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Original Article

Uropathogens and their Susceptibility to Common Antibiotics in Adult Patients Presenting to the Emergency Department of a Tertiary Care Hospital in Pakistan

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ABSTRACT

OBJECTIVE

To identify the prevalence of uropathogens and their susceptibility patterns to different antibiotics in adult patients presenting to the emergency department with lower urinary tract symptoms so that treating physicians can identify common pathogens and select a reasonable empirical antibiotic if needed.

METHODOLOGY

The study is a retrospective chart review conducted in the emergency department of Shifa International Hospital, Islamabad, Pakistan. All the patients diagnosed with urinary tract infection through dipstick in the emergency department whose urine cultures were positive were included in the study. The chart review was done from January, 2018 to December, 2018.

RESULTS

Out of 203 patients with positive urine dipstick, whose cultures sent from emergency only 64(31.3%) samples showed significant bacterial yield. Most patients included in the study were above 50 years of age (79.7%) with a male predominance (males 36, females 28). The most common organisms isolated was E.coli 44 (68.8%) followed by Klebsiella spp. 09(14%) and Enterococcus spp. 03 (4.7 %) respectively. Antibiotics which were found most sensitive against pathogens in our study included Imipenem (78.1 %), Nitrofurantoin (76.6 %) and Fosfomycin (76.6 %) respectively. On the other hand both penicillin's (Co-amoxiclave 80.8 %) and cephalosporin (Cefixime 84.4%, Ceftazidime 78.1 %, and Ceftriaxone 81.2 %) were highly resistant to most of microbial growth. Moderately resistant antibiotics included Co-Trimoxazole (71.4%), Ciprofloxacin (73.4%) and Gentamicin (48.4%) respectively. A high prevalence of carbapenums resistance Imipenem (9.4%), was also observed in this study.

CONCLUSION

Most uropathogens identified in patients presenting to the emergency department with urinary complains are sensitive to Fosfomycin, Nitrofurantoin, Gentamycin, and Imipenem which may be considered as empirical therapy in our settings.

KEYWORDS

Uropathogens, Emergency Department, Susceptibility Patterns, Pakistan

INTRODUCTION

Urinary tract infection (UTI) remains one of the most common presentations of patients presenting to the emergency department in developing countries. In the emergency department, UTI can be easily diagnosed in a patient with lower urinary tract symptoms by urinalysis or urine dipstick. [(1)] This early diagnosis prompts the emergency physician to start early empirical antibiotic therapy. Unfortunately, the widespread use of antibiotics against uropathogens has led to the emergence of antibiotic-resistant species.[(2)]

Gram-negative bacteria are increasingly becoming resistant to all the common antibiotics that are routinely prescribed in outpatient and inpatient settings. The infections caused by these bacteria are becoming more difficult to treat due to the misuse of antibiotics. Most community or hospital acquired UTIs are caused by Escherichia coli (E.coli) and Enterobacteriaceae, both of which are Gram-negative bacteria.[(3)] One of the unique features of these bacteria is to acquire genes that encode for multiple mechanisms causing antibiotic resistance, including extended-spectrum-lactamases (ESBLs), AmpC-β-lactamase, and carbapenemases.[(4)]

Most studies have identified E.coli as the most common causative bacterium. [5] Nowadays the emergence of ESBL E.coli, Vancomycin-Resistant E.coli (VRE) and Multi-Drug Resistance (MDR) E.coli are the organisms of growing concern. β-lactamase, which is prescribed by physicians in hospitals, are becoming inefficient because of weak activity against E.coli. The resistance mechanism of E.coli to β-lactamase is important because of the transmission of plasmid-mediated genes encrypting β-lactamase. On the other hand, Klebsiella is another bacterium which is developing resistance due to β-lactamase.[6]

For gram-negative bacterial infections mostly β-lactamase antibiotics are used. Trimethoprim-sulfamethoxazole, aminoglycosides, fluoroquinolones and a wide range of non-β-lactamase antibiotics are resistant to ESBL producing gram-negative bacteria. These antibiotics are usually linked with the worst outcomes when they are used against an Extended-spectrum β-lactamase (ESBL) creating strain. However, the use of third-generation cephalosporin with the combination of the β-lactamase inhibitor is supported in recent clinical trials.[7]

This study is designed to determine the prevalence and antibiotic susceptibility of uropathogens in adults presenting to the emergency department with urinary symptoms over a period of one year. Urine cultures are usually sent from the emergency department and empirical antibiotic therapy is started in the department. There is an increasing trend of development of resistance among uropathogens around the globe.

