Resistance Changes of *Escherichia Coli* to Cephalosporin in Erbil

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Abstract: Antibiotic resistance is a topic that is constantly being researched, and numerous studies are published each year with new data that can change or redefine our perspective on the problem. The emergence and spread of drug-resistant pathogens with new resistance mechanisms, leading to antimicrobial resistance, continue to jeopardize our ability to treat common infections. This necessitated the need for understanding the mechanism of action in each country due to the environmental changes. The study aimed at documenting the resistance of *E. coli* to Cephalosporin in Erbil, Kurdistan Region of Iraq. The study covers the periods from August to December 2018. Two hundred and two (202) samples were collected from infected patients in Erbil from different specimens. Four different groups of cephalosporin were tested against the resistance of E. coli. Ineffectiveness of the antibiotics used against *E. coli* was reported. *E. coli* is becoming stronger every month, according to our findings. The rising increase in the resistance of *E. coli* is a result of resistance to fluoroquinolones in *E. coli,* which causes other resistance mechanisms because it is often linked to other commonly used medicines. There is a need for proper investigation of *E. coli* resistance to the currently used antibiotic in each country because the continued resistance might require to change guidance of many severe infections. Continued research on medicinal plants is also needed to develop a compound against resistant microorganisms.

1. Introduction

The emergence and spread of drug-resistant pathogens with new resistance mechanisms, leading to antimicrobial resistance, continue to jeopardize our ability to treat common infections (Abdulrahman, 2021; Jasovský et al., 2016b). The rapid global spread of multi- and pan-resistant bacteria, which cause infections that are not treatable with existing antimicrobial medicines such as antibiotics, is especially concerning (Walsh & Toleman, 2012). Antibiotics are becoming increasingly ineffective as drug resistance spreads worldwide, resulting in more difficult-to-treat infections and death (Tacconelli et al., 2018). New antibacterial is desperately needed, for example, to treat carbapenem-resistant gram-negative bacterial infections identified on the WHO priority pathogen list (Huttner et al., 2013). However, if people do not change the way antibiotics are used now, these new antibiotics will suffer the same fate as the current ones and become ineffective (Huttner et al., 2013). High rates of resistance against antibiotics commonly used to treat common bacterial infections, such as urinary tract infections, sepsis, sexually transmitted infections, and some forms of diarrhea, have been observed worldwide, indicating that we are running out of effective antibiotics (Dalhoff, 2012). For example, in the countries reporting to the Global Antimicrobial Resistance and Use Surveillance System, the rate

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of resistance to ciprofloxacin, an antibiotic commonly used to treat urinary tract infections, ranged from 8.4 percent to 92.9 percent for *E coli* and from 4.1 percent to 79.4 percent for Klebsiella pneumoniae (GLASS) (Abdulrahman et al., 2019).

Escherichia coli bacteria, known as E. coli is a facultatively anaerobic, road shaped, and gram-negative bacteria that can mainly exist in the intestine of animals (Rafalskiy et al., 2020). Most of them are harmless to those organisms that they live in, but there are some pathogenic *E. coli*, which might cause food poisoning in their host. Some of the E.coli may cause respiratory illness, urinary tract infection, pneumonia and diarrhea (Rafalskiy et al., 2020). The resistance to Cephalosporin antibiotics can be due to some species' mechanisms. Poor penetration of the drug into bacteria reduces the affinity of PBP, Degradation of drugs by B-lactamases, and failure in the activation of Autolytic enzymes (Drawz & Bonomo, 2010). Currently, *Citrobacter freundii, morganella morganii, neissella E. coli, and gonorrhoeae* strains are also resistant to cephalosporin. Also, many others are developed resistance such as, *Providencia rettger, Pseudomonas aeruginosa, and serratia marcescens* strain (Drawz & Bonomo, 2010). Therefore, this research aims to understand the *E. coli* resistance and its changes to 4 groups of cephalosporin antibiotics: Cefuroxime, ceftriaxone, Cefotaxime, and cefexime. in a particular time in Erbil city.

