

## Antibiotic susceptibility and drug prescription pattern in uropathogenic *Escherichia coli* in district Muzaffarabad, Azad Jammu and Kashmir, Pakistan

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### Abstract

The present research study was done to determine the correlation between antibiotic susceptibility and drug prescription patterns in empirical treatment of uropathogenic *Escherichia coli* (*E. coli*) in two hospitals of district Muzaffarabad, Azad Kashmir, Pakistan.

One hundred uropathogenic *E. coli* clinical isolates were collected from UTI patients who attended the Combined Military Hospital (CMH) and Abbas Institute of Medical Sciences (AIMS), district Muzaffarabad, AJK. All isolates were subjected to antibiotic susceptibility against seven commonly prescribed antibiotics by Kirby-Bauer disk diffusion method. However, all the *E. coli* isolates were susceptible to Imipenem. Eight percent and 10% of isolates from CMH and AIMS were found to be resistant against Nitrofurantoin drug respectively. Similarly, 94% and 74% isolates from CMH and 60% and 64% isolates from AIMS were found to be resistant against Co-trimoxazole and Co-amoxiclavate, respectively. Pipemidic acid resistance was also detected in 76% and 60% isolates from AIMS and CMH, respectively. Ciprofloxacin resistance was also observed in 54% and 36% isolates from AIMS and CMH, respectively.

The finding of the study revealed that both hospitals have different drug susceptibility pattern against uropathogenic *E. coli*, which may be associated with patterns of drug prescription in empirical treatment of urinary tract infections. There is a vital need for appropriate development of hospital-specific antibiograms to determine appropriate empiric therapy of urinary tract infections.

**Keywords:** Antibiotic susceptibility patterns, *Escherichia coli*, Urinary tract infection patients, Empirical treatment.

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### Introduction

Urinary tract infections (UTI) are one of the most common

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bacterial infections diagnosed in both outpatients as well as in hospitalised patients. Each year 150 million cases of UTI are reported worldwide, resulting in a significant increase in healthcare associated expenditure.<sup>1</sup> Although UTI affects both sexes, it is more common in women than men. It has been reported that every second woman contract UTI at least once in her life.<sup>2</sup> More than 80% UTI infections are caused by *Escherichia coli* (*E. coli*), commensal gram-negative bacteria, inhabiting the colon of warm blooded animals.<sup>3</sup>

Empirical treatment based on global data of antimicrobial susceptibility is the most preferred method to treat UTI. This global antimicrobial susceptibility data is not constant and varies from time to time and from place to place.<sup>4</sup> Empirical treatment of UTI without local antimicrobial susceptibility data may lead to misuse of antibiotics and will end up in increasing antibiotic resistance. Updated knowledge of local hospital-based antibiotic susceptibility of uropathogens is important for ensuring appropriate therapy and minimising the threat of antibiotic resistance.

The present study was carried out to investigate the prevalence and antibiotic susceptibility patterns of *E. coli* isolated from patients affected with UTI against antibiotics frequently used in empirical treatment of UTI in two main hospitals, AIMS and CMH of district Muzaffarabad, Azad Jammu and Kashmir (AJK).

### Methods and Results

The study was carried out in the microbiology laboratory of Abbas Institute of Medical Sciences (AIMS) and Combined Military Hospital (CMH), district Muzaffarabad, AJK, Pakistan.

Urine samples were collected from the OPDs (outpatients departments) and indoor patients of two major hospitals from district Muzaffarabad, AJK, Pakistan. The duration of the study was eight months from November 2016 to June 2017.

Urine samples of 100 patients, comprising 50 males and 50 females, who attended the outpatient departments (OPDs) as well as indoor patients of the two hospitals and had clinical evidence of urinary tract infection, determined by physicians, were included in this study. The age of the

patients included ranged from 20 months to ≥ 68 years. Patients with history of hospital admission a week before their presentation in OPDs were excluded from the study to rule out hospital-acquired infections. The patients on antibiotic therapy were also excluded from the study.

