Original Article

A Study on Bacterial Etiology and Antibiotic Utilization Pattern among Inpatient with Urinary Tract Infections

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ABSTRACT

Background: Urinary tract infections constitute a significant public health problem and present an important cause of morbidity and mortality. Irrational antibiotic use leads to treatment failure, adverse drug reaction and development of antibiotic resistance. The main aim was to study the bacteriological aetiology, their sensitivity pattern and antibiotic utilization pattern which aids in evaluating the rationality of antibiotic therapy. **Materials and Methods:** This retrospective study was conducted for a period of 6 months. Case records of 400 patients were selected based on the study criteria. **Results:** In our study (52%) were male. Diabetes mellitus (36.14%) was the most common predisposing factor. *Escherichia coli* (42.03%) was the most frequently isolated bacteria among Gram negative species whereas *Enterococcus* species (59.49%) was predominant among Gram positive species. Cephalosporin (25.16%) were most commonly prescribed antibiotics. Piperacillin-tazobactam (30.16%) was the commonest empirical antibiotic. Total of 541 bacteria were isolated from 400 cultures and each isolate showed resistant to one or more antibiotics. Gram negative bacteria were highly susceptible to Meropenem, Piperacillin-tazobactam and Gentamicin, and they showed resistance to Cefixime followed by Cefazolin and Ciprofloxacin. Gram positive bacteria were highly sensitive to Linezolid, Vancomycin and Teicoplanin where as they are resistant to Cefixime, Ciprofloxacin and Ampicillin. **Conclusion:** In our study none of the antibiotics has 100% sensitivity towards both Gram positive and Gram-negative bacteria and there is increasing resistance towards commonly used antibiotics. So it is recommended that selection of antibiotic should be done based on culture sensitivity and patient response.

Keywords: Urinary tract infection, *Escherichia coli,* Piperacillin-Tazobactam, Gram negative, Diabetes mellitus.

INTRODUCTION

Urinary tract infections are a significant public health issue. With 150 million cases worldwide each year, Urinary Tract Infections (UTIs) are the most prevalent bacterial illnesses.[1] UTI prevalence rises with age, and in women over 65, it is roughly double what it is in the general female population.[2]

There are two types of these infections: Lower UTIs (cystitis) and Upper UTIs (pyelonephritis). Female gender, a past UTI, sexual activity, vaginal infection, diabetes, obesity, and genetic predisposition are some of the risk factors linked to cystitis. Both Gram-negative and Gram-positive bacteria, as well as a few fungi, are responsible for UTIs. Uropathogenic *Escherichia coli* is the most frequent culprit behind both simple and complex UTIs.[1]

Symptoms of UTI include urinary frequency, urgency, suprapubic discomfort, and

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dysuria.[3] Urine culture, microscopic urinalysis and dipstick urinalysis are the three main tests used in laboratory analysis for UTIs.[4]

For treatment of acute, uncomplicated UTI, first-line antibiotics include nitrofurantoin, cotrimoxazole, and Fosfomycin trometamol and Second-line medications include fluoroquinolones and beta-lactam agents.[4]

In the seriously ill patient, the traditional initial therapy is an IV fluoroquinolone, an aminoglycoside with or without ampicillin, or extended-spectrum cephalosporins with or without an aminoglycoside.[5]

Drug prescribing studies are essential to identify irrational prescribing patterns and aids in modification of current prescribing patterns through discussion on rational drug use or by suggesting measures to improve prescribing habits. The current study is an attempt to explore the prescribing patterns of antibiotics in the management of urinary tract infections.

MATERIALS AND METHODS

The study was a retrospective study carried out over a period of 6 months (April 2022–September 2022) among inpatient in tertiary care teaching hospital in South India. The patients above the age of 18 years diagnosed with UTI and urine culture positive patients were included in the study irrespective of gender, and other co-morbidities. Exclusion criteria for the study include patients below 18 years, pregnancy and lactating women, OPD patients, UTI caused by fungi and immunocompromised patient.