METHODS

The study design for this research is a retrospective chart review. This study has been conducted in the emergency department of Shifa International Hospital in Islamabad, Pakistan. The data collection period was one year, starting from January, 2018 to December, 2018. All the patients presenting to the emergency department aged 18 years and above with a positive urine dipstick test (Nitrite and Leukocyte esterase) and whose urine culture was sent were included in the study. Those who left the emergency department either on request or against medical advice were excluded from the study. Samples of urine were collected as per standard techniques (midstream urine/ clean catch) in the ER and sent to the microbiology laboratory. Urine specimens were inoculated onto cysteine lactose electrolyte deficient agar following standard procedures. Cultures showing significant bacterial growth were subjected to identification and sensitivity testing using the VITEK 2 system. Variables of interest were extracted from the chart review and the emergency medical records. The analysis was performed by using SPSS version 23. Frequencies with percentages were generated for categorical variables such as demographics, type of bacteria and resistance or sensitivity to different antibiotics. The study was approved by the Ethical Review Board of Shifa International Hospital.

		Frequency	Percent
Age	18-50	13	20.3
	50 and above	51	79.7
Gender	Male	36	56.2
	Female	28	43.8

Table1: Patients Demographics

RESULTS

Out of a total of 475 cases of suspected UTI, urine dipstick was positive in 203 cases of different ages and gender. Out of these 203 cases, 64 (31.3%) samples showed significant bacterial yield. Culture positive UTI was seen in 36 males (56.2 %) and 28 females (43.8 %) with a male to female ratio of 1.28:1. Most patients included in the study were above 50 years of age as shown in Table 1.

The most common organism isolated was E.coli 44 (68.8%), including E. coli ESBL 30(46.9%) and E.coli MDR 14(21.9%) as shown in Figure 1. E.coli was followed by Klebsiella spp. 09 (14 %), Enterococcus spp. 03 (4.7 %), Salmonella 02 (3.12%), Pseudomonas spp. 02(3.1%), Enterobacter spp. 02 (1.00 %) and Staph. Aureus 01(1.6%) in table 2.

There was no growth of Proteus spp. observed. Poly microbial growths which were obsserved in 05 samples counted as independent growths showed a combination of E.coli and Staph. Aureus in 02 cases, E.coli, and Enterococci spp. in 02 cases and E.coli and Klebsiella spp. in 01 cases respectively.

The bacterial yield was also analyzed with reference to gender to identify any difference in the causative uropathogens among males and females. E.coli ESBL was found more in females 16(57.1%) than in males 14(38.9%), while E.coli MDR was more common in males. On the other hand, Klebsiella was mostly seen in male urine samples. Other bacteria had almost equal growth in both genders. (Table 3)

Regarding antibiotic sensitivity in our study Imipenem(78.1 %), Nitrofurantoin (76.6 %) and Fosfomycin (76.6 %) turned out to be highest and almost equally sensitive against most of the bacteria. These are followed by Gentamicin (45.3%), Co-Trimoxazole (22.2 %), Ciprofloxacin (17.2 %), Ceftazidime (9.4 %), Ceftriaxone (7.8%),

	Bacterial yield	Frequency	Percent
Valid	E.coli (ESBL)	30	46.9
	E.coli (MDR)	14	21.9
	"KLEBSIELLA PNEUMONIAE (MDR)"	4	6.2
	KLEBSIELLA PNEUMONIAE	3	4.7
	"KLEBSIELLA PNEUMONIAE (ESBL)"	2	3.1
	PSEUDOMONAS AERUGINOSA	3	4.7
	PSEUDOMONAS AERUGINOSA (MDR)	2	3.1
	SALMONELLA SPP	1	1.6
	SALMONELLA PARATYPHI A	1	1.6
	"STAPHYLOCOCCUS AUREUS (MRSA)"	1	1.6
	ENTEROCOCCUS SPP	3	4.7
	Total	64	100.0

