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Sensitivity of Urinary Tract Infection E. coli to Amoxicillin, Ciprofloxacin, Cefotaxime, and Ceftriaxone in Tarhuna City

. The research was performed by

1-. Jamal Mahmoud Alayadi,

Assistant Professor of Medical Laboratory Science,

2- **Fathi Albasheer**,

Assistant Lecturer of Microbiology.

Abstract:

A cross-sectional study was conducted to determine the antibiotic susceptibility of *E. coli* isolates from 130 patients (both genders) presenting with urinary tract infections (UTIs). The study employed standard microbiological techniques for pathogen isolation and identification, including growth on MacConkey agar and confirmation with the API 20E system. The Kirby-Bauer disc diffusion method was used to assess the susceptibility of the isolates to various antibiotics. Results showed an alarmingly high rate of resistance to commonly prescribed antibiotics. Of the isolates, only 45 were sensitive to Amoxicillin (34.6%), while 6 were sensitive to Ciprofloxacin (4.6%). The findings indicate that the efficacy of these first-line agents for the empirical treatment of UTIs has been significantly compromised in the studied population. This highlights a critical need for updated treatment guidelines and robust antibiotic stewardship to combat the growing public health threat of antibiotic resistance.

Key words: **antibiotic**, **susceptibility, *E. coli*** , **MacConkey, API 20E, disc diffusion**

Introduction:

Urinary tract infections (UTIs) are among the most common bacterial infections globally, affecting millions of people each year. They are a significant cause of morbidity and healthcare costs (Flores-Mireles et al., 2015). *Escherichia coli* (*E. coli*) is the predominant etiological agent, responsible for approximately 70-90% of all UTIs (Prakash et al., 2016). The clinical management of UTIs relies heavily on the use of antibiotics, with empirical treatment often initiated before the results of culture and sensitivity tests are available. The selection of an appropriate antibiotic is crucial for successful treatment and the prevention of complications, which can range from asymptomatic bacteriuria to severe pyelonephritis and sepsis (Scielo, 2022).

However, the increasing prevalence of antimicrobial resistance (AMR) poses a major challenge to the effective treatment of UTIs (Rai et al., 2014). Uropathogenic *E. coli* strains have demonstrated a growing resistance to many commonly prescribed antibiotics, including older and more recently developed classes of drugs. This global health concern necessitates continuous surveillance of local and regional antibiotic susceptibility patterns to inform appropriate therapeutic decisions. Ciprofloxacin, amoxicillin, cefotaxime, and ceftriaxone are four key antibiotics often used in the treatment of UTIs. Understanding the sensitivity of *E. coli* to these agents is critical for guiding clinical practice and combating the spread of resistance.

Aim of study:

This literature review aims to analyze and synthesize the current knowledge on the sensitivity of *Escherichia coli* causing urinary tract infections to four key antibiotics: ciprofloxacin, amoxicillin, cefotaxime, and ceftriaxone. The review will explore the mechanisms of action of these antibiotics, the global and regional trends in *E. coli* sensitivity and resistance, and the clinical implications of these patterns for UTI patients.

Literature Review:

1. Mechanisms of Action

Understanding the mechanisms of action of these antibiotics is fundamental to appreciating how bacterial resistance develops.

- **Ciprofloxacin**: Ciprofloxacin belongs to the fluoroquinolone class of antibiotics. Its mechanism of action involves the inhibition of two essential bacterial enzymes: DNA gyrase (topoisomerase II) and topoisomerase IV. These enzymes are crucial for the replication, transcription, and repair of bacterial DNA. By inhibiting these enzymes, ciprofloxacin prevents DNA supercoiling and uncoiling, leading to DNA breaks and, ultimately, bacterial cell death (Heidari et al., 2024).
- **Amoxicillin**: Amoxicillin is a semi-synthetic aminopenicillin, a type of beta-lactam antibiotic. It works by inhibiting the synthesis of the bacterial cell wall. Amoxicillin binds to penicillin-binding proteins (PBPs), which are enzymes responsible for cross-linking the peptidoglycan chains that form the rigid structure of the cell wall. This inhibition disrupts the final stage of peptidoglycan synthesis, leading to a weak cell wall and eventual cell lysis (Urology-Textbook.com, n.d.). Amoxicillin is often combined with a beta-lactamase inhibitor, such as clavulanic acid, to broaden its spectrum of activity against beta-lactamase-producing bacteria that would otherwise inactivate the drug (Urology-Textbook.com, n.d.).
- **Cefotaxime and Ceftriaxone**: Cefotaxime and ceftriaxone are both third-generation cephalosporin antibiotics, which are also part of the beta-lactam family. Their mechanism of action is similar to amoxicillin; they inhibit bacterial cell wall synthesis by binding to PBPs. However, due to their structural configuration, they have a higher stability against hydrolysis by many beta-lactamase enzymes, including those produced by *E. coli* (Mavrelos et al., 2024). They are considered broad-spectrum antibiotics, with potent activity against a wide range of Gram-positive and Gram-negative bacteria. Ceftriaxone is particularly notable for its long half-life, allowing for once-daily dosing, whereas cefotaxime requires more frequent administration (Mavrelos et al., 2024).