A 20ml calibrated sterile screw-capped universal container was used to collect clean-catch midstream urine from the patients. The specimens were properly labelled, transported to microbiology laboratory and analysed within two hours. The patients were well instructed about the aseptic urine sample collection procedure. Prior to sample collection, verbal informed consent of all the patients was taken. The study was conducted after due ethical approval of hospital administration.

*E. coli* from urine sample was isolated with the help of a sterile 4.0mm calibrated platinum loop. A loopful (0.001 ml) of urine was inoculated on Cystine-Lactose-Electrolyte Deficient (CLED) agar (Oxoid, Thermo Scientific-UK) plates followed by incubation at 37°C for 24 hours. In case of no growth the plates were further incubated for additional 24 hours. The isolated bacterial colonies were counted and multiplied by 1,000 for the estimation of bacterial load/ml of the urine sample. A specimen was considered positive for UTI if the culture yielded a concentration of ≥10<sup>5</sup> CFU/ml. In addition to bacterial load, specimen having >5 pus cells per µl, observed under the microscope, were also considered positive. Cultural and biochemical characterisation of *E. coli* was performed according to Bergey’s manual of determinative bacteriology.<sup>5</sup> Antimicrobial susceptibility testing was performed on Mueller-Hinton agar using Kirby Bauer’s disk diffusion method.<sup>6</sup> The antibiotics used in empirical treatment of UTI in AIMS and CMH hospitals are Imipenem (10µg) Ciprofloxacin (5 µg), Cefixime (5µg), Co-amoxiclav (20µg), Pipemedic acid (20µg), Co-trimoxazole (25µg) and Nitrofurantoin (10 µg) obtained from Oxoid-Thermo Scientific, UK.

**Table-1:** Gender wise prevalence of UTI at AIMS and CMH.

Hospital	Age Group	Male [n(%)]	Female[n(%)]
AIMS (n=50)	20 months 68 year	17 (34)	33 (66)
CMH (n=50)	1-60years	16 (32)	34 (68)

AIMS: Abbas Institute of Medical Sciences; CMH: Combined Military Hospital; UTI: Urinary tract infection.

**Table-2:** Antibiotic response pattern of *E. coli* isolates from AIMS hospital.

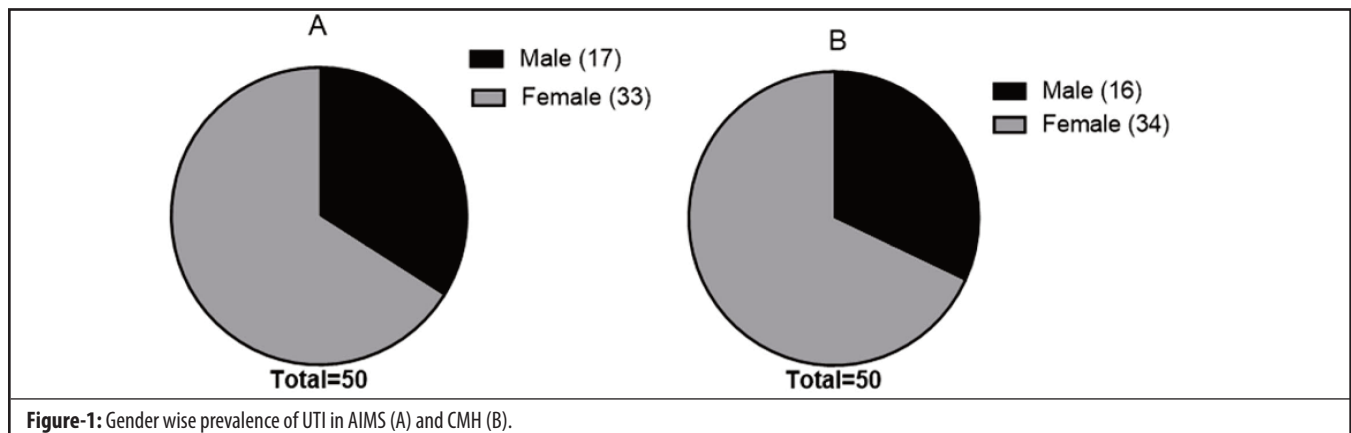
Drugs	Sample Size	Sensitive	Resistant [n(%)]
Imipenem	50	50	0 (0)
Ciprofloxacin	50	23	27 (54)
Cefixime	50	3	47 (94)
Co-Amoxiclave	50	18	32 (64)
Pipemedic Acid	50	12	38 (76)
Nitrofurantoin	50	45	5 (10)
Co-Trimoxazole	50	20	30 (60)