2. Material and Methods

2.1 Sampling

Two hundred and two (202) random specimens were sampled from a urine specimen, pyonephrosis drainage specimen, pus evacuated from Renal pelvis specimen, wound swab, vaginal swap specimen, aspiration specimen, PCN specimen, sputum specimen, deep wound swap, Subcutaneous pus specimen, Direct microscope, kidney specimen, abscess specimen, transplanted kidney, and leg ulcer specimen, between August to December 2018 (Kayfi & Abdulrahman, 2021; Mahmoud, et al., 2020).

2.2 Isolation, identification, and antimicrobial resistance testing of E. coli

In this study, two types of tests were used. Biochemical test, used for identifying the bacteria type. Which is mainly used to distinguish whether it is gram-positive or gram-negative bacteria. And second tests which were used for identifying other process are SIM (sulfur, indole, motility media). It is a differential medium for detecting the organism's ability to reduce sulfur and produce indole to swim through agar (detecting motile) (Lehman, 2014). Simmons's agar is used to test the organism's ability to utilize citrate. Kliger's iron agar is used to differentiate microorganisms basic on dextrose and lactose fermentation (Lehman, 2014). and Urease test used for detecting the organism's ability to produce an exoenzyme (Mahmoud & Abba, 2021).

2.3 Statistical Analysis

The data were analyzed using Statistical Analysis System (SAS) software (University version 9.4). Completed Randomized Design (CRD) was employed as the experimental design with three replications. One-way repeated ANOVA procedure was carried out, and means were subjected to post hoc Duncan's Multiple Range Test (DMRT) to find out significant differences in the means at $p \leq 0.05$ level (Abdulrahman et al., 2019).

3. Results

The (Table 1) below presents the total number of E. coli isolated from random specimens that were sampled from a Urine specimen, pyonephrosis drainage specimen, pus evacuated from Renal pelvis specimen, wound swab, vaginal swap specimen, aspiration specimen, PCN specimen, sputum specimen, deep wound swap, subcutaneous pus specimen, direct microscope, kidney specimen, abscess specimen, transplanted kidney, and leg ulcer specimen tested with four antibiotics.

Table 1: The total number of *E. coli* which they collected in any month

Antibiotics	August	September	October	Nov	December
Cefuroxime	14	7	10	11	6
Ceftriaxone	12	12	12	14	7
Cefotaxime	12	11	13	13	7
Cefexime	14	8	9	7	3

The results below show the percentage of *E. coli* resistance against Cefuroxime (Figure 1). The highest resistance was reported in 52 in August, followed by 45 in November, then 44 in October, 38 in September, and 23 in December.

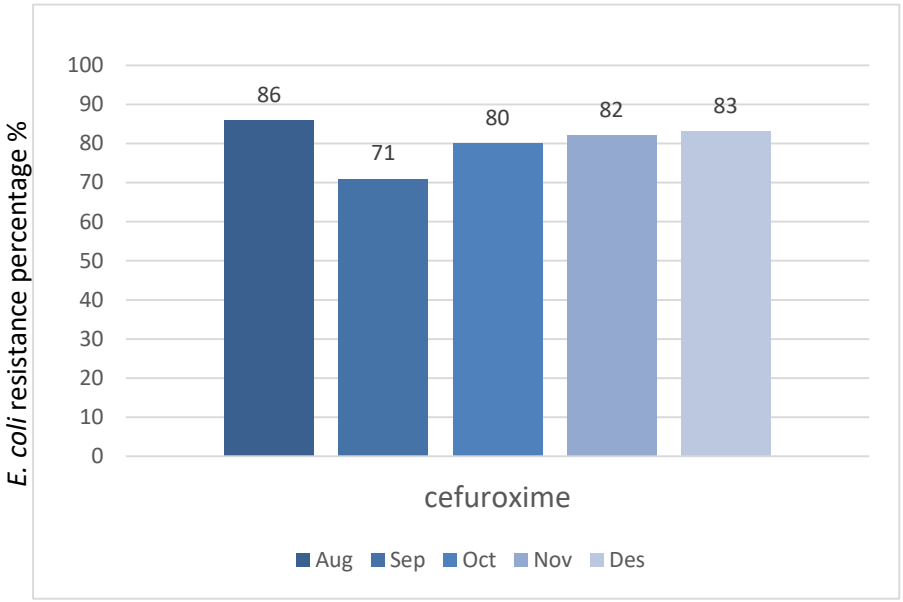

Figure 1: *E. coli* resistant to Cefuroxime during different months (Author, 2019)

