ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
Index Copernicus Value: 68 . 16
PubMed - National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 5, Issue –2, April - 2020, Page No. : 116 - 124

A Study of Antimicrobial Resistance and Susceptibility Pattern of Various Pathogens Causing Urinary Tract Infection in the Tertiary Care Teaching Hospital

[1]Lokeshwar.S, Pharm D 5th Year, Sri Ramachandra Institute of Higher Education and Research (DU), Porur, Chennai-600 116

[1]M D Suheil, Pharm D 5th Year, Sri Ramachandra Institute of Higher Education and Research (DU), Porur, Chennai-600 116

[1]Nithimol.S, Pharm D 5th Year, Sri Ramachandra Institute of Higher Education and Research (DU), Porur, Chennai-600 116

[1]Nowfiyasaharbanu M I, Pharm D 5th Year, Sri Ramachandra Institute of Higher Education and Research (DU), Porur, Chennai-600 116

[2]S. Karthik, Faculty of Pharmacy, Sri Ramachandra Institute of Higher Education and Research (DU), Porur, Chennai-600 116.

[2]G. Ragesh, Faculty of Pharmacy, Sri Ramachandra Institute of Higher Education and Research (DU), Porur, Chennai-600 116.

[2]P.Seenivasan, Faculty of Pharmacy, Sri Ramachandra Institute of Higher Education and Research (DU), Porur, Chennai-600 116.

Corresponding Author: S. Karthik, Faculty of Pharmacy, Sri Ramachandra Institute of Higher Education and Research (DU), Porur, Chennai-600 116.

Citation this Article: Lokeshwar.S, M D Suheil, Nithimol.S, Nowfiyasaharbanu M I, S. Karthik, G. Ragesh, P.Seenivasan, "A Study of Antimicrobial Resistance and Susceptibility Pattern of Various Pathogens Causing Urinary Tract Infection in the Tertiary Care Teaching Hospital", IJMSIR- April - 2020, Vol – 5, Issue -2, P. No. 116 – 124.

Type of Publication: Original Research Article.

Conflicts of Interest: Nil

Abstract

Introduction: Antibiotic resistance has become a serious public health concern with social and economic implications throughout the world are it community acquired or hospital acquired infections. Antibiotics are used only for the treatment of bacterial infections. Bacteria have evolved complex mechanisms to resist the action of antibiotics. They exhibit resistance based on the elaboration of an enzyme that renders antibiotic ineffective. The resistance and susceptibility pattern of UTI and UTI with Sepsis has been illustrated. A Urinary tract infection (UTI) is an infection in any part of urinary system like kidneys, ureters, bladder and urethra. Sepsis occurs when chemicals released in the blood stream to fight an infection trigger inflammation throughout the body.

Objectives: To identify antimicrobial resistance and susceptibility pattern of various pathogens causing urinary tract infection and UTI with sepsis in the tertiary care teaching hospital and to find out the

rational therapy for various pathogens causing urinary tract infections.

Materials and Method: It's a retrospective observational study carried out for 6 month. Patients who are diagnosed with Urinary tract infection and prescribed with antibiotics were included and Patient without culture sensitivity report was excluded. The data were analyzed with IBM.SPSS statistics software23.0 version.

Results: A total of 244 patients, the prevalence of UTI were higher in female (56%) than in male (44%) in the study. E.coli (53%) was found the most dominant bacteria among all isolated organisms, and second most prevalent organism was Klebsiella pneumonia (22%). Among the various antibiotics used for treating E.coli, the most susceptible antibiotic was found to be Piperacillin+Tazobactum (83%), Imipenem (100%)& Cefaperazone+sulbactum (57%).The most resistance antibiotic for E.coli was found to be Ampicillin (100%),Cefotaxime (90%) and Ciprofloxacin (100%).In higher end antibiotics, ertapenem shows higher susceptibility(63%) and resistance(36%) in male than female, and imipenem shows (60%) susceptibilty in female and (40%) in male for E..Coli, Where Ertapenem and imipenem shows (60%) and (50%) resistance in male for klebsiella pneumonia. Patients more than 60 years shown more resistance to most of the organism.The Hospital guidelines was compared with the Indian council of medical research (ICMR) guidelines in that patients with UTI- cystitis the treatment was found to be 52% appropriate and UTI-pyelonephritis it was found to be 91% appropriate.

