Section: Microbiology

Original Research Article

ANTIMICROBIAL RESISTANCE PROPERTIES OF UROPATHOGENIC ESCHERICHIA COLI IN ADULTS WITH URINARY TRACT INFECTION AND MOLECULAR CHARACTERISATION OF VIRULENCE FACTOR GENES IN RESISTANT STRAINS

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Abstract

Background: The ability of UPEC to cause urinary tract infection (UTI) is on the rise, while the ease of treating these infections due to multidrug resistance remains elusive. This study evaluated the prevalence of UPEC strains in adults with UTI, antimicrobial resistance pattern and the distribution of the most common virulence factor genes for multidrug resistance (MDR) by molecular methods. **Material & Methods:** *Escherichia coli* (E. coli) strains isolated from adult UTI patients admitted to Rajiv Gandhi Government Hospital, Chennai, were subjected to antibiotic susceptibility testing according to CLSI guidelines. The antibiotic resistance was determined by Extended-Spectrum Beta-lactamase (ESBL) and AmpC beta-lactamase screening. The presence of some virulence factors has been detected using PCR assay. **Results:** The study included 100 clinically significant consecutive, non-repetitive uropathogenic *Escherichia coli* isolates from patients with clinical diagnoses of UTI. Uropathogenic *E. coli* isolates were commonly isolated from medicine wards (40%). Around 93% of the isolates were associated with significant risk factors. Higher susceptibility was with Imipenem (91%) and Amikacin (91%). A higher proportion of UPEC isolates were resistant to most of the agents included in the antimicrobial panel (93%). Of all MDR isolates of UPEC, around 40% had ESBL-producing mechanisms of drug resistance. In genotype characterisation of the pan drug-resistant isolates, the "Fim H" gene was observed in (44.44%) of isolates, "Pap G" gene was observed in (11.11%) of isolates. **Conclusion:** The result showed that antibiotic resistance is escalating rapidly. UPEC strains causing infections are more likely to harbor certain virulence genes.

INTRODUCTION

Urinary tract infections represent the most common urologic disease encountered in humans in community-acquired and nosocomial bacterial infections. UTIs are the most common healthcare-associated infection in clinical practice and is mainly associated with different members of the family. Enterobacteriaceae and *Escherichia coli* is far by the most predominant pathogen.[3] UPEC (Uropathogenic *Escherichia coli*)is the causative agent of the vast majority of UTIs, accounting for about 70-90% of community-acquired UTIs and a significant proportion of Nosocomial UTIs (50%) and obviates the need for substantial medical costs.[4] UPEC clones are selected subsets of fecal flora that can adhere to host uroepithelial cells and mucous membranes and are considered a pre-requisite for establishing infectious diseases.[5] Given the complexities of human host defence systems, UPEC strains express many virulence factors to break the inertia of mucosal barriers.[6] The ability of UPEC to cause UTI is on the rise, while the ease of treating these infections due to multidrug resistance remains elusive. The difficulties encountered in treating these infections due to multidrug resistance necessitate updating the knowledge of their drug resistance in the given environment.[7] UPEC strains have many tools aiding their adaptation to dynamic

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microenvironments in the Urinary tract. Of these, the best-described virulence factors are involved in bacterial adhesion to the uroepithelium, and these proteinaceous structures are referred to as Fimbriae or pili.[8] UPEC strains possess Type 1 fimbriae and P fimbriae with fimH and papG as tip adhesion. The genes that confer these virulence properties are commonly located in specific regions of chromosomes termed "Pathogenicity islands" acquired by Horizontal gene transfer.[9,10] These virulence markers are expressed with different frequencies in the disease spectrum ranging from Asymptomatic bacteriuria to cystitis, urethritis, pyelonephritis, Acute urethral syndrome, complicated UTI, bacteremia, urosepsis and renal failure.

This study evaluated the prevalence of UPEC strains in adults with urinary tract infections, antimicrobial resistance pattern and the distribution of the most common virulence factor genes for multidrug resistance by molecular methods, which would aid in formulating effective infection control policies and antibiotic stewardship programme, thereby minimizing the spread of Anti microbial resistance.

MATERIALS AND METHODS

This cross-sectional study was conducted at the Institute of Microbiology, Rajiv Gandhi Government Hospital, Chennai, from March 2017 to September 2018 on 100 patients admitted to Rajiv Gandhi Government Hospital, Chennai. Informed consent for participating in the study and Institutional ethical committee clearance were obtained before starting the study.