**Table-3:** Antibiotic response pattern of *E. coli* isolates from CMH hospital.

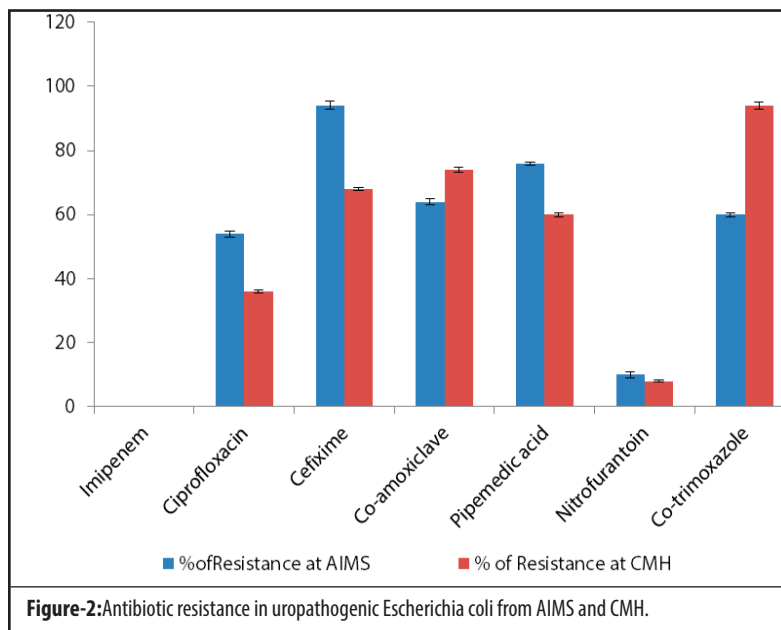
Drugs	Sample Size	Sensitive	Resistant [n(%)]
Imipenem	50	50	0 (0)
Ciprofloxacin	50	32	18 (36)
Cefixime	50	16	34 (68)
Co-Amoxiclave	50	13	37 (74)
Pipemedic Acid	50	20	30 (60)
Nitrofurantoin	50	46	4 (8)
Co-Trimoxazole	50	3	47 (94)

Antibiotic susceptibility results were interpreted according to the guidelines of the Clinical Laboratory Standards Institute (CLSI). Statistical analysis was performed using SPSS software (version 16.0, SPSS, Inc., Chicago, IL) and P < 0.05 was considered to be statistically significant.

The data obtained from this study showed that uropathogenic *E. coli* was present in all the samples irrespective of age (20 months to 68 years)(Table 1, Figure 1). However, UTI prevalence was higher in females than males (Figure1). All the 100 *E. coli* isolates, 50 each from AIMS and CMH were susceptible to Imipenem. Nitrofurantoin resistance was present in 5(10%, p=0.48) and 4(8%, p=0.01) isolates from AIMS and CMH,