Method of collection

The data's required for the study were collected from medical record department and microbiology department. Patients demographic details, general examination, Duration of stay in the hospital, Clinical findings, Microbial culture report, Antibiotic sensitivity report, Treatment chart, Name, category and combination of antibiotics prescribed, Dose of the drug and Route of administration were collected and recorded in the pre-designed data entry form.

For Culture method Non-radiometric automated aerobic culture and modified Kirby Bauer disc diffusion with or without MIC are used.

Ethical clearance

Ethical clearance for the study was obtained from the Institutional Ethics Committee (Ref No. FMIEC/CCM/233/2022), Father Muller Medical College Hospital, Mangalore.

Statistical analysis

Descriptive statistical tool such as frequency, percentage, mean, standard deviation are used to assess the pertinent data. Karl Pearson coefficient of correlation test was used to test for significant correlation using SPSS 23. *P*- values <0.05 were accepted as statistical significant.

RESULTS

Patient case records were reviewed and a total of 400 subjects were selected based on the study criteria. Gender wise distributions of the patients were analyzed (n=208, 52%) were males and (n=192, 48%) were female.

Age-wise distribution of patients

The age of patients ranged from 18 to 80 yrs. The most prevalent age group was found to be ≥65 years (41.25%). The distribution in other age groups is summarized in Table 1. Out of 400 patients; it was found that most of the patients were hospitalized for 0-10 days, followed by 10-20 days.

Frequency distribution of predisposing factors

81 (12.89%) patients out of 400 had no predisposing factors and a total of 628 predisposing factor were identified from 320 patients. 227(Male=109, Female=118) patients had diabetes mellitus (36.14%) which makes it the most common predisposing factor identified during the study Out of 208 male patients, 109 patients had diabetes. According to Karl-pearsons correlation, a statistical correlation was found between male gender and diabetic patients (p=0.0465). 194 patients had hypertension (30.89%), followed by 73 patients with catheter (11.62%) and 45 patients with CKD (Chart 1).

Microbiology of UTI

In the present study, 292 out of 400 cultures were mono-microbial (73%), 108 culture revealed poly-microbial growth (27%). A total of 541microbial isolate were identified from 400 specimens with an average of 1.3 pathogen per lesion. 383 out of 541 were gram negative bacteria (70.79%), 158 were gram-positive bacteria (29.20%). *Escherichia coli* was the most frequent bacteria isolated from 161cultures (42.03%) followed by *Enterococcus* species isolated from 94 cultures (59.49%), *Pseudomonas aeruginosa* isolated from 69 cultures (18.01%) and *Klebsiella pneumoniae* isolated from 57 cultures (14.88%). Out of 356 g negative bacteria isolated, the

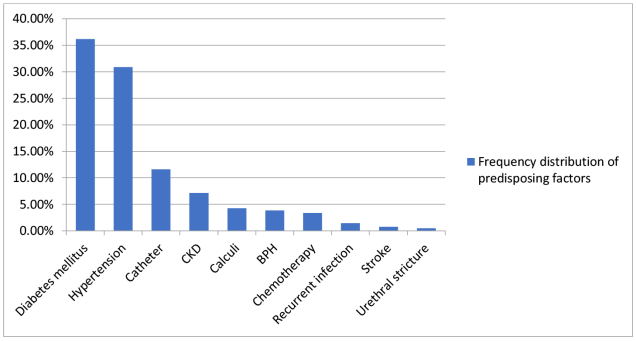

Chart 1: Frequency distribution of predisposing factor.

Table 1: Frequency distribution of isolated uropathogens according to gender.