Keywords: Urinary Tract Infection, ICMR, Sepsis, Antibiotics, Sensitivity, Resistance.

Introduction

Urinary tract infection (UTI) is an infection in any part of urinary system like kidneys, ureters, bladder and urethra. The different types of UTI can include Urethritis – infection of the urethra, Cystitis – infection of the bladder, Pyelonephritis – infection of the kidneys, Vaginitis – infection of the vagina. It is caused by a range of pathogens, but most commonly by Escherichia coli**,** Klebsiella pneumoniae**,** Proteus mirabilis**,** Enterococcus faecalis and Staphylococcus saprophyticus. High recurrence rates and increasing antimicrobial resistance among uropathogens threaten to greatly increase the economic burden of these infections [1]. With the exception of a spike in young women aged 14−24 years old, the prevalence of UTIs increases with age. The prevalence in women over 65 years of age is approximately 20%, compared with approximately 11% in the overall population. Between 50% and 60% of adult women will have at least one UTIs in their life, and close to 10% of postmenopausal women indicate that they had UTIs in the previous year. Etiology in older postmenopausal women varies depending on their health status, residential status (institutionalized or not), age, the presence of diabetes mellitus, history of/current catheterization, spinal cord dysfunction, and a history of antibiotic use. The frequency of uncomplicated cystitis in young sexually active women is approximately 0.5 episodes per person per year [2]. The peak rate of uncomplicated utis occurs during the years of maximum sexual activity, usually between the ages of 18 and 39. Uncomplicated recurrent utis are also frequent in young women. After a first episode of UTIs, 27% of women have a confirmed recurrence within the next 6 months, and 2.7% have a second recurrence within the same period of time. Recurrence is less common than with

uncomplicated UTIs, with 9% of females and 5.7% of males having a second episode within a year. Uro pathogenic Escherichia coli (UPEC) were the dominant infectious agent in both uncomplicated and complicated UTIs. Enterococcus spp. and Candida spp. Are substantially more common in complicated

Infections, while Staphylococcus saprophyticus (S. Saprophyticus) is rare. Infection with UPEC increases the likelihood of recurrence within 6 months [2]. Causes for UTIs are mainly Intercourse, Sex where women are more prone to UTIs than men because, in females, the urethra is much shorter and closer to the anus. Additionally, Vaginal atrophy. Chronic prostatitis in the forms of chronic prostatitis/chronic pelvic pain syndrome and chronic bacterial prostatitis may cause recurrent urinary tract infections in males, Urinary catheterization, Others like A predisposition for bladder infections related to genetics. Diabetes, being uncircumcised, and having a large prostate. In children UTIs are associated with vesicoureteral reflux. Signs and symptoms include Upper back and side (flank) pain, High fever, shaking and chills, Nausea, Vomiting, Pelvic pressure, Lower abdomen discomfort, painful urination, Blood in urine, Burning with urination, discharge [3]. Antibiotic are substances produced by various species of microorganisms that suppresses the growth of other microorganisms [4]. Bacteriological sensitivity testing was generally done by disk-agar diffusion method using standardized concentrations of antibiotics based on clinically attained plasma concentrations. Drug resistance refers to unresponsiveness of a micro organism to an Anti microbial agent (AMA), and is akin to the phenomenon of tolerance seen in higher organisms, Resistance may be developed by mutation or gene transfer, Cross resistance is acquisition of resistance to one AMA conferring resistance to another AMA, to which the organism has not been exposed, Bacteria may demonstrate any of five general mechanisms of antibiotic resistance like lack of entry and decreased cell permeability, greater exit and active efflux, Enzymatic inactivation of the antibiotic, Altered target or modification of drug receptor site, Synthesis of resistant metabolic pathways [5]. Sepsis is also called septicaemia which occurs when chemicals released in the blood stream to fight an infection trigger inflammation throughout the body. This can cause a cascade of changes that damage multiple organ system, leading them fail, sometimes even resulting in death.

Materials and Method

It is a retrospective observational study conducted for the period of six month in a tertiary care teaching hospital. Patients who are diagnosed with Urinary tract infection and prescribed with antibiotics and with culture Susceptibility were included. Patients without antibiotics susceptibility reports were excluded. The collected data were analysed with IBM.SPSS statistics software23.0 version. To describe about the data descriptive statistics frequency analysis, percentage analysis was used.