Table 2: Bacterial yield

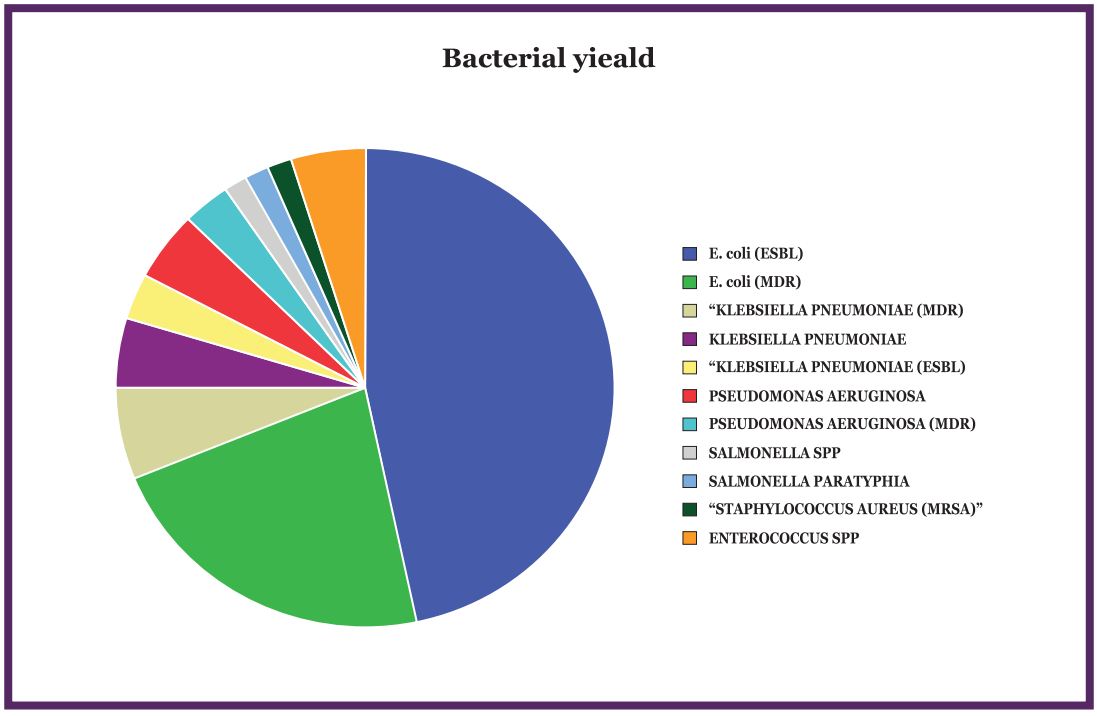

Figure: 1

			Gender		Total
			Male	Female	
Bacterial yield	E.coli (ESBL)	Count	14	16	30
		% within gender	38.90%	57.10%	46.90%
		% of Total	21.90%	25.00%	46.90%
	E.coli (MDR)	Count	9	5	14
		% within gender	25.00%	17.90%	21.90%
		% of Total	14.10%	7.80%	21.90%
	"KLEBSIELLA PNEUMONIAE (MDR)"	Count	4	0	4
		% within gender	11.10%	0.00%	6.20%
		% of Total	6.20%	0.00%	6.20%
	KLEBSIELLA PNEUMONIAE	Count	2	1	3
		% within gender	5.60%	3.60%	4.70%
		% of Total	3.10%	1.60%	4.70%
	"KLEBSIELLA PNEUMONIAE (ESBL)"	Count	1	1	2
		% within gender	2.80%	3.60%	3.10%
		% of Total	1.60%	1.60%	3.10%
	PSEUDOMONAS AERUGINOSA	Count	2	1	3
		% within gender	5.60%	3.60%	4.70%
		% of Total	3.10%	1.60%	4.70%
	PSEUDOMONAS AERUGINOSA (MDR)	Count	1	1	2
		% within gender	2.80%	3.60%	3.10%
		% of Total	1.60%	1.60%	3.10%
	SALMONELLA SPP	Count	1	0	1
		% within gender	2.80%	0.00%	1.60%
		% of Total	1.60%	0.00%	1.60%
	SALMONELLA PARATYPHI A	Count	0	1	1
		% within gender	0.00%	3.60%	1.60%
		% of Total	0.00%	1.60%	1.60%
	"STAPHYLOCOCCUS AUREUS (MRSA)"	Count	1	0	1
		% within gender	2.80%	0.00%	1.60%
		% of Total	1.60%	0.00%	1.60%
	ENTEROCOCCUS SPP	Count	1	2	3
		% within gender	2.80%	7.10%	4.70%
		% of Total	1.60%	3.10%	4.70%
	Total	Count	36	28	64
		% within gender	100.00%	100.00%	100.00%
		% of Total	56.20%	43.80%	100.00%

Table 3: Bacterial yields in Male and Female patients (n=64)

Amoxil/Clave. (7.8 %) and Cefixime (4.7 %) respectively.

