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Antibiotic Resistance: Investigating the Prevalence of Antibiotic Resistance in *E. Coli* Infections among Patients Treated with Ciprofloxacin versus Amoxicillin

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ABSTRACT

Among all gram-negative organisms that cause bacteremia, the most frequent one is *Escherichia coli*. **Objectives:** To determine the prevalence of antibiotic resistance towards *E. coli* infections in patients treated with ciprofloxacin and amoxicillin. **Methods:** This cross-sectional descriptive study was carried out at the Shahida Islam Medical College and Hospital for six months from July 2024 to December 2024. Isolates of specimens from various samples, such as blood, urine, stool, pus of the ear and skin were included. Isolates positive for *Escherichia coli* were included, while isolates from other organisms were excluded. Antibiotic sensitivity towards Ciprofloxacin and Amoxicillin was tested. SPSS version 25.0 was used for data analysis. Chi-square test was applied for statistical analysis, keeping $p<0.05$ as statistically significant. **Results:** The study analyzed 208 *E. coli* isolates, mostly from patients over 55 years and presenting with outpatient infections. Antibiotic resistance was significantly higher to amoxicillin (68.75%) compared to ciprofloxacin (41.35%) ($p<0.001$). Only 9.62% of isolates were sensitive to amoxicillin, while 44.71% were sensitive to ciprofloxacin. These findings highlight a concerning prevalence of resistance, particularly against amoxicillin, among *E. coli* infections. **Conclusions:** The results of this study reported a higher prevalence of antibiotic resistance to Amoxicillin when compared with the resistance towards Ciprofloxacin. Further, multicenter studies with a greater sample size would be better able to authenticate the findings observed in this research.

INTRODUCTION

Among all gram-negative organisms that cause bacteremia, the most frequent one is *Escherichia coli* [1]. Even then, published literature regarding the prognostic factors of *E. coli* associated bloodstream infections is limited, especially the local data. In the past couple of decades, a significant increase in antibiotic resistance towards *E. coli* infections has been observed, altering the patients' outcomes having bacteremia [2]. Multi and extended drug-resistant *E. coli* are becoming increasingly challenging as their incidence is rising, and so resistance to a broad range of Beta-lactams and other groups of anti-microbial agents as well [3]. Due to increased incidences, treatment options are becoming limited day by day, affecting *E. coli* linked infections to have a limited prognosis [4]. Adequate and prompt antibiotic therapy can affect the outcome of *E. coli* bacteremia. Due to the rising antibiotic resistance, an increase in the misuse of empirical antimicrobials can lead to a delay in the initiation of the appropriate therapy [5]. Having information about the *E. coli* bacteremia, whether empirical therapy is

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adequate, and the outcomes (prognosis) is vital for establishing strategies which might improve patient prognosis of patients with *E. coli* associated bacteremia [6]. The frequency of *E. coli* urinary tract infections (UTIs) is around 75-90 % worldwide. Studies have demonstrated escalating antibiotic resistance towards *E. coli* associated bacterial infections [7]. A study from Turkey reported 17 % *E. coli* strains showing uncomplicated infections, while 38 % showed complicated *E. coli* infections towards ciprofloxacin [8]. Ciprofloxacin resistance to *E. coli* has been reported to increase from 1.8 % to 15.9 % within the last decade in research from Switzerland [9]. Local data regarding resistance to antimicrobials is limited. *E. coli* is observed to be the most frequent source of infection (86.4 %), with resistance rising to as high as 27.4 % among outpatients while 72 % amongst admitted patients [10]. Factors associated with antibiotic resistance include senility, gender, immune-compromised patients, diabetes mellitus, recurrent infections, previous therapy with quinolones, hospital-acquired infections etc [11]. Only a handful of studies have been carried out in the local populations as well as in the developed populations, which have analyzed and compared the demographic data for determining prevalence and risk factors of antibiotic resistance using ciprofloxacin and/or amoxicillin [12]. Similarly, resistance to amoxicillin has also been reported in studies. However, data regarding it is scarce. Since the most commonly used antibiotics in both outpatients and admitted patients are ciprofloxacin and amoxicillin [13]. Antimicrobial resistance (AMR) is an ongoing worldwide issue that affects both developing and developed populations. For microorganisms' survival, AMR is regarded as a natural phenomenon. It is vital to slow down the development of AMR to maintain anti-microbial usefulness [14]. As AMR decreases the efficacy of treatment, it is pivotal to consider susceptibility testing in routine care for guiding individualized patient care as well as for surveillance of AMR [15].