Bacteria	Male(%)	Female(%)
Escherechia coli	72(44.72%)	89(55.27%)
Enterococcus species	63(50.4%)	62(49.6%)
Klebseilla pnemoniae	49(58.22%)	35(41.6%)
Pseudomonas aeruginosa	54(78.26%)	15(21.73%)
Acinetobacter	24(60%)	16(40%)
Staphylococcus species	12(41.3%)	17(58.62%)
Citrobacter	12(57.14%)	9(42.85%)
Proteus mirabilis	4(100%)	0

five most common were *Escherichia coli* (*n*=161; 42.03%), *Pseudomonas aeruginosa* (*n*=69; 18.01%), *Klebsiella pneumoniae* (*n*=57; 14.88%), *Klebsiella oxytoca* (*n*=27; 7.04%) and *Acinetobacter species* (*n*=24; 6.26%). According to Karl-persons correlation, a significant correlation was found between isolated bacteria and gender of the patient (*p*=0.0082). The most prominent bacteria involved in mono-microbial infection was *Escherichia coli* (*n*=143; 48.80%) followed by *Enterococcus* species (*n*=68; 23.2%), *Klebsiella pneumonia* (*n*=57; 19.52%), *Pseudomonas aeruginosa* (*n*=44;15.01%), *Enterococcus faecalis* (*n*=18;6.14%) and *Staphylococcus* species (*n*=8; 2.73%). *Enterococcus* species (*n*=26; 28.18%) was most prevalent bacteria in poly-microbial infections followed by *Pseudomonas aeruginosa* (*n*=25; 27.77%), *E. coli* (*n*=18; 20%), *Enterococcus faecalis* (*n*=9; 10%) and *Staphylococcus* species (*n*=8; 8.8%).

Prescription pattern of antibiotics

A total of 898 antibiotics were prescribed and with respect to the class of antibiotics, Cephalosporin (25.16%) were majorly prescribed, followed by Penicillin (24.05%). 400 empirical antibiotics were prescribed in 318 patients. Piperacillin-tazobactam (*n*=98, 30.81%), Ceftriaxone (*n*=69, 21.6%), Meropenem (*n*=49, 15.40%), Clindamycin (*n*=33, 10.37%) and Ceftriaxone-sulbactam (*n*=25, 7.86%) were the most commonly prescribed antibiotics and among these eligible patients, 26 (8.17%) received no empirical antibiotics. 498 definitive antibiotics were prescribed, Piperacillin–tazobactam (*n*=87, 29.29%) were majorly prescribed, followed by Meropenem (*n*=61, 20.53%), Linezolid (*n*=33, 11.11%), Ceftriaxone (*n*=30, 10.10%) and Levofloxacin (*n*=30, 10.10%).

Anti-biogram of Gram positive and Gram-negative bacteria

Cefixime (*n*=229), Cefzolin (*n*=217), Ciprofloxacin (*n*=207), Cefuroxime (*n*=196) and Co-trimoxazole (*n*=162) were found to be highly resistant in Gram negative bacteria. Meropenem (*n*=207), Piperacillin-tazobactam (*n*=200), Gentamicin (*n*=192), Ceftazidime (*n*=180) and Clindamycin (*n*=165) were the antibiotics to which gram-negative bacteria has maximum susceptibility. According to Karl-pearsons correlation, a significant correlation was found between gram negative isolates and susceptible antibiotics (*p*=0.0371). Gram positive bacteria had high resistant to antibiotics like Cefixime (*n*=109), Ciprofloxacin (*n*=106), Ampicillin (*n*=71), Imipenem (*n*=66) and Amikacin (*n*=59). They were highly sensitive to Linezolid (*n*=126), Vancomycin (*n*=113), Teicoplanin (*n*=102), Nitrofurantoin (*n*=70) and Imipenem (*n*=53).