Results

A Retrospective study was conducted for a period of 6 months. A total of 244 patients, case sheets were observed.The distribution of frequency of various isolated bacterial uropathogens were shown in Table-1. This study constitutes (97.4%) gram negative bacteria and only (2.6%) gram positive. Among the various antibiotics, highly susceptiblity for E.coli were Fosfomycin (100%) and Nitrofurantoin (97%), Amikacin (93%) and highly resistance to Cefalexin (100%), Levofloxacin (93%). Similarly for Klebseilla pneumonia, Susceptible to Piperacillin+Tazobactum

(95%), Nitrofurantoin (91%) and shown resistant to Ampicillin (100%), Amoxicillin+clavulanic acid (100%). The distribution patteren of higher end antibiotics with respect to resistance and susceptibility pattern of various micro-organisms isolated were shown in Table 2. In gender wise distribution the antibiotic susceptibility and resistance pattern, for E.coli ,Amikacin shown (61%) susceptiblity in female than (39%) in male, Nitrofurantoin shown 65% in female and 35% in male, Fosfomycin shown 60% in female and 40% in male. Similarly Ecoli shown more resistance to Amikacin in male (80%) than female (20%), Nitrofurantoin also shown higher resistance in male (100%) where ciprofloxacin, levofloxacin, cefuroxime, amoxicillin shown higher resistance in female, which is not statistically significant, as Amikacin (P value is 0.075), Nitrofurantoin (P value is 0.589) which is greater that 0.005. But for cotrimoxazole was found to have significant P value (0.015) . For Klebsiella pneumonia, gender wise distribution of antibiotic susceptibility and resistance pattern were observed in that levofloxacin, cefipime, shown higher resistance in female, which is statistically insignificant but gentamycin (P value is 0.012), Fosfomycin (P value is 0.001), ciprofloxacin (P value is 0.0379) was found to be significant. In age wise distribution, patients more than 60 years shown more resistance to cefazolin (89%), cefixime (80%), cefalexin (100%), and susceptablity to Fosfomycin(100%).patients between 40 - 60 years shows higher susceptibility colistin (100%), fosfomycin (100%), cefaperazone sulbactam (78%) and reistance to Vancomycin(100%). In 20 - 40 years cefalexin(100%), cefuroxime(89%), cefipime(80%) shown higher resistance and susceptibility to Fosfomycin(100%) and Piperacillin with tazobactum (100%). The distribution of UTI with Sepsis the resistance and susceptible pattern of E.coli and Staph.Aureus were shown in Table 3.

The Hospital guidelines was compared with the Indian council of medical research (ICMR) guidelines in that patients with UTI- cystitis the treatment was found to be 52% appropriate and UTI- pyelonephritis it was found to be 91% appropriate. Table 4.

Discussion

An observational retrospective study was conducted for duration of 6 months .Various pathogens are isolated from urine and blood cultures and reports are taken from the Medical record department throughout the study.

In this study out of 244 patients 137 (52%) were female than 107(48%) male which is in accordance with the study conducted by Azizun Nahar *et al* 2015 in their study female patient (73%) were more than male(27%) [6].This study constitutes more number of gram negative bacilli (96.4%) than gram positive organism (3.6%), This was concordant with the study conducted by Prakash *et al* where gram negative (90.32%) organism accounted more than gram positive (9.6%) organism.Among all organism isolated in the study E.coli accounted for more than fifty percent (53%) followed by 22% of Klebsiella pneumonia, Enterococcus faecalis (11%), Citrobacter koseri (3.3%) and Pseudomonas aeruginosa. Acinetobacter , Candida accounted less than (3%). Similar study were conducted by Prakash *et al* were organism like Ecoli (42.58%) isolated most followed by Klebsiella pneumonia(18.7%)and pseudomonas aeruginosa(13%).[7].In this study elderly male patient above 60 years of age showed higher prevalence of UTI (67.3%) compared with elderly female (23.7%).The reason for UTIs was due to prostate enlargement which