Inclusion Criteria

All patients over 18 years with a clinical diagnosis of Urinary tract infection and consecutive, non-repetitive, clinically significant isolates of *E. coli* from midstream clean catch urine samples were included.

Exclusion Criteria

Patients < 18 years of age on Antibiotic treatment and *Escherichia coli* isolates of repeat samples from the same patients were excluded.

Methodology

The significance of the *Escherichia coli* isolates was based on the presence of Gram-negative bacilli in Gram stain, significant quantitative growth in culture and biochemical reactions. All the samples were inoculated in Nutrient Agar, CLED and EMB agar. The isolates were then subjected to preliminary tests like Gram staining, Motility, Catalase test and Oxidase test. The Bacterial isolates, which were Gram-negative bacilli, catalase-positive, oxidase-negative and motile isolates, were subjected to biochemical reactions for further confirmation.

Antimicrobial susceptibility testing

Antimicrobial susceptibility was tested by the Kirby-Bauer disk diffusion method. Antimicrobial agents tested were Cefotaxime (30 µg), Cefepime (30 µg), Cefotaxime - Clavulinic acid (30/10 µg), Gentamicin (10 µg), Amikacin (30 µg), Norfloxacin (10 µg), Nitrofurantoin (300 µg), Imipenem (10 µg), Tetracycline (30 µg), Trimethoprim/Sulfamethoxazole (1.25/23.75 µg) and Cefoxitin (30 µg). As mentioned earlier, antibiotic resistance was determined according to the breakpoint proposed by CLSI. For quality control, *E. coli* ATCC®25922™ was used.

Detection of Antimicrobial Resistance

All the isolates were subjected to an Extended Spectrum Beta–lactamase (ESBL) screening test using cefotaxime (30 µg) and an AmpC beta-lactamase screening test using cefoxitin (30 µg). The positive isolates in the screening test were subjected to respective confirmatory tests using appropriate antibiotic discs (i.e., combined disc method).

The isolates resistant to cefoxitin (30 µg) were considered AmpC screening test positive. AmpC production was confirmed by placing cefoxitin and cefoxitin-cloxacillin at 20 mm apart in the Mueller Hinton agar plate. The test isolate that demonstrated a zone of inhibition of > 5 mm around the cefoxitin inhibitor than that around the cefoxitin alone was considered an AmpC producer. ESBL production was confirmed by the double disc synergy method. MBL(metallo beta-lactamase) production screening with Imipenem (IMP)disc and confirmation done by IMP-EDTA disc method

Molecular Characterisation

The Pan drug-resistant UPEC isolates were subjected to a conventional Polymerase chain reaction (PCR) to detect FimH and PapG genes.

Statistical Analysis

Statistical analyses were conducted using the Statistical Package for Social Sciences (SPSS-18). The population data were analysed using Pearson's Chi-Square analysis test.

RESULTS

During the study period, 100 clinically significant consecutive, non-repetitive uropathogenic *Escherichia coli* isolates from patients with clinical diagnoses of urinary tract infection were included in the study. Male predominance was reported, with a maximum of 30 patients (30%) in the age group of > 60. Uropathogenic E. coli isolates- 40(40%) were mainly from general medicine wards. Diabetes mellitus was the most common predisposing factor (52%) for UTI infection (Tables 1 and 2).

Table 1: Observation of demographic data

Parameters		Number of Isolates (%)
Gender	Male	54 (54%)
	Female	46 (46%)

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Age Group	18-20	3 (3%)
	21-30	10 (10%)
	31-40	8 (8%)
	41-50	29 (29%)
	51-60	20 (20%)
	>60	30 (30%)
Distribution of UPES isolates among various clinical settings	Distribution of UPES isolates (IMCU, ISCU, Uro-ICU)	6 (6%)
	General Medicine Wards	40 (40%)
	General Surgical Wards	21 (21%)
	Nephrology	31 (31%)
	Orthopaedics	2 (2%)

Table 2: Distribution of risk factors

Risk Factors	Number of Isolates (%)
Urethral stricture	52 (52%)
Urolithiasis	6 (6%)
BPH	5 (6%)
Diverticulum	5 (5%)
PCJ obstruction	4 (4%)
Renal cysts	3 (3%)
Immunosuppression	3 (3%)
Congenital abnormalities	3 (3%)
Neurogenic bladder	3 (3%)
Vesicoureteral reflux (VUR)	2 (2%)
Cystocoel	2 (2%)
Diabetes mellitus (DM)	2 (2%)
Post Renal Transplant	1 (1%)
Urological Interventions	1 (1%)
Previous UTI	1 (1%)