Escherichia coli was resistant to Cefixime (61.49%), Cefuroxime (59%) followed by Cefazolin (67.70%), Ciprofloxacin (55.90%), Co-trimoxazole (44.72%). *Klebsiella* species, the second most common species in our study were resistant towards Cefazolin (67.85%), Cefuroxime (63.09%), Ampicillin (55.95%), Cefixime (52.38%), Cotrimoxazole (51.19%). *Pseudomonas aeruginosa* were resistant towards Cefixime (73.91%), Ciprofloxacin (61.56), Nitrofurantoin (60.86%), Levofloxacin (53.52%), Ceftazidime (55.07%) (Table 2).

Escherichia coli was sensitive to Meropenem (73.91%), Piperacillin-Tazobactam (68.38%), Tigecycline (65.25%), Gentamicin (62.73%), ceftazidime (60.8%). *Klebsiella* species were sensitive to Amikacin (50%), Gentamicin (48.8%), Meropenem (42.85%), Levofloxacin (41.66%), Piperacillin-Tazobactam (39.28%). *Pseudomonas* was sensitive to Linezolid (59.48%), Piperacillin Tazobactam (44.92%), Meropenem (37.68%), Ceftriaxone (36.23%), Gentamicin (36.23%) (Table 3). *Staphylococcus* species showed resistant to Cefixime (15,51.72%), Ciprofloxacin (14,48.27%), Cefazolin (11,37.93%), Cefuroxime (10,34.48%), Levofloxacin (9,31.03%) *Enterococcus* showed resistance towards Cefixime (94, 75.2%), Ciprofloxacin (92, 73.6%), Imipenem (64, 51.2%), Ampicillin (64, 51.2%) and Amikacin (57, 45.6%). Whereas *Enterococcus* showed sensitivity towards Linezolid (106,84.81%) followed by Vancomycin (96,76.8%),

Table 2: Antibiotic resistance pattern in Gram negative bacteria.

Antibiotics	*Escherichia coli* (161)	*Klebsiella* species (84)	*Pseudomonas aeruginosa* (69)	*Acinetobacter* species (40)	*Citrobacter* Species (21)
Amoxicillin-clavulanic acid	36(22.36%)	35(41.66%)	2(2.89%)	25(62.5%)	6(28.57%)
Ampicillin	59(36.64%)	47(55.93%)	6(8.69%)	19(47.5%)	11(52.38%)
Piperacillin–sulbactam	30(18.63%)	34(40.41%)	20(28.98%)	20(50%)	6(28.57%)
Cefazolin	109(67.70%)	57(67.85%)	3(4.34%)	30(75%)	18(85.71%)
Cefuroxime	95(59%)	53(63.09%)	3(4.34%0	26(65%)	19(90.47%)
Cefotaxime	74(45.96%)	39(46.42%)	1(1.44%)	20(50%)	10(47.6%)
Cefaperazone-sulbactam	37(22.98%)	27(32.14%)	29(42.02%)	19(47.5%)	6(28.57%)
Ceftazidime	-	3(3.57%)	38(55.07%)	-	-
Cefixime	99(61.49%)	44(52.38%)	51(73.91%)	23(57.5%)	12(57.14%)
Ciprofloxacin	90(55.90%)	40(47.61%)	48(69.56%)	22(55%)	7(33.33%)
Levofloxacin	46(28.57%)	28(29.76%)	39(56.52%)	21(52.5%)	6(28.57%)
Gentamicin	24(14.90%)	22(26.19%)	37(53.62%)	18(45%)	3(14.28%)
Imipenem	28(17.39%)	33(39.28%)	38(55.07%)	26(65%)	5(23.8%)
Meropenem	17(10.55%)	26(30.95%)	33(47.82%)	23(57.5%)	6(28.57%)
Co-trimoxazole	72(44.72%)	43(51.19%)	21(30.43%)	21(52.5%)	5(23.8%)
Nitrofurantoin	24(14.90%)	33(39.28%)	42(60.86%)	16(40%)	8(38.09%)

Table 3: Antibiotic sensitivity pattern in Gram negative bacteria.

