



Subtraction antibiogram in most prevailing Uropathogen *Escherichia coli* over a period of 3 years. A study from Tertiary care health center in Himachal Pradesh.

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ABSTRACT:

Background : *Escherichia coli* is the most common cause of UTI worldwide. This study aimed to subtraction antibiogram for *E.coli* for the period of 3 years. **Material and Methods:** This retrospective study was carried out in the Department of Microbiology, DRPGMC, Kangra at Tanda. 16,142 urine samples were received in Microbiology laboratory for a period of 3 years.(May,2018- April,2021). Semi quantitative standard loop method was performed for urine culture on MacConkey agar. Culture plates were incubated for 18–24 hours at 37°C. Count of $\geq 10^5$ CFU/ml was considered significant growth. *E.coli* was identified by biochemical reactions. The antibiotic susceptibility testing (AST) was carried out using Kirby Bauer disc diffusion method. **Results:** Antibiotic resistance of *E.coli* to Nitrofurantoin increased from 2.2% to 8%, Cotrimoxazole: 43.6% to 51.1%, Norfloxacin 33% to 59.7%, Cefazolin 74.9% to 80.5% in 3 years. **Conclusion:** Increasing resistance to first line antibiotics for most common uropathogen *E.coli* is an alarming situation. Appropriate antimicrobial stewardship and guidelines of antibiotic usage should be followed strictly. Periodic instructions to clinicians regarding the AMR pattern should be provided to reduce evolving resistance.

KEY WORDS: UTI, *Escherichia coli*, Antimicrobial resistance, Uropathogenic

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I. INTRODUCTION

Urinary tract infections (UTIs) are among the most common types of bacterial infections occurring both in the community and healthcare settings [1]. Uropathogenic *Escherichia coli* (*E. coli*) (UPEC) is the prevailing etiologic agent of urinary tract infection around the globe[2]. Annually about 150 million people are being diagnosed with urinary tract infection across the world. Without exception women have a lifetime risk of developing UTI is 60%. by contrast, men have barely 13% risk in lifetime.[3]

More susceptibility to UTI in females to males is due to the short length of urethra, absence of prostatic secretion, pregnancy and contamination of the urinary tract with faecal flora.[4]

Increasing resistance has make treatment worrisome, and may lead to therapeutic block.[5] The treatment regimen of UTIs differs according to the age of the patient, sex, underlying disease, infecting agent, and whether there is lower or upper urinary tract involvement.[6] *Escherichia coli* shows resistance in the treatment of uncomplicated cystitis, the preferable antibiotics for empiric treatment include Nitrofurantoin, Cotrimoxazole and Norfloxacin.[7]

This study will help us to assess the subtraction antibiogram for *E.coli* in UTI from May ,2018 to April, 2021.

II. MATERIALS AND METHODS

The retrospective study was conducted in the Department of Microbiology, DRPGMC, Kangra at Tanda. 16,142 urine samples were received in the Laboratory from May 2018 to April 2021. Urine samples with significant growth of *E. coli* ($>10^5$ CFU/ml) were included in the study.

Cultures were done by a semi-quantitative standard loop method on Mac Conkey agar. Culture plates were incubated for 18–24 hours at 37°C. The urine specimen with a growth of $\geq 10^5$ CFU/mL of a single

microorganism or mixed flora with a predominant species was considered significant and defined as positive urine culture. Negative urine culture was defined as no growth, insufficient growth, or a mixed microbial flora with no predominant organisms.[8]E.coli was identified by standard biochemical reactions.

The antibiotic susceptibility testing (AST) was carried by Kirby Bauer disc diffusion method. The antibiotic discs (Himedia) were used including Nitrofurantoin(300µ), Norfloxacin(10µ), Cotrimoxazol(25µ) and Cefazolin(30µ) The interpretation of results was based on the recommendations of the Clinical Laboratory Standards Institute (CLSI).[9]

III. RESULTS

The antibiotic resistance rates to the first line antimicrobials to treat UTI in our setup were Nitrofurantoin, cotrimoxazole, norfloxacin & cefazolin.The trend of antibiotic resistance over the period of 3 years was analyzed. A total of 16,142 urine samples were received from May 2018 to April 2021.13236(81.9%) urine samples showed no growth ,insignificant & contamination. Positive growth with $\geq 10^5$ CFU/mL was seen in 2906 urine samples. E.coli isolates were 1433(49.3%).Year wise isolates for E.coli are given in table 1.