Table 4: Descriptive Analysis of antimicrobial sensitivity pattern for UPEC in a study group

Antimicrobial agent	No. of susceptible Isolates N (%)	No. of Resistant Isolates N (%)
Amikacin (30 µg)	91 (91)	9 (9)
Gentamicin (10 µg)	91 (91)	9 (9)
Cefotaxime	7 (7)	93 (93)
Cefotaxmine-clavulanic acid (30-10 µg)	37 (37)	63 (63)
Norfloxacin (10 µg)	5 (5)	95 (95)
Nitrofurantoin (300 µg)	62 (62)	38 (38)
Imipenem (10 µg)	91 (91)	9 (9)
Tetracycline (30 µg)	50 (50)	50 (50)
Cotrimoxazole (1.25 / 23.75 µg)	50 (50)	50 (50)
Cefoxitin	47 (47)	53 (53)

A high degree of resistance was observed for various classes of antimicrobial agents. Higher susceptibility was seen with Imipenem 91 (91%), Amikacin 91 (91%), and Gentamicin 91 (91%), followed by Nitrofurantoin (62%). Of the 100 isolates of UPEC from patients with clinical diagnosis of UTI, 7 (7%) isolates were observed to be sensitive to all the agents included in the antimicrobial panel. 93 (93%) proportion of UPEC isolates from patients were observed to be resistant to most of the agents included in the antimicrobial panel, which were mainly from medical wards (43.01%) (Table 3, 4).

Table 5: Observation of Antimicrobial resistance and susceptibility parameters of patients

Parameters	Isolates N (%)
Rates of extended-spectrum Beta Lactamases in UPEC isolates(n=93)	
No. of isolates positive in phenotype screening test	93
No. of ESBL producers - confirmed	37 (39.78%)
AMPC Beta Lactamases among UPEC isolates (n =93)	
No. of isolates positive in phenotype screening test	53
No. of AmpC producers - confirmed	35 (37.63%)
MBL production in UPEC isolates (n=93)	
No. of isolates positive in phenotype screening test	14
No. of MBL producers - confirmed	9 (9.7%)
Antimicrobial resistance spectrum among UPEC isolates (n=93)	
ESBL	37 39.78%, (p=0.012)
AMP C	35 37.63%, (p=0.010)
MBL	9 9.67%, (p=0.046)
ESBL + AMPC	7 7.52%, (p=0.044)
ESBL + MBL	3 3.22%, (p=0.002)
AMPC + MBL	2 2.15%, (p=0.001)

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The main potential risk factor for the development of MDR UPEC infection was reported Diabetes mellitus in 48 cases (51.61%), followed by Urethral stricture in 6 cases (6.45%). Out of 93 MDR isolates of UPEC, 37 isolates were (39.78%) ESBL producers of all isolates of UPEC, 35 isolates (37.63%) were confirmed to be AmpC Beta-Lactamase producers, and 9 isolates (9.67%) were confirmed to be MBL producers. The enzyme coproduction was reported in 12.9% of uropathogenic E. coli isolates. ESBL and AmP C coproduction were observed among most isolates, accounting for about 7.52% of the total isolates with enzyme coproduction. ESBL production was the most common resistance mechanism observed, accounting for 37 (39.78%) of the total isolates, followed by Amp C 35(37.63%) (Table 5).