Antibiotics	*Escherichia coli* (161)	*Klebsiella species* (84)	*Pseudomonas aeruginosa* (69)	*Acinetobacter* species (40)	*Citrobacter* Species (21)
Amoxicillin-clavulanic acid	64(39.75%)	22(26.19%)	1(1.44%)	7(17.5%)	2(9.52%)
Piperacillin–tazobactam	110(68.32%)	33(39.28%)	31(44.92%)	13(32.5%)	13(61.90%)
Cefazolin	42(26.08%)	17(20.23%)	1(1.14%)	4(10%)	2(9.52%)
Cefuroxime	34(21.11%)	18(21.42%)	1(1.14%)	3(7.5%)	4(19.04%)
Cefotaxime	41(25.46%)	19(22.61%)	2(2.89%)	3(7.5%)	6(28.57%)
Ceftriaxone	2(1.24%)	1(1.19%)	25(36.23%)	-	-
Ceftazidime	98(60.8%)	33(39.28%)	23(33.33%)	17(42.5%)	9(42.85%)
Levofloxacin	42(26.08%)	35(41.66%)	16(23.18%)	16(40%)	7(33.33%)
Gentamicin	101(62.73%)	41(48.80%)	25(36.23%)	14(35%)	11(52.38%)
Amikacin	77(47.82%)	42(50%)	22(31.88%)	10(25%)	7(33.33%)
Meropenem	119(73.91%)	36(42.85%)	26(37.68%)	10(25%)	16(76.19%)
Clindamycin	93(57.76%)	29(34.52%)	23(33.33%)	10(25%)	10(47.61%)
Nitrofurantoin	58(36.02%)	29(34.52%)	11(15.94%)	12(30%)	12(57.14%)
Tigecycline	105(65.25%)	25(29.76%)	11(15.94%)	4(10%)	8(38.09%)
Linezolid	13(8.07%)	13(15.47%)	41(59.42%)	14(35%)	2(9.52%)

Teicoplanin (91, 72.8%), Nitrofurantoin (57, 45.6%) and Imipenem (50, 40%).

DISCUSSION

Urinary tract infraction is huge burden on health care due to high prevalence of infection in both community and nosocomial settings. Irrational antibiotic use lead to treatment failure, adverse drug reactions, super infections, prolongation of the treatment, increased cost and development of antibiotic resistance.

According to patient's gender in the study, total uropathogens that were isolated for male (208/400) (52%) compared to female (192/400) (48%), this is in contrast with the study conducted by Nadeem *et al.* Fernando *et al.*[6,7] The high prevalence of male population in our study is because, for men aged above 65 years the incidence of UTI is estimated to increase 0.05 per person year. In our study male population were more (52.25%)

in age group greater than 65 years. Catheterization was also one of the reason for UTI and male population was predominant (72.6%) compared to female. The prevalence of symptomatic urinary tract infection in pregnant women has been 17.9% and in our study we have excluded pregnant and lactating women since it comes under our exclusion criteria. In our study, it was noted that Diabetes (36.14%) was the most common predisposing factor followed by hypertension (30.89%), catheter (11.2%). The findings are in accordance with the studies done by Swaine *et al* and Dilip *et al.*[9,10]

Our study observed that the gram negative bacteria (95.75%) were more prevalent than gram positive bacteria (4.25%). The findings are in accordance with the study done by Inam *et al* and Tigist, *et al.*[8,12] It was found that out of 383 gram negative bacteria, *E.coli* (42.06%) was the most common organism followed by *Pseudomonas aeruginosa* (18.02%), *K. pneumonia* (14.88%). It was observed that the study done by Das *et al.*[11] reported the most common pathogen isolated were *E. coli* (59.4%), *Klebsiella* species (15.7%), *Enterococcus faecalis* (8.1%). For gram positive bacteria out of 158, 79.61% were *Enterococcus* species followed by *Staphylococcus* species (18.32%). It was compared with studies conducted by Rama *et al.*[13]