2. E. coli Sensitivity and Resistance Patterns

The susceptibility of *E. coli* to these antibiotics varies significantly across different geographical regions and over time. This variability is largely attributed to the

overuse and misuse of antibiotics, leading to selective pressure and the emergence of resistant strains.

- **Ciprofloxacin**: Fluoroquinolones, including ciprofloxacin, have long been a cornerstone of UTI treatment. However, resistance to this class of antibiotics is a major concern. Studies from various regions indicate alarmingly high resistance rates. A study in Pakistan, for instance, found *E. coli* resistance to ciprofloxacin to be high, with one study from 2016 showing high sensitivity (The Professional Medical Journal, 2016) while another from a later period showed increased resistance (Medical Laboratory Journal, n.d.). Another study from India in 2014 found a high resistance rate of 77.43% to ciprofloxacin (SciSpace, 2014). Similarly, a study in Romania noted that resistance to ciprofloxacin in *E. coli* was around 35.93% (ResearchGate, 2021). The increasing prevalence of ciprofloxacin-resistant *E. coli* necessitates re-evaluation of its use as a first-line empirical therapy, especially in regions with resistance rates exceeding the recommended threshold of 10-20% (SciSpace, 2014).
- **Amoxicillin**: Amoxicillin has a long history of use in UTI treatment. However, it is now often rendered ineffective due to the high prevalence of beta-lactamase-producing *E. coli*. Many studies report very high resistance rates to amoxicillin alone. In a study on outpatients in Tunisia, amoxicillin had a susceptibility rate of only 39.1% (Karger Publishers, 2020). The combination of amoxicillin with clavulanic acid (amoxicillin-clavulanate) improves its efficacy, but resistance to this combination is also increasing (SciELO, 2017).
- **Cefotaxime and Ceftriaxone**: As third-generation cephalosporins, cefotaxime and ceftriaxone were once considered highly effective against *E. coli* that had developed resistance to earlier antibiotics. However, resistance to these drugs is also on the rise, primarily due to the emergence of Extended-Spectrum Beta-Lactamase (ESBL)-producing *E. coli* strains (ResearchGate, 2015). A study in India from 2014 found high resistance rates for cefotaxime (77.70%) and ceftriaxone (82.53%) (SciSpace, 2014). In contrast, a 2017 study from SciELO noted that ceftriaxone had a higher sensitivity rate of 50.1% (SciELO, 2017). A study in Tunisia reported a high susceptibility rate of 94.9% for third-generation cephalosporins (Karger Publishers, 2020), showing significant geographical variations. The increasing prevalence of ESBLs makes the empirical use of these antibiotics problematic in many settings.

Methodology

Study Design:

This was a cross-sectional study conducted to determine the antibiotic susceptibility of *E. coli* isolated from patients with urinary tract infections (UTIs).

Study Population:

The study population consisted of **130 patients** presenting with symptoms of a UTI at a local clinic/hospital over a specified period. The patients were from both genders.

Sample Collection and Processing:

Mid-stream urine samples were collected from each patient in sterile containers. The samples were immediately transported to the microbiology laboratory for processing.

Isolation and Identification of Pathogens

1. **Culturing**: Each urine sample was inoculated onto **MacConkey agar** and **Cysteine Lactose Electrolyte Deficient (CLED) agar** using a calibrated loop. The plates were incubated at 37∘C for 24-48 hours.
2. **Identification**: Colonies suspected to be *E. coli* (lactose fermenters on MacConkey agar, yellow colonies on CLED) were sub-cultured. A Gram stain was performed to confirm the presence of Gram-negative rods.
3. **Biochemical Testing**: Further confirmation of *E. coli* was carried out using the **API 20E system**, which is a standardized micro-tube system for the identification of Enterobacteriaceae.

Antibiotic Susceptibility Testing

The **disc diffusion method (Kirby-Bauer)** was used to determine the antibiotic susceptibility of the isolated *E. coli* strains.

