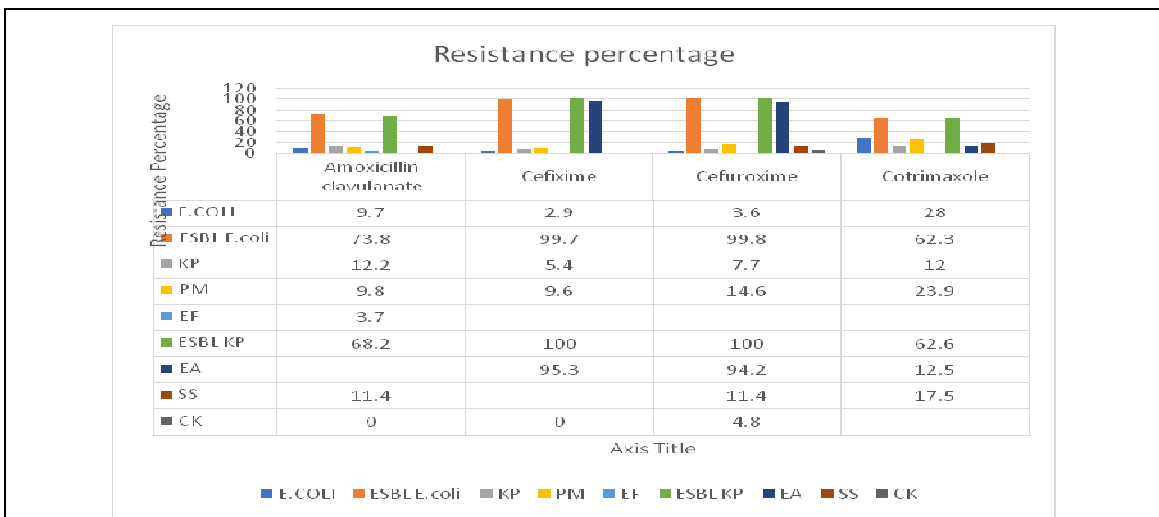


Figure 2. Percentage of organisms resistant to the test drug.

KP: *Klebsiella pneumoniae*, PM: *Proteus mirabilis*, EF: *Enterococcus faecalis*, ESBL KP: ESBL: Extended spectrum beta-lactamase *Klebsiella pneumoniae*, EA: *Enterobacter aerogenes*, SS: *Staphylococcus saprophyticus*, CK: *Citrobacter koseri*.

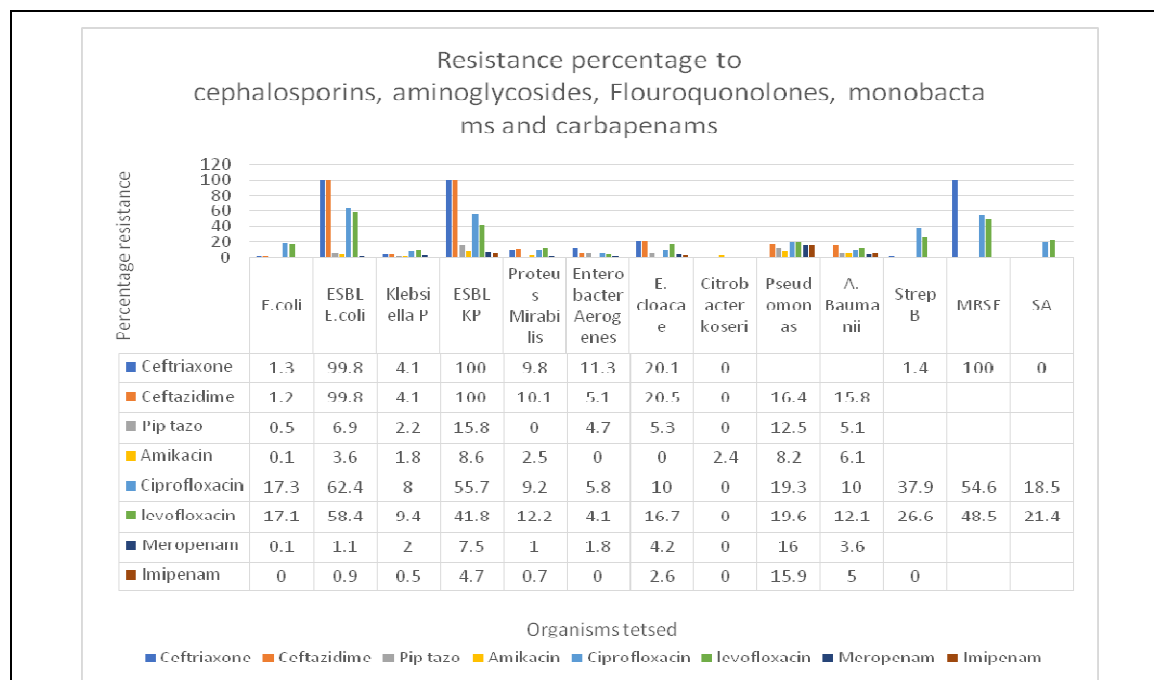


Figure 3. Percentage of organisms resistant to the test drug.