December has 83% of the bacterial resistance toward Cefuroxime (Figure 2). The study found E. coli resistant to Cefuroxime antibiotics in the examining period. In the reported cases the highest resistance was recorded in August, 12 out of 14 accounting to 86% of the total cases. The amount of reported cases has decreased in September, with only 7 cases, but 5 are resistant to the Cefuroxime antibiotics representing 71%. In October, the reported cases' percentage rose to 10, 8 become resistant to Cefuroxime, accounting for 80%. In November, it continuously increased to 11 cases 8 become resistance accounting to 82%.

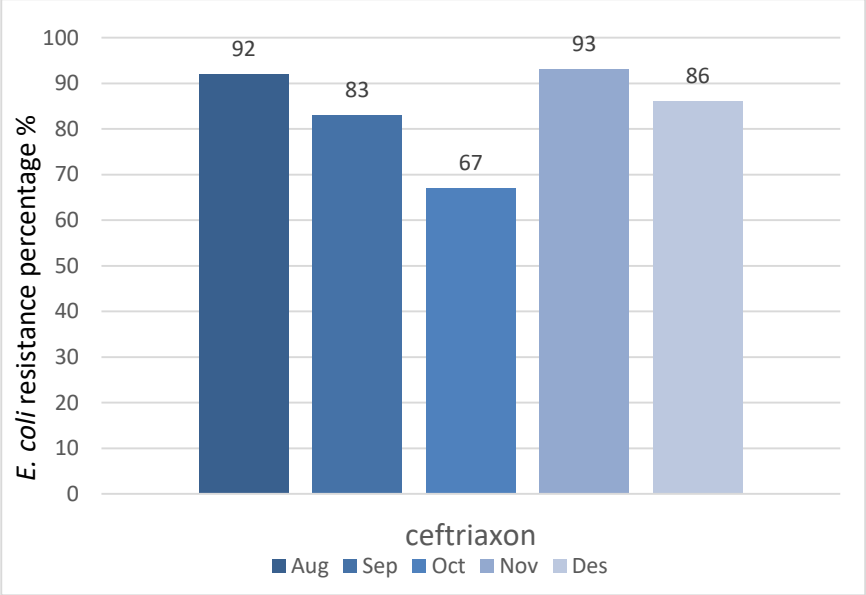

Figure 2: *E. coli* resistance to ceftriaxone during different months (Author, 2019)

Ceftriaxone was also used against *E. coli* from August to December. In August, the resistance had in much amount which measured 92%. the *E. coli* had resistance to 11 of them from 12. In September, that amount has decreased to 83%, for 10 of them had resistance among 12. It continued to decline till it got 67% in October. The *E. coli* were resistant for 8 of them among 12. It started to increase for the highest level in November which the antibiotics were sensitive to less amount of E. coli. It had resistance for 12 of them among 13. It was an average amount in December which the resistance was 86%, 1 among 7 (Figure 3).