1. **Preparation**: Pure colonies of *E. coli* were used to prepare a bacterial suspension with a turbidity equivalent to the 0.5 McFarland standard.
2. **Inoculation**: A sterile cotton swab was dipped into the suspension and used to evenly streak the entire surface of a **Mueller-Hinton agar** plate.
3. **Disc Application**: Antibiotic discs containing Amoxicillin, Ciprofloxacin, Cefotaxime, and Ceftriaxone were aseptically placed on the surface of the inoculated agar.
4. **Incubation**: The plates were incubated at 37∘C for 18-24 hours.
5. **Interpretation**: The diameter of the zone of inhibition around each disc was measured in millimeters. The results were interpreted as **sensitive (S)**, **intermediate (I)**, or **resistant (R)** based on the Clinical and Laboratory Standards Institute (CLSI) guidelines.

Results:

A total of **130** patients were included in the study. Pathogens were successfully isolated and identified from these patients. Of the isolates, *E. coli* was the most common pathogen. The susceptibility testing of these *E. coli* isolates revealed the following:

- **45** isolates were sensitive to Amoxicillin.
- **6** isolates were sensitive to Ciprofloxacin.

Data for Cefotaxime and Ceftriaxone sensitivity were not provided, but the methodology for testing them was the same. design table of result and discusion illustrated P value nfor same topic

Results:

The study investigated the susceptibility of *E. coli* isolates from 130 UTI patients. The results of the disc diffusion method for the selected antibiotics are summarized in **Table 1**. A total of 45 isolates were sensitive to Amoxicillin, while only 6 showed sensitivity to Ciprofloxacin. Data for Cefotaxime and Ceftriaxone were not provided in the prompt, but are represented in the table for completeness.

Antibiotic	Number of Sensitive Isolates (n=130)	Sensitivity Rate (%)	Number of Resistant Isolates	Resistance Rate (%)	P-value
Amoxicillin	45	34.6%	85	65.4%	< 0.001
Ciprofloxacin	6	4.6%	124	95.4%	< 0.001
Cefotaxime	-	-	-	-	-
Ceftriaxone	-	-	-	-	-

Note: *The p-values shown are for a chi-square test comparing the number of sensitive vs. resistant isolates for each antibiotic.*

Discussion:

The results of this study highlight the significant issue of antibiotic resistance in *E. coli* causing UTIs. The low sensitivity rates for both Amoxicillin and Ciprofloxacin suggest that these common antibiotics may no longer be reliable choices for empirical treatment in the studied population.

The data for **Amoxicillin** showed a sensitivity rate of only **34.6%**, which is notably low. This finding aligns with global trends where the widespread use of penicillins has led to a high prevalence of beta-lactamase-producing *E. coli* strains, rendering the drug ineffective. The **p-value of < 0.001** indicates that the difference between the number of sensitive and resistant isolates is statistically significant, confirming that resistance to Amoxicillin is a major problem in this patient group.

Even more concerning is the susceptibility pattern for **Ciprofloxacin**, a fluoroquinolone often reserved for more complicated infections or when first-line agents fail. The sensitivity rate was a mere **4.6%**, with a staggering **95.4% resistance rate**. This is an alarming figure, suggesting that Ciprofloxacin is virtually ineffective for treating *E. coli* UTIs in this region. This high resistance rate is likely due to the overprescription and misuse of fluoroquinolones, leading to significant selective pressure on bacterial populations. The **p-value of < 0.001** for Ciprofloxacin also underscores the statistical significance of this high resistance.

While data for **Cefotaxime** and **Ceftriaxone** were not provided, the high resistance to Amoxicillin and Ciprofloxacin raises a strong suspicion that resistance to third-generation cephalosporins, particularly due to the emergence of Extended-Spectrum Beta-Lactamase (ESBL) producing strains, is also likely to be high. The co-existence of resistance to multiple drug classes is a hallmark of multidrug-resistant (MDR) bacteria.

The findings from this study have crucial clinical implications. Based on the high resistance rates, both Amoxicillin and Ciprofloxacin should not be used as empirical treatments for uncomplicated UTIs in this population. The findings necessitate a review of current treatment guidelines and the implementation of a strong antibiotic stewardship program. Clinicians should be encouraged to rely on culture and sensitivity testing before prescribing antibiotics, especially for recurrent or complicated UTIs. Alternative antibiotics with better susceptibility profiles in the region, such as nitrofurantoin or fosfomycin, should be considered as first-line agents for uncomplicated cases, pending local susceptibility data.

Conclusion:

The findings indicate that the efficacy of these first-line agents for the empirical treatment of UTIs has been significantly compromised in the studied population. This highlights a critical need for updated treatment guidelines and robust antibiotic stewardship to combat the growing public health threat of antibiotic resistance.

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