On the other hand, both penicillin (Amoxil/Clave. 80.8 %) and cephalosporin (Cefixime 84.4%, Ceftazidime 78.1 %, Ceftriaxone 81.2 %) groups were highly resistant to most of the microbial growth. Moderately resistant antibiotics included Co-Trimoxazole (71.4%), Ciprofloxacin (73.4%) and Gentamicin (48.4%) respectively. Imipenem (9.4%), Fosfomycin (10.9 %) and Nitrofurantoin (15.6%) were the least resistant antibiotics identified by the study.

All those antibiotics which were not tested in a sample were identified as "not checked" and excluded during analysis. (Table 4)

Individual drugs were also analyzed by cross-tabulation with a bacterial yield to identify the exact patterns of resistance and sensitivity related to the drug. Different strains of E.coli (ESBL, MDR) Klebsiella Pneumonia (MDR, ESBL), Pseudomonas Aeruginosa (SPP., MDR) and Salmonella (SPP., PARATYPHI) were isolated and analyzed separately. As not all the antibiotics were tested in all the samples, all those antibiotics not tested were identified and excluded from calculations before analysis and reported separately. (Table: 5)

Drugs	Not Checked%	Sensitive%	Resistance%
Amoxil/Clave	9.4	7.8	80.8
Cefixime	10.7	4.7	84.4
Ceftazidime	12.5	9.4	78.1
Ceftriaxone	10.9	7.8	81.2
Co-Trimoxazole	6.3	22.2	71.4
Fosfomycin	12.5	76.6	10.9
Gentamicin	6.2	45.3	48.4
Imipenem	12.5	78.1	9.4
Nitrofurantoin	7.8	76.6	15.6
Ciprofloxacin	9.4	17.2	73.4

Table 4: Antibiotics cumulative resistance and sensitivity patterns to uropathogens

DISCUSSION

Urinary tract infection (UTI) is one of the most common diagnoses in patients presenting to the emergency department, which manifests as either fever in elderly or otherwise in all ages with symptoms of lower urinary tract symptoms (LUTS). Antimicrobial resistance is emerging in both complicated and uncomplicated UTI.[8] Frequent use of catheters in outpatient settings, bed-bound patients and elderly has increased the risk of UTI amongst this population.

In our study although 203 samples showed urine dipstick positive, cultures were positive in only 64 samples. A greater number of urine samples of patients showed isolation of bacteria in the elderly as compared to young patients (51 vs. 13). This correlates well with multiple studies reporting an increased incidence of UTI in the elderly. [9]

In community-acquired UTI, it is a well-known factor that females acquire this infection more often than males, however in our study; male patients had higher number of culture-positive samples. This difference may have been related to the fact because of being tertiary care center, most of our patient population includes chronically ill and debilitated males with indwelling Foley catheters.[10] This is also true in cases of inpatients with catheter associated chronically ill patients admitted to the hospital. In a recent hospital-based survey regarding catheter-associated urinary tract infection, it was seen that house officers had significant knowledge gaps regarding prevention of UTI and care of Foley's catheter as compared to residents and specialists.[11] As house officers deal with catheterization in most setups, it is imperative to ensure adherence to aseptic technique and proper care to prevent UTI.