is in concordant with study conducted by Devanand Prakash *et al* 2013, carried out a similar study showed high prevalence of UTI was in elderly male (71%) than females (27%)[7]. E.coli showed higher susceptibility towards Fosfomycin (100%), Amikacin (93%), Nitrofurantoin (97%) which was in accordance with study conducted by Uttam K. Das, *et al* 2018, where Amikacin(72.5%), showed higher susceptibility followed by Nitrofurantoin(83.6%) **[8].** In the study levofloxacin (93%), ciprofloxacin (90%), cefalexin (100%) shown higher resistance, A similar results was shown in Thakur, *et al* 2012. But which was contrast in case of susceptibility were Ceftazidime (72%) and cefotaxime (78%) showed higher susceptibility in Thakur, *et al* 2012 study [13]. where in this study ceftazidime (72%), cefotaxime (75%), showed more resistant.For klebsiella organism, Nitrofurantoin (91%) showed higher susceptibility, which is in contrast with study conducted by Azizun Nahar *et al* 2015**[6].**Where nitrofurantoin had shown 68% resistance in klebsiella sp, But in the study conducted by Uttam K. Das, *et al* 2018, Ampicillin (100%), amoxicillin+clavulanic acid (100%), cefazolin (90%), cefuroxime (89%), ceftazidime (85%) showed higher resistance[9] which correlates with this study were amoxicillin+clavulanic acid (97%), cefuroxime(90%) showed higher resistance. The study conducted by Chaitali pattanayaka *et al* 2013 showed cephalosporins were highly resistant to Enterobacter faecalis, Similarly in this study higher resistance were seen in cefotaxime (100%), cefalexin (100%) [9].

Higher susceptibility was shown in piperacillin tazobactum(100%), Fosfomycin(100%), amikacin(100%) and third generation cephalosporins (100%) in Citrobacter koseri which correlates with the study Hiba sami *et al* where imipenam(100%) amikacin showed high susceptibility[11].

In this study Highest Resistance was observed in Nitrofurantoin (86%) which does not correlate with study conducted by Hiba sami *et al* where Nitrofurantoin showed (67%) more susceptibility in Citrobacter koseri.[11].In this study, Ceftazidime(84%) showed more susceptibility and Nitrofurantoin(100%) showed high resistance to pseudomonas aeruginosa, which is in contrast with the study conducted by Chaitali pattanayaka *et al* where Ceftazidime (100%) was completely resistant were as Imipenam(40%), Gatifloxacin(41.7%) showed more susceptibility in their study[9].

In Enterobacter cloacae, highest Susceptibility were seen in fosfomycin (100%).Resistance were seen in Nitrofurantoin(100%),cefipime(100%),cefotaxime(100 %) which is similar to the study conducted by Giannoula *et al* where Fosfomycin showed (99%) Susceptibility, but in contrast to our study cefotaxime (98%) showed more susceptibility [12].

The susceptibility and resistance pattern for higher end antibiotic were studied for various organism in that E.coli showed more susceptibility to Imipenem(100%) and resistance to ertapenam(71%) which is not in concordant to the study conducted by A. J. Al-Zahran *et al* where meropenam(95.8%) showed susceptibility to E coli.[14].

In this study Klebsiella pneumonia, Colistin showed (100%) susceptibility and Ertapenem showed (100%) resistance where as in a study done by Prakash *et al* imipenem showed (70%) resistance and meropenam showed (80%) susceptibility[7].

Vancomycin showed (100%) susceptibility and Tetracycline showed (100%) resistance towards Entereobacter faecalis. A contrast result obtained from

Prakash *et al* their Impenenam have (100%) susceptibility[7].

In the study conducted by Prakash *et al* [7].The chi square test showed statistically significant variations(P< 0.05) at 95% CI for the infected and non infected male and female patients variables among all age groups , where as in this study chi square test showed statistically significant variations (P< 0.05) at 95% CI for the infected male and female variables among all age groups.

A study done by Thakur *et al* on Gender wise distribution of susceptibility and resistance pattern on isolated bacterial uropathogens, result showed that there was no statistical significance between resistance and susceptibility of various pathogens with gender [13]. Similar results were obtained in this study. Among all age group most of the resistance was observed from age group >60 years, one third of resistance was observed from age group 40-60 years, least was in 20-40 years. and susceptibility was higher in the age group (40- 60) when compared with 20-40 and >60 years in accordance with the study conducted by Thakur *et al*[13].