Klebsiella P: *Klebsiella pneumoniae*, *E. Cloacae*: *Enterococcus cloacae*, ESBL KP: ESBL: Extended-spectrum beta-lactamase *Klebsiella pneumoniae*, *A. baumannii*: *Acinetobacter baumannii* SS, Strep B: *Streptococcus* group B, MRSE: Methicillin-resistant staphylococcus epidermidis, SA: *Staphylococcus aureus*.

seen in 17.1% and 19.6% of non-ESBL *E. coli* and *P. aeruginosa*, respectively. Although it is not clear that at what level of resistance should quinolones be avoided, it is preferable to avoid quinolones as a favored choice of empirical antibiotics in our population. ESBL *E. coli* was sensitive to piperacillin-tazobactam,

amikacin, meropenem, and imipenem in 93.1%, 96.4%, 98.9%, and 99.1%, respectively. ESBL *E. coli* was resistant to amoxicillin-clavulanate, cotrimoxazole, ciprofloxacin, and levofloxacin in 73.8%, 62.3%, 62.4%, and 58.4%, respectively. ESBL *K. pneumoniae* was resistant to amoxicillin-

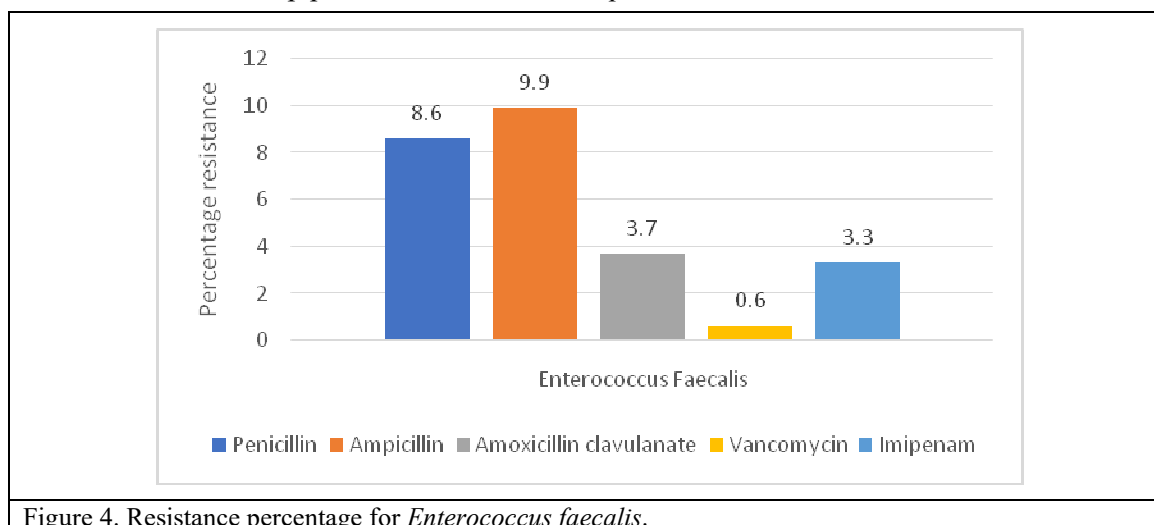


Figure 4. Resistance percentage for *Enterococcus faecalis*.

clavulanate, cotrimoxazole, ciprofloxacin, and levofloxacin in 68.2%, 62.6%, 55.7%, and 41.7%, respectively. This is consistent with other studies which show the co-resistance of ESBL-producing organisms to quinolones and cotrimoxazole.^{20,21} Antibiogram was concerning for *P. aeruginosa* with resistance to ceftazidime, ciprofloxacin, levofloxacin, meropenem, and imipenem in 16.4%, 19.3%, 19.6%, 16%, and 15.9% isolates respectively. Until recently, carbapenems were almost uniformly active against resistant Gram-negative organisms, but some strains have now developed very effective ways to deal with the carbapenems. There are various mechanisms by which these organisms achieve such a feat, by producing beta-lactamases that destroy the antibiotics, by blocking the entry of these antibiotics, or by efflux pumps that actively pump out these antibiotics.²² Enterococcus was sensitive to all primary enterococcal drugs. The growing resistance pattern suggests that antibiotics should be used responsibly and appropriately. Antibiotic stewardship is the need of an hour.

This study has certain limitations. It is a retrospective study and the clinical details of the patients, including the history of comorbidities in the form of diabetes mellitus, hypertension, stroke, bedridden status, presence of chronic kidney disease, presence or absence of indwelling catheters, obstruction, prior antibiotic exposure, etc., are not known. It is a single-center study involving patients who attended our hospital. This might not reflect the microbiological spectrum and antibiogram of the entire Bahraini community. Nitrofurantoin which is active against ESBL gram-negative organisms in multiple studies, has not been tested in our isolates. Nitrofurantoin might still be the preferred empirical oral therapy for lower UTI. A multi-center study in Bahrain would be required to get better knowledge about microbiological spectrum and antibiogram.

Conclusions

Gram-negative organisms are the predominant

cause of UTI in both genders. *E. coli* is the most common organism causing UTIs. *E. faecalis* is the most common Gram-positive organism causing UTI in our cohort. There is a high incidence of ESBL *E. coli* and *K. pneumoniae* in our community. There is alarmingly increased resistance of *P. aeruginosa* to carbapenems which will be a concern in the future. Cotrimoxazole should not be used, and quinolones should be avoided for empirical treatment of UTI. Amoxicillin-clavulanate, cefixime, and cefuroxime are suitable oral antibiotics for empirical treatment if suspicion for ESBL organisms is low. For sick patients requiring hospitalization, piperacillin-tazobactam, aminoglycosides, and carbapenems should be considered for empirical treatment. Antibiotic stewardship is the need of an hour.

Conflict of interest: None declared.

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