In community-acquired urinary tract infection, increasing drug resistance is a growing concern in patients presenting to the emergency department. First-line antibiotics like Co-amoxiclav, Ciprofloxacin, Ofloxacin, and Cephalexin are not helpful now in treating even uncomplicated urinary tract infection.[12] This trend was also observed in our study where most of these drugs

Bacterial													
Antibiotic		E.coli ESBL	E.coli MDR	KLEBPNEUMDR	KLEB-PNEU	KLEB-PNEU. ESBL	PSEUDO-MONAS AERU.	PSEUDO-MONAS AERU MDR	SALMO-NELLA SPP	SALMO-NELLA PARA.	STAPH. AUREUS MRSA	ENTERO-COCCUS SPP	TOTAL
Amoxil/Calve	S	1.60%	3.10%	0.00%	3.10%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	7.80%
	R	45.30%	18.80%	6.20%	1.60%	3.10%	0.00%	1.60%	1.60%	0.00%	1.60%	3.10%	82.80%
	N	0.00%	0.00%	0.00%	0.00%	0.00%	4.70%	1.60%	0.00%	1.60%	0.00%	1.60%	9.40%
Cefixime	S	0.00%	0.00%	0.00%	1.60%	0.00%	0.00%	0.00%	0.00%	1.60%	0.00%	1.60%	4.70%
	R	46.90%	21.90%	6.20%	1.60%	3.10%	0.00%	1.60%	1.60%	0.00%	0.00%	1.60%	84.40%
	N	0.00%	0.00%	0.00%	1.60%	0.00%	4.70%	1.60%	0.00%	0.00%	1.60%	1.60%	10.90%
Ceftazidime	S	1.60%	0.00%	0.00%	3.10%	0.00%	3.10%	0.00%	0.00%	0.00%	0.00%	1.60%	9.40%
	R	43.80%	20.30%	4.70%	1.60%	3.10%	0.00%	3.10%	0.00%	0.00%	0.00%	1.60%	78.10%
	N	1.60%	1.60%	1.60%	0.00%	0.00%	1.60%	0.00%	1.60%	1.60%	1.60%	1.60%	12.50%
Ceftriaxone	S	0.00%	0.00%	0.00%	3.10%	0.00%	1.60%	0.00%	0.00%	1.60%	0.00%	1.60%	7.80%
	R	45.30%	20.30%	6.20%	1.60%	3.10%	0.00%	1.60%	1.60%	0.00%	0.00%	1.60%	81.20%
	N	1.60%	1.60%	0.00%	0.00%	0.00%	3.10%	1.60%	0.00%	0.00%	1.60%	1.60%	10.90%
Co-Trimoxazole	S	6.30%	4.80%	1.60%	3.20%	0.00%	1.60%	0.00%	0.00%	1.60%	1.60%	1.60%	22.20%
	R	39.70%	17.50%	4.80%	1.60%	3.20%	0.00%	1.60%	1.60%	0.00%	0.00%	1.60%	71.40%
	N	0.00%	0.00%	0.00%	0.00%	0.00%	3.20%	1.60%	0.00%	0.00%	0.00%	1.60%	6.30%
Fosfomycin	S	40.60%	20.30%	4.70%	4.70%	3.10%	0.00%	1.60%	1.60%	0.00%	0.00%	0.00%	76.60%
	R	4.70%	1.60%	1.60%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	3.10%	10.90%
	N	1.60%	0.00%	0.00%	0.00%	0.00%	4.70%	1.60%	0.00%	1.60%	1.60%	1.60%	12.50%
Gentamicin	S	23.40%	7.80%	3.10%	3.10%	1.60%	3.10%	0.00%	0.00%	0.00%	0.00%	3.10%	45.30%
	R	23.40%	14.10%	3.10%	1.60%	1.60%	0.00%	3.10%	1.60%	0.00%	0.00%	0.00%	48.40%
	N	0.00%	0.00%	0.00%	0.00%	0.00%	1.60%	0.00%	0.00%	1.60%	1.60%	1.60%	6.20%
Imipenem	S	43.80%	17.20%	3.10%	1.60%	3.10%	4.70%	0.00%	1.60%	0.00%	0.00%	3.10%	78.10%
	R	1.60%	3.10%	1.60%	0.00%	0.00%	0.00%	3.10%	0.00%	0.00%	0.00%	0.00%	9.40%
	N	1.60%	1.60%	1.60%	3.10%	0.00%	0.00%	0.00%	0.00%	1.60%	1.60%	1.60%	12.50%
Nitrofurantoin	S	43.80%	18.80%	0.00%	3.10%	3.10%	1.60%	0.00%	1.60%	0.00%	1.60%	3.10%	76.60%
	R	3.10%	3.10%	6.20%	1.60%	0.00%	0.00%	1.60%	0.00%	0.00%	0.00%	0.00%	15.60%
	N	0.00%	0.00%	0.00%	0.00%	0.00%	3.10%	1.60%	0.00%	1.60%	0.00%	1.60%	7.80%
Ciprofloxacin	S	6.20%	0.00%	0.00%	3.10%	0.00%	3.10%	0.00%	0.00%	0.00%	1.60%	3.10%	17.20%
	R	39.10%	20.30%	6.20%	1.60%	1.60%	0.00%	3.10%	1.60%	0.00%	0.00%	0.00%	73.40%
	N	1.60%	1.60%	0.00%	0.00%	1.60%	1.60%	0.00%	0.00%	1.60%	0.00%	1.60%	9.40%