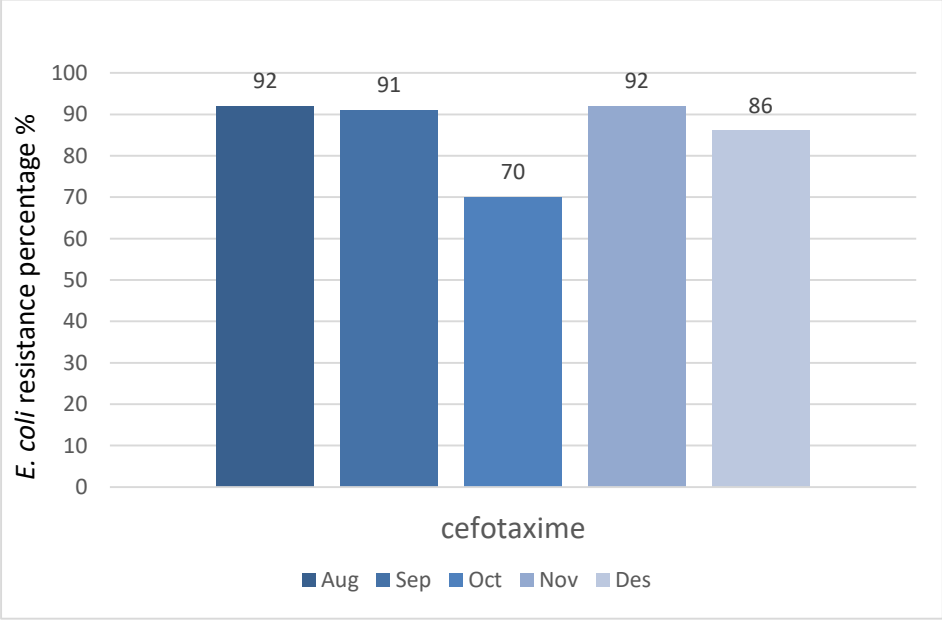

Figure 3: *E. coli* resistance to Cefotaxime during different months (Author, 2019)

E. coli resistance for Cefotaxime was 92% in August. It was resistant to 11 of them out of 12. It was almost the same in September, which was 91%, for 11 *E. coli* had resistance to 10 of them. October was the best mode for the Cefotaxime because there is less resistance, which can be measured by just

70%, among 13 just for 9 of them had resistance. It starts to get an increase in November to 92%, 12 out of 13. And it was normal in December that was 86%, 6 out of 7 (Figure 4).

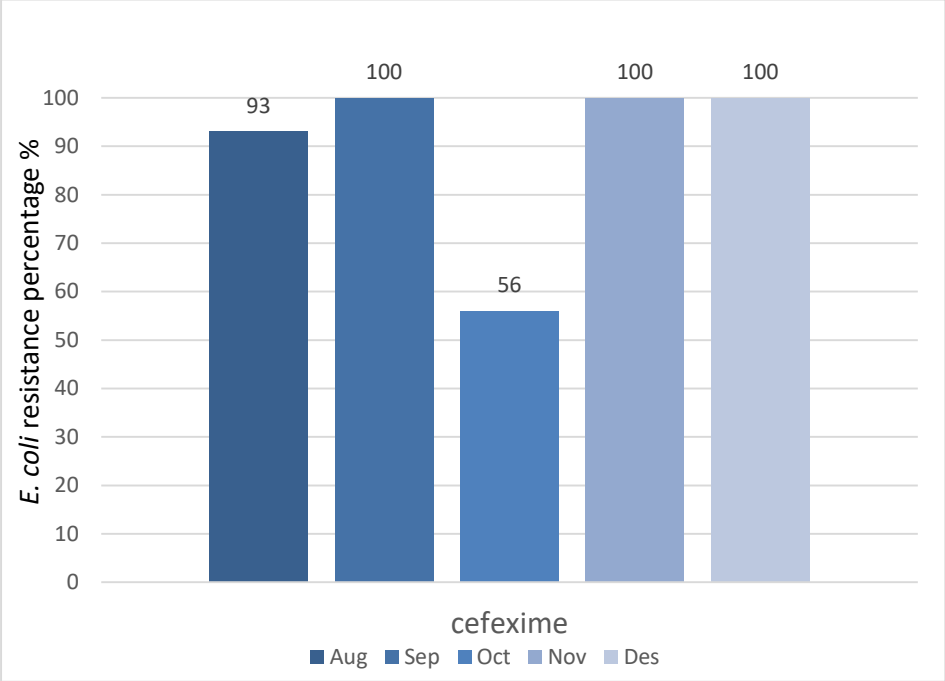

Figure 4: *E. coli* resistance to Cefexime during different months (Author, 2019).

Cefexime has been chosen as the most less effective antibiotic in this research. In August out of 13, 12 were ineffective against E. coli. In September, November and December Cefexime were not effective to any *E. coli* on this date, which means 100% resistance has been observed. But in October it was 56% which means it was resistance just to 5 of them among 9.