In our study it was found that 318 patients got empirical therapy out of which piperacillin-Tazobactam (30.81%) was the most commonly prescribed empirical antibiotic followed by Ceftriaxone (21.6%), Meropenem (15.40%), Clindamycin (10.37%) and in 26 cases there were no antibiotics prescribed as empirical therapy. This study is different from the studies conducted by Aykut *et al.*[14] which reported that the most common antibiotic started empirically were Ciprofloxacin (30.7%), Fosfomycin (10.7%), Ceftriaxone (9.3%). The reason for contrast being sepsis (78) the most common co-morbidity in our study. Hence Piperacillin-Tazobactam was most commonly prescribed.[14] Antibiotic resistant pattern in our study showed that *E. coli* was resistant to Cefixime, Cefuroxime followed by Cefazolin, Ciprofloxacin, Co-trimoxazole, Whereas sensitivity pattern showed sensitivity to Meropenem, Piperacillin-Tazobactam, Tigecycline, Gentamicin. This is almost similar to the observation reported by Arul *et al.*[15] In gram positive species *Enterococcus* showed resistance towards Cefixime, Ciprofloxacin, Imipenem, Ampicillin, and sensitive to Linezolid, Vancomycin, Teicoplanin, It was compared with the study conducted by Atreyi *et al.*[16] where the results showed sensitivity towards Vancomycin, Erythromycin, Linezolid and resistant to Erythromycin, Ciprofloxacin.

CONCLUSION

In our study, the most prevalent age group was between ≥65 year and majority of patients were male. Diabetes mellitus was the most common predisposing factor. Gram negative bacteria were the most commonly isolated pathogen. The majority of urine culture isolates were monomicrobial in nature. *Escherichia coli* is the most frequently isolated bacteria. Cephalosporins were the majorly prescribed class of antibiotics followed by Penicillins. Piperacillin-tazobactam was the most commonly prescribed empirical antibiotic. Gram negative bacteria were highly susceptible to Meropenem, Piperacillin-tazobactam, Gentamicin and Ceftazidime and they showed resistance to Cefixime followed by Cefazolin, and Ciprofloxacin. Gram positive bacteria were highly sensitive to Linezolid, Vancomycin and Teicoplanin where as they are resistant to Cefixime, Ciprofloxacin and Ampicillin. No antibiotic has 100% sensitivity in both gram positive and gram-negative bacteria. There is an increasing resistance to commonly used antibiotics hence antibiotic selection should be done based on culture sensitivity results and patients response. It can be concluded that our study may help in the rational prescription of antibiotics in the treatment of urinary tract infection.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

UTI: Urinary Tract Infection; **IV:** Intravenous; **SPSS:** Statistical Package for Social Sciences; ***E. coli*:** *Escherichia coli*.

SUMMARY

Urinary tract infraction is huge burden on health care due to high prevalence of infection in both community

and nosocomial settings. Gram negative bacteria were the most commonly isolated pathogen. *Escherichia coli* is the most frequently isolated bacteria. No antibiotic has 100% sensitivity in both gram positive and gram negative bacteria. There is an increasing resistance to commonly used antibiotics hence antibiotic selection should be done based on culture sensitivity results and patients response.