Table 1: Distribution of Urine samples annually and positive E.coli isolates.

Duration	Urine sample	E.coli	Percentage(%)
May 2018-April 2019	5902	560	9.4
May 2019-April 2020	5954	555	9.3
May 2020-April 2020	4286	318	7.4
Total	16,142	1433	8.8

Females were in predominance to males in our study with 5,535 males and 10,607. Male to female ratio was 1:1.9

Subtraction antibiogram pattern in different time frame(2018-2021) was analysed for nitrofurantoin, norfloxacin ,cotrimoxazole and cefazolin.Increase in resistance was seen in all of the antibiotics, least in nitrofurantoin and maximum in norfloxacin. Susceptibility trend of antibiotics is shown in table 2.

Table 2: Susceptibility trend of antibiotics for uropathogenic E.coli

Time Duration	Nitrofurantoin		Norfloxacin		Cotrimoxazole		Cefazolin	
	S	R	S	R	S	R	S	R
2018-2019	97.8%	2.2%	67%	33%	56.4%	43.6%	25.1%	74.9%
2019-2020	95.5%	4.5%	47.6%	52.4%	52.2%	47.8%	25%	75%
2020-2021	92%	8%	40%	59.7%	48.9%	51.1%	19.5%	80.5%

Nitrofurantoin showed least -5.8 % decrease in susceptibility from 2018 to 2021. Maximum -27% decrease in susceptibility was seen with Norfloxacin.

IV. DISCUSSION

In this study, we focused on the E. coli strains from urine samples and their susceptibility pattern to different groups of antibiotics which are commonly administered to treat the infections over the period of 3 years. E.coli was the most common bacterial isolate from urine samples.Females were more susceptible to UTI as compared to males due to the short length of urethra, absence of prostatic secretion, pregnancy and easy contamination of the tract with faecal flora.[4]

Study also focused on the antibiotic sensitivity pattern .The uncontrolled use of antibiotics and easy availability over the counter has led to an increase in resistance to E.coli.

Cotrimoxazole being first line empirical treatment in UTI. In our study we see an increasing trend in resistance for this drug. In 2018-19 resistance was 43.5% which increases to 47.7% in 2019-20 and 51.1% in 2020-21. In a study by Tavirani et al showed 62% of resistance in E.coli for cotrimoxazole.[10]

With increase in resistance to cotrimoxazole other alternatives in the first line for UTI are nitrofurantoin, norfloxacin and cefazolin. Changing trend of resistance was least seen in nitrofurantoin with 97.5% susceptibility at starting of study to 92% at the end. This could be due to nitrofurantoin has a single indication , narrow tissue distribution, narrow spectrum of activity, bactericidal activity against E. coli in urine at therapeutic doses, and limited contact with bacteria outside the urinary tract.[11]

The data from the present study reveals the high rate of Norfloxacin resistance in E. coli. The rise in resistance to Norfloxacin was highest in the 3 years. The fact can be explained as it is one of the commonly

prescribed drugs on an outpatient basis. It is of great concern that E. coli has developed a high rate of resistance against them as well. Other reason could be due to Covid pandemics urine samples were less for the year 2020 and 2021 due to non functional OPD's at regular basis and most of the urine samples were from comorbid IPD patients. It reflects that this useful antibiotic is instantaneously losing its efficacy in the treatment of UTI

Cefazolin is a first-generation parenteral cephalosporin, which is excreted through the kidneys. Although the resistance rate is increasing, it continues to remain as an important drug of choice for the treatment of acute. In our study we see remarkable increase in resistance from 74.9% in starting to study to 80.5% at the end of study similarly Chen et al in their showed resistance to E.coli 75% to 78%. [12]

V. CONCLUSION

According to the present study, male to female ratio for UTI was higher in females. E. coli is the most common cause of urinary tract infection. Increased trend of resistance toward the basic first line antibiotics has left the treatment option with limited antibiotics. Judicious and rational use of antibiotics and proper implementation of antibiotic stewardship policy in health care setup is necessary. Periodic assessment of antimicrobial resistance data should be done. Any increase and decrease in resistance should be noted and alarming issues should be considered. AMR data should be shared and discussed with clinicians on a regular basis.

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