4. Discussion

Antibiotic resistance is a complex issue but it is linked to the country's present healthcare delivery system. Antimicrobial resistance is a significant public health concern in Southeast Asian countries (Walsh & Toleman, 2012). In most Southeast Asian nations, little is known about the epidemiological implications of antibiotic resistance. Antimicrobial resistance is a significant public health concern, particularly in developing countries, where relatively easy access to and higher consumption of medicines has resulted in a disproportionately higher incidence of inappropriate antibiotic use and higher resistance levels than developed countries (Huttner et al., 2013). Disease resistance varies according to geography. As a result, local resistance patterns must be known (Abdulrahman et al., 2019). According to specific hospital-based data, antibiotic resistance is on the rise. It will become a more significant worry if not treated efficiently by current demands, as it has in other industrialized countries (Tacconelli et al., 2018). Despite numerous proposals and initiatives in recent decades, the world has failed to keep pace with microbes that are becoming increasingly resistant to available treatments, a phenomenon which is known as antimicrobial resistance (AMR) (Jasovský et al., 2016b). Although many international organizations, such as the World Health Organization, the European Centre for Disease Control, and the World Health Assembly, have highlighted antimicrobial resistance as a major public health issue, addressing the problem will be a significant challenge for policymakers and health care providers (Dalhoff, 2012). The World Health Organization has recommended a regional antimicrobial resistance strategy to reduce morbidity and death caused by antimicrobial

resistant infections and preserve the effectiveness of antimicrobial drugs in the treatment and prevention of microbial illnesses. Any antibiotic use contributes to increasing the number of microorganisms on which drugs can be used have no effect. AMR is thus an unavoidable phenomenon that undermines the effectiveness of both primary and modern medicine and affects people from birth to death (Jasovský et al., 2016b). Cephalosporin-resistant Escherichia coli producing extended-spectrum -lactamase (ESBL) or plasmid-mediated AmpC-lactamase (pAmpC) is common in both health care settings and the community (Jasovský et al., 2016a). The increasing prevalence of these organisms and their spread into nursing homes and the community has implications for the empirical management of patients with infections in which E. coli is suspected to be the causative pathogen (Bader, Hawboldt, & Brooks, 2010). Given the scarcity of clinical and microbiologic data on cephalosporin-resistant E. coli in the United States, we conducted this multicenter study to identify risk factors for acquisition and predictors of clinical outcome associated with these organisms (Park et al., 2012). In addition, we investigated the epidemiology of the relevant -lactamases and their relationship to antimicrobial susceptibility. The study finds out the continues resistance of *E. coli* against the used antibiotics in Erbil. The study is in conformity with the previous investigation carried out in other countries with regard *E. coli* resistance to the various used antibiotics. The current study found the *E. coli* resistance in Erbil, Kurdistan Region of Iraq to be five times higher than the previous report in other countries. According to Health Protection Surveillance Center in 2014 (McCloskey et al., 2014). The *E. coli* resistance to cephalosporin has been found in almost all countries and most of them are above 10% (Meyer et al., 2010). The rising increase in the resistance of *E. coli* is a result of resistance to fluoroquinolones in *E. coli*, and this causes other resistance mechanisms because it is often linked to other commonly used medicines. There is a need for proper investigation *of E. coli* resistance to the currently used antibiotic in each country because the continued resistance might require to change guidance of many severe infections. Continued research on medicinal plants is also required to develop a compound that will act against resistant microorganisms.

5. Conclusion

E. coli is widespread bacteria globally and has become resistant to many antibiotics, including cephalosporin. *E. coli* has increased enormously and rapidly to almost all antibiotics such as Cefuroxime, ceftriaxone, Cefotaxime, and cefexime, which are in the group of cephalosporin antibiotic used in this research. *E. coli* has evolved stronger than before by gaining those resistances daily. So in Erbil it also shows well defense against cephalosporin antibiotics. This condition exists because of not being well used by patients, overusing them, and wrong prescriptions from doctors. Despite the new efforts and existing antibiotics, more research is needed to develop and make new antibiotics that treat resistant strains of *E. coli*. And more recommendations to use those antibiotics to prevent it's spreading and keep the other antibiotics from weakening them against *E. coli*.

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