In UTI with Sepsis the organisms isolated were E.coli and staph.aureus. Amikacin(81%), imipenem (100%) and piperacillin tazobactum(83%), showed higher susceptibility where as Ampicillin (100%), Ciprofloxacin(100%) and Cefotaxime(90%) showed resistance to E.coli.

In Staph. aureus Linezolid (100%), Vancomycin (100%) and Clindamycin (90%) showed higher susceptibility, Erythromycin(75%), Ampicillin(59%) showed higher resistance in this study. In cystitis-UTIs, 51.7% of drugs prescribed by hospital guidelines were adherent to Indian council of medical research(ICMR) guidelines and 48.3% were not, similarly for pyelonephritis-UTIs, 91% of drugs were adherent to ICMR guidelines and 9% were Non adherent.

Conclusion

The study revealed that generally Urinary tract infections (UTI) is more prone to female than male. But in the study elderly male patient above 60 years were more prone to have UTI. Among various organism isolated E.Coli was more prevalent than other organism. The Hospital guidelines were compared with the Indian council of medical research (ICMR) guidelines and found deviation in it. Stringent policy should be adopted for adhering hospital guidelines with the international guidelines and revising it accordingly. This is because adhering to the prescribing hospital guidelines may avoid the inappropriate use of antibiotics. The routine antibiotic susceptibility testing's will also be helpful in providing rational therapy and thereby reduces the mortality and morbity. This enhances the quality of life of the patients.

Ethical clearance: A prior approval was obtained from the institutional ethical committee.

References

1. Webmed. Urinary tract infections. Available from https://www.webmed.com/women/guide/your-guide-urinary-tract-infections (Accessed March 5 2020).
2. Mayoclinic. Urinary tract infections. Available fromhttps://www.mayoclinic.org/diseases-conditions/urinary-tract-infection/symptoms-causes/syc-20353447 (Accessed March 5 2020)
3. Gordon L.Archer, Ronald E. Polk. Treatment and prophylaxis of bacterial infections. Anthony s. Fauci dennis l.kasper. Harrison's infectious disease.
4. Abdel-Moneim M. Galal, IdrissM. Al-Turk and Khalid D. Al-Zhrany, Mohamed K.

ibrahim.Antibiotic resistance in Gram negative pathogenic bacteria in hospitals drain in Al madina , Al- munnawara . Journal of taibah university for science.2010;(3):14-22.

5. R Nalini, J Ezhil Ramya. Recent Sensitivity Pattern of Escherichia Coli in Urinary Tract Infection. RRJMB.2014; 3(3).
6. Azizun Nahar1, Shahed Hasnat2, Hasina Akhter3, Nilufar Begum4Evaluation of antimicrobial resistance pattern of uropathogens in a tertiary care hospital in Dhaka city, Bangladesh.Journal of Public Health 2017; 7(2):1- 12
7. Devanand Prakash and Ramchandra Sahai Saxena Distribution and Antimicrobial Susceptibility Pattern of Bacterial Pathogens Causing Urinary Tract Infection in Urban Community of Meerut City, India.ISRN Microbiology,2013; 1- 13.
8. Uttam K. Das, Prithul Bhattacharjee*, Shubhaleena Debnath, Maitrayee Chakraborty, Ranjib Ghosh, Lakshman Das et al. Antibiotic sensitivity pattern of bacterial isolates from urine samples of admitted patients with urinary tract infection in a tertiary care teaching hospital of Tripura, India: a hospital record based study.2018;7(4). 585- 58
9. Chaitali Pattanayaka,Sunil K Patanaikb, Pratyay Pratim Dattaa, Parbaty Panda . A study on antibiotic sensitivity pattern of bacterial isolates in the intensive care unit of a tertiary care hospital in Eastern India".Int J Basic Clin Pharmacol. 2013; 2(2):153-159.
10. Dr. Anbumani Narayanasamy, M.Malika .Prevalance and susceptibility of extended spectrum beta -lactamasees in urinary isolates of escherichia coli in a teritary care hospital in chennai - south india.Internet journal of medical update. 2011; 6(1): 39-43.
11. Hiba Sami, Asfia Sultan, Meher Rizvi, Fatima Khan, Shariq Ahmad, Citrobacter as a uropathogen, its prevalence and antibiotics susceptibility pattern, Christ med Journal of Health and Research,2017; 23- 26.
12. Giannoula S. Tansarli, Starvros Athanasiou, Evaluation of Antimicrobial Susceptibility of Enterobacteriaceae causing Urinary Tract Infections in Africa, Antimicrobial agents and chemotherapy,2013;57(8):3628- 3639.
13. Thakur P, Ghimire P, Rijal KR Singh GK,Antimicrobial resistance pattern of Escherichia coli isolated from urine samples in patients visiting tertiary health care centre in eastern Nepal. Sunsari Technical College Journal, 2012; 1(1):22-26.
14. A. J. Al-Zahran and N. Akhtar, "Susceptibility patterns of extended spectrum beta-lactamase (ESBL)-producing Escherichia coli and Klebsiella pneumoniae isolated in a teaching hospital," Journal of the College of Physicians and Surgeons Pakistan. 2011, 21 (6): 342-346.