Table 3: MDR isolates and other parameters of patients

		Number of Isolates (%)
Distribution of sensitive strains of UPEC in UTI	No. of sensitive strains	93 (93%)
MDR isolates of UPEC in a study group	No. of resistant strains	48 (51.61%)
MDR isolates in various clinical settings (n=93)	Intensive Care Units	40 (43.01%)
	Medical wards	25 (26.88%)
	Surgical wards	17 (18.27%)
	Nephrology wards	7 (7.7%)
	Orthopaedics	7(7.52%)
Risk factors implicated in MDR UPEC infection (n=93)	Urethral stricture	6 (6.45%)
	Urolithiasis	6 (6.45%)
	Benign Prostatic Hyperplasia	5 (5.37%)
	Diverticulum	5 (5.37%)
	PCJ (Pelviureteric junction) obstruction	4 (44.44%)
	Renal cysts	4 (44.44%)
	Immunosuppression	4 (4.3%)
	Congenital abnormalities	3 (3.22%)
	Neurogenic bladder	3 (3.22%)
	Vesoco Ureteric Reflex	3 (3.22%)
	Cystocele	3 (3.22%)
	Diabetes Mellitus	2 (2.15%)
	Post Renal Transplant	2 (2.15%)
	Urological Interventions	2 (2.15%)
	Previous UTI	2 (2.15%)
Enzyme coproduction among the UPEC ISOLATES (n=93)	ESBL + AMP C	2 (2.15%)
	ESBL + MBL	2 (2.15%)
	AMP C + MBL	1 (1.07%)
Virulence genes (n=9)	Fim H	1 (1.07%)
	Pap G	1 (1.07%)
	Fim H + Pap G	1 (1.07%)

In genotype characterisation of the pan drug-resistant isolates, the "Fim H" gene was observed in 4 (44.44%) of isolates, and the "Pap G" gene was observed in 1 (11.11%) of isolates. These highly virulent resistant strains account for significant mortality and morbidity (Table 3, Figure 1).

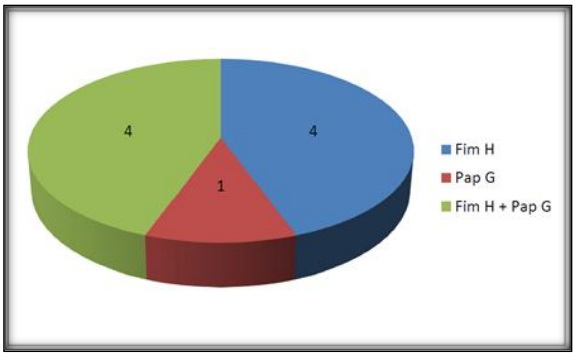

Figure 1: Observation of molecular characterisation of pan-drug-resistant UPEC isolates (n=9)

DISCUSSION

Urinary tract infections are among the most prevalent infections encountered worldwide. *Escherichia coli* is the cause of more than 80 percent of urinary tract infections in all age groups, in both ambulatory and hospitalised patients. The infection's severity often depends on the interplay between host susceptibility and virulence of the associated strains.[1-3] Hence, understanding the virulence properties of the pathogen aids the clinician to anticipate the development of complications, their potential outcomes and effective preventive measures. In view of these, the virulence markers may serve as an important epidemiological indicator in detecting UTIs by resistant isolates.[5,7]

In this study, among the 100 UPEC isolates, the maximum proportion of the subjects belonged to more than 60 years of age category (30%). This highlights that infection by highly virulent organisms is more common in the elderly who are immunocompromised, and this is concordant with a study by Usein et al., where highly virulent *E.co*li strains were isolated from adult UTI.[12] Male predominance, also observed in the present study, accounting for 54 %, Regarding speciality-wise distribution of UPEC, 40 % of isolates were from medical wards (40%). This was similar to a study conducted by Montaz H et al. on the virulence potential of UPEC in various clinical settings.[13] Significant risk factors for colonisation/infection with MDR organisms are selective antibiotic pressure, prolonged hospitalisation, instrumentation, etc. In this study, around 93 % of the isolates were associated with significant risk factors for UTI, and this correlates well with a study conducted by Santo et al. on risk factors for UPEC infections.[14]

The antimicrobial susceptibility pattern of UPEC revealed that 95% of isolates were resistant to cefotaxime, 93% to Nitrofurantoin, and 38% to Norfloxacin. Higher susceptibility was observed with Imipenem (31%) and Amikacin (91%), followed by Nitrofurantoin (62%). These findings were similar to the study conducted by Rezaee et al.[15] In the present study, 7% of isolates were observed to be sensitive to all the agents included in the antimicrobial panel. MDR isolates were reported to be significantly higher

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(93%). These MDR strains pose a serious threat in the management of patients due to transferable drug resistance and immune evasion mechanisms owing to the multitude of virulence factors, which correlates with the study conducted by Abe et al. on virulence factors of UPEC.[16]

MDR isolates with enzyme coproduction and surface adhesions were isolated in greater proportion from Intensive Care Units and Nephrology Units from patients with chronic UTI. A study by Caracuo et al. also showed similar results.[17] Around 88% of the MDR virulent isolates were associated with patients with significant risk factors, and Diabetes mellitus is the most common (48%), followed by obstructive lesions of the genitourinary tract, which is concordant with a study conducted by Navidina M et al.[18]