REFERENCES

1. Flores-Mireles AL, Walker JN, Caparon M, Hultgren SJ. Urinary tract infections: Epidemiology, mechanisms of infection and treatment options. Nat Rev Microbiol. 2015;13(5):269-84. doi: 10.1038/nrmicro3432, PMID 25853778.
2. Medina M, Castillo-Pino E. An introduction to the epidemiology and burden of urinary tract infections. Ther Adv Urol. 2019;11:1756287219832172. doi: 10.1177/1756287219832172, PMID 31105774.
3. Bono MJ, Leslie SW, Reygaert WC. Urinary tract infection; 2022.
4. Chu CM, Lowder JL. Diagnosis and treatment of urinary tract infections across age groups. Am J Obstet Gynecol. 2018;219(1):40-51. doi: 10.1016/j.ajog.2017.12.231, PMID 29305250.
5. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, *et al*. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the infectious diseases society of America and the European society for microbiology and infectious diseases. Clin Infect Dis. 2011;52(5):e103-20. doi: 10.1093/cid/ciq257, PMID 21292654.
6. Raja NS. Oral treatment options for patients with urinary tract infections caused by extended spectrum βeta-lactamase (ESBL) producing Enterobacteriaceae. J Infect Public Health. 2019;12(6):843-6. doi: 10.1016/j.jiph.2019.05.012, PMID 31176606.
7. Fernando MMPSC, Luke WANV, Miththinda JKND, Wickramasinghe RDSS, Sebastiampillai BS, Gunathilake MPML, *et al*. Extended spectrum beta lactamase producing organisms causing urinary tract infections in Sri Lanka and their antibiotic susceptibility pattern–A hospital based cross sectional study. BMC Infect Dis. 2017;17(1):138. doi: 10.1186/s12879-017-2250-y, PMID 28187754.
8. Khan IU, Mirza IA, Ikram A, Afzal A, Ali S, Hussain A, *et al*. Antimicrobial susceptibility pattern of bacteria isolated from patients with urinary tract infection. J Coll Physicians Surg Pak. 2014;24(11):840-4. PMID 25404444.
9. Chen SL, Jackson SL, Boyko EJ. Diabetes mellitus and urinary tract infection: Epidemiology, pathogenesis and proposed studies in animal models. J Urol. 2009;182(6):S51-6. doi: 10.1016/j.juro.2009.07.090, PMID 19846134.
10. Chandrasekhar D, Dollychan A, Roy BM, Cholamughath S, Parambil JC. Prevalence and antibiotic utilization pattern of uropathogens causing community-acquired urinary tract infection in Kerala, India. J Basic Clin Physiol Pharmacol. 2018;29(6):671-7. doi: 10.1515/jbcpp-2018-0015, PMID 30063465.
11. Das RN, Chandrashekhar TS, Joshi HS, Gurung M, Shrestha N, Shivananda PG. Frequency and susceptibility profile of pathogens causing urinary tract infections at a tertiary care hospital in western Nepal. Singapore Med J. 2006;47(4):281-5. PMID 16572238.
12. Mechal T, Hussen S, Desta M. Bacterial profile, antibiotic susceptibility pattern and associated factors among patients attending adult OPD at Hawassa University Comprehensive Specialized Hospital, Hawassa, Ethiopia. Infect Drug Resist. 2021;14:99-110. doi: 10.2147/IDR.S287374, PMID 33469325.
13. Alkhawaldeh R, Abu Farha R, Abu Hammour K, Alefishat E. The appropriateness of empiric treatment of urinary tract infections in a tertiary teaching hospital in Joran: A cross-sectional study. Antibiotics. 2022;11(5):629. doi: 10.3390/antibiotics11050629, PMID 35625272.
14. Başer A, Yilmaz A, Başer HY, Özlülerden Y, Zümrütbaş AE. Which patient should start empirical antibiotic treatment in urinary tract infection in emergency departments? Turk J Emerg Med. 2020;20(3):111-7. doi: 10.4103/2452-2473.290064, PMID 32832730.
15. Prakasam A, Kumar KD. A cross sectional study on distribution of urinary tract infection and there antibiotic utilization pattern in Kerala. Int J Res Pharm Biomed Sci. 2012;3(3):1125-113.
16. Chakraborty A, Pal NK, Sarkar S, Gupta MS. Antibiotic resistance pattern of *Enterococci* isolates from nosocomial infections in a tertiary care hospital in Eastern India. J Nat Sci Biol Med. 2015;6(2):394-7. doi: 10.4103/0976-9668.160018, PMID 26283837.