Legends Tables

Table 1: Distribution frequency of isolated bacterial uropathogens

S. N.	Organism	Frequency	Chi-square	P value
1.	E.Coli	108 (53%)	110.567	The P-Value is < .00001. The result is significant at p < 0.05.
2.	Kleb. pneumonia	45 (22%)		
3.	E.faecalis	23(11%)		
4.	Citrobacter koseri	7(3.3%)		
5.	Pseudomonas aeruginosa	6(2.9%)		
6.	Acinetobacter	3(1.4%)		
7.	Candida tropicalis	8(3.8%)		

Table 2: Distribution of Higher end antibiotics with Resistance and Susceptibility pattern of micro-organisms isolated

S. N.	Antibiotics	E.coli		Kleb. Pneumonia		Enterobacter faecalis	
		Susceptible	Resistance	Susceptible	Resistance	Susceptible	Resistance
1.	TETRACYCLINE	-	-	-	-	0	7(100%)
2.	ERTAPENEM	7(29%)	17(71%)	0	23(100%)	-	-
3.	COLISTIN/POLYMIXIN	20(100%)	0	16(100%)	0	-	-
4.	IMIPENEM	10(100%)	0	2(29%)	5(71%)	-	-
5.	VANCOMYCIN	-	-	-	-	5(100%)	0

Table 3: Distribution of UTI with Sepsis resistance and susceptible pattern of E- coli and Staph Aureus.

Antibiotics	E.Coli		Staph. Aureus	
	Susceptible	Resistance	Susceptible	Resistance
AMPICILLIN	0(0%)	10(100%)	9(41%)	16(59%)
CEFOTAXIME	1(10%)	10(90%)	14(70%)	6(30%)
CEFTAZIDIME	2(25%)	6(75%)	-	-
CEFEPIME	3(36%)	6(66%)	-	-
PIPERACILLIN+ TAZOBACTUM	5(83%)	1(17%)	-	-
IMIPENEM	4(100%)	0(0%)	-	-
AMIKACIN	9(81%)	2(19%)	-	-
CIPROFLOXACIN	0(0%)	9(100%)	18(78%)	5(22%)
CEFAPERAZONE+ SULBACTAM	4(57%)	3(43%)	-	-
LINEZOLID	-	-	6(100%)	-
VANCOMYCIN	-	-	5(100%)	-
CLINDAMYCIN	-	-	19(90%)	2(10%)
ERYTHROMYCIN	-	-	6(25%)	18(75%)
GENTAMYCIN	-	-	18(81%)	4(19%)

Table 4: Comparison of drug prescribed according to the ICMR guidelines in cystitis and pyelonephritis.

Condition	Organism	Drug prescribed	ICMR guidelines	Appropriateness	inappropriateness
CYSTITIS (N- 58)	E.Coli (N- 40) Kleb. Pneumonia (N- 18)	Nitrofurantoin Ciprofloxacin Amikacin Cef+ sulbac Colistin Ceftriaxone	Nitrofurantoin Ciprofloxacin Cefuroxime Cotrimoxazole Cefipime	30 (51.7%)	28 (48.3%)
PYELONEPHRITIS (N- 90)	E.Coli (N-63) Klebseilla pneumonia (N- 27)	Levofloxacin Imipenam Meropenam Fosfomycin	Piperacillin+ tazobactam Impenam Ertapenam Amikacin	82 (91%)	8 (9%)