This study aims to determine the prevalence of antibiotic resistance towards *E. coli* infections in patients treated with ciprofloxacin and amoxicillin.

METHODS

This cross-sectional descriptive study was carried out at the Shahida Islam Medical College and Hospital for six months from July 2024 to December 2024 after ethical approval from the institutional review board committee, IRB certificate no: SIMC/ET.C/00023/24. Isolates of specimens from various samples, such as blood, urine, stool, pus of the ear and skin were included. Isolates positive for Escherichia coli were included, while isolates from other organisms, such as *Staphylococcus aureus, Pseudomonas aeruginosa, Salmonella typhi, Klebsiella pneumoniae,* etc., were excluded from the study. Prior informed consent was taken. Antibiotic sensitivity towards Ciprofloxacin and Amoxicillin of 6 mm disks (5 µg) was obtained commercial market (Oxoid Limited, Basingstoke, Hampshire, England). Sensitivity towards antibiotics on the clinical isolates was tested through Muller-Hinton medium (Oxoid Limited, Basingstoke, Hampshire, England). The incidence of AMR to E. coli as reported in the local study was 16%; therefore, the sample size was calculated using the open EPI online software for sample size calculation. Keeping the following values, the sample size came out to be 207 [16]. Therefore, a total of 208 specimen isolates were included in the study. Sample size (n) = [DEFF*Np(1-p)]/[(d2/Z21-α/2*(N-1)+ p*(1-p)] (Table 1).

Table 1: Sample Size and Confidence Levels for Frequency in a Population

Variables	Percentage
Population size (for finite population correction factor or fpc) *(N):*	1000000
Hypothesized % frequency of outcome factor in the population *(p):*	16%+/-5
Confidence limits as % of 100 (absolute +/- %) *(d):*	5%
Design effect (for cluster surveys- DEFF):	1
Confidence Levels	**Sample Size (n)**
95%	207
80%	89
90%	146
97%	254
99%	357
99.9%	582
99.99%	814

Isolated colonies of *E. coli* from agar plates were included. The broth was incubated at 37°C for 8 to 24 hours. Broth incubation was carried out according to the guidelines of the National Committee for Clinical Laboratory Standards (NCCLS) in preparing Mueller-Hinton broth as well as agar medium. Using a 0.5 McFarland standard for reference, bacterial culture suspension was prepared having appropriate turbidity. A sterile cotton swab was dipped and streaked in 3 directions over Mueller-Hinton agar for obtaining uniformity in growth, according to the specifications of the manufacturer. For 5 minutes, plates were dried. Disks of Ciprofloxacin and Amoxicillin 5ug were prepared using sterile forceps. Discs were then placed 15 mm from the plate's edge and less than 25 mm from each other. Incubation of plates was carried out within 15 minutes after application of disks for 24 hours at 37°C. According to standard values of NCCLS, reference ranges used were >21 mm as sensitive, between 16 to 20 mm as intermediate resistant and 15 mm as resistant. Intermediate resistance (IR) was not termed as susceptible or sensitive organism against Ciprofloxacin and Amoxicillin. SPSS version 25.0 was used for data analysis. Numerical data (qualitative) was reported as frequency and

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percentages. Categorical (quantitative) data were recorded as mean and standard deviation. Chi-square test was applied for statistical analysis, keeping p<0.05 as statistically significant.

RESULTS

Out of the 208 *E. coli* isolates included in the study, 98 (47.12%) were from male patients and 110 (52.88%) from female patients. The majority of the patients, 160 (76.9%), were aged over 55 years. In terms of infection type, 167 (80.29%) cases were outpatient, followed by 22 (10.58%) post-surgical infections and 19 (9.13%) nosocomial infections. Regarding co-morbidities, 108 (51.92%) patients had diabetes, 93 (44.7%) had hypertension, 32 (15.38%) had COPD, and 26 (12.5%) reported other comorbid conditions (Table 2).

Table 2: Baseline Demographics and Clinical Characteristics of Isolates Included in the Study (n=208)

Variables		Frequency (%)
Gender	Male	98 (47.12 %)
	Female	110 (52.88 %)
Age >55 Years		160 (76.9 %)
Type of Infection	Out-patient	167 (80.29 %)
	Nosocomial	19 (9.13 %)
	Post-surgical	22 (10.58 %)
Co-morbidity	Hypertension	93 (44.7 %)
	Diabetes	108 (51.92 %)
	COPD	32 (15.38 %)
	Other	26 (12.5 %)

Findings show the sources of *E. coli* isolates varied among clinical specimens, with the most common being urine samples, followed by blood, stool and pus from ear and skin specimens. This distribution reflects the high prevalence of urinary tract infections among the specimen population included in the study (Figure 1).