S = Sentivie, R = Resistance, N = Not Checked

Table 5: Association of antibiotic resistance and sensitivity with bacterial growth

have very less antimicrobial activity against isolated uropathogens. General practitioners find it difficult to select appropriate empirical therapy for UTI in this era of resistant uropathogens. [13]

In recent years it has been observed that ciprofloxacin, which was once a novel first-line drug of choice for uncomplicated and complicated UTI has lost its efficacy completely due to extensive and irrational use of this broad-spectrum antibiotic. In our study, ciprofloxacin showed a slightly improved sensitivity, as compared to 1st, 2nd, or 3rd generation cephalosporin which is a matter of great concern about the emerging resistance of bacteria to cephalosporin in treating common uncomplicated infections.

Nitrofurantoin was found to be a reasonably high efficacious oral agent among all antimicrobials. It can be used against almost all uropathogens in the current setting and similar results were also reported from other studies. [14] For developing countries with very fewer resources, this is a cost-effective medication, especially in treating uncomplicated UTI and for its prophylaxis.

The other oral antimicrobial which showed efficacy against most of the uropathogens is Fosfomycin, which is available in the form of a dissolvable single-dose sachet and has shown promising results in uncomplicated UTI. [15] On the other hand, for complicated UTI intravenous antibiotics of moderate to high susceptibility are Gentamicin and Carbapenems (Imipenem, Meropenem). In recent years, Carbapenems are being used mostly for resistant and complicated cases like Pseudomonas infections. In a similar study carried out in Peshawar, Pakistan, ESBL E.coli was most sensitive to Carbapenems (97.72%) followed by amikacin (86.36%) and piperacillin/tazobactam (72.52%). [16] Studies have shown that E.coli is highly resistant to the commonly prescribed cefixime (3rd generation cephalosporin) in Pakistan and neighboring countries such as Iran and India. [16, 17]

A similar pattern of sensitivity was observed in Sri Lanka, however, the ESBL E.coli had a carbapenem resistance of 4.9% which is much higher compared to our study (1. 6% resistance to carbapenem). [18] It is alarming to see that there was a 9.4% prevalence of resistance to carbapenem by the prevailing uropathogens in our study. Carbapenem resistance is an emerging challenge for the physicians and it is imperative to control this by rational use of antibiotics.

CONCLUSION

Choosing antibiotics for the urinary tract infection is becoming difficult because of increasing emergence of resistance to commonly prescribed antibiotics. Although increasing antimicrobial resistance to uropathogens responsible for UTI is a great concern all over the world yet there is no alternative to the rational use of antibiotics to preserve long term efficacy of many excellent drugs. Still, drugs like Nitrofurantoin, Fosfomycin, certain aminoglycosides, and Carbapenems have excellent efficacy against resistant strains in treating urinary tract infections. The selection of empirical antimicrobials for UTI in an emergency should be guided by the local culture and sensitivity patterns and should be reviewed as soon as the culture report is available. Hospital-wide data and multicentric studies are required to further establish the antibiogram of the region.

LIMITATION OF THE STUDY

It is a single-center study and data was collected through the emergency department so, the findings of this research cannot be generalized due to its low sample size. As this study was based on retrospective chart review so we were unable to categorize patients according to their symptoms or clinical severity. Furthermore, the sources of samples like catheter or mid-stream urine sampling cannot be identified. Although standard sampling techniques are ensured in the department when a urine sample is collected, still we cannot differentiate between community-acquired and nosocomial infections.

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