Among the MDR UPEC isolates, 39.78% were phenotypically characterised as ESBL producers, 37.6% were AmpC producers, and 9.67% were found to be MBL producers. These pan-drug-resistant isolates pose a significant challenge in the management of UTIs. Similar findings were reported by Iqbal M et al.[19]

The Coexistence of different classes of beta-lactamases in a single isolate may pose diagnostic and therapeutic challenges. In this study, enzyme coproduction was evident in 12.90% of UPEC isolates, of which ESBL and AmpC coproduction was predominant, accounting for 7.52%. It correlates well with a study conducted by Mukherjee M et al. in Kolkata on MDR isolates of UPEC.[20] The emergence of resistant phenotypes occurs mainly due to antibiotic selection pressure accelerated by inappropriate dosage and duration of treatment. Hence, it is mandatory to perform antimicrobial susceptibility testing for all the agents in the panel rather than testing a single agent to extrapolate the results to other agents. Here, ESBL production was the predominant resistant mechanism observed.

Pandrug resistance in UPEC isolates is predominantly mediated by multidrug resistance transferrable plasmids. Hence, it becomes necessary to evaluate the virulence factors (especially adhesion coding operons) in these resistant isolates to curtail chronic infections and selective antibiotic pressure responsible for the prolonged survival and spread of these resistant isolates. Among the nine pan drug-resistant isolates, four isolates had Fim H gene, four had both Pap G and Fim H genes, and one isolate was positive for the Pap G gene, accounting for chronic infections due to antimicrobial resistance, which correlates well with a study by Vila J et al. on quinolone-resistant Uropathogenic *E. coli*.[21] Remarkably, fimbriation promotes adhesion to phagocytes and accounts for its intracellular survival within the macrophages. Type 1 fimbriae with Fim H as tip adhesion molecule is required for UTI and intracellular biofilm formation, suggesting various physiological implications. Enhanced bacterial adhesion to host cells constitutes a survival benefit. Fimbriation is considered an important virulence mechanism required to survive in the presence of extracellular antibacterial drugs, which occurs by up-regulating Fim H-mediated binding to macrophages.[22]

CONCLUSION

The present study reported a high rate of antimicrobial resistance among the most commonly used antimicrobial agents for treating UTIs caused by UPEC isolates. Among the UPEC isolates, 37 isolates (39.78%) were ESBL producers, followed by Amp C producers, 35 isolates (37.63%), and 9 (9.67%) isolates were MBL producers. Molecular characterisation of the pan drug-resistant UPEC isolates revealed a Fim H gene positivity rate of 44.4% and Pap G gene positivity rate of 11.11%, accounting for a higher degree of virulence in the strains implicated in chronic UTI in critically ill patients. Routine testing of these factors and co-relation with antimicrobial resistance is recommended. These findings will help understand the pathogenicity and proper management of UTI patients, thus decreasing the improper use of antibiotics.

REFERENCES

1. Stephenson S, Brown PD. Distribution of virulence determinants among antimicrobial-resistant and antimicrobial-susceptible Escherichia coli implicated in urinary tract infections. Indian J. Med. Microiol. 2016; 34: 448-456.
2. Anderson AC, Martin SM, SJ Hultgren SJ. Host subversion by the formation of intracellular bacterial communities in the urinary tract. MicrobesInfect. 2004; 6:1094-101.
3. Bernard MS, Hunter KF, Moore KN. A review of strategies to decrease the duration of indwelling urethral catheters and potentially reduce the incidence of catheter-associated urinary tract infections. Urol Nurs. 2012;32:29-37.
4. Ruiz J, Simon K, Horcajada JP, Velasco M, Barranco M, Roig G et al. Differences in virulence factors among clinical isolates of Escherichia coli causing cystitis and pyelonephritis in women and prostatitis in men. Journal of Clin. Microbiology. 2002; 40: 4445-49.
5. Chakraborty A, Adhikari P, Senoy S, Saralaya V. Molecular characterisation of Uropathogenic Escherichia coli isolates at a tertiary care hospital in South India. Indian J Med Microbiol 2017; 35:305-10.
6. Vijalalakshmi J, Hymavathi R, Renukadevi A, Anithalavanya, Ramanamma MV. Study of virulence factors in uropathogenic Escherichia coli. J Evol Med Dent Sci 2015;4:1297-1305.
7. Rahdar M, Rashki A, Miri HR, Rashki Ghalehnoo M. Detection of pap, sfa, afa, foc, and fim Adhesin-Encoding Operons in Uropathogenic Escherichia coli Isolates Collected From Patients With Urinary Tract Infection. Jundishapur J Microbiol 2015;8:e22647.
8. Oluwasola F, Kolawole DO, Lamikanra A. Antibiotic resistance and Virulence properties in Escherichia coli strains from cases of Urinary tract infections. Afr. J. Infect. Dis. 2013;7:1-7.
9. Mims AD, Norman DC, Yamamura RH, Yoshikawa TT. Clinically in apparent (asymptomatic) bacteriuria in ambulatory elderly men: epidemiological, clinical, and microbiological findings. J Am Geriatr Soc, 1990; 38:1209-14.
10. Neamati F, Firoozeh F, Safari M, Zibaei M. Virulence genes and antimicrobial resistance pattern in uropathogenic Escherichia coli isolated from hospitalised patients in Kashan, Iran. Jundishapur J Microbiol 2015; 8: e17514.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