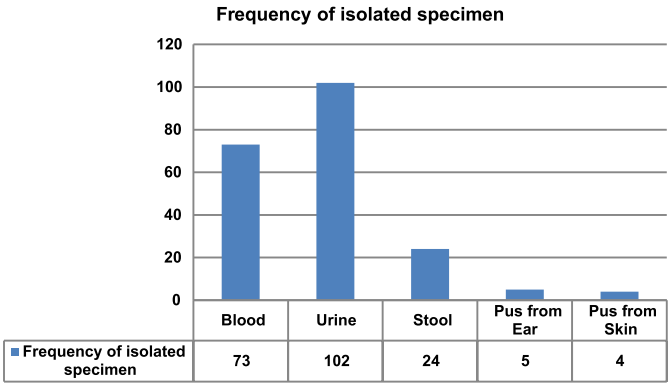

Figure 1: Route of *E. Coli* Isolated from Specimen (n=208)

Among the 208 clinical isolates tested, resistance to ciprofloxacin was observed in 86 (41.35%) isolates, while amoxicillin resistance was considerably higher at 143 (68.75%). Intermediate resistance was found in 29 (13.94%) isolates for ciprofloxacin and 45 (21.63%) for amoxicillin. Only 93 (44.71%) of the isolates were sensitive to ciprofloxacin compared to just 20 (9.62%) for amoxicillin. The difference in resistance patterns between the two antibiotics was statistically significant (p<0.001), indicating a markedly higher resistance of *E. coli* to amoxicillin than ciprofloxacin (Table 3).

Table 3: Antibiotic Resistance Ratio of Various Isolates Against Ciprofloxacin versus Amoxicillin (n=208)

Clinical Isolates of *E. Coli*	Ciprofloxacin (5 ug)	Amoxicillin (5 ug)	p-Value
Resistant (R): <15 mm	86 (41.35 %)	143 (68.75 %)	<0.001
Intermediate Resistance (IR): 16-20 mm	29 (13.94 %)	45 (21.63 %)	
Sensitive (S): >21 mm	93 (44.71 %)	20 (9.62 %)	

DISCUSSION

Among the 208 specimen isolates included in the study, the prevalence of resistance to Ciprofloxacin was 86 (41.35%), while that of Amoxicillin was 143 (68.75%). Higher rates of resistance were observed in isolates to Amoxicillin as compared with Ciprofloxacin. Likewise, among the specimen isolates, sensitivity with Ciprofloxacin was reported to be higher, 93 (44.71%) in comparison to Amoxicillin, 20 (9.62%). A significant difference of <0.001 was observed between the two antibiotics. Literature also reports similar results to the findings of this study. AMR, as reported in other research as well, shows that failure of treatment because of resistance by *E. coli* leads to higher mortality rates [17, 18]. Routine analysis of resistance development using *E. coli*, one of the most common gram-negative pathogens, was isolated in urine specimens [19]. This is in line with the published literature, where urinary tract infections have been observed as the major source of infection. Similar to the findings of our study, Ciprofloxacin has been reported to show good activity against *E. coli*, 27.02 % as compared to 44.71 % in our study [20]. In other studies, the range of Ciprofloxacin resistance by *E. coli* infections is between 10% and 40% [21]. Likewise, rising *E. coli* related infections to amoxicillin are also reported to be a major challenge to health care, with the highest reported incidence being resistant bloodstream infections [22]. However, in our study, the most common isolated specimens were urine samples, followed by blood. Since Amoxicillin is known to be the most commonly used first-line empirical antibiotic for commonly observed infections, many clinicians are in consideration of broadening the use of second and third-line antibiotics to counter resistance [23]. In line with the reported resistance to Amoxicillin (68.75%), a study reported 76 % resistance to *E. coli* associated infections [24]. In contrast, resistance to Ciprofloxacin in our study was at 41.35 % while in another research it was 54.2% [25].

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CONCLUSIONS

The results of this study reported a higher prevalence of antibiotic resistance to Amoxicillin when compared with the resistance towards Ciprofloxacin. Further, multicenter studies with a greater sample size would be better able to authenticate the findings observed in this research.

Authors Contribution

Conceptualization: SM
Methodology: NK
Formal analysis: MAZ, SLA
Writing review and editing: NK, MAZ, SLA, KA, AI

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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