**Figure-1:** Gender wise prevalence of UTI in AIMS (A) and CMH (B).



respectively. Resistance against Cefixime 47(94%, p-value 0.001), Co-trimoxazole 30(60%, p-value 0.005), Pipemidic acid 38(76%, p-value 0.001) and Co-amoxiclave 32(64%, p-value 0.03), Ciprofloxacin 27(54%, p-value 0.05) was observed in *E. coli* isolates from AIMS (Table 2). Similarly, resistance against Cefixime 34(68%, p-value 0.01), Co-trimoxazole 47(94%, p-value 0.001), Pipemidic acid 30(60%, p-value 0.005) and Co-amoxiclave 37(74%, p-value 0.001), Ciprofloxacin 18(36%, p-value 0.03) was found in *E. coli* isolates from CMH (Figure 2, Table 3).

## Discussion

Microbial infections of urinary tract are among the most frequently occurring bacterial infections across the globe. Empirical treatment based on global susceptibility data is the preferred method for treatment of urinary tract infections. However, this global antimicrobial susceptibility data is not constant across the globe.<sup>4</sup> This may lead to misuse of antibiotics and consequently antibiotic resistance development in microbes.

The present study provides valuable data to compare and monitor the status of antimicrobial resistance in uropathogenic *E. coli* in two main tertiary care hospitals of district Muzaffarabad. Both hospitals provide indoor and outdoor treatment facilities to the population of Muzaffarabad and the surrounding areas of district Muzaffarabad, while CMH additionally caters to armed forces and their families deployed in this region.

The current study showed higher prevalence of UTI in females (67%) than in males (33%) which is in line with other findings that UTI occur more frequently in females

than males.<sup>7</sup> This may be due to the general anatomical structure of the female body, such as shorter and wider urethra, close proximity of the urethral meatus to the anus, sexual intercourse, and poor hygienic conditions.<sup>8</sup> Cefixime resistance was observed in 94% and 68% of isolates from AIMS and CMH, respectively. Resistance against Ciprofloxacin was also higher in isolates from AIMS (54%) than CMH (36%). Similar level of resistance (57%) against ciprofloxacin was also reported.<sup>9</sup> High rates of resistance against Cefixime and Cotrimoxazole was also reported in *E. coli*, isolated in Shahid Sadoughi Hospital, Iran.<sup>10</sup> Co-amoxiclave resistance was found in 64% and 60% isolates from AIMS and CMH, respectively. Our data is supported by the finding that Co-amoxiclave resistance reached 48% in hospital and 32.6% in the community by 2014.<sup>11</sup>

Co-trimoxazole was present in 94% isolates from CMH and in 60% isolates from AIMS. Zachariah et al, also reported a higher incidence of 89% Co-trimoxazole resistance among *E. coli* isolated from TB patients who are using Co-trimoxazole prophylaxis, in Malawi. All the *E. coli* isolated in AIMS and CMH were susceptible to Imipenem. Shams et al. also reported 6% resistance in *E. coli* isolated from blood and urine specimens against Imipenem. The results of this study demonstrate a high level of resistant *E. coli* against Cefixime and Cotrimoxazole and maximum susceptibility against Imipenem, therefore Imipenem may be considered as a first-line empiric antibacterial agent for the treatment of *E. coli* driven UTI infections.<sup>12</sup> As MDR phenomenon among the microorganism is an evolving mechanisms, regular antimicrobial surveillance and monitoring studies should be conducted on local levels to provide physicians with knowledge about the most successful empirical treatment of UTIs.

## Conclusion

This study confirms that Cefixime, Cotrimoxazole, Co-amoxiclave and Pipemidic acid are not a first choice for treatment of UTI in district Muzaffarabad. Imipenem and Nitrofurantoin may be considered as a first choice empiric agent in district Muzaffarabad. Antibiotic resistance pattern of organisms change rapidly over a short period of time, therefore regular surveillance of antimicrobial susceptibility should be performed for ensuring appropriate therapy and overcoming evolution of antibiotic resistance.

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**Conflict of Interest:** None.

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