11. Performance Standards for Antimicrobial Susceptibility Testing. 27th ed. CLSI supplement M100. Clinical and Laboratory Standards Institute, Wayne, PA, USA, 2017.
12. Usein CR, Damian M, Tatu-Chitoiu D, Capusa C, Fagaras R, Tudorache D, et al. Prevalence of virulence genes in Escherichia coli strains isolated from Romanian adult urinary tract infection cases. J Cell Mol Med. 2001;5:303–10.
13. Momtaz H, Karimian A, Madani M, Safarpoor Dehkordi F, Ranjbar R, Sarshar M, et al. Uropathogenic Escherichia coli in Iran: serogroup distributions, virulence factors and antimicrobial resistance properties. Ann Clin Microbiol Antimicrob. 2013;12:8.
14. Santo E, Macedo C, Marin JM. Virulence factors of uropathogenic Escherichia coli from a university hospital in Ribeirao Preto, Sao Paulo, Brazil. Rev Inst Med Trop Sao Paulo. 2006;48:185–8.
15. Rezaee MA, Sheikhalizadeh V, Hasani A. Detection of integrons among multidrug-resistant (MDR) Escherichia coli strains isolated from clinical specimens in northern west of Iran. Braz J Microbiol. 2011;42:1308–13.
16. Abe CM, Salvador FA, Falsetti IN, Vieira MA, Blanco J, Blanco JE, et al. Uropathogenic Escherichia coli (UPEC) strains may carry virulence properties of diarrhoeagenic E. coli. FEMS Immunol Med Microbiol. 2008;52:397–406.
17. Caracciolo A, Bettinelli A, Bonato C, Isimbaldi C, Tagliabue A, Longoni L, et al. Antimicrobial resistance among Escherichia coli that cause childhood community-acquired urinary tract infections in Northern Italy. Ital J Pediatr. 2011;37:3-6.
18. Navidinia M, Najar Peerayeh S, Fallah F, Bakhshi B, Adabian S, Alimehr S, et al. Distribution of the Pathogenicity Islands Markers (PAIs) in Uropathogenic E.coli Isolated from Children in Mofid Children Hospital. Arch Pediatr Infect Dis. 2013;1:75–9
19. Iqbal M, Patel IK, Shah SH, Ain Q, Barney N, Kiani Q, et al. Escherichia coli's Susceptibility patterns: multidrug-resistant isolates' prevalence and extended-spectrum beta-lactamase phenotype. J Pak Med Assoc. 2002;52:407–11.
20. Mukherjee M, Basu S, Mukherjee SK, Majumder M. Multidrug-Resistance and Extended Spectrum Beta-Lactamase Production in Uropathogenic E. Coli which were Isolated from Hospitalised Patients in Kolkata, India. J Clin Diagn Res. 2013;7:449–53.
21. Vila J, Simon K, Ruiz J, Horcajada JP, Velasco M, Barranco M, et al. Are quinolone-resistant uropathogenic Escherichia coli less virulent? J Infect Dis. 2002; 186: 1039–42.
22. Blomfield IC, McClain MS, Eisenstein BI. Type 1 fimbriae mutants of Escherichia coli K12: characterization of recognized afimbriate strains and construction of new film deletion mutants. Mol Microbiol 1991;5:1439–45.

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